

medicina

BUENOS AIRES, VOL. 85 Supl. V - 2025



medicina

BUENOS AIRES, VOL. 85 Supl. V - 2025

COMITÉ DE REDACCIÓN

Sebastián F. Ameriso

FLENI, Buenos Aires, Argentina

Pablo J. Azurmendi

Instituto de Investigaciones Médicas A. Lanari, UBA, Argentina

Gabriela V. Carro

Hospital Nacional Prof. A. Posadas, Buenos Aires, Argentina

José H. Casabé

Instituto de Cardiología y Cirugía Cardiovascular, Hospital Universitario

Fundación Favaloro, Buenos Aires, Argentina

Hugo N. Catalano

Hospital Alemán, Buenos Aires, Argentina

Eduardo L. De Vito

Instituto de Investigaciones Médicas A. Lanari, UBA, Argentina

Elisa Estenssoro

*Hospital Interzonal de Agudos General San Martín de La Plata,
Buenos Aires, Argentina*

*Facultad de Ciencias Médicas, Universidad Nacional de La Plata,
Buenos Aires, Argentina*

Isabel Narvaiz Kantor

Organización Panamericana de la Salud (OPS/OMS) (ret.), Argentina

Basilio A. Kotsias

Instituto de Investigaciones Médicas A. Lanari, UBA, Argentina

Gustavo Kusminsky

Hospital Universitario Austral, Buenos Aires, Argentina

Oscar M. O. Laudanno

Instituto de Investigaciones Médicas A. Lanari, UBA, Argentina

Isabel A. Lüthy

Instituto de Biología y Medicina Experimental (IBYME),

Buenos Aires, Argentina

Domingo J. Palmero

Hospital de Infecciosas Dr. Francisco J. Muñiz

Instituto de Tisioneumonología Prof. Dr. Raúl Vacarezza,

Facultad de Medicina, UBA, Argentina

Guillermo B. Semeniuk

Instituto de Investigaciones Médicas A. Lanari, UBA, Argentina

Oswaldo J. Stringa

Hospital de Clínicas José de San Martín, UBA, Argentina

Carlos D. Tajer

*Hospital de Alta Complejidad El Cruce Néstor Kirchner,
Buenos Aires, Argentina*

MIEMBROS EMÉRITOS

Damasia Becú Villalobos

Instituto de Biología y Medicina Experimental-CONICET,

Buenos Aires, Argentina

María Marta de Elizalde de Bracco

*IMEX-CONICET-Academia Nacional de Medicina, Buenos Aires,
Argentina*

Guillermo Jaim Etcheverry

Facultad de Medicina, UBA, Argentina

Daniel A. Manigot

Hospital San Juan de Dios, Buenos Aires, Argentina

Rodolfo S. Martin

Facultad de Ciencias Biomédicas,

Hospital Universitario Austral, Buenos Aires, Argentina

La Tapa

El Partenón de Libros

(1983), Marta Minujín

MEDICINA (Buenos Aires) - Revista bimestral – ISSN 1669-9106 (En línea)

Registro de la Propiedad Intelectual N° 02683675

Personería Jurídica N° C-7497

Publicación de la Fundación Revista Medicina (Buenos Aires) Propietario de la publicación: Fundación Revista Medicina

Queda hecho el depósito que establece la Ley 11723

Publicada con el apoyo del Ministerio de Ciencia, Tecnología e Innovación Productiva.

MEDICINA no tiene propósitos comerciales. El objeto de su creación ha sido propender al adelanto de la medicina argentina.

Los beneficios que pudieran obtenerse serán aplicados exclusivamente a este fin.

Aparece en **MEDLINE (PubMed)**, **ISI-THOMSON REUTERS (Journal Citation Report, Current Contents, Biological Abstracts, Biosis, Life Sciences)**, **CABI (Global Health)**, **ELSEVIER (Scopus, Embase, Excerpta Medica)**, **SciELO, LATINDEX, BVS (Biblioteca Virtual en Salud)**, **DOAJ, Google Scholar y Google Books.**

Incluida en el Núcleo Básico de Revistas Científicas Argentinas del CONICET.

Directores Responsables:

Eduardo L. De Vito, Pablo J. Azurmendi, Isabel A. Lüthy, Domingo J. Palmero

Secretaría de Redacción: Ethel Di Vita, Instituto de Investigaciones Médicas Alfredo Lanari, Combatientes de Malvinas 3150,
1427 Buenos Aires, Argentina

e-mail: revmedbuenosaires@gmail.com – http://: www.medicinabuenosaires.com

Vol. 85, Supl. V, Noviembre 2025

Diagramación y Diseño: Andrés Esteban Zapata - aez.sgi@gmail.com

REUNIÓN ANUAL DE SOCIEDADES DE BIOCIENCIAS 2025 SAIC – AAFE

**LXX REUNIÓN ANUAL DE LA SOCIEDAD ARGENTINA DE INVESTIGACIÓN
CLÍNICA (SAIC)**

**LVII REUNIÓN ANUAL DE LA ASOCIACIÓN ARGENTINA DE FARMACOLOGÍA
EXPERIMENTAL (AAFE)**

17-20 de noviembre de 2025
Centro Metropolitano de Diseño - Ciudad Autónoma de Buenos Aires

EDITORES RESPONSABLES

Dr. Javier Cotignola
Dr. Ventura Simonovich

**2025 ANNUAL MEETING
OF BIOSCIENCE SOCIETIES SAIC – AAFE**

**LXX ANNUAL MEETING OF THE ARGENTINE SOCIETY
OF CLINICAL RESEARCH (SAIC)**

**LVII ANNUAL MEETING OF THE ARGENTINE SOCIETY
OF EXPERIMENTAL PHARMACOLOGY (AAFE)**

November 17-20th, 2025
Centro Metropolitano de Diseño - Ciudad Autónoma de Buenos Aires

RESPONSIBLE EDITORS

Dr. Javier Cotignola
Dr. Ventura Simonovich

LA TAPA

El Partenón de Libros (1983), Marta Minujín

Esta obra, reconstrucción simbólica de la democracia a través del acceso al conocimiento, representa para nosotros hoy el valor de la educación y ciencia argentina: una construcción colectiva, libre, pública y transformadora, que debe ser defendida frente a los intentos de censura, desfinanciamiento o privatización.

Foto: Roman März

CONSEJOS DIRECTIVOS

SAIC

Presidente:

Dr. Javier Cotignola
(Nodo FCEN)

Vicepresidente:

Dr. Hugo Ortega
(Nodo Litoral)

Secretaria:

Dra. Geraldine Gueron
(Nodo FCEN)

Tesorera:

Dra. Ayelén Toro
(Nodo FCEN)

Prosecretario:

Dr. Horacio Rodriguez
(Nodo Litoral)

Vocales:

Dr. Alejandro Español
Nodo: CEFYBO – Odontología

Dra. Mara Roxana
Rubinstein Guichon
Nodo: INFICA-FAVALORO-UCA

Dra. Luz Andreone
Nodo: Hospital Garrahan

Dr. Ariel Pablo Lopez
Nodo: Hospital De Clínicas

Dra. Vanina Da Ros
Nodo: IBYME - INGEBI

Dr. Ulises Orlando
Nodo: FMED

Dra. Silvina Álvarez
Nodo: NCO

Dra. Mónica Galleano
Nodo: FFYB

Dra. Carmen Stanganelli
*Nodo: Academia Nacional
de Medicina - Hospital Italiano*

Dra. Marcela Villaverde
Nodo: Instituto Ángel Roffo

Dr. Luis Di Ciano
Nodo: Instituto Lanari

Dra. Valeria Segatori
Nodo: Sur

Dra. Mariana Tellechea
Nodo: CEDIE

Revisores De Cuentas:
Titular

Dr. Carlos Bruque

Suplente

Dr. Pablo Sanchis

AAFE

Presidente:

Dr. Ventura Simonovich
Ciudad: Buenos Aires

Vicepresidente:

Dra. Susana Gorzalczany
Ciudad: Buenos Aires

Secretaria:

Dra. Guillermina Hernando
Ciudad: Bahía Blanca

Prosecretaria:

Dra. Natalia Alza
Ciudad: Bahía Blanca

Tesorero:

Dr. Jerónimo Laiolo
Ciudad: Córdoba

Protesorero:

Dr. Santiago Zugbi
Ciudad: Buenos Aires

Vocal Titular:

Dra. Daniela Quinteros
Ciudad: Córdoba

Vocal Suplente:

Dra. Alicia Penissi
Ciudad: Mendoza

Rev. De Cuenta Titular:

Dra. María Laura Barreiro Arcos
Ciudad: Buenos Aires

Rev. De Cuenta Suplente:

Dr. Uranga Leonardo Joaquín
Ciudad: Córdoba

**LAS SOCIEDADES QUE ORGANIZAN
ESTA REUNIÓN CONJUNTA
AGRADECEN EL APOYO DE**

ENTIDADES OFICIALES

**CONSEJO NACIONAL DE INVESTIGACIONES CIENTÍFICAS Y TÉCNICAS
FUNDACIÓN WILLIAMS**

ENTIDADES Y EMPRESAS AUSPICIANTES DE PREMIOS

**ASOCIACIÓN EDUARDO WILDE
ETC INTERNACIONAL
FUNDACIÓN CHERNY
FUNDACIÓN HONORIO BIGAND DE ASISTENCIA
Y DESARROLLO SOLIDARIO
FUNDACIÓN GADOR
MABXIENCE**

**LAS SOCIEDADES QUE ORGANIZAN ESTA REUNIÓN
CONJUNTA AGRADECEN LA PARTICIPACIÓN
Y COLABORACIÓN DE LAS SIGUIENTES EMPRESAS**

Estratégico
ONELAB

Premium
**THERMO FISHER SCIENTIFIC
ETC INTERNACIONAL**

Preferente
**ANALYTICAL
JENCK
WASSERBERG
TECNOLAB
MACROGEN
SARTORIUS
MICROLAT**

Asociado
**NORCES
INBIO HIGHWAY**

Colaborador
**BIO-OPTIC
BIODUNAMICS
NOVEGENE
VECTOR BUILDER
BRICK LABWARE**

También nos acompañan
**SF 500
GRIDX
INCUBANDO SALUD
PARQUE DE INNOVACIÓN
LOCI LABS**

PALABRAS DE BIENVENIDA DE LOS PRESIDENTES DE LAS SOCIEDADES

Es un verdadero honor darles la bienvenida a la LXX Reunión Anual de la Sociedad Argentina de Investigación Clínica (SAIC).

Este año compartimos el congreso con la Asociación Argentina de Farmacología Experimental (AAFE); haciendo que nuestro encuentro científico sea es un espacio de comunidad, reflexión y construcción colectiva.

Cada año, esta reunión nos recuerda por qué elegimos la ciencia como forma de vida. La investigación biomédica nos invita a explorar lo desconocido, pero también a hacerlo juntos, con diálogo, colaboración y compromiso. No se trata solo de producir conocimiento, sino de generar impacto: en la salud de las personas, en las políticas públicas y en el fortalecimiento de nuestras instituciones científicas.

Sabemos que no es un camino fácil. En la Argentina, investigar implica navegar entre la escasez de recursos, la inestabilidad y la falta de continuidad. Pero también significa ser parte de una tradición de creatividad, esfuerzo y excelencia que ha hecho de nuestra ciencia un ejemplo de resiliencia. La incertidumbre nos desafía, pero también nos impulsa a innovar, a vincularnos y a encontrar nuevas formas de crecer.

En este contexto, la SAIC se propuso profundizar su misión de integrar la ciencia básica con la investigación clínica y traslacional. Durante los últimos años, hemos trabajado para abrir la sociedad a nuevas disciplinas, fortalecer los consejos temáticos y crear espacios de encuentro entre investigadores, profesionales de la salud, bioinformáticos, biotecnólogos y emprendedores. Porque entendemos que la investigación traslacional no es una línea recta del laboratorio al hospital: es un entramado de saberes, instituciones y personas que buscan un objetivo común.

También creemos firmemente que la ciencia debe dialogar con la sociedad. Por eso, esta reunión incluye mesas redondas con asociaciones de pacientes, debates sobre políticas de salud y actividades de vinculación tecnológica y emprendedurismo científico. Nuestro desafío como comunidad científica es acompañar los descubrimientos con responsabilidad, ética y sentido social.

Agradezco profundamente al Consejo Directivo de la SAIC, al equipo organizador, a los coordinadores de simposios y mesas, a los jurados de premios y a todos los que hicieron posible esta reunión. Agradezco también a las instituciones que nos apoyan —universidades, organismos públicos, empresas y fundaciones— y, muy especialmente, a los jóvenes investigadores, que son el presente y el futuro de la ciencia argentina.

Que la 70ª Reunión Anual sea un espacio para compartir, inspirarse y generar nuevas ideas. Que cada simposio, cada póster y cada conversación renueven nuestro compromiso con una ciencia de calidad, abierta, colaborativa y con vocación de servicio.

Dr. Javier Cotignola
Presidente, Sociedad Argentina de Investigación Clínica (SAIC)

Es un honor darles la bienvenida a esta nueva edición del Congreso de la Asociación Argentina de Farmacología Experimental. Cada encuentro renueva algo más que un programa científico: fortalece nuestra convicción de que la ciencia se construye en comunidad, con diálogo, respeto y un propósito claro.

Agradezco profundamente a la Fundación Williams por su apoyo constante a la investigación científica; a la Comisión Directiva de la SAIC por compartir nuestra visión de una ciencia más integrada y traslacional; y a la Comisión Directiva de la AAFE por su trabajo incansable, generosidad y compromiso con el fortalecimiento de nuestra disciplina.

Sabemos que el contexto argentino para investigar es sumamente desafiante. Las limitaciones presupuestarias, la desinversión, la incertidumbre y, a veces, la falta de reconocimiento social ponen a prueba nuestra vocación. Sin embargo, a nivel global, la ciencia también enfrenta tensiones profundas: desinversión, la disolución de equipos de investigación, la presión por la inmediatez, el riesgo de la desinformación y el desafío de mantener la ética y el sentido humano del conocimiento.

Y, a pesar de todo, aquí estamos. Como escribió Charles Dickens en “Historia de dos ciudades”, ambientada en la Revolución Francesa: “Era el mejor de los tiempos y era el peor de los tiempos; la edad de la sabiduría y también de la locura; la época de las creencias y de la incredulidad; la era de la luz y de las tinieblas; la primavera de la esperanza y el invierno de la desesperación.”

Vivimos un momento de grandes dificultades, pero también de inmensas posibilidades, porque la creatividad florece precisamente en la escasez.

Hoy, en tiempos de inteligencia artificial, la interacción humana es más necesaria que nunca. Las máquinas procesan datos con una precisión asombrosa, pero solo las personas pueden interpretar, imaginar y decidir el rumbo de la ciencia. Hace unos años, Nassim Taleb, en su libro “Antifrágil”, planteó una idea inspiradora: que existen sistemas —y comunidades— que no solo resisten la incertidumbre, sino que se fortalecen gracias a ella. Creo que nuestro desafío es construir un sistema de investigación y desarrollo antifrágil, que se nutra de nuestras fortalezas y transforme cada obstáculo en una oportunidad de crecimiento.

Con ese espíritu, y junto con la SAIC, hemos creado el Consejo de Investigación Traslacional, una iniciativa que busca tender puentes entre la ciencia básica y la clínica, entre el laboratorio y la sociedad. Nos enorgullece que la IUPHAR haya reconocido esta propuesta y nos acompañe para que pueda replicarse en otras sociedades científicas del mundo.

Porque nadie investiga solo. Detrás de cada descubrimiento hay equipos, mentores, estudiantes y comunidades que sostienen el esfuerzo cotidiano. La farmacología argentina —como toda la ciencia argentina— ha demostrado una y otra vez que la inteligencia, el rigor y la pasión pueden transformar la adversidad en innovación.

Que este congreso sea, entonces, una celebración de esa inteligencia colectiva, de la colaboración y de la esperanza. Que cada charla, cada póster y cada conversación nos recuerden que la ciencia avanza no solo con datos, sino con vínculos, valores y propósito.

Muchas gracias por estar aquí, por seguir creyendo en la farmacología y en la ciencia argentina.

Con enorme alegría, declaro inaugurado el Congreso de la Asociación Argentina de Farmacología Experimental.

Dr. Ventura Simonovich
Presidente de la Asociación Argentina de Farmacología Experimental (AAFE)

AAFE CONFERENCE**Monday 17th November 2025 - 11:00 - 12:00 - Calle Principal****Chair: Natalia Alza****CROSSING THE TRANSLATIONAL GAP: THE JOURNEY OF PEGASUS AND ARISTAEUS
IN EXPERIMENTAL PHARMACOLOGY FOR NEURODEGENERATION****César Avila, Diego Ploper, Silvina Chaves, Esteban Vera Pingitore, Benjamín Socías,
Rodrigo Tomás-Grau and Rosana Chehín***Instituto de Investigación en Medicina Molecular y Celular Aplicada (IMMCA) (CONICET)- Universidad Nacional
de Tucumán (UNT)-Ministerio de Salud Pública de Tucumán-SIPROSA, San Miguel de Tucumán, Argentina.*

We originally discovered that certain tetracyclines possess a unique biophysical property: the ability to selectively bind cross- β structural pattern without interacting with native monomeric protein. This insight led to the development of two translational strategies targeting α -synuclein pathologies: the therapeutic agent Pegasus and the diagnostic platform Aristaeus. Pegasus (DAD9) is a first-in-class dopaminergic agonist with intrinsic neuroprotective activity and no off-target effects on conventional levodopa/carbidopa-sensitive pathways. Rationally designed by conjugating a non-antibiotic tetracycline scaffold with dopamine, it retains antioxidant, anti-inflammatory, and anti-aggregant properties, while selectively activating D1/D2 receptors. Efficacy was demonstrated in biophysical, cellular, and in vivo models. An IND-enabling package is currently under development. Aristaeus, based on the same molecular logic, replaces the conventional antibody-based biocapture element with

a rationally selected tetracycline, engineered to anchor onto polymeric or conductive surfaces while preserving selective affinity for amyloid aggregates. This innovation enables robust, scalable detection of α -synuclein aggregates in biological fluids, with potential applications in the early diagnosis of Parkinson's disease and adaptability to other proteinopathies, such as Alzheimer's disease. Both projects faced the translational "valley of death," but strategic private investment in IP protection, formulation development, and regulatory planning enabled Pegasus to advance toward IND status. This experience paved the way for the future positioning of Aristaeus, currently under national phase protection. This trajectory exemplifies how insights from fundamental biophysical experimentation can evolve into technological concepts with high impact, supporting the development of innovative therapeutic and diagnostic platforms for neurodegenerative diseases.

LANARI CONFERENCE**Monday 17th November 2025 - 17:30 - 18:30 - Calle Principal****Chair: Javier Cotignola****BEYOND THE SINGLE RECEPTOR: EXPLORING STEROID HORMONE SIGNALING
IN BREAST TUMOR CELLS****Adali Pecci***Instituto de Fisiología, Biología Molecular y Neurociencias*

Steroid hormone receptors (SHRs) belong to a broad family of ligand-activated nuclear receptors that, while structurally similar, display distinct functional behaviors. Each SHR comprises three main domains: an N-terminal activation function 1 (AF-1) domain, which is intrinsically disordered and ligand-independent; a central DNA-binding domain (DBD); and a C-terminal ligand-binding domain (LBD) that includes activation function 2 domain (AF-2), connected via a hinge region.

Traditionally, hormone response specificity was attributed solely to the ligand. Although this still holds for certain synthetic agonists, natural ligands often activate multiple

SHRs simultaneously, leading to broader physiological effects. Despite conserved features such as ligand-binding pockets and DNA recognition sequences, SHRs can trigger divergent—and sometimes opposing—biological outcomes in a tissue-specific manner. This raises a long-standing question: what truly defines the specificity of SHR-mediated actions?

Multiple factors contribute to this specificity, including receptor expression levels, intranuclear localization (i.e., the ability to form biomolecular condensates), chromatin accessibility, DNA sequence of target regions, and differential interactions with other transcription factors

and coregulators. Adding further complexity, SHRs can form heterocomplexes, allowing mutual regulation of transcriptional activity. This receptor crosstalk may be synergistic, enhancing hormonal signals, or antagonistic, involving competition for signaling pathways, cofactors, or genomic binding sites.

To investigate these mechanisms, we employed ChIP-seq, RNA-seq, and quantitative fluorescence microscopy in breast cancer cells. Our findings reveal a functional

crosstalk between SHRs and support emerging paradigms in hormone action specificity. From a pharmacological standpoint, deciphering these interactions is essential for the design of more effective endocrine therapies. Such strategies could reduce tumor resistance, limit metastatic potential, and expose new vulnerabilities in cancer cells. Ultimately, unraveling SHR crosstalk may reveal new vulnerabilities in tumor biology, offering promising avenues for cancer treatment.

DOSNE DE PASQUALINI CONFERENCE

Tuesday 18th November 2025 - 11:00 - 12:00 - Calle Principal

Chair: Isabel Lüthy

FROM FUNDAMENTAL IMMUNOLOGY TO PRECISION MEDICINE: DEVELOPMENT OF A THERAPEUTIC ANTI-MICA MONOCLONAL ANTIBODY AND VALIDATION OF SOLUBLE MICA IN LIQUID BIOPSIES AS BIOMARKER IN ONCOLOGY

Norberto Zwirner

IBYME

MICA (MHC class I chain-related protein A) is a promising target for precision oncology, as it is minimally expressed on normal cells but frequently upregulated in diverse tumor types. However, tumor cells can shed soluble MICA (sMICA), which antagonizes NKG2D-mediated immune responses and promotes immune evasion. In our laboratory, we have generated robust evidence supporting MICA as a relevant target for precision medicine. We developed an anti-MICA monoclonal antibody that exhibits antitumor activity and elucidated its mechanism of action. Within this framework, we also analyzed the competitive landscape and will discuss the scientific and operational challenges encountered during its preclinical development and potential translation into a therapeutic candidate. Concurrently, given that elevated sMICA levels are detectable in plasma or serum from

cancer patients, but existing immunoenzymatic assays suffer from limited sensitivity and matrix interference, we designed a highly sensitive Förster resonance energy transfer (FRET)-based heterogeneous immunoassay for early detection of sMICA. This method aims to validate sMICA as a diagnostic and prognostic biomarker, offering a novel approach for patient monitoring and therapeutic follow-up. Together, these two initiatives (the anti-MICA monoclonal antibody and the FRET-based sMICA assay) illustrate complementary technology transfer pathways, each presenting distinct scientific and operational challenges. We will outline the progression from basic research to translational application, highlighting key achievements and the hurdles encountered during interactions with CONICET and biopharmaceutical partners.

GENETIC CONFERENCE

Tuesday 18th November 2025 - 18:30 - 19:30 - Calle Principal

Chair: Cecilia Soledad Fernandez

EXPLORING GENETIC VARIABILITY IN MUSCULAR DYSTROPHIES: FROM DUCHENNE TO HISTORICAL FINDINGS

Florencia Giliberto^{1,2}

1 Laboratorio de Distrofinopatías, Cátedra de Genética, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires (UBA), Buenos Aires, Argentina. 2 Instituto de Inmunología, Genética y Metabolismo (INIGEM), UBA-CONICET, Buenos Aires, Argentina

Over the past decades, remarkable progress has been achieved in the molecular study of dystrophinopathies. In Argentina, our research program relies on a biobank of more than 3,000 samples from Duchenne and Becker muscular dystrophy (DMD/BMD) patients and families, providing the foundation for large national cohorts, innovative methods, and regional collaboration to advance diagnosis and care. We implemented a comprehensive molecular algorithm for DMD/BMD, achieving a 97% detection rate in more than 400 patients. This work not

only confirmed clinical diagnoses but also identified individuals eligible for pharmacogenetic therapies such as exon-skipping and nonsense read-through. Importantly, we provided the first meta-analysis of Latin American mutational frequencies, highlighting regional disparities in access to molecular diagnosis and treatment opportunities. Building on this foundation, we explored the role of genetic modifiers in disease progression. By stratifying Argentine patients into extreme phenotypes, we demonstrated the prognostic significance of ACTN3 variation

and its interaction with the location of DMD variants. This study, the first of its kind in Latin America, underscored the importance of considering both cis- and trans-acting genomic factors in predicting severity and in the design of clinical trials. Expanding the scope beyond male patients, we investigated skeletal muscle involvement in asymptomatic female carriers of DMD variants.

Whole-body MRI revealed a high prevalence of edema, fatty infiltration, and atrophy compared with healthy controls, even in the absence of clinical symptoms. These findings challenge the traditional view of carriers as unaffected and advocate for multidisciplinary surveillance and early intervention strategies. Finally, our work on Pompe disease highlighted the diagnostic pitfalls of

pseudodeficiency alleles. A controversial 2021 report that attributed Pompe disease to a 14th-century Italian mummy (Cangrande della Scala) based on misinterpretation of the GAA:c.271G>A variant, triggered our investigation. Using ACMG/ClinGen frameworks, we reclassified this variant as benign, preventing misdiagnosis and emphasizing the importance of rigorous variant curation. Together, these studies illustrate a translational trajectory bridging molecular discovery, clinical application, and public health impact, and highlight the value of integrating cutting-edge technologies with regional patient data to improve diagnostic accuracy, optimize therapeutic opportunities, and deepen understanding of disease heterogeneity in neuromuscular disorders.

TAQUINI CONFERENCE

Wednesday 19th November 2025 - 11:00 - 12:00 - Calle Principal

Chair: Débora Cohen

PLCS, CATIONS, AND THE CHEMISTRY OF FERTILIZATION AND DEVELOPMENT

Rafael A. Fissore

Department of Veterinary and Animal Sciences. University of Massachusetts

Calcium oscillations are the driving signal for egg activation and the initiation of embryonic development in mammals. The sperm factor PLC ζ 1 is the primary trigger of these oscillations. In mice, however, males lacking PLC ζ 1 remain subfertile, and our findings show that another PLC can function as a backup, providing limited fertility. Importantly, these PLCs act in an interdependent manner to ensure the timely onset of fertilization and developmental success.

Beyond calcium, two other divalent cations, zinc (Zn²⁺)

and magnesium (Mg²⁺), play indispensable roles in meiosis and early development. We identified TRP channels, specifically TRPV3 and TRPM7, as key regulators of Zn²⁺ and Mg²⁺ homeostasis during these stages. However, the mechanisms controlling the functional activity of these TRP channels and the cellular targets of these ions remain largely unknown. In this talk, I will highlight the critical steps regulated by these PLCs and TRP channels, discuss unresolved questions, and point to promising directions for future research.

SAIC-AAFE CONFERENCE

CELL SIGNALING PATHWAYS DRIVING CANCER PROGRESSION AND METASTASIS

Thursday 20th November 2025 - 11:00 - 12:00 - Calle Principal

Chairs: Ayelén Toro, Alejandro Urtreger

PROTEIN KINASE C IN TUMORIGENESIS AND METASTASIS

Marcelo G. Kazanietz

Department of Molecular and Cellular Pharmacology, Miller School of Medicine and Sylvester Comprehensive Cancer Center, University of Miami

Protein kinase C (PKC), a family of serine/threonine kinases, has been widely implicated in tumorigenesis and metastasis, albeit with a high degree of isozyme specificity. Most PKCs are activated by the lipid second messenger diacylglycerol (DAG) that is transiently generated upon stimulation of surface receptors. While PKC isozymes are rarely mutated in cancer, major imbalances in expression have often been linked to disease progression and aggressiveness. For example, abnormal overexpression of PKC epsilon, as observed in castration-resistant prostate cancer and non-small cell lung cancer (NSCLC), associates with the activation of proliferative and metastatic signaling pathways, and

additionally correlates with poor patient prognosis. PKC epsilon has also been found to be a crucial mediator of KRAS-driven lung tumorigenesis in non-small cell lung cancer (NSCLC), as established by a genetically engineered mouse model of PKC epsilon gene (PRKCE) deletion. Indeed, mutant KRAS-driven lung tumor formation is impaired in mice lacking either a single or both PRKCE gene alleles, emphasizing the relevance of PKC epsilon expression to disease progression. PKCs play prominent roles in regulating transcriptional networks involved in cell cycle regulation, epithelial-to-mesenchymal transition (EMT), inflammation, and immune evasion across different cancer types. Interestingly, hyperactivation of

specific PKC isozymes, particularly PKC alpha, has also been observed in models of triplenegative breast cancer (TNBC). This is reflected in its constitutive co-localization with sites of DAG generation in the cell periphery, and may relate to the abnormal overexpression of specific phospholipase C (PLC) isozymes responsible for DAG generation found in TNBC cellular models. Thus, addiction to deregulated DAG production and its rewiring effects through aberrantly expressed PKCs may represent a promising targetable vulnerability in cancer cells. Our

studies indicate that the DAG-PKC pathway is involved in multiple aspects of cancer progression, suggesting its aberrant activation as a marker of aggressiveness. The identification of downstream signaling and gene effectors of the DAG-PKC pathway will provide novel mechanistic insights into the tumorigenic activity and metastatic dissemination of cancer cells, while offering targeting strategies to improve the efficacy of chemotherapy and immunotherapy in cancer patients.

RHO GTPASES IN CANCER: REGULATORY NODES IN CELL MOTILITY SIGNALING

Mariana Cooke

Department of Molecular and Cellular Pharmacology, Miller School of Medicine and Sylvester Comprehensive Cancer Center, University of Miami

Cancer cells develop phenotypic traits that enhance their ability to grow indiscriminately and metastasize to local and distant sites. The Rho GTPases, a subfamily of the Ras superfamily comprising more than 20 small G-proteins, have emerged as fundamental signaling players in the control of actin cytoskeleton remodeling and in the regulation of proliferation, gene expression, cell metabolism, and the tumor microenvironment. Among the Rho GTPases, Rac1 has a prominent role in the formation of pro-motility actin-rich protrusions such as lamellipodia and ruffles, and it is recognized as a crucial factor in tumor growth and metastatic spread, rendering it an attractive target for cancer therapy. Aberrant Rac1 hyperactivation is a cancer hallmark and has been causally associated with cancer progression and chemo/radioresistance. Mechanistically, this is primarily due to abnormal overexpression and/or activation of Guanine nucleotide Exchange Factors (Rac-GEFs), which promote GDP/GTP exchange on Rac1, thereby activating it. Using unbiased expression and RNAi screening approaches, our laboratory identified distinct members of the large Rac-GEF family (>40 members) as effectors of

receptor tyrosine kinases (RTKs). For example, FARP1, ARHGEF39, and TIAM2 were established as the main Rac-GEFs driving the formation of actin-rich ruffles required for lung adenocarcinoma cell migratory and invasive activities in response to stimulation of EGFR, cMET, and AXL. RTK stimulation caused the subcellular relocalization of Rac-GEFs to peripheral ruffles, leading to compartmentalized Rac1 activation, as determined using a FRET biosensor. In castration-resistant prostate cancer models, VAV2 was found to be the most crucial Rac-GEF implicated in hypermotility phenotypes, suggesting significant cancer-cell-type specificity in Rac-GEF utilization. A comprehensive analysis of human specimens revealed up-regulation of these RacGEFs in cancer vs. non-tumoral areas, as well as significant associations with poor patient prognosis. These results were validated through comprehensive bioinformatics analysis. The ongoing efforts to design Rac-GEF/Rac1 inhibitors aim to develop preclinical platforms for targeted approaches, ultimately achieving the long-term goal of advancing cutting-edge personalized anticancer therapies.

SAIC CONFERENCE

Thursday 20th November 2025 - 15:00 - 16:00 - Calle Principal

Chair: Elba Vazquez

GLOBAL DNA METHYLATION AS A POTENTIAL LINK BETWEEN MATERNAL EARLY ADVERSITY AND INTERGENERATIONAL CONSEQUENCES

Eduardo Canepa

Laboratorio de Neuroepigenética y Adversidades Tempranas

Child maltreatment-related trauma represents one of the most harmful and widespread stressors in our society. The long-term consequences of exposure to maltreatment during childhood are well established and include adverse psychological, biological, and behavioral outcomes, as well as increased risk for mental and physical health problems. Recent evidence suggests that the heavy burden imposed by child maltreatment may not be limited to the adult life of the affected women, but can

also be transmitted to another, even more vulnerable population—their offspring. The prevailing paradigm posits that this intergenerational transmission likely occurs after birth, during infancy and early childhood, through the impact of maternal dysfunctional states related to childhood maltreatment on the quality of mother-child relationships and caregiving.

In this project, we seek to extend this paradigm by proposing that the process of intergenerational transmission

begins during fetal development. Data from human cohort studies and animal models suggest that the placenta provides a record of maternal exposure to adverse environmental experiences not only during pregnancy but also from earlier life periods, as reflected by changes in the transcriptome and epigenome. Thus, the placenta may contribute to fetal programming and, consequently, to the intergenerational transmission of the effects of maternal childhood maltreatment. The general aim is to provide experimental evidence linking maternal expo-

sure to early-life adversity with potential alterations in the placental epigenome —particularly in DNA methylation—and its role as a mediator in the establishment of attachment style.

Clarifying the molecular alterations underlying parental dysfunction in mothers with a history of childhood maltreatment will enable the development of biologically informed interventions aimed at disrupting the intergenerational transmission of its consequences.

Symposium 1 - SAIC - Monday 17th November 2025 - 9:30 - 11:00 - Auditorio

EXPERIMENTAL MODELS IN BIOMEDICINE: ALTERNATIVES, COMPLEXITY AND APPLICATIONS

Chairs: Hugo Ortega, Ayelen Toro

GENOME EDITED MOUSE MODELS FOR PRECLINICAL STUDIES

Martina Crispo

Unidad de Biotecnología en Animales de Laboratorio, Institut Pasteur de Montevideo

Martina Crispo leads the Laboratory Animal Biotechnology Unit (UBAL) at the Institut Pasteur de Montevideo, Uruguay, a regional reference center for the development and application of genetically engineered animal models. UBAL's mission is to provide innovative biotechnological tools to advance biomedical research, while ensuring high standards of animal welfare, scientific rigor, and ethical responsibility.

The unit has established robust platforms for generating, characterizing, and maintaining transgenic and gene-edited mouse models, with a strong focus on CRISPR/Cas9 technologies. Under Dr. Crispo's leadership, UBAL has

successfully created a wide range of genetically modified mouse lines, including knock-out, knock-in, and conditional models for the study of cancer, infectious diseases, immunology, and neurobiology. Several of these CRISPR-derived models represent pioneering developments in Uruguay and have become essential resources for local and international collaborations.

Through this integrated approach, the unit not only strengthens biomedical research capacity in Uruguay but also fosters a collaborative, responsible, and innovative scientific ecosystem across Latin America.

MICE WITH A MISSION: TRANSLATING PROSTATE CANCER COMPLEXITY THROUGH PATIENT-DERIVED XENOGRAFTS

Estefania Labanca

Department of Genitourinary Medical Oncology and the David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center, Houston, USA.

Treatment-refractory prostate cancer contributes to lethality. Advances in prostate cancer research have lagged behind other cancer types, largely due to the scarcity of models that accurately replicate both, disease progression and its microenvironmental dependencies. To help overcome this, we established the MDA PCa PDX series, a comprehensively characterized and clinically annotated collection of over 150 prostate cancer patient-derived xenografts (PDXs), accounting for the heterogeneous spectrum in prostate cancer that better represent disease biology. PDX-derived organoids have served as a complementary platform suitable for genetic manipulation and development of new PDX models, integrating model systems.

To further functionalize clinical observations and address challenges in modeling skeletal metastases, the main metastatic site in prostate cancer, models are applied *in vivo* intrabone and they mirror the characteristic bone-forming phenotype of human prostate cancer. The epithelial-stromal contributions driving bone metastases can be deconvoluted by cross-species characterization and signal molecular adaptations of tumors when within the bone niche. Further, with bidirectional interrogation, we can associate clinical findings to murine modeling. As proof-of-principle, we determined induced structural

remodeling across the bone–tumor interface and transcriptional reprogramming in both compartments when exploring the impact of bone-targeting in preclinical models of bone metastases.

Our models have been useful in to study the metastatic process and identify clinically relevant therapeutic targets. Namely, the bone-metastasis derived PDX, MDA PCa 118b that robustly remodels the microenvironment highly expresses growth factor FGF9 and one of its receptors, FGFR1. We have shown that FGFR1 increased rates of bone metastases and shortened survival in experimental mouse models of spontaneous metastases. Our findings were coupled with clinical studies, highlighting the relevance of these models for guiding patient management.

Additionally, we have mimicked the progression to therapy of patients in our model systems, revealing metabolic reprogramming upon treatment relapse. We identified enhanced metabolism of ketone bodies—fatty-acid-derivatives that can used as alternative energy fuel—occurring upon castration-resistant prostate cancer. Together *in silico*, *in vitro*, *in vivo* and patient studies proposed key ketogenic enzyme ACAT1 as a promising target for therapeutic intervention in treatment-refractory prostate cancer.

Overall, this valuable resource has allowed to understand tumor evolution, especially metastasis to bone

and resistance to therapy, enabling to translationally and mechanistically bridge the lab and clinic.

USING THE ZEBRAFISH LATERAL LINE TO STUDY THE DEVELOPMENT OF SENSORY SYSTEMS

Paola V Plazas^{1,2}

¹ CONICET, ² Instituto de Farmacología, Facultad de Medicina, UBA

The zebrafish is an exceptional vertebrate model for studying biological processes *in vivo* and within an intact organism. Its optical transparency during early development, external fertilization and rapid embryogenesis allow direct visualization and manipulation of cellular dynamics as they unfold. These features, combined with powerful genetic tools and transgenic lines, make zebrafish uniquely suited for studying the development and function of sensory systems in their native environment. The lateral line (LL) is a mechanosensory system that allows fish to detect water movement and pressure changes. It comprises a set of sensory organs, the neuromasts, composed of hair cells (HCs) that are innervated by sensory afferent neurons (ANs) and by efferent neurons that modulate their activity. Importantly, zebrafish LL HCs share structural, functional, and molecular characteristics with HCs of the mammalian inner ear. Due to their accessibility and conservation, they have been widely used as a model to investigate the genetic basis of hearing and balance.

Sensory circuits are assembled early in development. A remarkable feature of this process is that it relies on “spontaneous” electrical activity (SEA) generated within sensory organs. In our lab, we leverage the zebrafish LL system to investigate *in vivo* how SEA contributes to the

assembly of sensory circuits.

First, I will present our recent findings aimed at characterizing SEA in the developing LL. Using *in vivo* calcium imaging in transgenic larvae expressing GCaMP7 in LL HCs, we identified two types of calcium transients—spikes and waves—whose frequency and amplitude change over development. Notably, spike dynamics are modulated by efferent input, suggesting a role in shaping HC activity.

Additionally, I will discuss our work on the role of SEA in LL system assembly. By selectively silencing SEA in individual ANs via stochastic expression of the potassium channel hKir2.1, we observed abnormal development of central axonal arbors and reduced innervation areas. Time lapse imaging revealed that silenced axonal arbors displayed higher motility and lower density of varicosities, both features of immature neurons. Collectively, our results provide an *in vivo* demonstration that SEA plays a key role in the assembly of sensory circuits.

Finally, I will briefly highlight a recent study in which we used the zebrafish LL to evaluate the pathogenic nature of a novel genetic variant associated with sensory disorders, underscoring the translational relevance of this model.

FROM SOIL TO THE LABORATORY: *C. ELEGANS* AS AN ETHICAL ALTERNATIVE IN RESEARCH

Ximena Blanco Crivelli^{1,2}

¹ Universidad de Buenos Aires, Instituto de Investigaciones en Epidemiología Veterinaria (IIEV-UBA), ² Universidad de Buenos Aires, Facultad de Ciencias Veterinarias, Cátedra de Microbiología

Caenorhabditis elegans is a free-living, non-parasitic nematode with worldwide distribution. Newly hatched larvae measure ~0.25 mm in length, while adults reach ~1 mm. This species has a short life cycle, a high reproductive rate, and can be easily maintained in the laboratory on agar plates or in liquid culture using *Escherichia coli* OP50 as a food source, making it highly suitable for experimental studies. Since its establishment as a model organism in the 1960s, *C. elegans* has been widely used in research on neurobiology, apoptosis, physiology, microbiology, parasitology and toxicology.

Here, we investigated its potential as an alternative model for assessing tetanus toxin (TeNT) toxicity, aiming to replace guinea pigs and mice in potency assays. A strain

maintenance protocol was established, and toxicity tests were performed with TeNT at a concentration of 10^{-1} on strains N2 (wild-type, WT), CF512, CF1844 and LC80. Sensitivity was observed in the first three strains, with mortality as the response indicator. The WT strain was further tested against lower toxin dilutions (10^{-2} , 10^{-3} and 10^{-4}), showing no statistically significant differences compared with the control at 19 °C.

These findings support the use of *C. elegans* as a valuable alternative model for high-concentration TeNT toxicity testing and provide a foundation for future implementation of this approach in toxicological studies, in line with the 3Rs principles (Replacement, Reduction and Refinement).

Symposium 2 - SAIC - Monday 17th November 2025 - 13:00 - 14:30 - Auditorio ONCOPEDIATRICS
Chairs: Georgina Cardama, Hebe Duran

FROM REGISTRY TO PUBLIC POLICY: THE ARGENTINE PEDIATRIC ONCOLOGY REGISTRY (ROHA) AS A TOOL FOR EQUITY AND RESEARCH

Florencia Moreno

Coordinadora Programa Nacional de Cáncer Pediátrico. Directora del ROHA- Instituto Nacional del Cáncer- Ministerio de Salud

The Argentine Hospital Pediatric Oncology Registry (ROHA) was established in 2000 as an initiative aimed at consolidating information on cancer in children across the country. Over its 25 years of operation, it has become an essential tool not only for epidemiological surveillance but also for health system planning, the development of public policies, and the advancement of clinical and translational research in pediatric oncology.

A key turning point in this process was the adoption of the National Pediatric Oncology Law (Law 27.674) in 2022, which granted ROHA a central role as the technical and administrative backbone of this public policy. The law guarantees the right of all pediatric cancer patients to comprehensive health coverage and social benefits, using the registry as the reference platform for certification and entitlement. In this way, ROHA evolved from being a registry system into a true instrument for ensuring equity and access.

The value of the data collected lies in its high coverage (over 90% of cases nationwide) and its ability to integrate with national sources such as INDEC, DEIS, and RE-

NAPER. This integration has enabled the development of incidence, survival, and trend analyses that guide resource allocation, the organization of Pediatric Oncology Units, and the prioritization of treatment strategies.

The results achieved are significant: from the implementation of the Unique Pediatric Oncology Certificate (CUOP), which grants automatic access to social benefits, to the development of stratification and quality assessment tools for oncology services. Furthermore, ROHA has become an indispensable source for multicenter research at both the national and international levels, in collaboration with networks such as PAHO/WHO, IARC, SIOP, and other pediatric cancer registries in Latin America and Europe.

In summary, ROHA illustrates how epidemiological information can be transformed into concrete action. Its trajectory, from hospital-based registry to national public policy, demonstrates that the systematic production of reliable data not only enhances scientific knowledge but also guarantees rights and contributes to reducing inequities in health.

FOXP3 AS A THERAPEUTIC TARGET IN PEDIATRIC HIGH GRADE GLIOMA

Marianela Candolfi

*Instituto de Investigaciones Biomédicas (INBIOMED, CONICET-UBA), Facultad de Medicina, Universidad de Buenos Aires. Centro de Referencia en Investigación Oncopediátrica (CRIO), Argentina.
 maru.candolfi@gmail.com*

Pediatric high grade gliomas (pHGG) are aggressive and diffuse brain tumors that develop during childhood. Although they are considered rare diseases (~60 cases/year in Argentina), due to the lack of therapeutic options and their dismal prognosis they represent the leading cause of cancer-related death in children. Years of limited funding and unavailability of preclinical models and tissue samples has significantly delayed the development of effective therapies for pHGG. Consequently, these children are treated with the same standard therapy that also fails in adult glioma patients, i.e. surgery, radiotherapy and chemotherapy with temozolomide. Thus, it is urgent to develop novel therapies tailored to the unique biology of these tumors. The transcription factor *Forkhead Box Protein P3* (FOXP3) is crucial for the immunosuppressive function of regulatory T cells, constituting a promising target to boost immunity in cancer. Since FOXP3 has also been detected in tumor cells, our group has focused in the tumor intrinsic effects of Foxp3 for several years. We found that Foxp3 blockade elicits intrinsic and immune-mediated

antitumoral effects in breast cancer and adult glioblastoma. We have now explored the expression and function of FOXP3 in pHGG. These tumors overexpress Foxp3 compared to low-grade gliomas (pLGG), and this expression correlates with immunosuppressive and epithelial-mesenchymal transition markers. Both chemo- and radio-therapy further induce Foxp3 expression in pHGG cells and blockade of this response with a cell penetrating peptide that inhibits Foxp3 nuclear translocation (P60) elicits antitumoral effects, reducing viability, decreasing the expression of invasion-associated proteins, and enhancing chemo-radiosensitivity. In order to enhance the local availability of P60 in the tumor we developed an adenovector encoding P60 (Ad.P60). This vector efficiently transduces pediatric glioma cells and decreases both cell viability and resistance to several chemotherapeutic drugs, also showing an adequate safety profile in the brain of prepubertal mice. Our results indicate that FOXP3 exerts intrinsic pro-tumoral effects in pediatric glioma, and its local inhibition could enhance the treatment of these devastating tumors.

RETINOBLASTOMA: THE ROLE OF EARLY DETECTION AND REGIONAL RESEARCH IN IMPROVING OUTCOMES

Claudia Sampor
Hospital Garrahan

Retinoblastoma is the most common intraocular malignancy in childhood, accounting for approximately 3% of all pediatric cancers. While survival exceeds 95% in high-income countries, children in low- and middle-income settings continue to face a disproportionate burden, with survival rates frequently below 50%. In Latin America, progress has been heterogeneous, reflecting disparities in early diagnosis, access to specialized care, and availability of multidisciplinary treatment.

Timely diagnosis remains the cornerstone for achieving cure with minimal morbidity. Late presentation is still a frequent challenge across the region, leading to advanced disease stages and higher enucleation rates. Strengthening awareness among primary care providers, integrating referral networks, and implementing national early detection strategies have demonstrated measurable improvements in several countries. These efforts are essential to bridge the survival gap while preserving vision and quality of life.

Treatment strategies have evolved significantly in the past two decades, incorporating conservative approaches such as intra-arterial and intravitreal chemotherapy,

which allow ocular salvage and improved functional outcomes. However, the implementation of these modalities requires trained multidisciplinary teams and access to adequate infrastructure, elements not yet uniformly available across the region.

Collaborative preclinical and translational research in Latin America, particularly in Argentina, has generated valuable scientific evidence that contributes significantly to understanding retinoblastoma biology and resistance mechanisms, supports therapeutic innovation, and explores chemoresistance pathways and novel drug candidates for ocular tumors. These studies demonstrate that high-impact translational research can be successfully conducted in Latin America through regional and international collaboration.

The Latin American experience underscores that progress against retinoblastoma is possible when clinical excellence, research, and collaboration converge. Strengthening regional partnerships and ensuring equitable access to early diagnosis and modern treatment will be key to transforming survival and quality of life for every child with retinoblastoma.

A DIFFERENTIATION-BASED TRANSCRIPTIONAL SIGNATURE FOR RISK STRATIFICATION IN NEUROBLASTOMA

Federico Julián Garde¹, Daniela J. Di Bella², María Sol Ruz^{*1}, Abel Luis Carcagno^{*1}

1. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Departamento de Química Biológica.; Laboratorio de Diferenciación Celular y Cáncer

2. Harvard University; Department of Stem Cell and Regenerative Biology

fedegarde97@gmail.com

Neuroblastoma (NB) is the most common extracranial solid tumor in children, arising from the embryonic neural crest and characterized by impaired differentiation. Despite the advances in therapy, risk stratification remains challenging. Recent single-cell RNA sequencing (scRNA-seq) studies have provided unprecedented resolution of NB, revealing malignant populations that range from immature states to more differentiated phenotypes, providing an opportunity to link cellular differentiation programs to patient outcomes.

In this study, we integrated scRNA-seq data from three independent cohorts to construct a comprehensive atlas of primary NB tumors. Following Seurat-based integration and filtration of malignant cells, two principal states were identified: clusters 0 and 1. Alignment to a human fetal adrenal medulla reference revealed a differentiation landscape along the sympathoadrenal lineage, spanning from less-differentiated (Cluster 1) to more-differentiated

states (Cluster 0). The inferred developmental hierarchy was validated using trajectory analyses (CytoTrace2 and Monocle3) and functional enrichment.

Genes differentially expressed between these states were used to derive a novel differentiation-associated signature. As a proof of concept, we applied this signature to bulk RNA-seq data from NB patients at diagnosis and demonstrated its capacity to stratify patients into high- and low-risk groups (Cox regression analysis) and a correlation with the tumor INSS stage, suggesting that the underlying developmental composition could influence the response to therapy and the progression of the disease.

This study establishes a framework integrating single-cell analysis with prognostic stratification in NB, showing that developmental hierarchies inferred from scRNA-seq atlases can provide biologically interpretable signatures, enabling effective patient stratification.

Symposium 3 - SAIC - Monday 17th November 2025 - 15:00 - 16:30 - Auditorio**EXPOSURE TO POLLUTANTS AND THEIR IMPACT ON HUMAN HEALTH****Chairs: Andrea Randi, Claudia Cocca****EFFECT OF CHRONIC EXPOSURE TO URBAN AIR POLLUTION ON THE VISUAL PATHWAY****Ailen Gala Hvozda Arana^{1,2}***1 Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Ciencias Químicas. Cátedra de Química General e Inorgánica. Buenos Aires, Argentina, 2 CONICET- Universidad de Buenos Aires. Instituto de Bioquímica y Medicina Molecular (IBIMOL), Buenos Aires, Argentina.**agala@docente.ffyb.uba.ar*

Particulate matter (PM) present in air pollution has been shown to produce adverse effects on the eyes, with oxidative stress playing a key role in its physiopathological mechanisms. In the eye, the lens antioxidant system helps maintain the redox balance of nearby ocular structures. The aim of this study was to evaluate the redox environment in mouse lenses after exposure to urban air. Male Balb/c mice, 8 weeks old, were exposed to urban air (UA, n=18) or filtered air (FA, n=18) in exposure chambers located in the city of Buenos Aires (average PM level: $15.2 \pm 5.3 \mu\text{g}/\text{m}^3$). The animals were exposed for up to 12 weeks (CICUAL- REDEC-2025-578-E-UBA-DCT_FFYB). The animals were sacrificed, and the eyes were enucleated. The lenses were separated and lysed. In the lysate, the activities of antioxidant enzymes, the levels of reduced and oxidized glutathione, as well as protein oxidation, were assessed. In addition, SDS-PAGE analysis, circular dichroism (CD) and 1-anilinonaphthalene-8-sulfonic acid (ANS) fluorescence study were performed. No major differences were observed between groups after 1 and 2 weeks, except for an increase in SOD activ-

ity after 1 week (107%, $p < 0.05$). Glutathione reductase (GR) activity increased in the UA group after 4 weeks (47%, $p < 0.05$). After 12 weeks, Glutathione Peroxidase activity increased (63%, $p < 0.05$), whereas GR activity decreased (40%, $p < 0.05$), along with the GSH/GSSG ratio (62%, $p < 0.05$) in UA compared to FA. Moreover, protein oxidation significantly increased (113%, $p < 0.05$). SDS-PAGE revealed no changes in protein molecular mass, and CD/ANS studies showed no alterations in protein conformation.

These results suggest that exposure to urban air pollution alters the redox environment of the lens, which could affect the antioxidant defenses of nearby ocular structures. However, at these times, the shift towards a pro-oxidant environment did not alter the proteins conformation. The correlation between protein oxidation and the GSH/GSSG ratio indicates that the lens GSH pool may help prevent protein oxidation. The increased protein oxidation could lead to lens opacification, which may be a relevant mechanism in the development of cataracts.

ROLE OF COPPER IN GYNECOLOGICAL DISEASES: STUDY OF CHELATION AS A THERAPEUTIC STRATEGY IN ENDOMETRIOSIS**María Belén Delsouc***Laboratorio de Biología de la Reproducción (LaBiR), Facultad de Química, Bioquímica y Farmacia (FQByF), Universidad Nacional de San Luis (UNSL). Instituto Multidisciplinario de Investigaciones Biológicas de San Luis (IMIBIO-SL), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). San Luis, Argentina.*

Metals play an ambivalent role in gynecological health. Some, such as iron and copper, are essential for normal cellular function but can be toxic if accumulated in excess. Others, such as cadmium, lead, mercury, arsenic, and nickel, are dangerous even at low concentrations. All of these metals have been associated with disorders of the female reproductive system. Particularly, copper dyshomeostasis has been connected to ovarian cancer, endometrial cancer, polycystic ovary syndrome, uterine fibroids, and endometriosis. Copper, as an essential micronutrient, is obtained primarily through the diet and absorbed in the intestine and needs to be strictly regulated. It is essential for cell signaling, oxygen transport, and enzymatic activity in eukaryotic life forms. However, it contributes to pathological processes by acting as an endocrine disruptor and promoting oxidative stress when its homeostasis is altered. In endometriosis, elevated

levels of this metal have been detected in serum and urine samples from patients and even in the peritoneal fluid of C57BL/6 mice with surgically induced disease. Endometriosis is an estrogen-dependent disorder affecting approximately 5–15% of women of reproductive age. It is characterized by the growth of endometriotic-like tissue outside the uterine cavity, causing symptoms such as chronic pelvic pain, dysmenorrhea, dyspareunia, dysuria, and fertility problems. Despite its high prevalence and important impact on quality of life, there is still no cure, and the need for new therapeutic approaches is a research priority. At LaBiR (FQByF, IMIBIO-SL CONICET, UNSL), we evaluated the effect of copper chelation on the progression of endometriosis. Ammonium tetrathiomolybdate (TM) is a highly specific, low-toxic copper chelator with demonstrated antitumor activity. This drug was tested in a C57BL/6 mouse model of endometriosis,

generated by autologous uterine tissue transplantation to the intestinal mesentery. Our results indicate that TM exerts antiproliferative, antiangiogenic, and anti-inflammatory effects, modulates oxidative stress, and reduces the

expression of neurotrophins and sensory neuropeptides. These findings underscore the need to consider copper dyshomeostasis in endometriosis and to continue investigating the therapeutic potential of this class of drugs.

EXPOSURE TO INSECTICIDES DURING PREGNANCY: CHANGES IN ENZYME EXPRESSION IN THE PLACENTA

Natalia Guíñazú

Centro de Investigaciones en Toxicología Ambiental y Agrobiotecnología del Comahue (CITAAC), Consejo Nacional de Investigaciones Científicas y Tecnológicas (CONICET), Universidad Nacional del Comahue, Neuquén, Argentina.

Exposure to environmental chemicals during pregnancy, including organophosphate pesticides (OP), can affect the health of both the mother and the fetus, and have repercussions later in life. The Developmental Origins of Health and Disease (DOHaD) theory emphasizes the significant influence of early-life environments on long-term health outcomes. This aligns with the World Health Organization's life course approach, highlighting early-life factors' role in future health. In the last decade, the placenta has become a new focus within DOHaD research. The placenta expresses enzymes relevant to pesticide detoxification and other cellular processes. Esterases are classified into A, B, and C esterases as they interact with OP. The paraoxonases (PON-1, 2, and 3) and the carboxylesterases (CES-1, 2 and 3) are A and B-esterases able to metabolize OP. CES are inhibited by OP in comparison to PON that aren't.

The present study aimed to determine whether PON and CES are modulated in the placenta of pregnant women residing in an intensive pesticide use scenario. Healthy pregnant women who lived in rural and urban surroundings were recruited between 2018 and 2022. Participants

were classified according to their residential settings in rural (RG) or urban (UG) groups. The placentas were collected and the levels of the OP chlorpyrifos (CP) were studied by GC-MS. The enzyme activity and the transcript expression of PON and CES were also determined in this organ. CP was more frequently detected in RG (74 %) and showed significantly higher levels (ng/g lw) in RG (mean= 101.1, range <LOD-1,558) compared to UG (mean= 25.12, range <LOD-705.72). CES and PON (arylesterase and lactonase) activities were significantly upregulated in RG vs UG. Higher CES1, CES2 and PON2 mRNA transcript levels were found in RG vs UG. CP concentration and CES1 and CES2 mRNA levels showed a positive and significant correlation.

The RG placentas showed elevated CP concentrations and alterations in esterases, which elucidate the impact of pesticides on CES and PON regulation. These findings highlight the need for further investigation into the effects of pesticide exposure during pregnancy and to deepen the knowledge about the function that esterases play in the placenta.

IMIDACLOPRID AS AN ENDOCRINE DISRUPTOR ACTIVATES ARYL HYDROCARBON RECEPTOR AND INDUCES MAMMARY TUMOR GROWTH AND PROGRESSION IN HER2-POSITIVE SYNGENEIC MOUSE MODEL

Sol Buján¹, Noelia Miret^{1,2}, Alejandro Nicola Candia¹, Carolina Pontillo^{1,3}, Florencia Chiappini^{1,3}, Maria Agustina Leguizamón^{1,3}, Matías Fernández¹, Sofía Martín Mena^{4,5}, Melisa Bressan⁵, Gabriel Scicolone^{4,5}, Marianela Candolfi¹, Andrea Randi^{1,3}

1. CONICET-Universidad de Buenos Aires, Instituto de Investigaciones Biomédicas (INBIOMED), Buenos Aires, Argentina; Laboratorio de Efectos Biológicos de Contaminantes Ambientales

2. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. Departamento de Fisicomatemática, Cátedra de Física, Junín 956, Buenos Aires, Argentina.; Laboratorio de Efectos Biológicos de Contaminantes Ambientales

3. Universidad de Buenos Aires, Facultad de Medicina, Departamento de Bioquímica Humana, Ciudad de Buenos Aires, Argentina.; Laboratorio de Efectos Biológicos de Contaminantes Ambientales

4. CONICET- Universidad de Buenos Aires, Instituto de Biología Celular y Neurociencias "Prof E. De Robertis" (IBCN), Buenos Aires, Argentina

5. Universidad de Buenos Aires, Facultad de Medicina, Departamento de Biología Celular, Histología, Embriología y Genética. Buenos Aires, Argentina.; Laboratorio de Neurobiología del Desarrollo

sol_bujan@hotmail.com

Although widely detected in human samples, information on the toxicology of neonicotinoid insecticides remains limited. Recently, we reported that imidacloprid (IMI) exposure in mice induces alterations in mammary gland architecture and preneoplastic lesions, suggesting endocrine disruption (ED). Our group demonstrated that IMI enhances cell proliferation, migration, and metallo-

protease activity in HER2(+) LM3 murine mammary cancer cells. In breast cancer, G protein-coupled estrogen receptor (GPER) content was associated with adverse clinical features. Some EDs activate the aryl hydrocarbon receptor (AhR), triggering tumor-promoting effects. Tryptophan 2,3-dioxygenase 2 (TDO2) degrades tryptophan producing kynurenine, which triggers immune tol-

erance. We aimed to investigate the IMI action on AhR activation (immunofluorescence, RT-qPCR) in LM3 cells, and to assess its impact on tumor growth, metastasis (histopathology), and GPER expression (Western blot) in a syngeneic LM3 mouse model. Results showed that IMI (0.1, 10 μ M) increased AhR expression and its nuclear translocation in LM3 cells. Furthermore, IMI promoted tumor growth (IMI 10 mg/kg b.w.) and a reduction in tumor cell doubling time in 30-day treated mice. Increased pulmonary micrometastases were observed at all doses

tested (0.01; 0.1; 10 μ M). Besides, IMI enhanced the CYP1A1 mRNA expression, suggesting an activation of the nuclear AhR pathway, while it reduced TDO2 mRNA levels in tumors. We also found enhanced levels of GPER and ERK1/2 activation. Our findings suggest that exposure to IMI at environmentally relevant doses activates the AhR and GPER pathways, promoting tumor growth and pulmonary metastasis in a murine HER2(+) mammary cancer model.

Symposium 4 - AAFE - Monday 17th November 2025 - 15:00 - 16:30 - Salón 2

FROM COMPUTER AND BENCH TO BEDSIDE: EMERGING PERSPECTIVES AND INNOVATIVE TOOLS IN PRECISION MEDICINE

Chair: Santiago Zugbi

MODEL-INFORMED PRECISION DOSING: COMPUTATIONAL TOOLS IN CLINICAL PHARMACOKINETICS

Lucas Brstilo

Unidad de Tratamientos Innovadores, Hospital Garrahan.

Model-informed precision dosing represents a shift from “fixed-dose medicine” to personalized medicine, optimizing therapeutic outcomes while minimizing risks for each patient. This approach integrates population

pharmacokinetic models, drug concentrations obtained through therapeutic drug monitoring, and patient-specific characteristics to provide individualized dosing recommendations.

BIG DATA AND PERSONALIZED MEDICINE: TURNING DATA INTO CLINICAL DECISIONS

Giovanna Aschettino

Unidad de Genómica, Hospital Garrahan

This presentation will focus on the experience of how integrating clinical and genomic data is supporting the optimization of clinical decision-making. Examples of large-scale data analysis and transformation for patient

diagnosis and treatment will be discussed, as well as the importance of multidisciplinary work to optimize diagnostic and therapeutic strategies.

APPLIED GENOMICS IN THE HOSPITAL SETTING: CHALLENGES IN PERSONALIZED MEDICINE

María Sol Touzon

Unidad de Genómica, Hospital Garrahan.

This talk will address the role of applied genomics in the clinical and healthcare setting, highlighting the challenges and opportunities of integrating genomics into personalized medicine. It will examine how genomic tech-

nologies are transforming the diagnosis, prognosis, and treatment of diverse diseases, enabling approaches tailored to the molecular characteristics of each patient.

Symposium 5 - SAIC - Tuesday 18th November 2025 - 15:00 - 16:30 - Auditorio

INNOVATION IN REPRODUCTION AND FERTILITY

Chairs: Susana Theas, Verónica Bosquiazzo

HDL CHOLESTEROL METABOLISM AND OOCYTE BIOLOGY: IMPACT ON FEMALE FERTILITY

Dolores Busso^{1,2}

1 Laboratory of Nutrition, Metabolism and Reproduction, Research and Innovation Center, Universidad de Los Andes, Santiago, Chile. 2 Center of Interventional Medicine for

Precision and Advanced Cellular Therapy (IMPACT), Santiago, Chile.

Excess cholesterol in animal cells induces efflux to high-density lipoproteins (HDL) and hepatic excretion by reverse cholesterol transport. In different species, including humans, HDL is the only lipoprotein found in substantial amounts in ovarian follicular fluid (FF). FF HDL size and composition correlate with embryo quality, suggesting that HDL metabolism can influence oocyte biology. Knock-out mice for the main HDL receptor Scavenger Receptor Class B Type 1 (SR-B1 KO) exhibit cholesterol-rich, dysfunctional HDL and female infertility. We showed that oocytes from these mice accumulate unesterified cholesterol (UC) during follicular development, and that ovulated eggs show high rates of parthenogenetic meiotic resumption and mortality. Loading wild-type (WT) mouse eggs with UC using methyl- β -cyclodextrin-cholesterol (M β CD-chol) results in their spontaneous activation and increased lability, demonstrating that UC excess in KO eggs is the leading cause of their dysfunction. Indeed, administration of the lipid-lowering drug probucol to SR-B1 KO females reestablishes their fertility along with a reduction in UC in oocytes and ovulated eggs.

We hypothesized that disruptions in UC levels in eggs may induce the spontaneous opening of PM channels, which normally mediate Ca²⁺ influx after oocyte fertilization, i.e., CaV3.2 and TRPV3, thereby explaining the spontaneous activation phenotype of KO eggs. Using the specific sensor FURA, we evaluated Ca²⁺ dynamics in M β CD-chol-loaded eggs and observed that, while most WT eggs underwent one or more [Ca²⁺]_i rises and activated, most eggs from dKO CaV3.2/TRPV3 mice were resistant to M β CD-chol-induced activation. In sum, the dysfunction and lability in eggs with excess cholesterol may be partly explained by the spontaneous opening of PM calcium channels, as well as by their mitochondrial dysfunction and lipid storage defects. Based on the current evidence, we propose that a well-regulated and largely unexplored system of cholesterol traffic between FF HDL and oocytes may be required for their homeostasis and could have significant implications for human female fertility. These results are particularly important considering that lipids, including cholesterol, are usually not evaluated in infertile patients.

SPERM AS A CONTRACEPTIVE TARGET: EXPANDING THE FUTURE OF NON-HORMONAL BIRTH CONTROL

Guillermina M. Luque

Instituto de Biología y Medicina Experimental (IBYME-CONICET), Ciudad Autónoma de Buenos Aires, Argentina.

The sperm-specific calcium channel CatSper is a compelling target for developing non-hormonal contraceptives due to its critical role in sperm motility and exclusive expression in sperm cells. Pharmacological inhibition of CatSper offers a unique opportunity to block fertilization without affecting other physiological systems. However, the goal of using CatSper as a contraceptive has not been achieved so far. One reason is that the complex structural organization of CatSper has impeded heterologous reconstitution of the channel to study its regulation in vitro. To address this, we conducted a high-throughput screening to detect new drugs capable of blocking CatSper using Fluorescent Cell Barcoding with a membrane potential assay to assess CatSper function by flow cytometry, a method developed and validated by our laboratory. We screened 6924 compounds and identified, among others, a lead compound ("compound 8"), not previously reported, as a promising CatSper inhibitor. This compound showed inhibitory effects in mice, humans and rabbits at low micromolar concentration without affecting sperm viability. While the IC₅₀ in mouse sperm is 5.1 μ M, human sperm is significantly more sensitive, with IC₅₀ values of 0.12 μ M. Addition-

ally, compound 8 showed direct inhibition of CatSper in mouse sperm, validated by patch-clamp. Using a computer-assisted sperm analysis (CASA) system, we observed significant changes in key kinetic motility parameters, similar to the phenotype observed in CatSper1-null sperm in mice, humans and rabbits. Notably, the effect on sperm motility persisted even after inhibitor removal in all experimental models, suggesting the impact is not immediately reversible. Compound 8 did not induce DNA fragmentation, compromise plasma membrane integrity, or alter mitochondrial activity in human sperm, confirming the impairment in motility is due to CatSper inhibition. The inhibitor also produced a marked reduction in fertilization rates during in vitro fertilization in mouse sperm and complete inhibition in female rabbits after artificial insemination with rabbit sperm exposed ex vivo. Interestingly, the inhibitory effect was observed in both human and rabbit semen, suggesting potential use as male or female contraceptive. These findings indicate the identified compound holds significant potential for developing non-hormonal contraceptives, highlighting CatSper inhibition's strong translational and therapeutic potential.

WHEN THE EMBRYO TALKS: HOW QUALITY SHAPES ENDOMETRIAL IMMUNITY

Rosanna Ramhorst

CONICET, Universidad de Buenos Aires. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales IQUIBICEN, Buenos Aires, Argentina.

Embryo implantation relies on precise immunological homeostasis that activates regulatory circuits between two key partners: the embryo and the receptive endometrium. The embryo produces soluble ligands and expresses receptors for diverse autocrine and paracrine factors, while the endometrium releases mediators that regulate embryo proliferation, differentiation, adhesion, and invasiveness. In this sense, decidualization of endometrial stromal cells is a multistep process generating mature decidual cells and senescent decidual cells. Mature decidual cells secrete pro implantation factors and migrate to encapsulate the embryo, whereas senescent cells produce proinflammatory mediators (SASP factors) that also contribute to implantation. However, dysregulation of these processes or their microRNA-mediated control can perpetuate inflammation, compromising endometrial receptivity and health.

To explore whether embryo quality influences the immunomodulatory endometrial milieu, we analyzed the effect of soluble factors secreted by human embryos of varying developmental competence obtained from assisted reproductive technology treatments. Our findings indicate that decidualized cells act as biosensors of embryo

quality, selectively promoting implantation of competent embryos. Developmentally impaired human blastocysts are not inert; rather, they actively trigger exacerbated inflammatory responses resembling menstruation.

Specifically, decidualized cells exposed to factors from developmentally impaired embryos increased production of active IL-1 β and chemokines, enhancing neutrophil recruitment and activation compared with responses to normally developing embryos. Moreover, factors from impaired embryos skewed dendritic cells toward an inflammatory phenotype and limited regulatory T-cell recruitment, reinforcing a proinflammatory microenvironment unfavorable for implantation. In contrast, signals from competent embryos sustained a tolerogenic immune profile that supports successful implantation.

Collectively, these findings suggest that soluble embryonic signals are sensed and amplified by decidual cells, which then transmit distinct immunological cues to immune cells. This dynamic interaction determines whether the endometrial immune environment becomes receptive or inflammatory, thus favoring implantation of viable embryos while promoting the elimination of developmentally compromised ones.

GLUCOSE AND PYRUVATE DIFFERENTIALLY MODULATE METABOLIC AND REDOX DYNAMICS DURING CAPACITATION TO ENABLE FERTILIZATION COMPETENCE IN MOUSE SPERM

Jael Dafne Herzfeld¹, Lucas Nicolás González¹, Candela Senosiain¹, María Eugenia Matzkin², Patricia Sara Cuasnicú³, Débora Juana Cohen¹, Vanina Gabriela Da Ros¹

1. IBYME; Laboratorio de Biología de las Gametas

2. IBYME; Laboratorio de Fisiología Testicular

3. IBYME; Laboratorio de Mecanismos Moleculares de la Fertilización

jaael.h@gmail.com

Male infertility remains a prevalent condition, with many cases unexplained due to our limited understanding of sperm physiology. Capacitation—the process by which ejaculated sperm acquire fertilizing ability within the female reproductive tract—requires the coordinated activation of signaling and metabolic pathways. Although glucose, pyruvate, and lactate are present in the female tract and commonly included in *in vitro* capacitation media, how each substrate contributes to sperm mitochondrial activity and fertilization ability has not been fully elucidated. In a previous study, using a mouse model, we showed that sperm capacitated in a glucose-only medium were able to undergo normal acrosome reaction and develop hyperactivation but displayed a delay in acquiring fertilizing ability. To gain deeper insights into this phenomenon, we evaluated the capacitation status

of sperm under glucose-only conditions. We found that glucose alone increased oxidative stress, evidenced by elevated reactive oxygen species (ROS), lipid peroxidation, and DNA fragmentation. Furthermore, when sperm were incubated with glucose and pyruvate, no increases in ROS or DNA fragmentation were detected. Remarkably, antioxidant supplementation in a glucose-only medium preserved redox balance and restored fertilization performance to control levels. Altogether, these findings demonstrate that glucose is not a metabolically neutral substrate; when present alone, it induces oxidative stress that compromises sperm function. These insights provide a new perspective on unexplained infertility and suggest strategies to improve assisted reproduction outcomes.

Symposium 6 - AAFE - Tuesday 18th November 2025 - 15:00 - 16:30 Salón 2

RESEARCH IN OPHTHALMOLOGY FROM BASIC SCIENCE TO APPLIED RESEARCH IN THE PATIENT

Chair: Daniela Quinteros

RESEARCH IN OPHTHALMOLOGY: IDENTIFYING PROBLEMS TO STUDY THEM AND TRANSLATING RESULTS INTO BETTER PATIENT CARE

José D. Luna Pinto

Centro privado Romagosa SA y Fundacion VER.

We propose evidence-based narrative medicine as a necessary step in the translational research roadmap. Precision medicine is paving the way for personalised risk assessment, and its application in clinics specialising in retinal diseases has the potential to transform current treatment paradigms. This roadmap identifies two complex obstacles to advancing research from basic clinical practice to direct application. Overcoming them requires the development of transformative and complex relationships between the various actors involved. We suggest that by identifying problems in everyday practice and studying them using the scientific method,

it is possible to learn and develop transformative—or translational—strategies to address them. This allows professionals themselves to adopt and recommend evidence-based strategies and interventions aligned with high-level guidelines. Our model encompasses all aspects of care that converge in the professional-patient relationship and determine the therapies and decisions that patients make regarding their treatment. We offer an innovative approach to studying, teaching and improving therapeutic intimacy and the integrative effectiveness of the doctor-patient relationship, within the rapid advances of medicine in the field of the retina.

CHITOSAN-TPP NANOGELS: AN OCULAR DELIVERY SYSTEM FOR FOLIC ACID

Agustina Alaimo

Laboratorio Interdisciplinario de Dinámica Celular y Nano-herramientas. Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Instituto IQUBICEN-CONICET.

Folic acid (FA) is an essential nutrient with therapeutic potential for ocular disorders, but its use is limited by poor ocular bioavailability. This study aimed to develop chitosan (CS)-based nanogels (NGs) as a drug delivery system to improve FA transport and release in the eye, focusing on corneal permeation. The NGs were characterized using various techniques. Dynamic light scattering (DLS) showed a hydrodynamic diameter of 312.4 ± 8.2 nm and a low polydispersity index (Pdl) of 0.28, indicating a uniform particle size. Scanning electron microscopy (SEM) confirmed their spherical morphology. In vitro drug release studies demonstrated a sustained release of FA, best described by the Higuchi model, which suggests a diffusion-controlled mechanism. Mucoadhesion studies, based on zeta potential (ζ) measurements,

revealed a significant decrease from +36.9 to +18.1 mV. This confirmed the strong electrostatic interaction between the positively charged NGs and the negatively charged ocular mucin layer, enhancing their adhesion to eye tissues. Ex vivo corneal permeation studies on rabbit corneas showed that encapsulated FA permeated 2.6 times more slowly than free FA. This indicates a sustained release profile, which could improve therapeutic efficacy and reduce the frequency of administration. In conclusion, these results demonstrate that CS NGs are a promising ocular delivery system for FA. Their controlled release and enhanced bioadhesion could significantly improve folic acid's ocular bioavailability, offering a new strategy for treating eye diseases that require sustained drug release.

LIPID NANOPARTICLES FOR OCULAR ADMINISTRATION: THERAPEUTIC ALTERNATIVES FOR GLAUCOMA AND UVEITIS

María Lina Formica

Departamento de Ciencias Farmacéuticas-Facultad de Ciencias Químicas. Universidad Nacional de Córdoba. Unidad de Investigación y desarrollo en Tecnología Farmacéutica- UNITEFACONICET.

According to the WHO, 750 million people suffer from ocular disorders, but the eye's barriers make drug administration difficult. This necessitates high, frequent doses or invasive techniques, which cause side effects and poor adherence. To solve this, we developed a new type of lipid nanoparticle (LNEi) as a drug delivery platform for ophthalmic medications, prioritizing its potential for industry transfer. We validated our platform for treating glaucoma and uveitis. For glaucoma, we formulated LNEi with acetazolamide (AZM), a drug with low ocular bioavailability. Compared to conventional lipids (LNEc), our AZM-loaded LNEi showed a more potent and prolon-

ged hypotensive effect, significantly reducing intraocular pressure (IOP) in rabbits without causing corneal toxicity. For uveitis, we loaded a corticosteroid into LNEi. These nanoparticles also showed high encapsulation efficiency and did not cause ocular damage. Administered subconjunctivally, they alleviated inflammation in the anterior chamber in an induced uveitis model, achieving therapeutic results with lower doses than those used in clinical practice. These advances demonstrate the potential of our lipid nanoparticles to improve the efficacy of ocular treatments, offering a new perspective for the therapy of these pathologies

PRECLINICAL MODELLING OF RETINAL DEGENERATION: MELATONIN DELIVERY SYSTEMS

Daniela Quinteros

*Departamento de Ciencias Farmacéuticas-Facultad de Ciencias Químicas. Universidad Nacional de Córdoba.
Unidad de Investigación y desarrollo en Tecnología Farmacéutica- UNITEFA-CONICET.*

Melatonin (Mel) is a promising neuroprotective agent with antioxidant and anti-apoptotic properties. While it has shown positive results in treating retinal diseases when administered orally, its effectiveness is limited by poor ocular penetration. To overcome this, we developed protein-based nanoparticles using human serum albumin (HSA) and ethyl cellulose (NCEC) to deliver Mel. These nanoparticles are biocompatible and capable of sustained drug release. In vitro and ex vivo studies confirmed that both NCECMel and Np-ASH-Mel systems improved ocular permeation and provided a prolonged release profile, suggesting they can enhance Mel's ocular bioavailability compared to oral administration. To further assess their therapeutic potential, we developed a retinal degeneration (RD) model in New Zealand rabbits by injecting a combination of glutamate (GLUT) and buthionine sul-

foximine (BSO) to induce oxidative stress and cytotoxicity in retinal ganglion cells. This model effectively mimics the progressive degeneration seen in ocular neurodegenerative diseases. We then investigated the neuroprotective effects of Mel solution, NCECMel (topical), and NpASH-Mel (subconjunctival). The results showed that both nanoparticle systems effectively protected retinal ganglion cells, significantly improving cell viability and reducing apoptosis compared to a control Mel solution. These findings demonstrate that Np-ASH-Mel and NCECMel are safe and effective strategies for treating neurodegenerative ocular diseases. The successful application of these nanoparticle-based delivery systems opens new avenues for developing innovative therapies to improve the quality of life for patients with these challenging condition

Symposium 7 - AAFE - Tuesday 18th November 2025 - 17:00 - 18:30 - Salón 2

PHARMACOLOGICAL NANOTECHNOLOGY: A NEW PARADIGM IN DRUG DELIVERY

Chair: María Laura Barreiro

NANOTECHNOLOGY: FROM SUSTAINABLE SYNTHESIS TO BIOMEDICAL APPLICATIONS

Martín Federico Desimone

Instituto Química y Metabolismo del Fármaco (IQUIMEFA); Facultad de Farmacia y Bioquímica (FFyB-UBA)

Nanotechnology offers a transformative approach to addressing challenges in modern medicine, from targeted drug delivery to tissue regeneration. This work explores a holistic approach to nanomedicine, beginning with the sustainable production of nanomaterials and culminating in their diverse biomedical applications. I first highlight the importance of "green synthesis," a process that leverages plant extracts as eco-friendly reducing and capping agents to produce nanoparticles, circumventing the need for toxic chemicals. The efficiency and environmental benefits of this method are shown to be a superior foundation for creating therapeutic agents. Building

upon this foundation, we demonstrate the versatility of these materials in several key areas. We present the use of nanostructured lipid systems illustrating how precise delivery can enhance efficacy and minimize side effects. The controlled release capabilities of biomaterials are also explored through the fabrication of sustained-release films for transdermal delivery and silica-collagen scaffolds for growth hormone applications. Furthermore, I will discuss the immunomodulatory potential of nanomaterials, examining how the adsorption of proteins on silica nanoparticles can influence biological responses.

NANOMEDICINES IN 2025: ACHIEVEMENTS AND REMAINING CHALLENGES

Eder Lilia Romero

Centro de Investigación y Desarrollo de Nanomedicinas (CIDeN), Universidad Nacional de Quilmes

Where do we stand, thirty years after the introduction of the first nanomedicine to the pharmaceutical market? There was no unprecedented therapeutic revolution. Nanomedicines did not deliver the "miracle cures" that had once been anticipated. However, according to Gartner's hype cycle, we are now on the slope of enlightenment: at this stage, we can predict with increasing accuracy how nanoparticulate materials interact with diverse biological microenvironments. We can better correlate their structural characteristics with their functions, and we have

gained deeper insight into their potential toxicities and how to mitigate them. Yet, key questions remain: Have we achieved therapies more successful than those introduced in the 1990s? And why does the preclinical phase remain such a bottleneck, with so few formulations managing to advance beyond it? The main reasons can be summarized as follows: i) Preclinical models, whether based on 2D cultures or animal studies, fail to adequately recapitulate the true spatial microenvironment of human pathologies. As a result, much of preclinical nanomedici-

ne remains far from predictive. ii) The large-scale manufacture of nanomedicines under GMP conditions is highly complex. Scaling up production introduces unprecedented challenges, such as the need to monitor nanoparticle size in liquid media in real time. iii) Rigorous characterization is essential, as the nanoscale architecture of these systems determines their therapeutic efficacy, toxicity,

and stability. iv) Finally, there are no globally harmonized regulatory frameworks—not even regarding basic aspects such as nomenclature or the upper limit of the nanoscale. In this context, I will review the current landscape of clinical nanomedicine, highlighting both the most promising strategies and emerging fields of application

INNOVATIONS IN ONCOLOGICAL NANOMEDICINE BASED ON FUNCTIONAL NANOPARTICLES

Romina Glisoni

Instituto de Nanobiotecnología (NANOBIOTEC UBA-CONICET). Departamento de Microbiología, Inmunología, Biotecnología y Genética. UBA

This work summarizes recent advances from our group on the design and development of functional nanoparticle platforms for cancer therapy and diagnosis. We focus on innovative nanomedicine strategies that enhance therapeutic efficacy, improve diagnostic imaging, and increase safety in oncological applications. Our research includes the green synthesis of polymer-stabilized gold nanoparticles loaded with radiosensitizing agents to improve treatment outcomes in melanoma, employing environmentally friendly methods that align with sustainable chemistry principles. Additionally, we have developed glycosylated polymeric micelles as imaging agents for sentinel lymph node mapping in breast cancer, facilitating more accurate and less invasive diagnostics. Furthermore, polymeric micelles encapsulating antitumoral compounds have demonstrated potent efficacy in aggressive breast cancer

models, highlighting the potential for targeted drug delivery to overcome resistance and reduce side effects. These studies showcase the versatility of nanoparticle engineering to overcome biological barriers, achieve targeted delivery, and integrate therapeutic and diagnostic functionalities (theranostics). Our multidisciplinary approach combines physicochemical characterization, in vitro biological evaluation, and translational considerations, aiming to accelerate clinical application. Overall, our work contributes to advancing multifunctional nanoplateforms that address key challenges in precision oncology, including enhanced targeting, controlled drug release, and combined therapeutic-imaging capabilities. Future perspectives will focus on scaling up production, regulatory pathways, and fostering collaborations to facilitate the translation of these technologies into clinical practice.

MULTIFUNCTIONAL NANOPLATFORMS FOR TARGETED DELIVERY OF ANTITUMOR AGENTS

Mónica Cristina García

Unidad de Investigación y Desarrollo en Tecnología Farmacéutica (UNITEFA)

This presentation will focus on the development and application of multifunctional nanotechnology platforms for advanced cancer therapies. Hybrid nanoplateforms for the targeted delivery of antitumor agents are a promising strategy for improving therapeutic efficacy and reducing side effects in cancer treatment. The design of various hybrid nanoplateforms based on magnetic nanoparticles and lipid nanosystems functionalized with inorganic na-

noparticles will be discussed, highlighting their ability to respond to specific endogenous signals and exogenous stimuli, as well as their potential for controlled drug delivery and biological performance. Through these advanced systems, it is possible to overcome current challenges in the administration of oncological drugs, moving towards more personalized, safe, and effective therapeutic options.

Symposium 8 - SAIC - Oncology - Wednesday 19th November 2025 - 13:00 - 14:30 – Auditorio
BIOLOGICAL CLOCKS AND METABOLIC PATHWAYS IN CANCER PROGRESSION
Chairs: Ana Fernanda Castillo, Mariano Gabri

TIME MATTERS: THE BIOLOGICAL CLOCK IN BRAIN TUMOR GROWTH AND TREATMENT

Mario E. Guido

*CIQUIBIC – CONICET. Departamento de Química Biológica Ranwel Caputto. Facultad de Ciencias Químicas.
 Universidad Nacional de Córdoba. Córdoba. Argentina
 mario.guido@unc.edu.ar*

Biological clocks are intrinsic timekeeping systems that regulate physiology and metabolism in nearly all cells, including cancer cells. Disruption of circadian rhythms,

often caused by shift work or artificial lighting, is associated with metabolic disorders and increased cancer risk. Glioblastoma (GBM), a grade 4 glioma, is one of

the most aggressive brain tumors, characterized by rapid growth, therapy resistance, and a median survival of 14 months. Despite advances in surgery, radio-, and chemotherapy, current treatments remain largely ineffective, underscoring the need for novel approaches.

Our studies revealed that GBM cells in culture preserve a functional circadian oscillator that drives rhythms in clock gene expression, lipid metabolism, and reactive oxygen species. We demonstrated temporal variation in chemotherapy efficacy: tumor-bearing mice treated with the proteasome inhibitor Bortezomib at night exhibited greater benefit than those treated during the day. Moreover, tumor inoculation at different times influenced growth rates, suggesting that both the tumor clock and host circadian state regulate progression.

Pharmacological modulation of circadian machinery also affected GBM biology. Inhibition of glycogen synthase kinase-3 (GSK-3) with CHIR99022 altered viability, migration, cell cycle, and redox status, while increasing the content of lipid droplets and its daily oscillation. Com-

bined treatment of CHIR99022 with temozolomide (TMZ) enhanced cytotoxicity compared to TMZ alone. In contrast, the disruption of the molecular clock gene *Per2* impacted both migration and proliferation, highlighting the role of circadian regulators in tumor growth.

Preliminary findings further show that GBM cells express non-visual photopigments sensitive to the blue spectrum such as Opn3 (encephalopsin) and Opn4 (melanopsin). Remarkably, one hour of blue light exposure inhibited cell proliferation, suggesting a novel light-dependent mechanism with therapeutic potential.

Finally, circadian rhythms were found to shape immune cell dynamics in mice, with elevated levels of NKT cells, neutrophils, and PD1⁺ T cells during the early day as compared to the night. Taken together, these findings highlight the relevance of photobiology and chronotherapy, suggesting that synchronizing therapeutic interventions with biological time—and potentially leveraging blue light stimulation—could enhance treatment efficacy while minimizing adverse effects in GBM management.

A LIPID METABOLISM ENZYME AND ITS IMPACT ON CANCER: THE ROLE OF ACYL-COA SYNTHETASE 4 AS A METABOLIC REGULATOR AND THERAPEUTIC TARGET

Paula Mariana Maloberti

Universidad de Buenos Aires, Facultad de Medicina, Departamento de Bioquímica Humana, Buenos Aires, Argentina. CONICET - Universidad de Buenos Aires, Instituto de Investigaciones Biomédicas (INBIOMED), Buenos Aires, Argentina.

Reprogramming lipid metabolism promotes tumor progression, highlighting arachidonic acid (AA) and its metabolites, the eicosanoids, whose intracellular regulation is crucial. Acyl-CoA Synthetase 4 (ACSL4), which preferentially activates polyunsaturated fatty acids such as AA has emerged as a key regulator in both physiological and pathological contexts. Its expression has been reported in triple-negative breast cancer (TNBC), castration-resistant prostate cancer (CRPC), and liver and colon tumors. We identified ACSL4 as a therapeutic target in TNBC, showing that it promotes cell proliferation, migration, invasion, and tumor growth through the modulation of oncogenic pathways, including mTOR, and mechanisms associated with therapy resistance, as revealed by transcriptomic and proteomic analyses. ACSL4 regulates mitochondrial function and contributes to metabolic reprogramming in breast cancer cells by modulating genes associated with bioenergetics. It increases parameters such as maximal respiration and spare respiratory capacity, while also enhancing glycolysis. Our laboratory developed PRGL493, a specific ACSL4 inhibitor. In TNBC and CRPC models, PRGL493 reduced proliferation and invasion and restored sensitivity to hormonal and chemotherapeutic agents, leading to significant tumor growth in-

hibition in vivo. Furthermore, international studies tested the inhibitor in diverse disease models including cancer, demonstrating its therapeutic potential. Extending these studies to epithelial ovarian cancer, PRGL493 markedly decreased proliferation, migration, and spheroid formation. PRGL493 inhibits ABCG2-mediated efflux in SKOV-3 and OV-90 cells, reducing multidrug resistance and sensitizing ovarian cancer cells to standard drugs such as carboplatin, paclitaxel, and doxorubicin. We further investigated the transcriptional regulation of ACSL4 and its functional relationship with the androgen receptor (AR) in TNBC. AR represses ACSL4 expression, while ACSL4 inhibition reactivates AR signaling in quadruple-negative breast cancer cells. Combining PRGL493 with the AR antagonist bicalutamide produced a synergistic effect, further suppressing proliferation, migration, and invasion, and reducing extravasation in the Tg(fli1:EGFP) zebrafish model, a valuable tool to visualize tumor cell dissemination through blood vessels. Overall, our results establish ACSL4 as a key therapeutic target that integrates oncogenic signaling and metabolic pathways. Its inhibition limits tumor progression and overcomes drug resistance, providing strong proof of concept for clinical translation and opening new avenues for cancer therapy.

UNDERSTANDING THE IMPACT OF CIRCADIAN RHYTHMS ON RESISTANCE MECHANISMS TO TARGETED AND IMMUNE CHECKPOINT INHIBITORS IN ADVANCED NON-SMALL CELL LUNG CANCER

Diego Enrico
AAOC

Targeted therapies and immune checkpoint inhibitors (ICIs) have transformed the management of advanced non-small cell lung cancer (aNSCLC), contributing to a substantial improvement in overall survival over the past two decades. Despite these advances, both intrinsic and acquired treatment resistance remain major barriers to achieving durable clinical benefit. Primary resistance often reflects limited oncogene dependency or the presence of concurrent biological drivers, whereas secondary resistance typically emerges through adaptive mechanisms triggered by selective therapeutic pressure. Resistance to targeted therapies is increasingly well understood, involving on-target mutations, bypass signaling activation, and phenotypic plasticity, enabling the development of more precise therapeutic strategies.

In contrast, resistance to immunotherapy is frequently primary and mechanistically complex, arising from dynamic interactions among tumor cells, the immune system, and the tumor microenvironment. Secondary resistance may also develop following initial responses, particularly when only partial tumor regression is achieved. Although several resistance pathways have been proposed, their clinical relevance is only beginning to be elucidated.

Emerging data highlight a significant role of circadian rhythms in shaping cancer progression and therapeutic

response. Core circadian clock components regulate key oncogenic and tumor-suppressor pathways and influence multiple cancer-related processes, including apoptosis, cell cycle control, DNA repair, immune surveillance, inflammation, angiogenesis, and MAPK signaling. Preclinical studies demonstrate that circadian oscillations modulate immune cell trafficking and function, suggesting their potential to influence ICI activity.

In this context, retrospective clinical studies across multiple tumor types reveal that administering ICIs earlier in the day is associated with improved survival compared with late-day dosing. A recent randomized phase III trial in aNSCLC confirmed that early ICI administration significantly enhances both progression-free and overall survival, independent of PD-L1 expression, and is accompanied by distinct CD8+ T-cell activation patterns.

As the interplay between circadian biology, oncogenic signaling, and immune dynamics becomes increasingly evident, targeting the circadian machinery represents a promising therapeutic frontier. A deeper understanding of how circadian rhythms influence resistance mechanisms to targeted therapies and immunotherapy may guide optimized treatment sequencing and inform future drug development.

DRUGGING KETONE BODIES METABOLISM IN ADVANCED PROSTATE CANCER.

Pablo Sanchis^{1,2,3,4}, Agustina Sabater^{1,3,4,5}, Jiabin Dong⁴, Peter DA Shepherd⁴, Elba Vazquez^{1,5}, Christopher Logothetis⁴, Geraldine Gueron^{1,5}, Estefania Labanca⁴

1. Laboratorio de Inflamación y Cáncer, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina.

2. CONICET-Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires C1428EGA, Argentina.

3. Universidad Argentina de la Empresa (UADE), Instituto de Tecnología (INTEC), Buenos Aires, Argentina.

4. Department of Genitourinary Medical Oncology and The David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center, Houston, USA.

5. CONICET-Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina;
pablosanchis@gmail.com

The complexity of metabolic pathways driving prostate cancer (PCa) progression remains poorly understood. We previously identified a metabolic shift from elevated glycolysis to enhanced ketone body (KB) metabolism in castration-resistant PCa (CRPC), accompanied by increased expression of key ketolytic/ketogenic enzymes—ACAT1, OXCT1, and BDH1. Among these, ACAT1 stood out as a promising druggable target, with its upregulation correlating with reduced patient survival. Here, we evaluate the potential of ACAT1 inhibition with arecholine hydrobromide (AH) as a therapeutic strategy for advanced PCa. AH induced cytotoxicity in PC3 and C42B cells (100 μ M, 96h), with greater sensitivity observed in 22Rv1 cells (50 μ M), and also reduced ACAT1 and phospho-ACAT1 levels (Western blot, immunofluorescence; $P < 0.05$). KB metabolism is tightly linked to

lipid dynamics. Accordingly, the cytotoxic effect of AH was accompanied by an increase in lipid accumulation (Bodipy 493/503), lipid uptake (Bodipy 500/510) and ATP content ($P < 0.05$). We also assessed the effect of AH in MDA-PCa-PDX-183 and 203 derived organoids. AH reduced cell viability, notably in MDA-PCa-PDX-203, the longitudinal CRPC sample from the same donor as MDA-PCa-183-PDX. In vivo, AH (50 mg/kg/day i.p.) significantly decreased tumor volume in sham-castrated MDA-PCa-PDX-183-bearing mice, but not in castrated ones, consistent with the observed castration-induced ACAT1 downregulation. Furthermore, AH reduced tumor volume and intratumoral KB levels in MDA-PCa-203-PDX. These findings underscore the pivotal role of KB metabolism in PCa progression and position ACAT1 as a compelling therapeutic target, particularly in the CRPC setting.

Symposium 9 - AAFE - Wednesday 19th November 2025 - 15:00 - 16:30 - Salón 2
INTEGRATING DIET, MICROBIOTA, AND METABOLOMICS IN TRANSLATIONAL RESEARCH
Chair: Claudia Guerrero

INTEGRATING DIET, MICROBIOTA, AND METABOLOMICS TO STUDY INTESTINAL INFLAMMATION.”
CURRENT RESEARCH STATUS

Pablo Romagnoli

Centro de Investigación de Medicina Traslacional “Severo Amuchastegui” (CIMETSA). Unidad Asociada a CONICET (Res 2247/23). Instituto Universitario de Ciencias Biomédicas de Córdoba (IUCBC)

Current clinical studies integrate omics techniques, clinical history, and dietary data through Big Data analysis and machine learning. This approach has allowed the discovery of metabolic and microbial subtypes, the development of personalized predictive models, and the creation of platforms that combine dietary, microbiota, and metabolomics data associated with different pathologies. These advances are emerging clinical applications such as nutritional precision medicine, personalized prevention for chronic diseases, and the design of new therapies based on dietary interventions, synbiotics, and microbiota transplantation. The intestinal mucosa is an incredibly complex internal surface that is continuously exposed to a multitude of microorganisms that constitute

the microbiota. This microbiota influences multiple systems in our body. In particular, the development of the immune system is influenced by the interactions between the intestinal mucosa, the microbiota, and the metabolites generated in response to dietary nutrients. To design potential interventions to treat inflammatory bowel diseases (IBD), which are increasingly affecting our population, it is necessary to investigate how the composition of the microbiome, as well as the metabolites generated in response to diet, influence intestinal mucosal homeostasis. We believe that the results of studying the interactions occurring in the intestinal mucosa will provide fundamental information for developing new therapies needed for IBD.

METABOLIC-NUTRITIONAL STATUS AND MICROBIOTA COMPOSITION DIFFERENTIATE PREGNANT WOMEN SUFFERING FROM MALNUTRITION FROM THOSE WITH A HEALTHY DIET

Marcela Paz Sosa

Cátedra de Farmacología Clínica. IUCBC. UNVM

Malnutrition has a strong negative impact on health and, therefore, on a country's economic well-being. In low-income areas of Córdoba, malnutrition in children can reach 47%, not only due to nutritional deficiencies but also due to overweight or obesity. Furthermore, almost 80% of pregnant women in these communities are overweight. Since a pregnant woman's nutrition determines the composition of her microbiota and the metabolites it produces, impacting the harmonious physiological development of her unborn child, implementing nutritional intervention during pregnancy could prevent developmental problems and reduce the future incidence of obesity in newborns and, consequently, in our population. Our hypothesis is that “metabolic-nutritional status and

microbiota composition differentiate pregnant women suffering from malnutrition from pregnant women with a healthy diet”. To investigate this hypothesis, we propose 1) determining the nutritional status, 2) defining the metabolic status, and 3) defining the microbiota composition during the first trimester of pregnancy. Our project aims to understand the nutritional status and precise composition of the microbiota during the first trimester of pregnant women in our population in order to design future nutritional strategies based on native foods that restore the microbiota of malnourished pregnant women, thereby restoring a healthy metabolic-nutritional status and the normal development of their future newborn.

LUMINAL IGG IDENTIFIES BACTERIA INVOLVED IN THE PATHOGENESIS OF IBD

Martín Amé

Cátedra de Farmacología clínica. UNVM

The intestinal mucosa is continuously exposed to microorganisms grouped together as the microbiota. The microbiota influences the development of the entire immune system through interactions with the intestinal mucosa. The intestinal mucosal immune system responds to the microbiota of the gastrointestinal tract through cellular and humoral responses. The humoral immune response

to the microbiota has historically been associated with immunoglobulin (Ig) A. However, there is increasing evidence of the role of IgG in protecting the intestinal mucosa from bacterial invasion. Inflammatory bowel disease (IBD) is a group of pathological entities that includes Crohn's disease and ulcerative colitis. Its pathophysiology still remains unclear. We designed a cross-sectional

clinical study to investigate the hypothesis that luminal IgG identifies specific microbiota involved in intestinal inflammatory processes. To do so, we recruited 15 participants with ulcerative colitis, 15 with Crohn's disease, and 15 in the control group. Using 16S sequencing, we identified specific species and metabolic pathways that characterized each group. We obtained feces samples from all participants and developed a flow cytometry method to quantify and determine the viability of the fixed

microbiota. We found that patients with Crohn's disease had lower amounts of bacteria per mg of fecal matter when compared to the control group, $p < 0.05$. We believe that determining the identity of IgG-coated bacterial species in inflammatory processes in patients with IBD in Argentina will be useful for identifying biomarkers that characterize the pathogenesis of IBD in our community. The results of this project will allow us to design new treatment strategies for IBD.

Symposium 10 - SAIC - Wednesday 19th November 2025 - 17:00 - 18:30 - Salón 1
BREAKING BALANCE: HORMESIS, AGE AND LEGACY IN METABOLIC DISORDERS
Chairs: Julieta Trinks, Esteban Martín Repetto

A DEADLY BALANCE: HORMETIC STRESS RESPONSES DRIVE BETA CELL FATE IN DIABETES

Marcelo J. Perone

Immuno-Endocrinology, Diabetes & Metabolism Laboratory, Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Pilar, Argentina.

Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.

Pancreatic β -cells produce insulin, the hormone essential for glucose uptake and metabolic homeostasis. Diabetes mellitus results from β -cell dysfunction or loss, due to autoimmune destruction in type 1 diabetes (T1DM) or insufficient compensation for insulin resistance in type 2 diabetes (T2DM). In T2DM, insulin resistance combined with progressive β -cell failure leads to inadequate insulin secretion, impaired glucose uptake, and chronic hyperglycemia, whereas T1DM is marked by (near)-absent circulating insulin.

β -cells must sustain episodic periods of high secretory activity (a form of physiological cellular stress), which requires a functional and healthy endoplasmic reticulum (ER). The ER is essential for proinsulin folding, and maintaining proteostasis is critical for β -cell function and survival under both physiological and pathological conditions. Excessive ER stress leads to cellular dysfunction, dedifferentiation, trans-differentiation, and ultimately β -cell death, as observed in both types of diabetes. Growing evidence links β -cell ER stress and maladaptive unfolded protein response (UPR) signaling to the initiation and progression of diabetes. Several monogenic diabetes forms also show excessive ER stress. Notably, β -cell ER stress arises at both early and late stages of T1DM and T2DM, though causality remains unproven. Given the importance of a healthy ER in β -cells, therapeutic

interventions that modulate ER stress may be harnessed. Modulation of the UPR with small molecules could shift β -cells between maladaptive and adaptive states, suppressing harmful pathways while preserving protective ones. In this context, ER stress-alleviating compounds such as tauroursodeoxycholic acid and 4-phenylbutyrate have been clinically investigated. Although definitive evidence is lacking that targeting ER stress responses can improve β -cell function and survival in diabetes, emerging insights into the intracellular signals that restore ER homeostasis are encouraging. The mechanisms leading to the loss of functional β -cell mass in diabetes are well characterized; however, far less is known about the counter-regulatory processes that preserve β -cell survival and function, particularly under conditions requiring insulin production beyond physiological limits. I will present evidence showing the benefits of a small molecule that attenuating ER stress in β -cells delays the onset of hyperglycemia in NOD mice, a model of T1DM. I will also reveal a newly identified molecular mechanism demonstrating that minimal ER stress is required to trigger an adaptive, pro-survival hormetic response that enhances β -cell resilience to cytotoxic inflammatory insults - a phenomenon not previously documented in β -cells.

MASLD AS A CHALLENGE: UNDERSTANDING AGE-RELATED PROGRESSION AND TRANSLATIONAL MODELS

Catalina Atorrasagasti^{1,2}

1 Programa de Hepatología Experimental y Terapia Génica, Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Pilar, Argentina. 2 Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease, affecting ~38% of the global adult population, closely linked to obesity, diabetes, and cardiovascular risk. It

encompasses a broad spectrum, from simple steatosis to metabolic dysfunction-associated steatohepatitis (MASH), which can progress to fibrosis, cirrhosis, liver failure, or hepatocellular carcinoma (HCC). While most

individuals remain at the steatosis stage, up to 40% progress to MASH, 9–20% develop advanced fibrosis or cirrhosis, and about 3% of MASH cases eventually lead to HCC. The variability in prevalence and outcomes across age groups highlights the complexity of MASLD epidemiology. Age is a major driver of MASLD: among older adults, prevalence ranges from 32.8% to 50.1%, with the highest rates in men aged 45–49 years and women aged 50–54 years. Sex further modulates disease course, with men disproportionately affected in midlife, while women lose protection after menopause. Aging further worsens disease by reducing regeneration, increasing oxidative stress, and driving chronic inflammation, heightening liver vulnerability.

Current therapeutic strategies focus on lifestyle interventions and glycemic control, while Resmetirom is the first drug approved for MASH, limited to patients with advanced fibrosis. Despite multiple targets under study, translation remains limited by inadequate preclinical models. A critical gap in preclinical research is that most experimental studies rely on young animals, which fail to reflect the progressive course of MASLD as it emerges

and advances in adult populations. Moreover, biological sex is increasingly recognized as a determinant of disease risk and outcome yet is often overlooked in both basic and translational studies.

This presentation will review key aspects of MASLD, from its epidemiological impact to current therapeutic challenge, and will emphasize the importance of incorporating age and sex as key biological variables to enhance the translational relevance of MASLD models. Accounting for these factors helps capture the complexity and heterogeneity observed in human disease. I will present our findings showing that middle-aged mice progress to more advanced disease stages, with greater hepatic injury and distinct histological and transcriptomic alterations compared with younger animals, further modulated by sex. Furthermore, bioinformatic strategies that combine transcriptomic, phenotypic, and histopathologic metrics provide a quantitative assessment of how well preclinical models reproduce human MASLD, offering an objective framework to evaluate model relevance and to guide biomarker discovery and therapeutic testing.

THE HIDDEN LEGACY: HOW PATERNAL DIABETES SHAPES OFFSPRING METABOLISM

Evangelina Capobianco

Centro de Estudios Farmacológicos y Botánicos (CEFyBO)- UBA-CONICET. Facultad de Medicina. Buenos Aires, Argentina.

Diabetes mellitus is one of the most impactful chronic diseases worldwide. Fetal exposure to maternal diabetes is linked to postnatal metabolic disorders such as obesity, diabetes, and hypertension. Over the last decade, numerous studies have shown that, in addition to the well-recognized importance of maternal intrauterine influence, environmental factors, lifestyle exposures, and paternal metabolic health prior to conception also play a critical role in determining offspring health. The offspring of parents with diabetes, upon reaching reproductive age, may transmit metabolic disorders such as diabetes or obesity to subsequent generations, thereby contributing to the exponential increase in the global prevalence of these conditions.

A key focus in understanding paternal programming is the placenta, particularly given the fetal origin of its trophoblast component, and the important contribution of the paternal genome to its development. The growing recognition of the placenta as a central mediator in the intrauterine programming of postnatal disease highlights the need to include placental development and function in studies of paternal metabolic disorders.

In this talk, we will explore data from a model of paternal diabetes that reveals placental alterations and early met-

abolic changes in the offspring. These findings provide a foundation for understanding how paternal diabetes can shape fetal development and long-term health, including susceptibility to liver diseases. Notably, studies examining the effects of paternal diabetes on placental function and offspring health remain limited, and this area of research warrants further investigation to uncover critical molecular mediators and windows of vulnerability.

Based on this evidence, we propose the following working hypothesis: Paternal diabetes affects the development of germ cells, in which certain epigenetic marks are retained and subsequently impair feto-placental development, with consequences for offspring health. In this way, paternal diabetes intergenerationally transmits abnormalities in glucose and lipid metabolism and programs a pro-oxidant and pro-inflammatory state, associated with alterations in the expression and function of peroxisome proliferator-activated receptors (PPARs).

PPARs are nuclear receptors activated by lipid-derived ligands that regulate the transcription of genes involved in lipid and carbohydrate metabolism, antioxidant and anti-inflammatory processes, immune response, as well as cellular differentiation and development.

SPEXIN REGULATES THE FUNCTIONALITY OF WHITE ADIPOSE TISSUE IN A SEX-DEPENDENT MANNER.

Carolina Carla Garraza, Sabrina Eliana Gambaro, Ana Alzamendi, María Amanda Rey, Andrés Giovambattista, María Guillermina Zubiria

Instituto Multidisciplinario de Biología Celular (IMBICE) - La Plata, Bs. As.

caro.garraza9@gmail.com

Spexin (SPX) is an adipokine involved in modulation of white adipose tissue (WAT) biology. Previously, we showed beneficial metabolic effects in obese SPX-treated mice from both sexes under Fructose Rich Diet (FRD) intake. However, it remains unexplored the potential sex dimorphism in these effects, particularly in WAT functions. For this aim, four groups of male and female mice (C57BL/6J) were studied: CTR mice, FRD mice (10 weeks of 20% w/v fructose intake), and two similar groups treated with SPX for the last ten days (ip. 29 µg/kg/day; CTR-SPX and FRD-SPX). WAT depots (subcutaneous (sWAT) and gonadal (gWAT)) were dissected, weighted and used for quantification of ob, Adiponectin, pparγ2 and galr2 by qPCR. SPX significantly reduced the masses of sWAT and gWAT in obese male and female mice (PFRDxSPX=0.015, PFRDxSPX=0.019,

respectively) and also counteracted the hypertrophy in the gWAT of both sexes. SPX strongly decreased the mRNA levels of ob and pparγ2 in gWAT from FRD mice, reducing them to baseline levels (PFRDxSPX=0.0086; PFRDxSPX=0.028, respectively), being this effect more pronounced in females (P=0.058, P=0.004, respectively). In sWAT, SPX reduced ob in obese females and pparγ2 in obese males (P<0.0001). Regarding galr2, only gWAT from obese females have increased receptor expression (P<0.0001), which was normalized with SPX (P<0.0001). Finally, SPX decreased il6 and il1β expressions in male and female gWAT explants incubated with lipopolysaccharide (P=0.029 and P=0.016, respectively). Overall, SPX produced more significant improvements in gWAT of female mice, emphasising the importance of sex in modulating SPX's effects on WAT functions.

Symposium 11 - SAIC - Thursday 20th November 2025 - 9:00 - 10:30 - Salón 1

PRECISION HUMAN GENETICS: SEQUENCING, BIOMARKERS, AND ARTIFICIAL INTELLIGENCE

Chairs: Melisa Taboas, Mariana Tellechea

LONG READ SEQUENCING: APPLICATIONS AND CHALLENGES IN DIAGNOSIS OF HUMAN GENETIC DISEASES

Aldana Claps

Departamento de Diagnóstico del Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán". Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina

Long read (LR) third-generation sequencing has taken a more prominent role in recent years, especially by allowing for better analysis of genome rearrangements, repetitive sequences, modified bases and regions with high sequence identity. Other methods based on short read sequencing do not efficiently assemble these challenging regions. Oxford Nanopore Technologies (ONT) use flow cells with nanopores embedded in an electro-resistant membrane. Each nanopore corresponds to its own electrode connected to a channel and sensor chip, which measures the electric current that flows through the nanopore. When a molecule passes through a nanopore, the current is disrupted to produce a characteristic 'squiggle'. The squiggle is then decoded using basecalling algorithms to determine the DNA or RNA sequence in real time. This characteristic allows the implementation of Adaptive Sampling (AS), a sequencing strategy that enriches regions of interest by rejecting reads mapping to off-target regions. Our group began applying ONT sequencing in 2020 for the genetic diagnosis of congenital adrenal hyperplasia (CAH) caused by 21-hydroxylase deficiency. This autosomal recessive monogenic disorder is due to pathogenic variants

in the CYP21A2 gene. A major diagnostic challenge is the presence of the CYP21A1P pseudogene, which shares 98% sequence identity with CYP21A2, leading to frequent misalignment when using short-read approaches. Currently, we are expanding the application of ONT sequencing to disorders caused by repeat expansions, including Fragile X syndrome and Friedreich's ataxia, which are associated with expansions in the FMR1 and FXN genes, respectively. In addition to repeat length, promoter methylation status plays a crucial role in the pathogenic mechanism of both conditions. ONT, with its capacity for direct methylation calling, offers a unique advantage in simultaneously characterizing repeat size and methylation patterns in a single assay. ONT LRs, combined with AS, represents a powerful and efficient strategy for interrogating these loci. By overcoming the historical limitations of short-read sequencing, ONT LRs sequencing provides a more comprehensive view of genome architecture. Its introduction into our diagnostic workflows has enabled a deeper understanding of these genetic disorders and is improving our ability to resolve complex loci, characterize disease-causing variants, and study epigenetic contributions to disease.

ANALYSIS OF GENOMIC BIOMARKERS IN LIQUID BIOPSY: FROM DIGITAL PCR TO NGS

Lucía Daniela Espeche
Biomakers S.A.

Cancer remains the second leading cause of death world- wide, and selecting the appropriate therapy is crucial to

improving patient survival. The detection of genomic biomarkers in tumor samples is now a pillar of precision medicine. While tissue biopsy remains the gold standard for both diagnosis and determining treatment, liquid biopsy has emerged as a minimally invasive and promising alternative. Liquid biopsy involves the analysis of blood or other body fluids to detect molecular alterations, circulating tumor cells, and tumor-derived metabolites. This approach offers several advantages: it is non-invasive, easy to obtain, provides a more comprehensive representation of the tumor's molecular landscape, enables real-time monitoring of disease progression, and is less dependent on pre-analytical variables for test success. Two key technologies have enabled the clinical application of liquid biopsy in cancer: digital PCR (dPCR) and next-generation sequencing (NGS). Digital PCR provides

highly sensitive and quantitative detection of known mutations, such as the EGFR p.(T790M) resistance variant in non-small cell lung cancer, and is particularly useful for targeted mutation monitoring during therapy. On the other hand, NGS allows comprehensive genomic profiling by simultaneously analyzing multiple genes and alterations, offering broader insights into tumor heterogeneity and resistance mechanisms. However, expanding the number of targets without compromising sensitivity has been a significant challenge in the field. Together, these technologies have expanded the utility of liquid biopsy across various stages of cancer management. Despite ongoing challenges, such as low ctDNA abundance and standardization of workflows, liquid biopsy combined with advanced molecular platforms is becoming an essential tool in precision oncology.

APPLICATION OF AI TOOLS IN ADDRESSING GENETIC VARIANTS ASSOCIATED WITH ABNORMALITIES IN THE SYNTHESIS AND ACTION OF THYROID HORMONES

Juan Nicola

Departamento de Bioquímica Clínica. Facultad de Ciencias Químicas. Universidad Nacional de Córdoba. Centro de Investigaciones en Bioquímica Clínica e Inmunología, Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET)

The rapid expansion of next-generation sequencing technologies has greatly increased our understanding of the genetic factors that contribute to thyroid disorders. However, interpreting genetic variants identified through these approaches remains challenging. Artificial intelligence (AI) tools are emerging as transformative allies in this field, offering new strategies to improve variant interpretation and diagnostic outcomes for patients with genetic endocrine disorders.

This symposium will explore the application of AI-driven methodologies, including machine learning-based variant effect predictors and integrative frameworks for clinical genomic data interpretation, to address unresolved questions in thyroid genetics. AI-based predictors, when trained on functional, evolutionary, and structural features, can prioritize rare missense variants, refine ACMG/AMP-based classification, and reduce the number of variants of uncertain significance.

Beyond prediction, integrating AI with functional datasets, imaging modalities (e.g., thyroid scintigraphy), and

electronic health records paves the way for multidisciplinary frameworks that link genotype to phenotype more accurately. These approaches improve variant classification and enhance personalized risk assessment, prognosis, and treatment decision-making in endocrine practice. The symposium will also address the limitations and ethical considerations of AI applications. These include algorithmic bias, lack of interpretability, and disparities in genomic datasets. These issues may hinder the equitable deployment of these technologies in diverse populations. There will be an emphasis on the need for continuous benchmarking against experimental data, reporting standards, and international collaboration to validate AI-derived predictions in clinically relevant settings.

By showcasing state-of-the-art advances and real-world applications, this session aims to demonstrate how AI can bridge the gap between genomic discovery and clinical care in thyroid genetics, thereby accelerating the integration of precision medicine into routine practice.

AN IN VIVO ASSAY TO DETERMINE THE PATHOGENICITY OF TWO GENETIC VARIANTS IN IGF1 USING A ZEBRAFISH MODEL

Macarena Recalcatti¹, Michella Braccalenti¹, Lucía Salatino², María Celia Fernández¹, Ayelén Martín¹, Horacio Domené¹, Patricia Pennisi¹, Paola Plazas², Sabina Domené¹

1. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET-FEI-División de Endocrinología, Hospital de Niños Ricardo Gutiérrez Buenos Aires, Argentina.

*2. Instituto de Farmacología, Facultad de Medicina, Universidad de Buenos Aires (UBA), Paraguay 2155, C1121ABG, Buenos Aires, Argentina.; Laboratorio de Neurobiología del desarrollo de sistemas sensoriales
macarenaluciarecalcatti@gmail.com*

The insulin-like growth factor 1 (IGF1) is highly conserved among vertebrates and plays a central role in pre- and postnatal growth. IGF1 deficiency due to homozygous

pathogenic variants in IGF1 gene leads to intrauterine and postnatal delay of growth often associated with deafness and mental retardation.

Our objective was to develop a functional assay to determine the pathogenicity of two human variants in IGF1 found in patients with severe growth retardation using the zebrafish model. While the patient with p.Ser35Cys has normal hearing and cognitive development close to normal, the patient with p.Tyr60His has mental retardation and deafness.

We performed overexpression assays using WT IGF1 mRNA and variants, microinjecting them into zebrafish embryos followed by phenotype scoring.

Overexpression of WT IGF1 mRNA resulted in embryos with cyclopia (37%), pericardial edema (52%), yolk edema (54%), and tail malformation (43%). Conversely, overexpression of variants p.Ser35Cys and p.Tyr60His

resulted in embryos with significantly less malformations ($p < 0.05$), pericardial edema (7%; 0%), yolk edema (17%; 5%), and tail malformation (10%; 0%) respectively. Cartilage development was evaluated using Alcian Blue. Overexpression of WT IGF1 mRNA led to a significant decrease in cartilage length compared to uninjected embryos. Interestingly, overexpression of p.Tyr60His variant did not affect cartilage length while p.Ser35Cys led to a shortening similar to that obtained with WT IGF1.

In conclusion, our study suggests that the pathogenic nature of p.Tyr60His is due to a lack of function, while p.Ser35Cys retained minimal biological activity. This assay will allow the study of future IGF1 variants.

Symposium 12 - SAIC - Thursday 20th November 2025 - 13:00 - 14:30 - Salón 1
AI IN HEALTH SCIENCES
Chairs: Juan Bizzotto, Juan Orlowski

CLINICAL PHENOTYPES IDENTIFIED WITH PERIPHERAL BLOOD TRANSCRIPTOMICS AND AI

Santiago Miriuka
Fundación FLENI

Artificial intelligence (AI) is transforming how health systems turn data into earlier, safer, and more personalized decisions. This talk will discuss the technologies and practices that support this change—in particular, how AI and transcriptomics can make a difference. Using whole-blood transcriptomes as a “liquid biopsy,” I will explore how gene-expression signatures from a standard blood draw, when integrated with routine risk factors, can predict the presence and burden of coronary artery calcification (CAC) on CT, a robust marker of subclinical atherosclerosis. I will outline the end-to-end approach: rigorous

RNA processing; feature selection and model training; strict cross-validation; and calibration to translate scores into clinically meaningful risk strata. To open the model’s “black box,” I will connect predictions to biology via pathway-level interpretation. I will also discuss limitations—pilot-scale cohorts, potential confounding, and generalizability across sites—and the validation required before deployment. Finally, I will look ahead to the future of AI in omics medicine, where multimodality meets algorithms to improve clinical outcomes.

WHEN TO SEEK ANSWERS FROM AI, AND WHEN TO TURN TO THE CELL: A NOVEL VESICLE-BASED PLATFORM FOR PERSONALIZED CANCER VACCINES

Guido Nicolás Molina
SphereBio

Cancer remains a leading cause of mortality worldwide, responsible for one in six deaths. Unlike therapeutic approaches that directly target tumor cells, cancer vaccines must activate dendritic cells (DCs) to cross-present tumor antigens to CD8⁺ T lymphocytes. One of the major challenges for cancer vaccines is personalization and antigen selection: highly heterogeneous tumors with multiple subclones, such as glioblastoma, require broad antigen coverage to prevent immune escape. Synthetic neoantigen vaccines are expensive, slow to manufacture, and often fail to include sufficient antigenic diversity. Moreover, another key challenge is to achieve efficient cross-presentation for CD8⁺ T-cell priming, which can be enhanced by cytosolic delivery of antigens into DCs for endogenous MHC-I presentation.

At SphereBio, we have developed a delivery platform based on engineered extracellular vesicles (EVs)

equipped with fusogenic proteins (SphereProteins) to enhance cytosolic delivery, mimicking viral mechanisms. Using model antigens, these vesicles markedly improved DC-mediated CD8⁺ T-cell activation and proliferation *ex vivo*, illustrating that engineered vesicles can be leveraged to achieve efficient antigen cross-presentation.

In parallel, to select the antigens to be carried by the vesicles, we explored AI-driven pipelines for epitope prediction but found that this reductionist approach is insufficient for highly heterogeneous tumors. As an alternative, we established a method to generate artificial cell-derived vesicles from HEK293 cells, capable of carrying autologous whole tumor lysates, thereby representing the complete antigenic complexity of each patient’s tumor. To further optimize vesicle functionality, we are developing SphereEngine, an AI platform for the design of membrane proteins that regulate endosomal escape,

targeting, and immunomodulation, in partnership with Innovative and AWS.

Finally, to explore patient stratification and potential differential responses to vaccination, we applied AI-based analyses to glioblastoma datasets, which revealed transcriptomic subtypes with distinct immune microenviron-

ments and survival profiles.

In conclusion, developing this platform has shown us where AI adds value to our approach, and where turning to the cell to extract its biological complexity gives us a true differentiator. Together, these insights define a path toward next-generation, personalized cancer vaccines.

DEEP LEARNING PREDICTS DNA MISMATCH REPAIR DEFICIENCY IN COLORECTAL CANCER FROM ROUTINE HISTOLOGY SLIDES

Ana Gorodisch^{1,2}

¹Kuvia, Buenos Aires, Argentina

²Instituto Tecnológico de Buenos Aires (ITBA), Buenos Aires, Argentina

Background: DNA Mismatch Repair (MMR) is a key molecular biomarker in colorectal cancer with major prognostic and therapeutic relevance. Tumors with deficient MMR (dMMR) are typically associated with microsatellite instability (MSI), whereas those with proficient MMR (pMMR), with microsatellite stability (MSS). Current detection methods rely on costly, limited-access molecular tests. Digital pathology enables the use of artificial intelligence (AI) to infer molecular status from histology. This study builds upon previous work presented at the Journal of Clinical Oncology (2024), advancing the detection of MMR status directly from hematoxylin and eosin (H&E) stained slides using AI to expand access to precision diagnostics.

Methods: Several deep neural network architectures were evaluated on high-resolution .SVS images. The training and internal validation dataset included 690 colorectal cancer slides from TCGA and CPTAC, comprising 101 cases with MSI/dMMR and 589 with MSS/pMMR. An independent external cohort from a private pathology lab, consisting of 120 cases (34 MSI/dMMR, 86 MSS/pMMR), was used to assess model generalization. The training

protocol followed a 5-fold Monte Carlo cross-validation, with results reported as mean $\pm$ standard deviation.

Results: On the TCGA-CPTAC cohort, the best-performing model achieved an accuracy of $93.0\% \pm 0.7$, sensitivity of $80.0\% \pm 7.0$, specificity of $95.0\% \pm 1.0$, PPV of $75.0\% \pm 4.0$, and NPV of $97.0\% \pm 0.9$. When tested on the external cohort, the model showed strong generalization with an accuracy of $87.4\% \pm 3.0$, sensitivity of $76.8\% \pm 1.5$, specificity of $90.7\% \pm 6.1$, PPV of $73.8\% \pm 8.4$, and NPV of $92.9\% \pm 4.6$.

Conclusions: These findings highlight the ability of AI to accurately predict molecular events from routine histology, strengthening the role of digital pathology as a transformative tool in modern oncology. The model's robust performance is being further enhanced by retraining with over 1,000 local slides to achieve performance comparable to molecular reference methods. This approach also proves scalable: prior work on endometrial cancer achieved promising results, and current efforts aim to transfer these optimizations to validate the model across multiple oncologic contexts.

DIGITAL TWINS OF HISTOLOGY: REPROGRAMMING THE PATHOLOGIST'S EYE WITH AI FOR PROGNOSTIC STRATIFICATION IN CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

Guillermo Blanco

Laboratorio de Inmunotoxicología (LIT) IDEHU-CONICET, Hospital de Clínicas "José de San Martín" Facultad de Medicina Universidad de Buenos Aires (UBA), Buenos Aires, Argentina

Chronic Lymphocytic Leukemia (CLL) exhibits heterogeneous clinical outcomes, yet the classification of intermediate aggressive subtypes, such as Accelerated CLL, remains dependent on subjective histological criteria based on Hematoxylin and Eosin (H&E) staining. This diagnostic gap represents a perfect opportunity to apply principles of Artificial Intelligence (AI) and high-dimensional data science to a ubiquitous, low-cost clinical asset.

This presentation outlines a novel methodology that transforms standard H&E images into quantitative, single-cell feature maps—a form of morphological spatial analysis. We implemented a robust, traceable pipeline using Ilastik and CellProfiler to segment thousands of individual CLL cells from lymph node biopsies, measuring hundreds of morphological parameters (e.g., size, texture, nuclear ir-

regularity) per cell.

Using unsupervised techniques (Seurat 5 and Monocle3 trajectory analysis) and pathologist-guided machine learning, we demonstrated that high-dimensional morphometrics can successfully and independently distinguish aggressive from indolent CLL cases. Aggressive disease was defined by the enrichment of a specific morphometric cluster corresponding to Paraimmunoblasts (PIB) and Prolymphocytes, while indolent cases were dominated by small lymphocytes.

By creating a "digital twin" of the tissue morphology, we provide objective metrics of cellular state, offering a complementary approach to current diagnostic criteria.

Furthermore, we will introduce ongoing work that uses spatial registration (H&E to IHC) and scRNA-seq com-

munication analysis (CellPhoneDB) to link these morphometrically aggressive cell clusters to key functional drivers, such as M2 macrophage polarization (efferocytosis axis: MerTK-GAS6) and metabolic reprogramming

(HIF-1 α). This work proves the concept that deep feature engineering on simple histological images can yield actionable, prognostic insights, bridging traditional pathology with advanced computational biology.

Roundtable 1 - SAIC - Tuesday 18th November 2025 - 9:00 - 10:30 - Auditorio

RARE DISEASES: FROM TRANSLATIONAL RESEARCH TO COMMUNITY ENGAGEMENT

Chair: Liliana Dain

This roundtable aims to bridge the gap between scientific research and the daily challenges faced by patients and families living with rare diseases.

Three researchers will present advances in the study, diagnosis, and potential treatment of rare disorders developed within the academic and clinical research community. Following these presentations, a discussion will be held with representatives from ALAPA (Latin American

Alliance for Rare Diseases) and patient and parent associations, fostering dialogue on how to translate scientific progress into tangible improvements in care, awareness, and public policy.

The activity seeks to promote collaboration between researchers, clinicians, and advocacy groups, emphasizing the importance of patient-centered research and the value of collective efforts in addressing rare diseases.

Javier Santos: Rare Disease Research Program at FCEN-UBA

Valeria Tripodi: Advances in the Diagnosis and Treatment of CoQ10 Deficiency-Related Disorders in Argentina

Bruno Berardino: Evaluation of Differentially Expressed miRNAs in Girls with Rett Syndrome as Diagnostic and Prognostic Biomarkers of Clinical Severity

Carolina Oliveto: ALAPA

Patients and Parents Associations

Roundtable 2 - SAIC - Tuesday 18th November 2025 - 15:00 - 16:30 - Salón 1

INNOVATION, TECHNOLOGY TRANSFER, AND ENTREPRENEURSHIP IN BIOMEDICAL SCIENCES

Chairs: Daniel Alonso, Graciela Ciccía

This roundtable will bring together key players from the scientific and technological ecosystem to discuss the challenges and opportunities involved in translating biomedical research into tangible products and innovations. Two startups will share their experience along the path “*from the bench to the product*”, highlighting the lessons learned, obstacles faced, and strategies that enabled them to transform laboratory results into real-world health solutions.

In addition, representatives from incubators and acceler-

ators—including *GridX*, *SF500*, *Parque de Innovación*, and *Incubando Salud*—will join the discussion, offering their perspectives on supporting science-based projects, funding mechanisms, and the role of public initiatives in strengthening the innovation ecosystem.

This activity aims to foster dialogue among researchers, entrepreneurs, and institutions, encouraging a culture of technology transfer and the development of projects with social and economic impact.

Adriana de Siervi: CSO y Co-Founder Oncolig

Juan Pablo Tosar: CSO y Founder B4-RNA

Claudio Cocconi: Coordinador General en Incubando Salud - Desarrollo de negocios

Romina Casadevall: GRIDX Partner – Scientific Explorer

AAFE AWARD - ANNUAL AWARD TO THE BEST WORK IN PHARMACOLOGY

Tuesday 18th November 2025 - 9:00 - 10:30 - Salón 2

Jury: Ventura Simonovich, Susana Gorzalczany, José Luna Pinto**Chair:** Guillermina Hernando**RIFAXIMIN A AND ITS BACTERICIDAL ACTIVITY AGAINST STAPHYLOCOCCUS AUREUS IN DAIRY COWS: IN VITRO STUDY UNDER SIMULATED MAMMARY GLAND CONDITIONS****Florencia Aliverti¹, Daniel Buldain¹, Julia di Filippo¹, Laura Marchetti¹, Mariana Lucas², Nora Mestorino¹**¹. Faculty of Veterinary Science, Universidad Nacional de La Plata, Argentina.; Laboratory of Pharmacological and Toxicological Studies -LEFyT-². Universidad del Salvador, Pilar, Argentina.; Faculty of Agrarian and Veterinary Sciences.

florence.aliverti@fcv.unlp.edu.ar

Rifaximin α (RIF α) is a semisynthetic antimicrobial with local action, effective against Gram-positive and Gram-negative bacteria, and used to treat bovine mastitis caused by *Staphylococcus aureus*. Data on its pharmacodynamic profile against this pathogen are scarce. This study aimed to evaluate the in vitro antibacterial activity of RIF α under simulated mammary conditions. Isolates were obtained from milk samples of dairy cows in Buenos Aires, Argentina, and identified by culture and biochemical tests; *S. aureus* ATCC 29213 served as a control. Six RIF α -susceptible isolates were tested by broth microdilution to determine minimum inhibitory concentrations (MICs) at pH 7.4, 6.5, 5.0, and in serum- or milk-supplemented media. Time-kill assays were conducted at 0.5 to 8 $\times$ MIC, with colony-forming units recorded up to 24

h. Antibacterial effect (E) was established classifying the antimicrobial activity as bacteriostatic ($E = 0$), bactericidal ($E \leq -3$), or virtual eradication ($E \leq -4$). MICs ranged from 0.004–0.125 $\mu\text{g/mL}$ depending on conditions. Significant bacterial reduction occurred after 2–4 h, becoming evident after 12 h. The effect was both time- and concentration-dependent, reaching stable bactericidal activity at 4–8 $\times$ MIC. In serum or milk, RIF α at 8 $\times$ MIC achieved a bactericidal index ($E = -3$), more marked than under pH changes alone. In conclusion, RIF α showed potent activity against *S. aureus* from bovine mastitis, with efficacy linked to drug concentration and exposure time. These findings support its therapeutic potential and underscore the need to consider mammary physiological conditions to optimize its effectiveness.

PH/THERMO-RESPONSIVE MAGNETIC NANOPLATFORMS FOR ADVANCED TAMOXIFEN-BASED BREAST CANCER THERAPY**Jazmín Torres^{1,2}, Luciana B. Lopes³, Paula M. Uberman^{1,2}, Mónica C. García^{1,4}**¹ Universidad Nacional de Córdoba (UNC), Facultad de Ciencias Químicas (FCQ), Departamento de Ciencias Farmacéuticas, Ciudad Universitaria, X5000HUA, Córdoba, Argentina.² Consejo Nacional de Investigaciones Científicas y Técnicas, CONICET, Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, UNITEFA, Córdoba, Argentina.³ Departamento de Farmacología, Instituto de Ciencias Biomédicas, Universidad de São Paulo, São Paulo, SP, Brasil.⁴ Consejo Nacional de Investigaciones Científicas y Técnicas, CONICET, Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, UNITEFA, Córdoba, Argentina.

jaz.torres.006@unc.edu.ar

Breast cancer is highly prevalent and the leading cause of cancer-related death in women. Tamoxifen (TMX) is one of the standard treatment; however, its unfavorable physicochemical and biological properties limit clinical use, a drawback addressable through nanomedicine. The pH gradient and temperature change between normal and tumor tissues can serve as internal triggers for TMX release from nanosystems. Here, stimuli-responsive hybrid magnetic nanoplateforms (HMNP), functionalized with L-cysteine–hyaluronic acid (L-Cys-HA), were

developed for TMX delivery to improve breast cancer therapy efficacy and safety.

HMNP were synthesized from magnetite nanoparticles by co-precipitation and functionalized with pre-synthesized L-Cys-HA. TMX was incorporated via electrostatic interactions ($\text{NH}_3^+/\text{COO}^-$) and loading efficiency (η) quantified by UV-Vis. Structural, morphological, and interfacial characterizations were performed. In vitro release studies evaluated biopharmaceutical performance. Biological activity was tested in 2D/3D breast cancer cultures, in-

cluding HA pretreatment to study internalization. Cytotoxicity in non-tumor cells, hemocompatibility (*ex vivo*), and antiangiogenic potential (chick chorioallantoic membrane (CAM) model), were also assessed.

HMNP showed pseudospherical morphology, uniform nanoscale size, and negative electrokinetic potential, favoring efficient TMX incorporation (>85%). TMX release was controlled and responsive to acidic pH and hyperthermia, confirming dual stimuli sensitivity. *In vitro*,

HMNP-TMX preserved or improved antitumor efficacy in 2D cultures and enhanced activity in 3D models. HA pretreatment suggested CD44-mediated internalization. HMNP-TMX exhibited higher cytocompatibility and lower hemolysis than free TMX. The CAM assay confirmed retention of TMX's antiangiogenic activity.

HMNP-TMX constitute an advanced nanoplatform for targeted and controlled TMX delivery, offering a promising strategy to improve breast cancer therapy.

SYNERGISTIC TRYPANOCIDAL ACTIVITY OF BENZNIDAZOLE AND NIFURTIMOX: IN VITRO EVIDENCE SUPPORTING COMBINATION THERAPY FOR CHAGAS DISEASE

María Sol Magi¹, Cinthia Stempin², Alvaro Federico Jimenez Kairuz³, Mónica Cristina García³

1. Universidad Nacional de Córdoba (UNC), Facultad de Ciencias Químicas (FCQ), Departamento de Ciencias Farmacéuticas - Consejo Nacional de Investigaciones Científicas y Técnicas, CONICET, Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, UNITEFA, Córdoba Argentina.

2. UNC, FCQ, Departamento de Bioquímica Clínica - CONICET, Centro de Investigaciones en Bioquímica Clínica e Inmunología, CIBICI, Córdoba Argentina.; Bioquímica Clínica

3. UNC, FCQ, Departamento de Ciencias Farmacéuticas - CONICET, UNITEFA

maria.sol.magi@unc.edu.ar

Despite advances in Chagas disease research, therapeutic options remain limited to benznidazole (BNZ) and nifurtimox (NFX), two drugs developed more than 50 years ago. Although effective in the acute phase, their use is restricted by toxicity, emerging resistance, and reduced efficacy in chronic disease. Optimizing antichagasic pharmacotherapy is therefore a pressing need. In this sense, combination therapy represents a promising approach, as BNZ and NFX may exert complementary mechanisms, enhancing trypanocidal efficacy. In this study, the *in vitro* activity of the combination BNZ-NFX was evaluated against *Trypanosoma cruzi* (Tulahuen strain) using the checkerboard test. Epimastigotes were tested as a screening model, followed by assays in the infective trypomastigote stage. Drugs were assayed at concentrations ranging from 0 to 200 μ M and 0 to 50 μ M, respectively. Parasite inhibition was quantified by MTT

assay ($\lambda=570$ nm) in epimastigotes and by flagellar motility under inverted microscopy (Neubauer chamber) in trypomastigotes. Both drugs exhibited concentration-dependent activity, with IC_{50} values of (104.5 ± 5.1) μ M for BNZ and (115.9 ± 5.5) μ M for NFX in epimastigotes, and (11 ± 1) μ M and (6.0 ± 0.1) μ M, respectively, in trypomastigotes. Isobologram analysis (Chou-Talalay method) confirmed synergism, with a combination index of 0.4 ± 0.1 in trypomastigotes. Notably, equimolar mixtures of 6.25 μ M of each drug achieved the same efficacy as 50 μ M administered individually, representing an 8-fold dose reduction. These findings provide robust *in vitro* evidence of BNZ-NFX synergy, supporting their potential as a combined therapy with improved efficacy, reduced toxicity, and better clinical tolerability, as a promising strategy for future *in vivo* studies.

EVALUATION OF THE MULTITARGET POTENTIAL OF PHYTOCANNABINOID FRACTIONS AGAINST ALZHEIMER'S DISEASE

Florencia Antonella Musso¹, Ana Clara Pascual², Sabrina Rosicler Salas², Pablo Milano², Ana Paula Murray¹, Susana Juana Pasquaré²

1. INQUISUR (CONICET - UNS), Bahía Blanca, 8000, Argentina. Depto. de Química-UNS.; Laboratorio de Productos Naturales y Análogos Sintéticos Bioactivos (PRONABIO)

2. INIBIBB (CONICET - UNS), Bahía Blanca, 8000, Argentina. Depto. de Biología, Bioquímica y Farmacia-UNS.; Laboratorio de Cannabinología-INIBIBB-UNS-CONICET

florencia.musso@uns.edu.ar

Alzheimer's disease (AD) is a multifactorial neurodegenerative disorder for which current therapies are mainly symptomatic. Thus, the search for multitarget agents remains a major challenge. Cannabis sativa represents a promising source of bioactive metabolites with neuroprotective potential.

In this study, an ethanolic extract of *C. sativa* inflorescences was screened for acetylcholinesterase (AChE) inhibitory activity through a bioassay-guided fractionation

approach, leading to the identification of subfractions enriched in the phytocannabinoid acids (PCa) tetrahydrocannabinolic acid (THCA) and cannabidiolic acid (CBDA). The subfraction with the highest THCA content exhibited the strongest enzymatic inhibition. This prompted us to evaluate THCA in a dose-response assay on endocannabinoid 2-arachidonoylglycerol (2-AG) hydrolysis in an experimental model of synaptic amyloidosis induced by β -amyloid oligomers, as occurs in AD. At 30

μM , THCA reduced monoacylglycerol lipase (MAGL) activity, the main enzyme responsible for 2-AG degradation, thereby potentially increasing the availability of this neuroprotective endocannabinoid, previously reported to be reduced in AD.

Further enzymatic assays demonstrated that THCA, CBDA, as well as the 1:1 and 1:5 THCA:CBDA subfractions inhibited MAGL activity, while CBDA and 6:1 THCA:CBDA subfraction stimulated diacylglycerol lipase

(DAGL), a key enzyme for 2-AG biosynthesis.

Together, these results suggest a dual mechanism exerted by PCa, enhancing cholinergic neurotransmission (via AChE inhibition) and restoring 2-AG levels (via MAGL or DAGL modulation), potentially contributing to synaptic function. Our results emphasize the therapeutic potential of PCa as multitarget modulators in AD. Future in vivo studies will be essential to validate efficacy and safety, consolidating their role as candidates for AD treatment.

SUBSPICATIN L AND K: COMPOUNDS FROM *SENECIO VIRA-VIRA* WITH POTENTIAL TO REVERSE MULTIDRUG RESISTANCE IN LEUKEMIA CELLS

Jazmin lavallen¹, Ignacio Lopez Enrico¹, Basso Ana Valentina¹, Jeronimo Laiolo², Mariana Belen Joray¹, Maria Cecilia Carpinella¹

1. Centro de Investigación y Desarrollo de Inmunología y Enfermedades Infecciosas (CIDIE; CONICET-UCC); Productos naturales

2. Instituto de Investigación Médica Mercedes y Martín Ferreyra (INIMEC; CONICET-UNC); Laboratorio de microbiología
lavallenjazmin@gmail.com

P-glycoprotein (P-gp) is a membrane transporter strongly associated with multidrug resistance (MDR) due to its ability to expel chemotherapeutic agents from tumor cells, thereby reducing their intracellular concentration and limiting treatment efficacy. A screening of plant extracts identified *Senecio vira-vira* as a promising source of metabolites with P-gp inhibitory activity (Laiolo et al., 2021). To isolate and characterize the active constituents, the ethanol extract of this species was subjected to a bio-guided fractionation strategy. Successive chromatographic techniques allowed the purification of the most active fractions, and structural elucidation by one- (1H and 13C) and two-dimensional (COSY, HMBC, HSQC) NMR led to the identification of two eremophilane-type sesquiterpenes: Subspicatin L and Subspicatin K.

Both metabolites were evaluated in vitro in chronic myeloid leukemia cell lines, sensitive (K562) and resistant

(Lucena 1), using functional assays. Neither compound exhibited cytotoxicity at 100 μM . In intracellular accumulation assays with doxorubicin and rhodamine 123 by flow cytometry, both metabolites enhanced drug retention. Subspicatin L showed strongest activity, with minimum effective concentrations (MECs) ranging from 3.15 to 6.25 μM , while Subspicatin K was MECs between 12.5 and 25 μM . The increased intracellular levels of doxorubicin translated into enhanced cytotoxicity, evidencing reversal of resistance, with MECs of 6.25 μM for Subspicatin L and 12.5 μM for Subspicatin K. Complementary assays in peripheral blood mononuclear cells and human erythrocytes confirmed the absence of significant toxicity. Overall, the results demonstrate that Subspicatin L and K inhibit P-gp-mediated efflux, promote intracellular drug accumulation, and restore sensitivity to chemotherapeutics.

HELJA INTERFERES WITH INFLUENZA VIRUS INFECTION IN MDCK CELLS

Melisa Belén Radicioni¹, Alejandra Figari², Marianela Del Río¹, Carlos Cimmino², Osvaldo Uez², Andrea Lerman², Mariana Regente¹

1. Instituto de Investigaciones Biológicas (UNMdP-CONICET); Grupo de Investigación "Biología Integrada de Organismos Fotosintéticos"

2. Instituto Nacional De Epidemiología (INE) "Dr. Juan H. Jara", Administración Nacional De Laboratorios E Institutos De Salud "Dr. Carlos Malbrán"

melisaradicioni@mdp.edu.ar

Influenza virus circulates worldwide and remains a major cause of respiratory illness. The increasing resistance of Influenza strains to conventional antiviral drugs underscores the need for novel therapeutic strategies. In this context, phytomedicine has gained attention as a promising therapeutic alternative, since plant-derived bioactive compounds often exhibit complex mechanisms of action that may reduce the viral spread. Among these molecules, lectins are relevant due to their ability to bind carbohydrates and glycoconjugates, a property associated with antimicrobial and antiviral effects. In our laboratory, a mannose-binding sunflower lectin, Helja, was isolated and previously shown to interact with Influenza virus in indirect assays. The aim of the present study was to an-

alyze the antiviral capacity of Helja against different Influenza strains through infection inhibition assays. MDCK cells seeded at 80% confluence in 48-well plates were inoculated with 4 HAU/25 μL of H1N1, H3N2, and B Victoria strains, with or without preincubation with Helja at 10, 50, and 100 $\mu\text{g/mL}$. Cultures were incubated at 37°C and 5% CO_2 , and infection progression was monitored by cytopathic effect every 12 hours for 36 hours. In addition, cell viability was assessed at 36 hours post-infection using the MTT assay. Results demonstrated that Helja preincubation reduced viral infection in host cells, with a clear decrease in cytopathic effect and higher cell viability in treated wells relative to controls without lectin. These findings suggest that Helja interferes with influenza A and

B infection in MDCK cells and highlight its potential as a candidate for developing novel antiviral agents.

SAIC AWARD - FUNDACIÓN CHERNY - MULTIDISCIPLINARY CALL

Tuesday 18th November 2025 - 15:00 - 16:30 - Auditorio

Jury: Monica Costas, Marianela Candolfi, Noelia Weisstaub, Manuel Muñoz, Fernando Dominici

COMPARATIVE ONCOLOGY IN MAMMALS: COOPERATIVE LIFESTYLES CO-EVOLVE WITH LOWER CANCER PREVALENCE

Catalina Sierra¹, Julián Maxwell², Nicolás Flaibani³, Constanza Sánchez de la Vega⁴, Alejandra Ventura², Nicolás José Lavagnino³, Matías Blaustein¹

1. Universidad de Buenos Aires. Facultad de Ciencias Exactas y Naturales. Departamento de Fisiología, Biología Molecular y Celular. Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3). Buenos Aires, Argentina.

2. CONICET - Universidad de Buenos Aires. Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE). Buenos Aires, Argentina.

3. CONICET - Universidad de Buenos Aires. Instituto de Ecología, Genética y Evolución de Buenos Aires (IEGEBA). Buenos Aires, Argentina.

4. CONICET - Universidad de Buenos Aires. Instituto de Cálculo (IC). Buenos Aires, Argentina.
catalinasierra9@gmail.com

The tree of life offers unlimited inspiration for designing novel therapeutic strategies against cancer. By combining ecology, evolutionary biology, veterinary medicine, and clinical research, comparative oncology aims to better understand cancer, particularly by highlighting species that are strongly susceptible or resistant to cancer and identifying the molecular and cellular mechanisms underlying these differences. Here, we hypothesized that cancer prevalence and mortality risk might have been fine-tuned by evolution. Using public databases, we show that species with cooperative habits have lower cancer prevalence and mortality risk. By developing a mathematical model, we provide a mechanistic explanation: an oncogenic variant that elicits higher cancer mortality in older and less reproductive individuals is detrimental to cooperative mammalian societies but can lead to a counterintuitive overcompensation in population size and fit-

ness within competitive contexts. The phenomenon of a population increasing in response to a decrease in its per capita survival rate is called the hydra effect, a process never explored in the field of cancer before. Therefore, cancer can be considered as a selected mechanism of biological obsolescence in competitive species. Altogether, we propose that cancer evolution and progression, as complex phenomena, must be studied as multi-level selection processes, exploring how increasing cancer mortality rates impact population structure as a function of ecological and behavioral aspects of each species, allowing molecular mechanisms of cancer resistance to evolve in cooperative and caring societies. These results encourage deeper cooperation between clinicians and comparative oncologists to advance cancer prevention and treatment strategies.

AMYLOID-BETA REGULATES ASTROCYTIC GLUCOSE METABOLISM AND INSULIN SIGNALING IN EXPERIMENTAL MODELS OF ALZHEIMER'S DISEASE

Melisa Bentivegna¹, Carlos Pomilio¹, Melina Bellotto¹, Nicolás González Pérez¹, Soledad Rossi¹, Amal Gregosa¹, Daiana Vota², Fátima Merech², María Marta Bonaventura¹, Jessica Presa¹, Ángeles Vinuesa¹, Victoria Lux-Lantos¹, Soledad Porte Alcon², Flavia Saravia¹, Juan Beauquis¹

1. Instituto de Biología y Medicina Experimental (IBYME), CONICET

2. Dpto. de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires
melisa.bentivegna@gmail.com

Alzheimer's disease (AD) is the most prevalent neurodegenerative disorder, characterized by amyloid beta (A β) plaques, neuroinflammation and cognitive impairment. Metabolic disturbances, particularly brain insulin resistance, are increasingly recognized as central features of AD pathophysiology. Astrocytes, essential for brain energy metabolism, exhibit a loss of homeostatic functions in AD. Even though the main astrocytic glucose transporters are non-insulin dependent, insulin may regulate astroglial glucose metabolism. Our objective was to evaluate insulin signaling and astrocyte metabolism in the PDAPP-J20 transgenic mouse model of familial AD and

in mouse primary astrocyte cultures exposed to A β . Adult PDAPP-J20 mice showed hyperinsulinemia, hippocampal insulin resistance and astrocytic proinflammatory activation. The reactive glial phenotype was accompanied by decreased insulin receptor levels in this chronic setting. Exposure of primary astrocytes to A β induced proinflammatory activation, oxidative stress and loss of glutamate transporter EAAT2, crucial for neuroprotection. Even though A β -exposed astrocytes showed increased insulin receptor levels in this acute setting, insulin-induced phosphorylation of the receptor was hampered. Amyloid-treated astrocytes also showed increased glu-

cose uptake and lactate release in a time- and nutrient availability-dependent manner. Insulin treatment was associated with a recovery of mitochondrial health and increased amyloid uptake, highlighting a pro-homeostatic role for the hormone. Our results underscore the inter-

play between insulin signaling and astrocyte metabolism at different experimental and temporal settings of amyloid pathology. Understanding these mechanisms may help to design therapeutic strategies aimed at restoring metabolic balance and mitigating neurodegeneration.

STRATEGIES FOR BREAST CANCER TREATMENT: DESIGN OF NEW NANOFORMULATIONS TO INHIBIT STAT3 SIGNALLING PATHWAY

Ariadna Birocco^{1,2}, Agustín Blachman^{1,2}, Delfina Cesare¹, Rocío Dadino¹, Sergio Moya³, Graciela C. Calabrese^{1,2}

1. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Biología Celular y Molecular

2. Instituto de Química y Fisicoquímica Biológicas (IQIFIB) UBA-CONICET, Ciudad Autónoma de Buenos Aires, Argentina.

3. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Biología Celular. Ciudad Autónoma de Buenos Aires, Argentina
birocco.ariadna@gmail.com

Metastasis remains the leading cause of therapeutic failure in breast cancer (BC). BC stem-like cells (BCSLCs) represent a small subset of poorly-differentiated tumor cells, considered responsible for tumor dissemination, that exhibit an invasive, highly proliferative phenotype, partly attributed to deregulation of the STAT3 transcription factor pathway. Also, BCSLCs overexpress CD44, a receptor capable of binding various extracellular matrix components, such as dermatan sulfate (DS). Our research group previously reported chitosan and DS polyelectrolyte complexes (PECs) that selectively target CD44, being an innovative strategy that could modulate pharmacological stress tolerance to 5-Fluorouracil in colorectal cancer. This study explores the design, production and characterization of PECs loaded with: (1) the anti-STAT3 antihelminthic Flubendazole (Flu), recently repurposed as antitumoral, and (2) an anti-STAT3 siR-

NA, as selective nanocarriers to target CD44+ cells, for the modulation of tumor progression and dissemination. Both nanoformulations are synthesized by ionic gelation, and the uptake of BC cells correlates to the level of expression of CD44: no surface functionalization is required for the intracellular drug delivery, as the presence of DS guarantees their distribution. PECs-Flu inhibit nuclear translocation of pSTAT3, while PECs-siRNA lower STAT3 expression. Particularly in MDA-mb-231 human BC cell line, PECs-Flu induce G2/M cell cycle arrest and apoptosis; significantly inhibit migration, reduce metalloproteinase-2 activity and suppress BCSLCs growth. In summary, these versatile nanosystems are a potential new strategy in the selective delivery of drugs to poorly-differentiated BC cells, contributing to metastasis inhibition and minimizing the side effects of conventional chemotherapeutics.

IL-1B PRIMING TRIGGERS AN ADAPTIVE STRESS RESPONSE THAT ENHANCES PANCREATIC B-CELL RESILIENCE TO SUBSEQUENT CYTOTOXIC INFLAMMATORY INSULT

Carolina Sétula¹, Ingrid Pensado-Evans¹, Andrea Scelza-Figueroa¹, Miranda Sol Orellano¹, Ignacio Rodríguez-Valero¹, Eduardo Spinedi², Raghavendra G. Mirmira³, Marcelo Javier Perone¹

1. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Pilar, Argentina.; Immuno-Endocrinology, Diabetes & Metabolism Laboratory

2. La Plata Medical School, Universidad Nacional de La Plata, Argentina.; Centre of Experimental and Applied Endocrinology (CENEXA, UNLP-CONICET)

3. The University of Chicago, Chicago, Illinois, USA.; Department of Medicine and the Kovler Diabetes Center
carolinasetula@gmail.com

Insulin-producing β -cells fine-tune glycemia; their dysfunction and/or loss underlies both type 1 and type 2 diabetes. Inflammatory cytokines induce endoplasmic reticulum (ER) stress, driving β -cell apoptosis and contributing to diabetes development. Hormesis is a phenomenon by which low doses of a cytotoxic agent benefit organisms.

We aimed to explore the role of IL-1 β -mediated hormesis in defending β -cells against dysfunction and death induced by pro-inflammatory cytokines (CYT).

INS-1E rat insulinoma or isolated mouse islets were cultured in RPMI 10S, conditioned with IL-1 β low (IL-1 β 10pg/ml/72h) and challenged with CYT (IL-1 β 100pg/

ml+IFN- γ 5ng/ml; +TNF- α 8ng/ml for islets). Apoptosis was assessed by HO/PI(microscopy) and Annexin-V/7AAD(flow cytometry); NO by Griess; mRNA by qPCR; proteins by WB and immunofluorescence; luciferase reporter assays; global expression by RNA-seq; and β -cell function by glucose-stimulated insulin secretion (GSIS) followed by insulin ELISA.

IL-1 β low reduced CYT-induced NO secretion, I κ B α phosphorylation, and decreased NF- κ B p65 nuclear translocation and transcriptional activity in INS-1E(p<0.05). IL-1 β low attenuated IL-1 β mRNA levels while upregulating IL-1Ra(p<0.05), reduced apoptosis/death after CYT/16h, with protection lasting up to 48h(p<0.05), hampered

the CYT-induced increases in DP5 and PUMA mRNA, CHOP and cleaved caspase-3 ($p < 0.05$) and counteracted the rise in Bax/Bcl-2 mRNA ratio ($p < 0.01$). IL-1 β low mitigated the CYT-induced decline in β -cell identity and maturity markers and enhanced GSIS in INS-1E and mouse islets. IL-1 β low increased eIF2 α phosphorylation in INS-

1E while reducing ATF4 and increased ER chaperones BiP and GRP94 ($p < 0.05$). RNA-seq analysis revealed protective transcriptome modulation following IL-1 β low priming and CYT challenge. Therapies harnessing the hormetic response could enhance β -cell function and survival in diabetes.

EPIGENETIC FACTOR KANSL2 REGULATES RIBOSOME BIOGENESIS AND CELL HETEROGENEITY IN GLIOBLASTOMA

Nicolás Budnik¹, Agustín Ezequiel Morellato¹, Carol Fagundez¹, Ken Kobayashi², Joaquín M. Espinosa³, Carolina Perez-Castro¹

1. Instituto de Investigación en Biomedicina de Buenos Aires (IBioBA) - CONICET -Partner Institute of the Max Planck Society. Buenos Aires, Argentina.; Laboratorio de células madre tumorales y plasticidad celular

2. Departamento de Fisiología, Biología Molecular y Celular (FBMC), Instituto de Biodiversidad y Biología Experimental Aplicada (IBBEA-CONICET-UBA), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina.; Laboratorio de Agrobiotecnología

3. Linda Crnic Institute for Down Syndrome, University of Colorado Anschutz Medical Campus, Aurora, CO, USA and Department of Pharmacology, University of Colorado Anschutz Medical Campus, Aurora, CO, USA.; Espinosa Lab
nicobudnik@gmail.com

Glioblastoma (GBM) is a highly aggressive brain tumor characterized by heterogeneity and the persistence of glioblastoma stem-like cells (GSCs), which sustain plasticity and therapeutic resistance. KANSL2 is a subunit of the Non-Specific Lethal (NSL) complex with histone acetyltransferase activity through KAT8/MOF. We have previously determined that KANSL2 is critical for GBM tumorigenesis. In support, patient-derived datasets (TCGA) revealed elevated expression of KANSL2 in GBM compared to normal brain (GTEx), correlating with ribosome-related transcriptional programs and tumor stemness. In GBM cell lines, KANSL2 localized to nucleoli, and its silencing reduced rRNA precursor expression, protein synthesis, and H4 acetylation at rDNA promoters. Conversely, KANSL2 overexpression enhanced ribosomal gene expression and proliferative capacity.

Transcriptomic profiling of patient-derived GBM spheroids with KANSL2 knockdown confirmed a reduction of ribosomal gene expression and the induction of Hippo pathway components, notably YAP1. KANSL2 depletion also induced proneural-to-mesenchymal transition, increasing migration and angiogenesis while reducing tumorigenic potential in vivo. Mechanistically, we uncovered a reciprocal regulation: KANSL2 limits YAP1 activity by promoting its phosphorylation and cytoplasmic retention, while YAP1 is required to sustain KANSL2 and NSL complex expression. This feedback loop integrates ribosome biogenesis, epigenetic control, and YAP1 signaling to determine GBM cell states. Altogether, our findings identify KANSL2 as a novel nucleolar epigenetic regulator that couples ribosome synthesis to cellular plasticity, highlighting its potential as a therapeutic target in GBM.

SAIC AWARD - FUNDACIÓN GADOR - BIOINFORMATICS AND NOVEL THERAPEUTIC TARGETS

Tuesday 18th November 2025 - 17:00 - 18:30 – Auditorio

Jury: Ezequiel Lacunza, Luis Diambra, Dario Fernandez Do Porto, Alberto Penas Steinhardt

Premio Gador-01

MATERNAL AGING AND IMPLANTATION: A COMPREHENSIVE ANALYSIS OF EMBRYO-ENDOMETRIAL INTERACTION

Ana Schafir¹, Lara Castagnola¹, Alejandra Marilina Fernandez², Laura Fernández¹, Lourdes Materazzi¹, Marcela Irigoyen³, Antonio Cattaneo³, Diego Gnocchi³, Gustavo Martínez³, Silvina Ponce Dawson², Soledad Gori¹, Claudia Pérez Leirós¹, Vanesa Hauk¹, Lía Isabel Pietrasanta², Esteban Grasso¹, Rosanna Ramhorst¹

1. IQIBICEN, UBA-CONICET; Laboratorio de Inmunofarmacología

2. Instituto de Física de Buenos Aires; Centro de Microscopía Avanzada

3. Fertilis, Medicina Reproductiva.

aschafir@qb.fcen.uba.ar

Advanced reproductive age (ARA) is associated with increased infertility and embryo poor quality. While most studies on reproductive aging focus on ovarian decline, the endometrium and its interaction with the embryo remains understudied. Here, we investigated how aging affects the embryo-endometrial dialogue, integrating

bioinformatic and in vitro approaches to uncover molecular and biomechanical disruptions that compromise implantation.

We constructed an interactome network using transcriptomic data from day-5 blastocysts and secretory-phase endometrial biopsies, identifying ligand-receptor pairs

enriched in pathways related to cell adhesion, immune modulation, and tissue remodeling. Using Atomic Force Microscopy (AFM), we evaluated the effects of soluble factors secreted by the embryo on the nanomechanical properties of stromal cells. Decidualization induces a significant decrease in stiffness, while soluble factors from arrested-development embryos reversed this. To assess the impact of aging, we analyzed endometrial samples from ARA women (>36), revealing 1,089 differentially expressed genes enriched in inflammation, stress response, and senescence-related pathways. We treated decidualized human endometrial stromal cells with thapsigargin, to induce a stressed and inflamma-

tory phenotype. AFM showed that stress prevented the biomechanical changes by decidualization, restoring stiffness to pre-differentiation levels. Furthermore, in a trophoblast-spheroid implantation assay, the Tg-treated cells impaired spheroid expansion. These findings reveal that successful implantation depends on a finely regulated dialogue between embryo and endometrium. ARA disrupts this, compromising endometrial receptivity. Our study introduces cellular mechano-competence as a novel determinant of implantation success and a new bioinformatic tool to explore new avenues in reproductive medicine.

TARGETING RAC1 AS A NOVEL STRATEGY TO REDUCE INFLAMMATION AND LIVER DAMAGE IN ACUTE LIVER FAILURE

Bárbara Bueloni¹, Esteban Fiore¹, María José Cantero¹, Lucía Lameroli¹, Catalina Atorrasagasti¹, Andrea Barquero², Lucía Gandolfi Donadio³, Matías Ciarlantini³, Julieta Comin³, Guillermo Mazzolini¹, Juan Bayo¹

1. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Pilar, Buenos Aires, Argentina.; Programa de Hepatología Experimental y Terapia Génica
2. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), CONICET-Universidad de Buenos Aires, Ciudad Universitaria, Ciudad Autónoma de Buenos Aires, Argentina
3. Instituto Nacional de Tecnología Industrial (INTI), Av. General Paz 5445, San Martín Buenos Aires, Argentina; Departamento de Ingredientes Activos y Biorrefinerías
bbueloni-conicet@austral.edu.ar

Acute liver failure (ALF) is a life-threatening condition with limited treatment options, underscoring the need for novel therapeutic targets. RAC1, a Rho GTPase, regulates inflammation and oxidative stress, key drivers of ALF. We aimed to evaluate the therapeutic potential of RAC1 inhibition in ALF.

Transcriptomic datasets from HBV- and APAP-related ALF patients (GSE38941 and GSE80751) were analyzed. The RAC1 inhibitor 1D-142 was tested in three murine ALF models (ConA, APAP, D-Gal/LPS) and on primary cultures and cell lines. RNA-seq from murine livers were correlated with human datasets. Immune infiltration, reactive oxygen species, cytokine profiling, NF- κ B activation and apoptosis were evaluated by flow cytometry, qPCR, immunofluorescence and caspase activity assay. Human liver explants were treated ex vivo with 1D-142.

Bioinformatic analyses identified RAC1 as an upstream regulator in human ALF, associated with inflammation,

oxidative stress, and cell death. In murine models, 1D-142 reduced liver damage, even when administered at advanced stages. Mechanistically, 1D-142 mitigated ROS production in hepatocytes, immune cell infiltration and cytokine production. It also reprogrammed macrophages toward an anti-inflammatory phenotype while reducing their migration and viability and directly protected hepatocytes from apoptosis. Liver transcriptomics revealed that 1D-142 modulates RAC1-driven transcriptional programs dysregulated in human ALF and restored hepatocyte metabolic pathways. In human explants, 1D-142 decreased transaminase release and modulated cytokine expression.

This study identifies RAC1 as a central regulator of inflammation and oxidative stress in ALF. Its pharmacological inhibition provides hepatoprotection across preclinical models and human liver explants, highlighting RAC1 as a promising therapeutic target with translational potential.

THYROID HORMONES CONTRIBUTE TO JAK/STAT PATHWAY ABNORMAL ACTIVATION, PROMOTING T-CELL LYMPHOMA DISSEMINATION

María Mercedes Debernardi¹, Lucero Alvarado¹, Alejandro Correa², María Victoria Revuelta³, Helena Sterle¹, Gonzalo Gonzalez¹, María Teresa García de Dávila⁴, Johanna Abigail Díaz Albuja¹, Alejandra Paulazo¹, Florencia Menay¹, Cynthia Rosembli¹, Leandro Cerchietti³, Graciela Cremaschi¹, Florencia Cayrol¹

1. Instituto de Investigaciones Biomédicas (BIOMED-UCA-CONICET); Laboratorio de Neuroinmunomodulación y Oncología molecular
2. Instituto Carlos Chagas; Laboratorio de biología básica de células madre
3. Weill Cornell Medicine; Hematology and Oncology Division
4. Hospital Británico; Departamento de Patología
debernardimercedes@gmail.com

Abnormal JAK/STAT pathway activation is widespread in virtually all T-cell lymphoma (TCL) subtypes. However,

er, activating mutations are insufficient to drive leukemic cell proliferation, which also requires enhanced upstream signaling. We have described that thyroid hormones (THs) contribute to the malignant phenotype of TCL by inducing intracellular transcriptional programs through integrin $\alpha v \beta 3$ activation. Here, we evaluate the effect of THs on the JAK/STAT pathway and its implications on TCL therapy. We found that THs induce the activation of STAT1, 3, and 5, including the upregulation of target genes and metalloprotease activity. Furthermore, we observed that the integrin $\alpha v \beta 3$ inhibitor, cilengitide, not only reverts these effects but also enhances the anti-lymphoma activity to a greater extent than the JAK1/2 inhibitor, ruxolitinib, when combined with bexarotene, a synthetic retinoid clinically used for cutaneous TCL treatment. Furthermore, we explored the mechanisms of

action of cilengitide and bexarotene combination using preclinical TCL in vivo models and proteomic analysis. We found that this combinatorial protocol significantly reduced tumor STATs phosphorylation, matrix metalloproteinase activity, and the number of metastatic foci by regulating proteins involved in cell proliferation, angiogenesis, metabolism, and immune response. In addition, we observed that high integrin $\alpha v \beta 3$ messenger RNA levels are enriched in pathways associated with lymphoma progression and reduce overall survival in samples from patients with TCL. Our findings support the therapeutic potential of targeting THs signaling through integrin $\alpha v \beta 3$ inhibition in combination with bexarotene as a less toxic therapeutic strategy to mitigate aberrant JAK/STAT activation and limit lymphoma dissemination.

HYDROGEL-BASED DRESSING FOR SUSTAINED RELEASE OF MESENCHYMAL STEM CELL-DERIVED EXOSOMES IN WOUND HEALING

Mikele Amondarain¹, Ailén Iribarne^{1,2}, María Belén Palma^{1,2}, Luciano Jorge Melli³, Lucía N. Moro¹, Gustavo Sevlever¹, Santiago G. Miriuka¹, Marcela García², José Luis Pedraz³, Carlos Luzzani⁴

1. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN).

2. Cátedra de Citología, Histología y Embriología, FCM, UNLP.

3. Instituto de Investigaciones Biotecnológicas IIBIO-UNSAM, Argentina.; IIBIO

3. Grupo NanoBioCel, Laboratorio de Farmacia, Facultad de Farmacia, Universidad del País Vasco (UPV/EHU), Vitoria-Gasteiz, España. Centro de Investigación Biomédica en Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Instituto de Salud Carlos III, Madrid, España.; Laboratorio de Farmacia, Facultad de Farmacia, Universidad del País Vasco (UPV/EHU), Vitoria-Gasteiz, España.

4. Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI).; Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN).
amondarain.m@gmail.com

Chronic wounds remain an unsolved clinical challenge, often resistant to current therapies and leading to prolonged suffering, infections, and increased healthcare costs. Mesenchymal stem cell (MSC)-derived exosomes have emerged as promising regenerative agents, but their therapeutic use is hindered by rapid clearance and instability. We developed a novel hydrogel-based dressing engineered for the sustained release of human MSC-derived exosomes. Exosomes were isolated, comprehensively characterized by nanoparticle tracking analysis, TEM, and lyophilized to ensure long-term stability. In vitro, exosome-loaded hydrogels promoted fibroblast and keratinocyte proliferation and significantly accelerated wound closure in scratch assays. Live/Dead staining confirmed excellent biocompatibility, while XTT assays demonstrated enhanced metabolic activity. Migration assays showed increased fibroblast motility, and qPCR revealed upregulation of collagen I and elastin, confirming a pro-regenera-

tive transcriptional profile. Importantly, microscopy demonstrated gradual and continuous uptake of exosomes from the hydrogel reservoir.

In vivo, in a murine full-thickness dermal wound model, application of exosome-loaded hydrogels resulted in faster wound closure compared with untreated and hydrogel-only controls. Histological analysis revealed improved re-epithelialization, enhanced angiogenesis, and reduced scar formation, supporting both regenerative and functional repair.

By combining stability, biocompatibility, and controlled release, this platform provides an “off-the-shelf” advanced therapy with strong translational potential for both acute and chronic wounds. Our findings highlight the unique ability of lyophilized MSC-derived exosomes embedded in a hydrogel matrix to promote efficient, scar-free healing, offering a disruptive, accessible, and patient-friendly alternative to current treatments.

UNVEILING THE ROLE OF AGE IN MASLD PROGRESSION AND BIOLOGICAL PROCESS ACTIVATION

Lucía Lameroli Mauriz^{1,2}, Andrea Scelza^{1,3}, Miranda Orellano^{1,3}, Brian Martínez Ruiz^{1,2}, Juan Bayo^{1,2}, Esteban Fiore^{1,2}, María Jose Cantero^{1,2}, Barbara Bueloni^{1,2}, Mailin Casadei^{1,2}, Guillermo Mazzolini^{1,2}, Catalina Atorrasagasti^{1,2}

1. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Universidad Austral;

2. Programa de Hepatología Experimental y Terapia Génica

3. Laboratorio de Inmuno-endocrinología, Diabetes & Metabolismo

llameroli-iimt@austral.edu.ar

Although age is a known risk factor for the severity and progression of Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD), its contribution to liver injury and molecular alterations remains poorly understood. Current animal models fail to fully recapitulate the clinical setting, as aging is often overlooked. This study investigates age-dependent differences in MASLD progression and benchmarks our model against others through integrative bioinformatic analyses.

Young (2-month-old, Y) and middle-aged (10-month-old, MA) male C57BL/6N mice were fed chow (CD) or high-fat diet (HFD) for 20 weeks. Metabolic and biochemical parameters were measured, and liver tissue analyzed by histology and RNAseq. Differentially expressed genes were identified followed by GO enrichment. We reanalyzed data from 39 models and computed the MASLD Human Proximity Score (MHPS), ranking models by transcriptomic, phenotypic, and histopathologic similarity

to human disease.

MA mice developed insulin resistance and more severe hepatic injury than Y mice after HFD, with elevated transaminases. HFD increased cholesterol. NAFLD activity scores indicated greater liver injury in MA animals. Histologically, MA-HFD mice displayed broader lipid droplet distribution, hepatocellular hypertrophy, inflammation, and fibrosis. Transcriptomic analysis revealed diet- and age-specific responses: Y-HFD mice upregulated angiogenesis and ECM genes, while MA-HFD mice upregulated inflammatory pathways and downregulated energy metabolism, including ATP processes, suggesting impaired energy homeostasis. Comparative MHPS analysis ranked the MA-HFD model among the closest to human MASLD and higher than Y-HFD, highlighting metabolic relevance and translational value.

These findings identify age as a critical modifier of liver injury, providing a more faithful preclinical MASLD model.

SAIC AWARD - IRENE FARYNA Y ROBERTO RAVEGLIA - ONCOLOGY

Wednesday 19th November 2025 - 15:00 - 16:30 - Auditorio

Jury: Vanina Medina, Martin Monte, Gabriel Fiszman, Estefania Labanca

MODULATION OF CARBONIC ANHYDRASE IX AND HYPOXIA-INDUCED METABOLIC AND IMMUNE DYSREGULATION IN TUMOR MICROENVIRONMENT: A PATH TOWARDS MORE EFFECTIVE IMMUNOTHERAPY FOR LUNG CANCER

Mariel Alejandra Fusco¹, Carlos Rafael Picón², Marco Aurelio Díaz Gutierrez¹, Juan Miguel Bayo Fina¹, Constanza Arriola Benitez¹, Flavia Piccioni¹, María Florencia Mercogliano³, Noelia Gomez¹, Mara Stinco¹, Nicolás Minatta², Ricardo Amorín², Manglio Miguel Rizzo², Mariana Malvicini¹

1. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Av. Presidente Perón 1500 (B1629ODT) Derqui-Pilar, Buenos Aires, Argentina

2. Hospital Universitario Austral, Av. Presidente Perón 1500, Pilar, Buenos Aires, Argentina; Servicio de Oncología

3. Instituto de Biología y Medicina Experimental (IBYME) - CONICET, Vuelta de Obligado 2490, CABA, Buenos Aires, Argentina.; Laboratorio de Inmunología Tumoral
marief.fusco@outlook.com

Immunotherapy using checkpoint inhibitors (ICIs) has transformed the treatment of advanced non-small cell lung cancer (NSCLC); however, poor response rates and the development of resistance remain significant clinical challenges. A prominent resistance mechanism is the hypoxic tumor microenvironment (TME), that promotes the expression of carbonic anhydrase IX (CAIX) facilitating an acidic, lactate-rich TME, which is highly immunosuppressive. Analysis of public datasets revealed that high CAIX expression is associated with reduced median survival in lung cancer patients ($p < 0.001$). Furthermore, CAIX expression strongly correlated with HIF-1 α , PD-L1, Foxp3, LAG-3 and TGF β supporting a link between hypoxia-driven metabolic alterations and immune suppression in the TME. Preliminary analysis of a local cohort ($n=34$) treated with immunotherapy indicated that patients with a high glycolytic/hypoxic TME exhibited less clinical benefit. We evaluated metabolic reprogramming induced by

hypoxia and its impact on immune cell function, and the potential of a CAIX inhibitor (4Mu) to reverse these effects. Exposure of lung cancer cells to hypoxia increased mRNA of CAIX and lactate transporter, enhanced lactate levels, and reduced extracellular pH. These metabolic shifts were accompanied by the induction of an M2 profile in macrophages and impaired antigen-specific splenocyte proliferation ($p < 0.01$). 4Mu downregulated CAIX, restored extracellular pH, decreased lactate secretion, and rescued lymphocyte proliferative capacity ($p < 0.01$). In vivo, 4Mu reduced CAIX expression, mitigated the anti-inflammatory macrophage profile, and enhanced T-cell infiltration. The combination of 4Mu with ICI therapy synergistically inhibited tumor growth and significantly increased immune infiltration, providing evidence for the therapeutic potential of combination to improve immunotherapy efficacy.

THERAPEUTIC INHIBITION OF FOXP3: A DUAL-FUNCTION MOLECULE IN PEDIATRIC GLIOMA

Matias Garcia Fallit^{1,2}, Jorge A. Peña Agudelo^{1,2}, Nazareno Gonzalez^{1,2}, Melanie Pérez Küper^{1,2}, Yamila Zampini^{1,2}, Alejandro J. Nicola Candia^{1,2}, Maicol Suarez Velandia^{1,2}, Bautista Gattelet^{1,2}, Joel Szczerba^{1,2}, Sergio Caraballo Hurtado^{1,2}, Ana

Clara Romero¹, Cristian Sobarzo¹, Ivana Sánchez Rojas¹, Hebe Durán^{2,4}, Marina Perona^{2,4}, Emilio de Simone⁵, Carla Giampaoli⁶, Carla Caruso¹, Alexis Descourvieres^{3,6}, Flavia Zanetti⁷, Noelia Casares⁸, Teresa Lozano⁸, Juan José Lasarte⁸, Guillermo Videla Richardson⁹, Marta M. Alonso⁸, Marianela Candolfi^{1,2}

1. Instituto de Investigaciones Biomédicas (INBIOMED, CONICET-UBA), Facultad de Medicina, Universidad de Buenos Aires, Argentina;

2. Consorcio de Referencia en Investigación Oncopediátrica (CRIO);

3. Departamento de Fisiología, Biología Molecular y Celular, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Argentina;

4. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina

5. Cátedra de Fisiología Animal, Facultad de Ciencias Veterinarias, Universidad de Buenos Aires, Argentina; Lab. de Diagnóstico de Metabolismo Óseo y Mineral

6. Alianza Argentina de Pacientes (ALAPA); ALAPA

7. Instituto César Milstein (CONICET); Lab. Fitopatología y Parasitología Molecular

8. Programa de inmunología e inmunoterapia, Centro de Investigación Médica Aplicada (CIMA, CCUN), Pamplona, España; Instituto de Investigación Sanitaria de Navarra (IDISNA);

9. Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI), Buenos Aires, Argentina.; Lab. de Investigación Aplicada a Neurociencias (LIAN)

mati.garciafallit@gmail.com

Pediatric diffuse gliomas are considered rare diseases (60 cases/year in Argentina), but due to its dismal prognosis they represent the leading cause of cancer-related death in children. The transcription factor Forkhead Box Protein P3 (FOXP3) constitutes a promising target to inhibit regulatory T cell-mediated immunosuppression and has also been detected in tumor cells. In this study, we explored the expression and function of FOXP3 in experimental pediatric gliomas. We found that FOXP3 is overexpressed in high-grade gliomas (pHGG) compared to low-grade gliomas (pLGG), and significantly correlates with immunosuppressive and epithelial-mesenchymal transition markers, particularly in pHGG. We detected FOXP3 in pediatric glioma biopsies and cell cultures, and upregulation was observed following chemo-radiotherapy ($p < 0.05$). Inhibition of FOXP3 nuclear translocation using a cell penetrating peptide (P60) boosted

lymphocytic activation and reduced pHGG cell viability, decreased the expression of invasion-associated proteins, and enhanced chemo-radiosensitivity. To improve the local bioavailability of P60, we used two strategies: (i) a cyclic variant of the peptide (CM1315), which displayed greater stability and efficiency at inhibiting FOXP3 than P60 in vitro and (ii) an adenovector encoding the P60 peptide (Ad.P60). This vector efficiently transduced pediatric glioma cells and decreased both cell viability and resistance to several chemotherapeutic drugs ($p < 0.05$). In prepubertal mice treated with an intracerebral injection of Ad.P60, no signs of neurotoxicity were observed in the brain parenchyma. Our results indicate that FOXP3 exerts intrinsic pro-tumoral effects in pediatric glioma, and its local inhibition could enhance the treatment of these devastating tumors.

REPURPOSING HEMOSTATIC DRUG DESMOPRESSIN AS A COADJUVANT THERAPEUTIC STRATEGY IN OSTEOSARCOMA: IMPACT ON TUMOR AGGRESSIVENESS AND COMBINATIONAL BENEFITS WITH ANTIANGIOGENIC AGENT BEVACIZUMAB

Luisina M. Solernó¹, Candela Llavona², Zahira Y. Saud², Mariana Onassis³, M. Florencia Gottardo¹, Martín Ledesma², Daniel F. Alonso¹, Juan Garona²

1. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional (COMTra)

2. Hospital de Alta Complejidad El Cruce; Unidad de Investigaciones Biomédicas en Cáncer (IBioCan), Centro de Medicina Traslacional (CEMET)

3. Hospital Interzonal de niños "Eva Perón"
lusolerno@gmail.com

Osteosarcoma (OSA) is known for its elevated mortality rates, early metastasis, and poor response to chemotherapy and targeted therapies like bevacizumab (BEVA). Desmopressin (dDAVP), a drug commonly used for hemostasis, has been repurposed for cancer treatment by targeting AVPR2 receptor on endothelial and tumor cells. However, its therapeutic activity in OSA remains unknown.

The main objective was to develop a coadjuvant strategy focused on dDAVP repositioning to increase the efficacy of anti-VEGFA mAb BEVA in OSA. In vitro, bioinformatic, and in vivo methods were used across human (MG-63/

U2-OS) and murine (K7M3) OSA models, and microvascular cell lines (HMVEC-L/HMEC-1).

Bioinformatic analysis showed a negative correlation between AVPR2 expression and proliferation, metastasis, and angiogenesis markers. High levels of AVPR2 were linked to better survival rates (TCGA-SARC-n=256, and TARGET-OSA-n=89, RNA-Seq databases). In vitro, dDAVP induced AVPR2-dependent cytostatic mechanisms, reducing OSA growth, mitosis, and chemotaxis, while promoting apoptosis. It showed a strong anti-angiogenic effect, impairing migration, tube morphogenesis, and growth of vascular endothelial cells, particularly

when combined with BEVA on cultures incubated with OSA-conditioned medium. In animal models, dDAVP treatment (12µg/kg-i.v., three times/week) significantly reduced tumor growth, lung metastasis and early angiogenesis. Its concomitant combination with BEVA (5mg/kg-i.p., two times/week) inhibited OSA growth, enhancing the efficacy of BEVA alone, and aggressiveness markers

like mitotic index, desmoplasia, vimentin expression and tumor necrosis. Results were significant at $p < 0.05$ (t test/ANOVA).

These results support the potential clinical translation of dDAVP as a promising, cost-effective, and adjuvant therapeutic strategy for OSA, particularly in combination with BEVA.

INTERPLAY BETWEEN THE ANDROGEN RECEPTOR AND ACSL4 AS THERAPEUTIC TARGETS IN BREAST CANCER

Melina Andrea Dattilo¹, Paula Fernanda Lopez¹, Yanina Benzo¹, M. Mercedes Bigi¹, Adrián Mansini², Luke Hoeppner³, Cristina Paz¹, Ernesto J. Podestá¹, Paula Mariana Maloberti¹

1. Universidad de Buenos Aires, Facultad de Medicina. Departamento de Bioquímica Humana. Buenos Aires, Argentina; CONICET - Universidad de Buenos Aires. Instituto de Investigaciones Biomédicas (INBIOMED).; Laboratorio de Regulación del Ácido Araquidónico y Señalización Celular

2. Rush University, Department of dermatology. IL, USA.

3. University of Minnesota, The Hormel Institute, MN, USA.

mdattilo@fmed.uba.ar

Acyl-CoA synthetase 4 (ACSL4) contributes to the progression of aggressive tumors, including breast cancer, where its overexpression is linked to poor prognosis. In triple-negative breast cancer (TNBC), which lacks estrogen and progesterone receptors and exhibits normal HER2 expression, the androgen receptor (AR) has emerged as a therapeutic target in the AR-positive subset. However, effective treatment options remain scarce for AR-negative TNBC. This study investigated the reciprocal regulation between ACSL4 and AR and evaluated whether their combined targeting could provide a novel therapeutic approach in breast cancer. In MDA-MB-231 cells, AR overexpression reduced ACSL4 promoter activity, mRNA, and protein levels. In MCF-7 cells dihydrotestosterone treatment decreased ACSL4 promoter activity, while the AR antagonist bicalutamide (BICA) increased it. Site-directed mutagenesis of the AR element

further confirmed this regulatory mechanism. Moreover, ACSL4 overexpression in MCF-7 TetOff/ACSL4 cells diminished AR expression, whereas silencing ACSL4 in MDA-MB-231 restored AR levels. ACSL4 inhibition with PRGL493 also enhanced AR expression in MDA-MB-231 and BT-20 cells. Building on this, we hypothesized that ACSL4 inhibition could restore AR expression and sensitize AR-negative TNBC to antiandrogen therapy. Consistently, the combination of PRGL493 and BICA produced a synergistic reduction in cell proliferation, migration, and invasion in MDA-MB-231 cells. This effect was validated in vivo using zebrafish xenografts, where dual treatment was more effective in inhibiting tumor extravasation than either drug alone. Together, these findings reveal a reciprocal regulation between ACSL4 and AR highlighting dual inhibition as a promising therapeutic strategy in breast cancer.

DECIPHERING THE ROLE OF PROGESTERONE RECEPTOR ISOFORMS IN BREAST CANCER PROGNOSIS AND TREATMENT

Leo Saldain¹, Lucas Lemos¹, Andrés Elia¹, Luisa Ambrosio¹, Gabriela Pataccini¹, María Florencia Abascal¹, Caroline Lamb¹, Silvia Inés Vanzulli¹, Karin Villar², Javier Burruchaga², Florencia Torres², Martín C Abba³, Claudia Lanari¹, Paola Rojas¹

1. IBYME; Carcinogénesis Hormonal

2. Hospital de Agudos "Magdalena V de Martínez"; Oncología

3. Universidad de La Plata; CINIBA

leosaldain@gmail.com

Luminal breast carcinomas with predominance of progesterone receptor isoform A (PRA) over isoform B (PRB; PRA-H) may benefit from antiprogesterin therapy. PRA-H tumors are less proliferative but more metastatic than PRB-H tumors (PRB>PRA). We aimed to clarify the prognostic and therapeutic implications of the PR isoform ratio. Using the mifepristone-sensitive PRA-H murine C7-2-HI carcinoma and two PRB-H variants (C7-HI, C7-2-HIR), we evaluated survival after tumor removal under IACUC-approved criteria. Median overall survival (OS) was 92 days (C7-2-HIR), 212 days (C7-2-HI), and

>300 days (C7-HI) ($p < 0.01$). Exome and RNA-Seq analyses confirmed enrichment of proliferative pathways in PRB-H tumors and metastatic pathways in PRA-H tumors. In a patient cohort (33 PRA-H, 16 PRB-H; primary tumors ≤ 15 mm²), lymph node metastases were more frequent in PRA-H. However, PRB-H patients exhibited significantly worse OS (115 vs 186 months, $p < 0.0065$) and DFS (87 vs undefined months, $p < 0.0001$). We are generating metastatic engineered cell line models to further test mifepristone combinations. In T47D-PRA cells, which readily produced lung metastases, tamoxifen plus

mifepristone enhanced growth inhibition ($p < 0.01$), consistent with trends observed in ex vivo cultures from three PRA-H patients. These findings suggest that mifepristone may improve tamoxifen efficacy in this subgroup. In conclusion, despite their greater metastatic potential,

PRA-H tumors are associated with better prognosis than PRB-H tumors. The paradoxical observation that PRB-H patients had poorer DFS even when lymph node-negative suggests differences in metastatic patterns and/or reduced sensitivity to endocrine therapy.

WILDE ASSOCIATION / GENETIC COUNSELING AWARD: HUMAN GENETICS

Wednesday 19th November 2025 - 17:00 - 18:30 – Auditorio

Jury: Maria Sol Ruiz, Carlos David Bruque, Viviana Dalamon, Rita Vazdez

CYTOGENETIC AND CYTOGENOMIC APPROACH TO PATIENTS WITH NEURODEVELOPMENTAL DISORDERS (NDDs): IDENTIFICATION AND CHARACTERIZATION OF CHROMOSOMAL ABNORMALITIES

Ana Goussies, Candela Ruiz, Cynthia Bravo, Andrea Rodríguez, Alexis Aranda, Tania Castro, Aldana Claps, Carolina Dellamea, Pablo Dellamea, Lilian Franzi, Fabiana Guerrisi, Paola Jablonski, Julieta Laiseca, Beatriz Ledesma, María Ester Mollica, Wanda Montes, Claudina Picon, Melisa Taboas, Evelyn Torchinsky, Roxana Cerretini

Centro Nacional de Genética Médica (CENAGEM), ANLIS "Dr. Carlos Malbrán", Ministerio de Salud de la Nación, Buenos Aires. Argentina; Departamento de diagnóstico genético

anagoussies@yahoo.com

Neurodevelopmental disorders (NDDs) comprise a heterogeneous group of conditions affecting communication, learning, behavior, and motor control. Intellectual disability (ID) is a major public health challenge in Latin America, with prevalence above 10%¹. We aimed to achieve the frequency of chromosome abnormalities in NDD patients. We conducted a retrospective study of patients referring to the CENAGEM, between January 2021 and July 2025. A total of 1,976 cytogenetic analyses were performed, and 17.8% showed pathogenic findings. 79 individuals with NDDs were analyzed: 43 with global developmental delay, 23 ID, and 13 multiple congenital anomalies. Patients with Down syndrome were excluded.

Cytogenetic studies were performed on peripheral blood lymphocyte cultures using GTW banding. To enhance resolution, molecular techniques were applied: FISH (29%),

MLPA (13%), array-CGH (14%), and SKY (5%). Structural abnormalities accounted for 55% of cases, numerical abnormalities for 42%, non-identified markers for 3%, and mosaicism for 17%. The most frequent alterations were deletions (16%), unbalanced translocations (12%), and pseudo-isodicentric chromosomes (7%). Additional findings included duplications, inversions, Robertsonian and balanced translocations, rings, isochromosomes, X monosomy, X tetrasomy, and mosaic tetraploidy.

Our results underscore the importance of combining classical cytogenetics with high-resolution molecular techniques to improve diagnostic yield, refine recurrence risk estimates, and strengthen counseling. Early etiological diagnosis enables tailored interventions and informs public health strategies. Complementary techniques allowed 27 cases to be resolved, with a diagnostic yield of 34%.

MODELING ARRHYTHMOGENIC CARDIOMYOPATHY WITH AN ISOGENIC IPSC PLATFORM: RESOLVING THE PATHOGENICITY OF A VARIANT OF UNCERTAIN SIGNIFICANCE

Guadalupe Amin, Mateo Lacava, Constanza Confinio Malecki, Sheila Lucia Castañeda, Federico Zabalegui, Joaquin Smucler, Ariel Waisman, Lucia Natalia Moro

Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

guadalupeamin06@gmail.com

Pathogenic variants in desmosomal genes cause arrhythmogenic cardiomyopathy (ACM), characterized by fibrofatty replacement and arrhythmias; PKP2 accounts for ~20–45% of cases and PKG for ~1–3%. iPSCs and CRISPR/Cas9 enable isogenic, human iPSC-CM models, to interrogate disease mechanisms. We hypothesized that CRISPR/Cas9 introduction of PKP2/PKG mutations into iPSCs would enable the creation of cellular models that recapitulate ACM phenotypes and facilitate variant classification. The objective of this work is to model ACM in vitro through the generation of iPSC lines carrying variants associated with ACM, and their differentiation into cardiomyocytes.

We generated three iPSC lines: PKG-knockout (PKG-KO), PKP2-knockout (PKP2-KO), and a PKP2 missense VUS (p.S140F). After differentiation into contractile, metabolically matured ventricular iPSC-CMs, we profiled intercalated-disc proteins and cytoskeletal alignment. PKG-KO iPSC-CMs showed increased PKP2 with decreased DSP and N-cadherin; PKP2-KO lacked DSP and displayed disorganized N-cadherin. Quantitative image analysis revealed impaired actin alignment in both knockout line versus wild type, consistent with intercalated-disc disruption. PKP2-KO and PKP2-S140F showed altered expression of des-

mosomal and junctional genes, and contractibility. Under a 7-day pro-adipogenic medium exposition, Oil Red O quantification indicated higher neutral-lipid accumulation in PKP2-S140F and PKP2-KO than in wild type. These results validate an isogenic human platform for ACM modeling: knockout lines recapitulate junctional and

structural defects, and the PKP2-S140F VUS exhibits adipogenic and junctional abnormalities consistent with deleterious impact. The platform enables functional evaluation of variants of uncertain significance at scale and supports discovery of pathogenic mechanisms and development of targeted strategies for ACM.

IDENTIFICATION OF NOVEL HUB GENES IMPLICATED IN THE PHISIOPATHOLOGY OF MYELOYD- PLASTIC SYNDROMES (MDS) AND SF3B1 VARIANTS

Marco Lincango¹, Jacqueline González², Alicia Enrico³, María Jazmín Toloza¹, Noemí Pintos⁴, Agustina Fiorito¹, Luis Cinarra⁵, Carlos Fondevila⁶, Miguel González⁷, Marcelo Iastrebnier⁸, Jorge Arbelbide⁹, Graciela Salinas¹⁰, Hugo Ferro¹¹, Inés Engelberger⁹, Irene Larripa¹, Carolina Belli¹

1. Instituto de Medicina Experimental (IMEX-CONICET)/ Academia Nacional de Medicina; Laboratorio de Genética Hematológica

2. Hospital General de Agudos Carlos Durand

3. Hospital Italiano La Plata

4. Sanatorio Dr. Julio Méndez

5. Sanatorio Integrado de la Ciudad S.A.

6. Clínica Bazterrica

7. Instituto de Investigaciones Hematológica (IIHEMA)/ Academia Nacional de Medicina; IIHEMA

8. Sanatorio Sagrado Corazón

9. Hospital Italiano Buenos Aires

10. Rhesus Hematología Clínica S.A.

11. Consultorios Hematológicos S.R.L.

lincango_marco@hotmail.com

MDS with splicing factor SF3B1 mutations represent a distinct subtype characterized by the presence of ring sideroblasts. These variants promote aberrant 3' splice site usage, compromising biological processes. However, the precise molecular mechanisms linking SF3B1 mutations to disease pathogenesis remain incompletely defined. We analyzed public RNA-seq datasets (GSE114922, GSE128429, GSE132836) to identify differentially expressed genes (DEGs) and alternative splicing events in SF3B1mut patients. Both approaches were validated experimentally in 97 samples from MDS patients (SF3B1mut and SF3B1wt, also SRSF2 and U2AF1-wt) and healthy controls (HC). A set of 1342 DGEs were identified in SF3B1mut. Our pipeline allowed to select and validate the hub genes set: MRRF, NDUFA8, GAR1, RBM25, and ACD as strong predictors of SF3B1 status. From 1269 individualized aberrant splicing events, we confirmed those previously described of OXA1L, TMEM14C, and

a novel event in WRN. The integration of the transcriptomic and splicing profiles in non-supervised analyses clustered SF3B1mut among MDS and differentiate them from HC (explained variance= 62%). Also revealed negative correlations between aberrant splicing events, impairing mitochondrial function, and the expression levels of key genes related with genomic instability and apoptosis. Our findings reveal a parallel interplay between alternative splicing and gene expression regulation, highlighting the dysregulation of key hub genes driving oxidative stress (NDUFA8), impaired mitochondrial function (MRRF, TMEM14C, OXA1L), increased apoptosis and inflammasome activation (RBM25), as well as genomic instability and telomere maintenance (WRN, ACD, GAR1). These findings highlight new players that may provide substantial clues in the physiopathology of MDS with variants in SF3B1.

SAIC AWARD - FUNDACIÓN BIGAND - MULTIDISCIPLINARY CALL FOR YOUNG INVESTIGATORS

Thursday 20th November 2025 - 9:00 - 10:30 - Auditorio

Jury: Elba Vazquez, Juan Garona, Eduardo Canepa, Clara Patricia Setton, Ana Sahores

GUT MICROBIOME SIGNATURE IN COLORECTAL CANCER: IDENTIFICATION OF TAXONOMIC AND FUNCTIONAL BIOMARKERS WITH POTENTIAL FOR EARLY DETECTION AND TARGETED THERAPIES IN AN ARGENTINE PATIENT COHORT

Florencia Adriana Lohmann¹, Lucía Manuela Herrera¹, Fabiana Alejandra Ferro², Juan Pablo Santino², Laura Raquel Soto¹, Andrea Romina Cajal¹, Hernán García Rivello², Marcela Alejandra Martínez von Scheidt², Walter Hernán Pavicic¹, Carlos Alberto Vaccaro², Tamara Alejandra Piñero¹

1. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB), Hospital Italiano de Buenos Aires (HIBA) - Universidad del Hospital Italiano de Buenos Aires (UHIBA) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina.

2. Hospital Italiano de Buenos Aires, Argentina.

florencia.lohmann@hospitalitaliano.org.ar

Colorectal cancer (CRC) is a multifactorial disease in which the gut microbiota modulates carcinogenesis through interactions with genetic, environmental, and physiological factors influencing tumor onset and progression. Taxonomic and functional profiling of the microbiome in sporadic CRC may reveal microbial signatures with diagnostic, prognostic, and therapeutic value. To address this, we conducted the characterization of the gut microbiome in an Argentinian cohort comprising 109 CRC patients and 117 matched controls integrating clinical and epidemiological data to identify microbial biomarkers for targeted interventions. Fecal samples underwent 16S rRNA V4-region sequencing. Microbial composition, functional profiles, and co-occurrence networks were explored. Random Forest (RF) classifier was trained using nine variables, optimized by cross-validation, and evaluated for performance metrics and feature importance. Alpha and beta diversity showed no significant group-level differences, suggesting greater

interindividual variability. CRC samples exhibited higher abundances of *Fusobacterium*, *Escherichia-Shigella*, and *Alistipes*. CRC-associated metabolic pathways favored L-valine degradation, de novo purine synthesis, and a modified tricarboxylic acid cycle (TCA), supporting tumor proliferation, whereas controls exhibited pathways linked to intestinal homeostasis and short-chain fatty acid (SCFAs) production. Co-occurrence networks highlighted proinflammatory microbial interactions in CRC. A RF classifier achieved an average AUC=0.867, identifying age and *Parasutterella excrementihominis*, *Bacteroides coprocola*, *Varibaculum timonense*, *Alistipes obesi*, *Blautia glucerasea*, *Butyrivibrio paravirosa*, *Bacteroides barnesi* and *Ruminococcus callidus*, suggesting microbiome profiles as potential biomarkers for patient classification and CRC progression. As the first comprehensive gut microbiome analysis in Argentine CRC patients, this investigation lays the groundwork for regionally tailored translational research and precision medicine strategies.

IGF-1-ENRICHED EXTRACELLULAR VESICLES ORCHESTRATE HEPATOCYTE PROLIFERATION AND IMMUNE REPROGRAMMING TO RESTORE LIVER REGENERATIVE CAPACITY AFTER RESECTION, EVEN IN FIBROTIC LIVERS

Mailín Casadei¹, María José Cantero¹, Bárbara Bueloni¹, Fátima Huamán¹, Lucía Lameroli¹, Natalia Pacienza², Catalina Atorrasagasti¹, Juan Bayo¹, Guillermo Mazzolini¹, Esteban Fiore¹

1. Instituto de Investigaciones en Medicina Traslacional (IIMT), Universidad Austral CONICET, Buenos Aires, Argentina.; Programa de Hepatología Experimental y Terapia Génica

2. Universidad Favaloro-CONICET, Buenos Aires, Argentina; Instituto de Medicina Traslacional, Trasplante y Bioingeniería (IMeTyB),

mcasadei50@gmail.com

Background: Impaired regeneration after liver resection may lead to liver failure, a risk exacerbated in fibrosis. Extracellular vesicles (EV) from mesenchymal stem cells (MSC) reproduce their immunomodulatory and regenerative properties, representing a promising cell-free therapy. We previously showed that MSCs from human umbilical cord (HUCPVC), engineered to express insulin-like growth factor I (IGF-1), act via EV carrying IGF-1. **Aim:** to evaluate the effect of IGF-1-carrying EV on liver regeneration in partial hepatectomy (PH) models of healthy and fibrotic livers. **Methods:** EV were isolated from HUCPVC transduced with adenoviruses encoding GFP (GFP-EV) or IGF-1 (IGF-1-EV). Adult C57BL/6 mice underwent 66% PH and received saline, GFP-EV, or IGF-1-EV (50 µg, i.v.). At 36h and 72h, liver tissue, hepatocytes, and macrophages were analyzed. Regeneration was assessed by liver index (LI), liver regeneration rate (LRR), PCNA immunostaining, and qPCR. Additional experi-

ments were performed in fibrotic mice subjected to PH. **Results:** At 36h post-PH, IGF-1-EV reduced ALT levels and increased PCNA+ hepatocytes, indicating an early proliferative response. By 72h, IGF-1-EV-treated mice showed significant increases in LI, LRR, and PCNA+ hepatocytes. Proliferative markers (cyclin D1, IGF-1, HGF) were upregulated at both time points. Inflammatory cytokines (TNFα, IL-1β, IL-6, iNOS) were reduced at 72h, while IL-10 and Arg1 increased. These effects were confirmed in vitro in isolated hepatocytes and macrophages. In fibrotic livers, IGF-1-EV enhanced regeneration and reduced fibrosis.

Conclusion: IGF-1-EV constitute a novel, cell-free therapy that enhances liver regeneration and modulates inflammation, offering potential benefit for patients with compromised regenerative capacity, including cirrhosis and small-for-size syndrome."

MANGANESE-INDUCED MITOCHONDRIAL DYSFUNCTION AND REMODELING OF ER-MITOCHONDRIA CONTACTS IN HIPPOCAMPAL NEURONS

Soledad Porte Alcon¹, Valentina Saud¹, Carlos Pomilio¹, Nicolás González Pérez¹, Melina Belloto¹, Melisa Bentivegna¹, Jessica Presa¹, Facundo Dallo¹, Martín Carrera¹, Juan Beauquis¹, Monica Kotler², Flavia Saravia¹

1. Departamento de Química Biológica, FCEN-UBA; Laboratorio de Neurobiología del Envejecimiento

2. Departamento de Química Biológica, FCEN-UBA, IQUIBICEN-CONICET; Laboratorio de Disfunción Celular en Enfermedades Neurodegenerativas y Nanomedicina

s.portealcon@gmail.com

Manganese (Mn) is a trace metal essential for brain function and development. However, excessive exposure represents a health risk due to long-term neurological effects. Mn accumulates in the brain, predominantly in the basal ganglia, leading to motor dysfunction. Affected individuals also exhibit memory loss and cognitive impairment, indicating that the hippocampus is an additional target of Mn neurotoxicity. At the cellular level, mitochondria are primary sites of Mn accumulation, where the metal impairs organelle dynamics, reduces energy production, and enhances the generation of reactive oxygen species (ROS). Although progress has been made in understanding Mn-induced neurodegeneration, the contribution of mitochondria–endoplasmic reticulum (ER) contact sites (MERCs) remains poorly defined. MERCs are specialized domains that regulate lipid metabolism, autophagy, and mitochondrial function, and their

remodeling has been linked to neurodegenerative disease. Here, we examined whether MERCs are altered in Mn-induced hippocampal damage, employing both in vitro and in vivo models of overexposure. In HT22 cells, Mn reduced viability, increased ROS, and promoted mitochondrial fragmentation. Treated cells also showed lipid droplet accumulation and impaired autophagic flux. Colocalization studies revealed enhanced ER-mitochondria contacts, associated with elevated expression of the tethering proteins VAPB and PTIP51. In vivo, intrastriatal Mn administration produced neuronal loss in the striatum and altered the cytoarchitecture of the CA1 hippocampal region, accompanied by higher VAPB and PTIP51 expression. Together, these results suggest that MERCs remodeling occurs during Mn exposure and may contribute to hippocampal vulnerability.

A NOVEL GENE THERAPY STRATEGY FOR TRIPLE-NEGATIVE BREAST CANCER: DIRECT AND IMMUNOMEDIATED EFFECTS OF FOXP3 BLOCKADE

Alejandro Nicola Candia¹, Nazareno Gonzalez¹, Matias García Fallit¹, Yamila Zampini¹, Melanie Pérez Küper¹, Jorge A. Peña Agudelo¹, Ana Clara Romero¹, Guillermo Videla Richardson², Sergio Caraballo¹, Maicol Suarez Velandia¹, Joel Szczerba¹, Emilio DeSimone³, Carla Giampaoli³, Alejandro Jorge Urtreger⁴, Laura Beatriz Todaro⁴, Juan José Lasarte⁵, Flavia Zanetti⁶, Marianela Candolfi¹

1. INBIOMED-UBA-FMED; Desarrollo de inmunoterapias contra el cáncer

2. Instituto Fleni

3. Instituto de Estudios de la Inmunidad Humoral "Prof. Ricardo A. Margni"

4. Instituto de Oncología "Angel H. Roffo"

5. Programa de inmunología e inmunoterapia, Centro de Investigación Médica Aplicada, Pamplona, España

6. Instituto César Milstein (CONICET)

alenicola90@gmail.com

FOXP3, a transcription factor essential for regulatory T cell (Treg) function, constitutes a promising target to reverse immunosuppression in cancer. FOXP3 is also expressed in tumor cells, but its intrinsic role is poorly understood. Our meta-analysis revealed that FOXP3 is upregulated in breast tumors, specially in triple-negative breast cancer. Single-cell sequencing revealed that FOXP3 is present in Tregs and TNBC cells. FOXP3 overexpression in TNBC correlated with immunosuppressive and EMT markers and worse survival. A positive feedback was found between FOXP3 and TGF- β expression in TNBC cells, and radiotherapy and chemotherapy further increased FOXP3 expression. Functional blockade with a cell penetrating peptide (P60) that inhibits FOXP3, elicited cytotoxicity and enhanced chemo-radio-resistance in TNBC cells. To improve delivery in vivo, we used an

adenoviral vector encoding P60 (Ad.P60), which inhibited tumor growth of EO771 tumors and decreased tumor Treg infiltration, without affecting the spleen. Ad.P60 significantly boosted the efficacy of dendritic cell (DC) vaccines in this tumor model, leading to 80% survival. To evaluate the immune-mediated effects of Ad.P60 ruling out its tumor intrinsic actions, we inoculated mice with a breast cancer cell line (LM38-LP) that lacks FOXP3. Local injection of Ad.P60 in combination with DC vaccines promoted tumor infiltration of CD8+IFN γ + T cells, but led to only 30% long-term survival. Our findings suggests that blockade of tumor intrinsic and immune-mediated effects of FOXP3 with Ad.P60 could constitute a promising therapeutic approach to combine with immunotherapy and standard therapy to improve the treatment of TNBC.

HIGH-RESOLUTION LIVE IMAGING OF CYTOPLASMIC AND STORE-DERIVED CALCIUM DYNAMICS UNCOVERS OSCILLATORY REGULATION AND COORDINATED STORE-ENTRY MECHANISMS IN MOUSE SPERM ACROSOMAL EXOCYTOSIS

Martina Griguoli¹, Sebastián Manikis¹, Gustavo Scanavachi², David Torres Hernández³, Mariano G. Buffone¹, Ana Romarowski¹

1. Instituto de Biología y Medicina Experimental (IBYME-CONICET), Buenos Aires, Argentina; Biología Celular y Molecular de la Reproducción

2. Harvard Medical School, Boston, MA, USA; Kirchhausen Lab

3. Instituto de Biotecnología, Universidad Nacional Autónoma de México (UNAM), Cuernavaca, Morelos, México; Laboratorio Nacional de Microscopía Avanzada (LNMA)

martugr@live.com.ar

Sperm capacitation enables acrosomal exocytosis (AE), essential for fertilization. Progesterone (PRG) induces AE by increasing intracellular Ca^{2+} ($[\text{Ca}^{2+}]_i$), but the origin and functional role of these fluxes remain unclear. Conventional fluorescence analyses require manual region-of-interest (ROI) selection, a laborious process that limits reproducibility.

Here, we present the first high-resolution live imaging of cytoplasmic and organellar Ca^{2+} dynamics during AE in capacitated mouse sperm. Using a triple-probe strategy with two Ca^{2+} indicators of different affinities (Fluo-5N AM and Calbryte 590 AM) and an AE marker (PNA-Alexa 647), we achieved discrimination between cytoplasmic and store-derived Ca^{2+} signals and defined multiple PRG-induced dynamic patterns. Our results show that low-level Ca^{2+} oscillations are the most frequent response to PRG and correlate with reduced AE. Sperm that underwent AE did not exhibit regular oscillations in

amplitude or frequency. Thapsigargin, a SERCA inhibitor, suppressed oscillations while enhancing PRG-induced AE, indicating an inhibitory role of oscillations in AE regulation in mouse sperm. Under low extracellular Ca^{2+} , PRG stimulation abolished oscillations and failed to trigger efficient AE, while store release alone induced only minimal AE. Together, these findings demonstrate that intracellular stores contribute to the exocytotic signal but extracellular influx is essential. Moreover, PRG-induced oscillations required both extracellular entry and SERCA-mediated Ca^{2+} uptake. Finally, we developed an open-source automated pipeline for region-specific fluorescence quantification, significantly reducing analysis time and increasing objectivity.

In summary, this work introduces a powerful imaging and analysis framework, reveals new regulatory roles of Ca^{2+} oscillations, and provides insights into the coordinated mechanisms driving AE.

SACERDOTE DE LUSTIG / MABXIENCE AWARD - NEUROSCIENCES

Thursday 20th November 2025 - 13:00 - 14:30 - Auditorio

Jury: Leonardo Romorini, Lucia Crivelli, Mariana Feld, Fernando Pitossi

NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A BIOMARKER IN LATE-ONSET ALZHEIMER'S DISEASE AND ITS POSSIBLE ASSOCIATION WITH PLASMA METAL LEVELS

Sebastián Molinari^{1,2}, Cecilia Catanesi², Julia Tau¹, Carina Tersigni³, M. Victoria Cabassi³, M. Belén Ventura⁴, Carilina Dalmaso⁵, Alfredo Ramirez⁶, Diana Cristalli⁷, Nicolás Irureta⁸, Nathalie Arnal¹

1. Instituto de Investigaciones Bioquímicas de La Plata (INIBIOLP),

2. Instituto Multidisciplinario de Biología Celular (IMBICE);

3. Facultad de Cs Exactas -UNLP; Lab. Salud Pública

4. Facultad de Cs Veterinarias-UNLP; Lab. de Nutrición mineral

5. Unidad Ejecutora de Estudios en Neurociencias y Sistemas Complejos

6. Department of Psychiatry and Psychotherapy, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany.; Division of Neurogenetics and Molecular Psychiatry

7. Centro de día JESI

*8. Hospital Interzonal General de Agudos Prof. Dr. Rodolfo Rossi; servicio de neurología
sebiolinari75@gmail.com*

Late-onset Alzheimer's disease (LOAD) is the most prevalent form of dementia in individuals over 65 years old, representing a growing health challenge in Argentina and worldwide. Its etiopathogenesis is multifactorial, involving genetic, metabolic, and immunological factors. It has been hypothesized that copper (Cu) overload contributes to β -amyloid peptide toxicity, while the neutrophil-to-lymphocyte ratio (NLR) has emerged as a potential inflammatory biomarker in LOAD.

This study included 216 participants over 55 years of age of both sexes: 101 controls, 74 with mild cognitive impairment (MCI), and 41 with LOAD from La Plata. NLR, plasma levels of Cu and zinc (Zn), and genetic variants of apolipoprotein APOE (2, 3, and 4) were measured. Currently, the ApoE4 variant is firmly considered a risk factor for LOAD development. Our results showed a significant

increase in Cu and Zn in LOAD compared to MCI, although the Zn level was lower in LOAD than in the control group. NLR was elevated in LOAD compared to the control group, remaining significant when regrouping LOAD+ versus LOAD- (controls + MCI). In logistic regressions, NLR was associated with LOAD (OR=1.39; 95% CI=1.04–1.86; $p=0.0269$), though robustness decreased when age, sex, and APOE4 were included. Cu showed a trend toward association ($p=0.071$), while Zn was not significant. ROC analysis for NLR yielded an AUC=0.5946 ($p=0.0218$), with a Youden index of 17.35. These findings suggest that, despite its moderate discriminatory capacity, NLR is an accessible, cost-effective, and non-invasive biomarker with potential utility for early LOAD detection, especially in primary care settings.

METFORMIN ALLEVIATES HIPPOCAMPAL ALTERATIONS AND MICROGLIAL DYSFUNCTION IN EXPERIMENTAL MODELS OF DIABETES AND ALZHEIMER'S DISEASE

Carlos Pomilio, Nicolás González Pérez, Soledad Porte Alcon, Valentina Saud, Luciano Arcucci, Melina Bellotto, Ángeles Vinuesa, Melisa Bentivegna, Facundo Dallo, Jessica Presa, Juan Beauquis, Flavia Saravia

IByME (CONICET) - Depto de Química Biológica (FCEyN-UBA); Laboratorio de Neurobiología del Envejecimiento

carlosjpomilio@gmail.com

Type 2 diabetes mellitus (T2DM) is a major risk factor for Alzheimer's disease (AD), and both conditions share pathogenic mechanisms including hippocampal insulin resistance, synaptic dysfunction, and neuroinflammation. As no effective treatments are available for AD, drug repurposing strategies are of increasing interest. Epidemiological evidence suggests that metformin, the first-line therapy for T2DM, may lower the risk of developing AD. Here, we investigated its neuroprotective potential using complementary in vivo and in vitro models of diabetes and AD-related brain pathology. C57BL/6J mice fed a high-fat diet (HFD) displayed systemic and hippocampal insulin resistance and cognitive deficits, whereas PDAPP-J20 transgenic mice exhibited robust amyloid pathology. In both models, metformin treatment (240 mg/kg, i.p., 3 times per week, 3 weeks) improved hippocampal-dependent memory. In HFD mice, metformin enhanced insulin signaling (evaluated by AKT

phosphorylation), increased synaptophysin levels, and reduced microglial reactivity. In AD mice, metformin reduced hippocampal amyloid burden (both parenchymal and perivascular) and restored homeostatic microglial marker TMEM119. In both models, metformin reversed microglial dystrophy and autophagosome accumulation, evidenced by decreased p62 accumulation. Complementary studies in BV2 microglial cells revealed that metformin restored autophagic flux disrupted by either palmitate-induced insulin resistance or amyloid- β fibrils, leading to reduced IL-1 β and TNF α expression in palmitate-exposed cells and enhanced amyloid phagocytosis and clearance. Together, our findings indicate that metformin exerts convergent protective effects in models of T2DM and AD by modulating microglial autophagy and neuroinflammation. These results provide preclinical evidence supporting the repositioning of metformin as a candidate therapeutic strategy for AD.

WHOLE-BODY MRI REVEALS SUBCLINICAL MUSCLE INVOLVEMENT IN FEMALE CARRIERS OF DUCHENNE MUSCULAR DYSTROPHY-RELATED VARIANTS

Alejandra P. Vigliano¹, Leonela Luce^{2,3}, José Manuel Pastor Rueda⁴, Hernán Chaves¹, Lilia Mesa⁵, Micaela Carcione², Chiara Mazzanti², Carmen Llames Massini², Pamela Radic⁶, Claudia Cejas¹, Florencia Giliberto²

1. Fleni, CP 1428, Buenos Aires, Argentina.; Departamento de Diagnóstico por Imágenes

2. Laboratorio de Distrofinopatías, Cátedra de Genética, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires (UBA), C1413AAD, Buenos Aires, Argentina.; Instituto de Inmunología, Genética y Metabolismo (INIGEM), CONICET - Universidad de Buenos Aires (UBA), C1120AAR, Buenos Aires, Argentina;

3. John Walton Muscular Dystrophy Research Centre, Translational and Clinical Research Institute, Newcastle University and Newcastle Hospitals NHS Foundation Trust, NE1 3BZ, Newcastle upon Tyne, UK.

4. Fleni, C1428AQK, Buenos Aires, Argentina.; Departamento de Neurología

5. Fundación Favaloro, C1093ABG, Buenos Aires, Argentina.; Instituto de Neurociencias

6. Laboratorio de Genética Molecular de la Hemofilia, Instituto de Medicina Experimental (IMEX), CONICET - Academia Nacional de Medicina, C1425AUM, Buenos Aires, Argentina.; Laboratorio de Genética Molecular de la Hemofilia, IMEX

avigliano@flenf.org.ar

Duchenne muscular dystrophy (DMD) is an X-linked disorder caused by pathogenic variants in the DMD gene, resulting in reduced or absent dystrophin, affecting 1 in 3,500–5,000 male births worldwide. Female carriers of pathogenic DMD variants have historically received little clinical attention, although some develop muscle weakness or cardiomyopathy. This study aimed to characterize skeletal muscle involvement in asymptomatic female carriers compared to healthy controls using whole-body MRI (WB-MRI) and to explore correlations with clinical and genetic data. We conducted a cross-sectional study including 29 obligate or genetically confirmed female carriers of DMD variants and 30 non-carrier controls. All participants underwent WB-MRI, evaluated with qualitative grading scales for edema, fatty infiltration, and atrophy. Carriers also had neurological examinations, serum creatine kinase (CK) testing, DMD genetic screening, and

X-chromosome inactivation (XCI) studies. All 29 carriers displayed MRI abnormalities, involving a significantly larger proportion of skeletal muscles than controls (85% vs 27% of 48 muscles, $p < 0.001$). Edema, fatty infiltration, and atrophy were more frequent in carriers (62.5% vs 8%; 81% vs 35%; 81% vs 25%, all $p < 0.001$), particularly in calves, thighs, and pelvic muscles. Gastrocnemius, soleus, and gluteus maximus were the most affected. No correlation was found between MRI abnormalities and clinical findings, CK levels, XCI or variant type. Female DMD carriers, even when asymptomatic, exhibit widespread subclinical muscle involvement. These findings challenge the traditional view of carriers as unaffected and highlight the urgent need for awareness, systematic evaluation, and development of dedicated guidelines to improve multidisciplinary care in this underrecognized population.

PRODUCT PRESENTATIONS BY SPONSORS

MEDICINA (BUENOS AIRES) 2025; 85 (Supl. V): 56-57

Sartorius Talk - Tuesday 18th November 2025 - 12:00 - 13:00 - Calle Principal**KEYS TO ACCELERATE YOUR DISCOVERIES: CASES SHARED BY IBYME**

Join this space where researchers will share how they

overcame key experimental challenges to advance our understanding of complex biological systems.

FROM STATIC TESTING TO REAL-TIME KINETICS**Alejandro Cagnoni***IByME*

Galectin-1 (GAL1) regulates tumor angiogenesis and immunosuppression, making it a key therapeutic target in cancer. In our laboratory, we developed neutralizing monoclonal antibodies against GAL1 and characterized them using Biolayer Interferometry (BLI).

This technology allowed us to precisely measure the affinity and kinetic constants of antibody-GAL1 interactions, overcoming the limitations of traditional methods

and providing reproducible and detailed data on their functionality.

The use of BLI accelerated the evaluation of antibodies and supported the development of therapeutic strategies with potential application in cancer and other pathologies associated with aberrant angiogenesis and immunosuppression.

OVERCOMING THE CHALLENGES OF STUDYING 3D MODELS**Nahuel Villarreal***IByME*

In our project, we analyzed the growth and dynamics of three-dimensional intestinal organoids using a real-time imaging system. This technology allowed us to accurately quantify the area and morphological changes of the organoids over time, preserving the integrity of the samples and avoiding destructive interventions. Furthermore, the use of fluorescent channels allowed us to discriminate cell populations and simultaneously assess processes such as cell proliferation and death. The use of

this automated approach was key to overcoming one of the main challenges in studying 3D models: the need to obtain quantitative and reproducible measurements under physiological conditions. Without this technology, it would have been necessary to manually capture images in each well at different times and analyze them individually using software such as ImageJ, a much more laborious process, prone to variability, and with lower temporal resolution.

CONCLUSION AND Q&A**Lucrecia Agnetti***Sartorius***ETC Talk - Wednesday 19th November 2025 - 12:00 - 13:00 - Calle Principal****ELEMENT'S AVITI24™: A MULTIOMIC NGS PLATFORM FOR DEEPER BIOLOGICAL INSIGHTS****Solomon Hailu***Element Biosciences*

The AVITI™ benchtop sequencer delivers high-quality data with flexible throughput and a low cost per gigabase. Featuring dual independent flow cells, scalable output, and open FASTQ integration, AVITI is designed

for efficient and accessible next-generation sequencing (NGS). Building on this foundation, the AVITI24™ platform expands throughput by 50%, reduces sequencing costs by 30%, and introduces powerful high-dimensional

single-cell multiomics capabilities. With support for up to two million cells per dual sided run in 24 hours, AVITI24 enables simultaneous profiling of RNA, proteins, and cell morphology - delivering subcellular resolution and rich spatial context. More than identifying which molecules are present, AVITI24's 5D multiomics reveals where molecules are located, how they interact, respond to stimuli, and change over time. By integrating gene expression,

protein activity, cell morphology, spatial organization, and dynamic responses, AVITI24 delivers a comprehensive view of cellular function and dysfunction. Powered by Teton™ and Teton Atlas™ chemistries, AVITI24 is a dual-purpose system that combines advanced multiomics with standard NGS - offering unmatched versatility for decoding biological complexity.

Tecnolab Talk - Thursday 20th November 2025 - 12:00 - 13:00 - Calle Principal

ddPCR: FROM THEORY TO PRACTICE - APPLICATIONS THAT MAKE A DIFFERENCE

María Fernanda Lazzarino

Tecnolab S.A.

Data from qPCR experiments are collected at the quantification cycle (Cq) within each enzymatic reaction curve. Therefore, optimization is critical for each primer pair, ensuring that reaction efficiency is consistent across all samples and acceptable (between 90% and 110%), with sample contaminants diluted adequately to ensure that all reactions and associated Cq values fall within the efficient range of the respective standard curves. Poorly optimized reactions can result in artifactual Cq values and misinterpreted data that are difficult or even impossible to reproduce. For absolute quantification, data analysis is further complicated by the different sources of DNA from which the samples and standard curves are derived, with unique backgrounds and contaminants that can variably affect the activity of Taq polymerase, giving misleading results. Droplet Digital PCR (ddPCR) has been commercially available since 2011 by Biorad. As with qPCR, ddPCR technology utilizes Taq polymerase in a standard PCR reaction to amplify a target DNA fragment from a complex sample using pre-validated primer or primer/probe assays. However, there are two distinct differences: 1) the partitioning of the PCR reaction into thousands

of individual reaction vessels before amplification, and 2) the acquisition of data at the reaction endpoint. These factors offer the advantage of direct and independent quantification of DNA without standard curves, giving more precise and reproducible data versus qPCR, especially in the presence of sample contaminants that can partially inhibit Taq pol and/or primer annealing. In addition, end-point measurement enables nucleic acid quantitation independently of the reaction efficiency, resulting in a positive-negative call for every droplet and greater amenability to multiplexed detection of target molecules. Due to these distinctive characteristics, ddPCR has become the tool of choice in applications such as: monitoring of minimal residual disease in liquid biopsy, detection and monitoring of resistance to antimicrobial therapies, detection of mutational variants, gene expression studies, CNV, linkage analysis, detection of gene editing, epidemiological monitoring in environmental samples, detection and quantification of infectious agents below the detection limit of qPCR, quantification of multiplex assays, gene therapy, etc.

ORALES 1 - SAIC - ONCOLOGÍA 1 BIOMARCADORES Y BLANCOS TERAPÉUTICOS

DATE & TIME: 17/11/2025 9:30 - 11:00 H

Chairs: Fernanda Rubio, Catalina Lodilinsky

1. O1-01. A NOVEL PATIENT-DERIVED HISTIOCYTOSIS CELL LINE OF THE CENTRAL NERVOUS SYSTEM UNVEILS GALECTIN-1 AS A PROMISING TARGET

Aylen Camila Nogueira¹, Jorge Peña Agudelo², Fidel Sosa³, Facundo Rodríguez⁴, Sofía Chemes⁵, Mónica Mezmezián⁶, Gustavo Sevelever⁷, Laura Galluzzo Mutti⁸, Gabriela Lamas⁹, Carina Santa Cruz¹⁰, Fabiana Lubieniecki¹¹, Mariana Candolfi¹², Guillermo Videla Richardson¹³, Gabriel Rabinovich¹⁴

1. Instituto de Biología y Medicina Experimental (IBYME), Ciudad Autónoma de Buenos Aires, Argentina.; Laboratorio de Glicomedicina

2. Facultad de Medicina, Universidad de Buenos Aires, Ciudad Autónoma de Buenos Aires, Argentina.; Instituto de Investigaciones Biomédicas (INBIOMED, CONICET-UBA)

3. Fundación para la lucha contra las enfermedades Neurológicas de la Infancia (FLENI), Belén de Escobar, Argentina.; Departamento de Neurocirugía

4. Fundación para la lucha contra las enfermedades Neurológicas de la Infancia (FLENI), Belén de Escobar, Argentina.; Departamento de Neurocirugía

5. Fundación para la lucha contra las enfermedades Neurológicas de la Infancia (FLENI), Belén de Escobar, Argentina.; Laboratorio de Investigación Aplicada a Neurociencias (LIAN)

6. Fundación para la lucha contra las enfermedades Neurológicas de la Infancia (FLENI), Belén de Escobar, Argentina.; Departamento de Neuropatología y Biología Molecular

7. Laboratorio de Investigación Aplicada a Neurociencias (LIAN); Fundación para la lucha contra las enfermedades Neurológicas de la Infancia (FLENI), Belén de Escobar, Argentina.

8. Hospital de Pediatría J. P. Garrahan, Buenos Aires, Argentina.; Departamento de Patología Pediátrica

9. Hospital de Pediatría J. P. Garrahan, Buenos Aires, Argentina.; Departamento de Patología Pediátrica

10. Hospital de Pediatría J. P. Garrahan, Buenos Aires, Argentina.; Departamento de Patología Pediátrica

11. Hospital de Pediatría J. P. Garrahan, Buenos Aires, Argentina.; Departamento de Patología Pediátrica

12. Instituto de Investigaciones Biomédicas (INBIOMED, CONICET-UBA); Facultad de Medicina, Universidad de Buenos Aires, Ciudad Autónoma de Buenos Aires, Argentina.

13. Fundación para la lucha contra las enfermedades Neurológicas de la Infancia (FLENI), Belén de Escobar, Argentina.; Laboratorio de Investigación Aplicada a Neurociencias (LIAN)

14. Instituto de Biología y Medicina Experimental (IBYME), Ciudad Autónoma de Buenos Aires, Argentina.; Laboratorio de Glicomedicina

aylen.nogueira@gmail.com

Histiocytosis of the central nervous system (CNS) is a rare pediatric neoplasm with poorly understood biology and its diagnosis can be challenging. Patient-derived models are essential for mechanistic studies and preclinical testing, yet remain largely unavailable for this disease. We established a new cell line, GP4, from pediatric CNS histiocytosis. Phenotypic analysis confirmed a histiocytic identity, with strong CD14 and CD68 positivity by flow cytometry. Galectin-1 (Gal-1) and Galectin-3 (Gal-3) are glycan-binding proteins with es-

established pro-tumoral roles in multiple cancers, including gliomas. We previously found in glioblastoma patient-derived models, that Gal-1 promotes tumor cell survival, proliferation, and migration. In this study we found robust Gal-1 and Gal-3 expressions in GP4 by immunofluorescence staining. RT-qPCR analysis aimed at comparing bulk biopsy and GP4 cell line showed higher GAL1 mRNA levels in GP4. Additionally, lectin array profiling identified a unique glycosylation signature in this cell line. To investigate the relevance of these lectins, we knocked down Gal-1, Gal-3, or both in GP4 cells. Gal-1 silencing increased tumor cell death and reduced viability, supporting a pro-tumoral role in this histiocytic context. On the other hand, Gal-3 knockdown and combined silencing produced minimal changes, suggesting a dominant role for Gal-1 in maintaining viability. Thus, establishment of GP4 cell line may contribute to the study of a poorly represented disease in experimental and translational research. Our findings also reinforce the conserved pro-tumoral role of Gal-1 across different CNS tumors, placing this lectin as a promising therapeutic target.

2. O1-02. DECIPHERING THE ROLE OF THE LONG NON-CODING RNA (lncRNA) PCGEM1 IN PROSTATE CANCER PROGRESSION

Sabrina Ledesma-Bazan¹, Pablo Sanchis², Rocío Seniuk³, Gastón Pascual⁴, María Jimena Rada⁵, Elba Vazquez⁶, Geraldine Gueron⁷, Javier Cotignola⁸

1. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina.; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina.; Laboratorio de Inflamación y Cáncer

2. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina.; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina.; Universidad Argentina de la Empresa (UADE), Instituto de Tecnología (INTEC), Buenos Aires C1073AAO, Argentina 4 Department of Genitourinary Medical Oncology and The David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; Laboratorio de Inflamación y Cáncer

3. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina.; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina.; Laboratorio de Inflamación y Cáncer

4. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina.; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina.; Laboratorio de Inflamación y Cáncer

5. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina.; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina.; Laboratorio de

Inflamación y Cáncer

6. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina.; Laboratorio de Inflamación y Cáncer

7. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina.; Laboratorio de Inflamación y Cáncer

8. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina.; Laboratorio de Inflamación y Cáncer

sabriedesma13@gmail.com

Long non-coding RNAs (lncRNAs) have emerged as critical regulators of prostate cancer progression. Previous results showed that PCGEM1, a lncRNA expressed in prostate cancer cells, may be a central hub in a competing endogenous RNA (ceRNA) network that could be involved in the progression to castration resistance. In this study we analyzed the potential clinical relevance of PCGEM1 and characterized its role in prostate tumor biology. Survival analyses in the TCGA-PRAD cohort showed that high levels of PCGEM1 were significantly associated with a lower risk of progression (HR=0.54, 95%CI= 0.35-0.83, $p=5.1e-3$) and there was a decreasing expression trend for higher ISUP grades ($p\text{-trend}=0.002$). Subsequently, PC3 prostate cancer cells were transfected with an over expressing vector. PCGEM1 overexpression significantly reduced cell viability ($p<0.01$), clonogenic capacity ($p<0.01$), and 3D spheroid size ($p<0.0001$), suggesting decreased proliferative and anchorage-independent growth potential. Phalloidin staining revealed that PCGEM1 induced a more elongated shape. Wound healing assays showed that PCGEM1 overexpression impaired migratory capacity. No significant changes were observed in the expression of canonical epithelial or mesenchymal markers at the mRNA level, indicating that the observed effects were not driven by a classical EMT program. Finally, proteomic profiling of PCGEM1-overexpressing cells highlighted consistent enrichment in pathways related to translation, ribosome function, and protein homeostasis, as well as immune and stress-response processes. These results indicate that PCGEM1 regulates key features of prostate tumor cells. However, we cannot discard that some of the effects are partially associated to the stress response triggered by PCGEM1 high expression.

3. O1-03. EXPLORING LNCRNA DYSREGULATION IN COLORECTAL CANCER FOR PRECISION MEDICINE AND NON-INVASIVE DIAGNOSIS

Marcela Astiz¹, Mariano Di Tommaso², Natividad Perlo³, Rocio Laurini⁴, Leandro Spalletti⁵, Malena Solis⁶, Federico Campomenosi⁷, Aimara Juarez⁸, Camila Landa⁹, Eugenia Salas¹⁰, Eduardo Alach¹¹, Martin Abba¹², Ezequiel Lacunza¹³

1. Facultad de Ciencias Médicas, UNLP, La Plata, Buenos Aires, Argentina; Centro de Investigaciones Inmunológicas Básicas y Aplicadas (CINIBA)

2. Hospital Interzonal General de Agudos San Roque, Gonnet, La Plata, Buenos Aires, Argentina.; Servicio de Gastroenterología

3. Hospital Interzonal General de Agudos San Roque, Gonnet, La Plata, Buenos Aires, Argentina.; Servicio de Gastroenterología

4. Hospital Interzonal General de Agudos San Roque, Gonnet, La Plata, Buenos Aires, Argentina.; Servicio de Gastroenterología

5. Hospital Interzonal General de Agudos San Roque, Gon-

net, La Plata, Buenos Aires, Argentina.; Servicio de Gastroenterología

6. Hospital Interzonal General de Agudos San Roque, Gonnet, La Plata, Buenos Aires, Argentina.; Servicio de Gastroenterología

7. Hospital Interzonal General de Agudos San Roque, Gonnet, La Plata, Buenos Aires, Argentina.; Servicio de Gastroenterología

8. Hospital Interzonal General de Agudos San Roque, Gonnet, La Plata, Buenos Aires, Argentina.; Servicio de Gastroenterología

9. Hospital Interzonal General de Agudos San Roque, Gonnet, La Plata, Buenos Aires, Argentina.; Servicio de Gastroenterología

10. Facultad de Ciencias Médicas, UNLP, La Plata, Buenos Aires, Argentina; Centro de Investigaciones Inmunológicas Básicas y Aplicadas (CINIBA)

11. Hospital Interzonal General de Agudos San Roque, Gonnet, La Plata, Buenos Aires, Argentina.; Servicio de Gastroenterología

12. Facultad de Ciencias Médicas, UNLP, La Plata, Buenos Aires, Argentina; Centro de Investigaciones Inmunológicas Básicas y Aplicadas (CINIBA)

13. Facultad de Ciencias Médicas, UNLP, La Plata, Buenos Aires, Argentina; Centro de Investigaciones Inmunológicas Básicas y Aplicadas (CINIBA)

marce.astiz.15@gmail.com

Colorectal cancer (CRC) screening via colonoscopy is essential for early detection and prevention. However, the molecular diversity of lesions calls for precision medicine. Long non-coding RNAs (lncRNAs) are involved in tumorigenesis, making them promising biomarkers and therapeutic targets. In previous bioinformatics analyses we compared normal vs. adenoma, normal vs. tumor, and inter-tumor differences by CRC CMS subtypes (CMS1-4) to identify lncRNA signatures with high accuracy, prognostic significance, and predictive value. We selected lncRNAs from normal/adenoma-tumor comparisons and CMS association, then assessed the expression of CRNDE, UCA1 (normal-tumor dysregulation), COLCA1 (CMS3), EGFR-AS1 (CMS2), AFAP1-AS1 (CMS1), and HAND2-AS1 (CMS4) in 76 pre-surgical colorectal biopsy samples (17 paired tumor-normal, 20 CRC biopsies, 19 healthy controls) using Real-Time qPCR. These lncRNAs were also tested in matched plasma samples. RNA-seq was performed on a subset of tumors and NAT (n=8). All assessed lncRNAs showed greater expression variability in tumors than in healthy biopsies, with 10-30% exhibiting higher expression, highlighting inter-tumor heterogeneity ($p<0.05$). CRNDE and UCA1 were upregulated in some tumors and downregulated in others, indicating distinct dysregulation patterns ($p<0.05$). AFAP1-AS1 and EGFR-AS1 expression varied by colon location (right/left) in agreement with CMS1 and CMS2, while COLCA1 was expressed in the right colon and rectum. HAND2-AS1 was less detectable. UCA1 and EGFR-AS1 were the most readily detectable in plasma from both healthy control and CRC patients, supporting their potential as liquid biopsy markers. These findings emphasize CRC's molecular heterogeneity and position lncRNAs as biomarkers for early detection and subtype-specific management, with potential for non-invasive blood diagnostics.

4. O1-04. IGF1R NUCLEAR LOCALIZATION IN PEDIATRIC GLIOMAS: U87-SPHEROID CHARACTERIZATION USING A COMBINATION OF IGF1R/IR INHIBITOR OSI906 AND TEMOZOLAMIDE AS TARGETED THERAPY

Matías Luis Senovieski¹, Florencia Clément², Evelin Barrios³, Ayelen Martín⁴, Patricia Pennisi⁵

1. Centro de investigaciones endocrinológicas "Dr. Cesar Bergada", CEDIE, CONICET, FEI, Div. Endocrinología Hospital de Niños "Dr. Ricardo Gutierrez", Ciudad Autónoma de Buenos Aires, Argentina.; Factores de Crecimiento y Biología Tumoral

2. Centro de investigaciones endocrinológicas "Dr. Cesar Bergada", CEDIE, CONICET, FEI, Div. Endocrinología Hospital de Niños "Dr. Ricardo Gutierrez", Ciudad Autónoma de Buenos Aires, Argentina.; Factores de Crecimiento y Biología Tumoral

3. Centro de investigaciones endocrinológicas "Dr. Cesar Bergada", CEDIE, CONICET, FEI, Div. Endocrinología Hospital de Niños "Dr. Ricardo Gutierrez", Ciudad Autónoma de Buenos Aires, Argentina.; Factores de Crecimiento y Biología Tumoral
4. Centro de investigaciones endocrinológicas "Dr. Cesar Bergada", CEDIE, CONICET, FEI, Div. Endocrinología Hospital de Niños "Dr. Ricardo Gutierrez", Ciudad Autónoma de Buenos Aires, Argentina.; Factores de Crecimiento y Biología Tumoral
5. Centro de investigaciones endocrinológicas "Dr. Cesar Bergada", CEDIE, CONICET, FEI, Div. Endocrinología Hospital de Niños "Dr. Ricardo Gutierrez", Ciudad Autónoma de Buenos Aires, Argentina.; Factores de Crecimiento y Biología Tumoral
- mosenovieski@cedie.org.ar

Pediatric central nervous system tumors—especially gliomas—are the most common solid tumors in children. Previously we found that in pediatric gliomas, nuclear localization of IGF1R is significantly associated with high-grade tumors and increased mortality risk. Current standard treatment for high-grade gliomas includes surgical resection followed by radiotherapy and Temozolomide (TMZ) chemotherapy, though optimal regimens remain to be defined. We aimed to characterize the in vitro and in vivo response of glioma cells to IGF1R inhibition using OSI906, alone or in combination with high or low TMZ doses. We used U87MG glioblastoma cells expressing wild-type IGF1R (WtU87) or a mutant form that cannot translocate to the nucleus (MutU87). We performed in vitro (Wt U87-, MutU87- derived spheroids) and in vivo (sc injection, nude male mice) studies to test OSI906, TMZ or the combination of both drugs, added to the culturing media (40 or 100 nM TMZ, 5uM OSI) or orally administered to the mice. In 3D spheroid cultures, both lines were sensitive to TMZ ($p < 0.03$), but MutU87 spheroids did not respond to OSI906. The combination of OSI906 and TMZ did not enhance MutU87 spheroid volume reduction. In vivo, WtU87-derived tumors grew faster and larger than MutU87 tumors ($p < 0.05$), and only WtU87 tumors showed sensitivity to OSI906, especially when combined with low-dose TMZ ($p < 0.02$). These findings indicate that nuclear IGF1R enhances sensitivity to IGF1R-targeted therapy, suggesting that in pediatric gliomas with nuclear IGF1R, treatment with inhibitors like OSI906 may allow for reduced TMZ dosing and potentially avoid radiotherapy in young children.

5. O1-05. CIRCULATING MICRORNAS LINKED TO PI3K/AKT/MTOR/S6 PATHWAY AS BIOMARKERS OF THERAPEUTIC RESPONSE AND TREATMENT ADJUSTMENT FOR LUMINAL BREAST CANCER

Micaela Vivanco¹, Florencia Cascardo², Federico Waisberg³, Juan Elías Gomez⁴, Adriana De Siervi⁵, Paola De Luca⁶, Virginia Novaro⁷

1. IBYME; Proteínas Quinasas y Oncología Molecular
 2. IBYME; Proteínas Quinasas y Oncología Molecular
 3. Instituto Alexander Fleming; Oncología Mamaria
 4. Instituto Alexander Fleming; Oncología Mamaria
 5. IBYME; Proteínas Quinasas y Oncología Molecular
 6. IBYME; Proteínas Quinasas y Oncología Molecular
 7. IBYME; Proteínas Quinasas y Oncología Molecular
- mica.vivanco.ibyme@gmail.com

Given the limited availability of validated predictive biomarkers for targeted therapies, we investigated plasma-derived microRNAs (miRNAs) as potential tools to guide therapeutic intervention in breast cancer (BC). Through bioinformatic analyses and literature review, we selected miR-16-5p, miR-21-5p, miR-103a-3p, miR-145-5p, and miR-195-5p, all linked to the PI3K/AKT/mTOR/S6 pathway. Their expression was evaluated by RT-qPCR in plasma samples from BC patients and healthy donors, showing a relative increase in patients. Independent validation using the GSE73002 dataset (N=1280) confirmed these findings in tumor samples. In addition, analysis of TCGA BRCA data revealed prognostic associations, where elevated levels of miR-16-5p, miR-103a-3p, and miR-145-5p ($p < 0.05$) correlated with reduced survival. To explore their predictive value, we conducted a prospective study in patients with advanced

luminal BC (N=24), assessing circulating miRNAs before initiation of CDK4/6 inhibitor therapy and every 3-6 months during ≥ 2 years of follow-up. Preliminary data indicate that after 18 months CDK4/6 inhibitor treatment reduces plasma miR-145-5p levels ($p = 0.0293$) in all patients, while miR-21-5p shows a non-significant downward trend in patients who relapse on therapy. Additional validation on an expanded set of samples is ongoing. Collectively, these results support the use of plasma-derived miRNAs as minimally invasive biomarkers with potential clinical utility of liquid biopsies in monitoring therapeutic response. Such biomarkers might contribute to a more precise integration of PI3K inhibitors, ultimately improving patient stratification and optimizing treatment strategies in advanced luminal BC.

6. O1-06. UNRAVELING RUNX GENE REGULATION IN HUMAN TRIPLE NEGATIVE BREAST CANCER USING LONG-READ TRANSCRIPTOMICS

Facundo Luis Couto¹, Camila Falguera², Natalia Brenda Fernández³, Natalia Rubinstein¹

1. Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3-FCEN-UBA); CONICET; Mecanismos Moleculares de la Metástasis
 2. Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3-FCEN-UBA); Mecanismos Moleculares de la Metástasis
 3. Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3-FCEN-UBA); CONICET; Mecanismos Moleculares de la Metástasis
 4. Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3-FCEN-UBA); CONICET; Mecanismos Moleculares de la Metástasis
- couto.facundo@gmail.com

Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer for which there are currently no effective targeted therapies, with surgery, radiation, and chemotherapy remaining the only available clinical options. Unfortunately, approximately 35% of TNBC patients will develop metastases due to the limited efficacy of these treatments. Intratumoral heterogeneity observed in breast cancer is one of the main causes of therapeutic failure. Variations in genetic and epigenetic features within subsets of cancer cells can alter both prognosis and drug response. To study intratumoral heterogeneity, our laboratory employs two cell culture models: adherent cells (standard culture) and cells grown under forced suspension conditions, which mimic two distinct phenotypes/stages of tumor progression. Unpublished data from our laboratory show increased expression of pluripotency and tumor dormancy genes in suspended cells compared to adherent cells. However, gene expression analysis by real-time PCR is technically limited to a small number of genes. The aim of this work was to perform a transcriptomic analysis (cDNA-seq) using long-read nanopore sequencing technology to compare the expression profiles of both cell populations and gain insights into the underlying mechanisms. Sample preparation, data generation, and bioinformatic analyses were all conducted in-house. Ongoing analyses have identified 10 genes including metabolic, stress, drug resistance genes, among others, whose expression is differentially affected by RUNX transcriptional inhibition depending on the culture model. These findings point to potentially distinct RUNX-dependent regulatory mechanisms across tumor subpopulations, which are currently under our investigation.

7. O1-07. EXPLORING GABAB RECEPTOR AS A POTENTIAL THERAPEUTIC TARGET IN PANCREATIC DUCTAL ADENOCARCINOMA

Martina I. Buset¹, Nadia N. Safronchik², M. Florencia Gottardo³, Giselle V. Ripoll⁴, Noelia P. Di Giorgio⁵

1. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional (COMTra)
2. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional (COMTra)
3. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional (COMTra)
4. Universidad Nacional de Quilmes; Centro de Oncología

*Molecular y Traslacional (COMTra)*5. *Universidad Nacional de Quilmes; Centro de Oncología**Molecular y Traslacional (COMTra)*

mbuset.998@gmail.com

GABA, the primary inhibitory neurotransmitter in the central nervous system (CNS), is synthesized by glutamic acid decarboxylase (GAD). Beyond the CNS, GABAergic components, including GAD1 and GABAB receptors (GABABR), are present in peripheral tissues, such as the pancreas, and have been implicated in tumorigenesis and tumor immunity. This study explores the therapeutic potential of GABABR in pancreatic ductal adenocarcinoma (PDAC), a highly lethal malignancy with limited treatment options. Transcriptomic analysis of Gad1 and GABABR subunits (Gabb1r/Gabb2r) were conducted using TCGA and GTEx datasets in Gepia2/UCSC/XENA platforms. Gad1 was significantly overexpressed in PDAC tissue ($p < 0.05$), although it showed no association with survival outcomes. In contrast, Gabb1r was decreased in PDAC ($p < 0.0001$) and its upregulation in PDAC patients correlated with improved overall ($p < 0.01$) and disease-free survival ($p < 0.05$). Both Gabb1r and Gabb2r expression tended to low levels in advanced stages of the disease, although only Gabb2r was statistically different between stage I and II ($p < 0.01$). Gene enrichment analysis associated high Gabb1r expression levels with downregulation of translation, post-translation modifications, vesicle transport and DNA replication pathways. Baclofen (300 μ M), a specific GABABR agonist, significantly inhibited proliferation by 60% in PANC02, while only 15% in PANC-1 in preliminary MTT assays. In conclusion, these findings suggest that Gabb1r upregulation is linked to favorable prognosis and reduced tumor progression. This suggests that repurposing GABABR agonists could be of interest as adjuvant agents to standard therapies for PDAC. Further studies are undoubtedly needed to fully understand the role of GABAB receptor in this pathology. Supported by UNQ-CONICET-ANPCYT.

8. O1-08. ROLE OF VAV2 AND RAC1 IN HEAD AND NECK SQUAMOUS CELL CARCINOMA PROGRESSION

Franco Chiaraluce¹, Maximiliano Aparicio², Cecilia Farré³, Gustavo Chapo⁴, Xosé Bustelo⁵, Mauricio Menacho Márquez⁶1. *Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).*2. *Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).*3. *IDICER (CONICET-UNR); Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB). Facultad de Ciencias Médicas. Universidad Nacional de Rosario.*4. *Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).*5. *CSIC-USAL; Centro de Investigación del Cáncer de Salamanca*6. *Facultad de Ciencias Médicas. Universidad Nacional de Rosario. IDICER (CONICET-UNR); Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).*
francolautarochiaraluce@gmail.com

Rac1, a Rho GTPase, is critical for regulating cell migration, proliferation, and cytoskeletal dynamics. In head and neck squamous cell carcinoma (hNSCC), Rac1 is linked to epithelial-mesenchymal transition (EMT), enhancing invasiveness and chemoresistance. Vav2, a guanine nucleotide exchange factor (GEF), activates Rac1 and has been implicated in hNSCC progression and poor prognosis in previous studies. This study evaluated the role of Vav2 and Rac1 in oral carcinogenesis and resistance. Using a carcinogenesis model with NQO administration in C57Bl6 mice, Vav2 knockout animals exhibited delayed tumor

onset and a significant reduction ($p < 0.01$) in tumor number per mouse. Histological analysis showed fewer malignant squamous cell carcinoma lesions, with subtle alterations in differentiation markers (keratins 1, 14, filaggrin) and decreased COX-2 expression, without changes in proliferation (BrdU), p53, or mTOR activation (phospho-S6). Pharmacological inhibition of Rac1 with 1A-116 and A41 for three weeks reduced tumor burden, albeit not significantly, suggesting partial Rac1 involvement in tumor progression. These results support that Vav2-mediated Rac1 activation contributes to hNSCC development and that targeting this axis may modulate tumor progression. Our findings align with reports demonstrating that the EGFR-Vav2-Rac1 signaling axis drives hNSCC invasiveness and poor outcomes. Further studies are warranted to explore therapeutic targeting of this pathway to improve hNSCC treatment.

9. O1-09. EXPLORING THE ROLE OF RAC1 IN CHOLANGIOCARCINOMA PROGRESSION

Mirco Mian¹, Sandra A Ostoih², Elena Echave³, Luciano E Anselmino⁴1. *Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).*2. *Hospital Provincial del Centenario. Rosario; Servicio de Oncología*3. *Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Departamento de Anatomía Patológica*4. *Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).*

mircomian08@gmail.com

Cholangiocarcinoma (CCA) is a rare biliary tract cancer with limited treatment options and poor prognosis. Surgery offers potential cure but is feasible in only 25-30% of patients. Chemotherapy combined with immunotherapy shows promise in trials, though clinical outcomes remain inconsistent. Our study focused on RAC1, a key regulator of actin cytoskeleton remodeling involved in cell proliferation and migration, hypothesizing its role in CCA aggressiveness. Analysis of public gene expression databases (GEO, TCGA, Array-Express) indicated significantly elevated RAC1 mRNA expression in tumor tissues compared to normal bile duct tissues ($p < 0.001$). We performed immunohistochemistry on patient samples using a RAC1-GTP-specific antibody to detect active RAC1 levels. Quantitative fluorescence microscopy revealed a marked increase of active RAC1 in CCA tumor tissues versus controls ($p < 0.001$), supporting database findings at the protein level. Functionally, RAC1 inhibition was assessed in HuCCT1 human CCA cells treated with selective inhibitors 1A-116, 1D-142, and A41. All inhibitors significantly decreased cell proliferation in a dose-dependent manner, highlighting RAC1's contribution to tumor growth. These results underscore RAC1 as a driver of CCA progression and a promising biomarker for tumor aggressiveness. Its inhibition impairs tumor cell proliferation, suggesting potential for targeted therapies. Further investigations will explore RAC1's involvement in invasion and metastasis and evaluate the therapeutic efficacy of RAC1 inhibitors in preclinical models and clinical settings.

ORALES 2 - SAIC - MEDICINA REGENERATIVA Y NANOMEDICINA

DATE & TIME: 17/11/2025 9:30 - 11:00 H

Chairs: Esteban Fiore, Ale Guberman

10. O2-01. ENHANCING MSC-DERIVED EXTRACELLULAR VESICLE PRODUCTION WITH IMT504 FOR LIVER FIBROSIS THERAPY

María José Cantero¹, Mailin Casadei², Barbara Bueloni³, Fátima Huamán Ormeño⁴, Joaquín Grimaldi⁵, Lucía Lameroli⁶, Catalina Atorrasagastu⁷, Natalia Pacienza⁸, Juan Bayo⁹, Guillermo Mazzolini¹⁰, Esteban Fiore¹¹1. *Instituto de Investigaciones en Medicina Traslacional (IIIMT),*

CONICET-Universidad Austral. Buenos Aires, Argentina; Laboratorio de Hepatología experimental y Terapia Génica
 2. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral. Buenos Aires, Argentina; Laboratorio de Hepatología experimental y Terapia Génica
 3. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral. Buenos Aires, Argentina; Laboratorio de Hepatología experimental y Terapia Génica
 4. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral. Buenos Aires, Argentina; Laboratorio de Hepatología experimental y Terapia Génica
 5. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral. Buenos Aires, Argentina; Laboratorio de Hepatología experimental y Terapia Génica
 6. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral. Buenos Aires, Argentina; Laboratorio de Hepatología experimental y Terapia Génica
 7. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral. Buenos Aires, Argentina; Laboratorio de Hepatología experimental y Terapia Génica
 8. Instituto de Medicina Traslacional, Trasplante y Bioingeniería (IMeTTYB), Universidad Favaloro-CONICET, Buenos Aires, Argentina; Laboratorio de Regulación Génica y Células Madre
 9. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral. Buenos Aires, Argentina; Laboratorio de Hepatología experimental y Terapia Génica
 10. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral. Buenos Aires, Argentina; Laboratorio de Hepatología experimental y Terapia Génica
 11. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral. Buenos Aires, Argentina; Laboratorio de Hepatología experimental y Terapia Génica
 mcantero-conicet@austral.edu.ar

Background: Mesenchymal stem cell (MSC)-derived extracellular vesicles (EVs) are emerging as a promising platform for delivering therapeutic factors in regenerative medicine. Human umbilical cord perivascular cells (HUCPVCs) represent a valuable MSC source due to their accessibility and rapid proliferation. IMT504 is an oligodeoxynucleotide previously shown to stimulate MSC proliferation in bone marrow and mobilization into peripheral blood. **Aims:** To evaluate whether pre-stimulation of HUCPVCs with IMT504 modulates EV production and to assess their therapeutic potential in experimental liver fibrosis. **Methods:** HUCPVCs from three independent donors were pre-treated or left untreated with IMT504 until passage 4. Cell culture supernatants were collected after 48 h in FBS-deprived medium. EVs were isolated by ion-exchange chromatography and characterized for particle concentration and size distribution by Nanoparticle Tracking Analysis (NTA). Antifibrotic effects of EVs from IMT504-treated (EVs/IMT504) or control cells (EVs/Ctrl) were evaluated in a thioacetamide-induced liver fibrosis mouse model (200 mg TAA/kg, 3 doses/week). From week 6, EVs were injected intravenously every 5 days for 3 doses. At week 8, livers were collected and collagen deposition quantified by Sirius Red staining. **Results:** EV yield from IMT504-treated cells was three-fold higher than in controls and exhibited a more heterogeneous size distribution. In vivo, treatment with either EVs/IMT504 or EVs/Ctrl similarly reduced collagen deposition in liver tissue, indicating that IMT504 pre-stimulation increases EV production without compromising their antifibrotic efficacy. **Conclusion:** Pre-stimulation of HUCPVCs with IMT504 enhances EV production while preserving their antifibrotic activity, representing a promising strategy to improve the scalability of EV-based therapies.

- 11. O2-02. IMT504 Accelerates Liver Regeneration after Partial Hepatectomy in Mice: Involvement of GLAST+ Wnt1+ Bone Marrow Stromal Progenitors**
 Maximiliano Borda¹, Lucía Cafaro², Romina Sierra³, Mercedes Díaz Pedraza⁴, Camila Becerra⁵, Agustina Ábalo⁶, María José Karolewski⁷, María José Cantero⁸, Máximo Schiavone⁹, Guillermo Mazzolini¹⁰, Montaner Alejandro¹¹, Esteban Juan

Fiore¹², Jorge B. Aquino¹³

1. Instituto de Investigaciones en Medicina Traslacional, CONICET-Universidad Austral; Developmental Biology & Regenerative Medicine Laboratory
 2. Instituto de Investigaciones en Medicina Traslacional, CONICET-Universidad Austral; Developmental Biology & Regenerative Medicine Laboratory
 3. Instituto de Investigaciones en Medicina Traslacional, CONICET-Universidad Austral; Developmental Biology & Regenerative Medicine Laboratory
 4. Instituto de Investigaciones en Medicina Traslacional, CONICET-Universidad Austral; Developmental Biology & Regenerative Medicine Laboratory
 5. Instituto de Investigaciones en Medicina Traslacional, CONICET-Universidad Austral; Developmental Biology & Regenerative Medicine Laboratory
 6. Instituto de Investigaciones en Medicina Traslacional, CONICET-Universidad Austral; Developmental Biology & Regenerative Medicine Laboratory
 7. Hospital Universitario Austral; Servicio de Anatomía Patológica
 8. Instituto de Investigaciones en Medicina Traslacional, CONICET-Universidad Austral; Gene Therapy Laboratory
 9. Instituto de Investigaciones en Medicina Traslacional, CONICET-Universidad Austral; Developmental Biology & Regenerative Medicine Laboratory
 10. Instituto de Investigaciones en Medicina Traslacional, CONICET-Universidad Austral; Gene Therapy Laboratory
 11. Fundación Pablo Cassará; Instituto de Ciencia y Tecnología Dr. César Milstein
 12. Instituto de Investigaciones en Medicina Traslacional, CONICET-Universidad Austral; Gene Therapy Laboratory
 13. Instituto de Investigaciones en Medicina Traslacional, CONICET-Universidad Austral; Developmental Biology & Regenerative Medicine Laboratory
- maxiborda23@gmail.com

The immunomodulatory oligodeoxynucleotide (ODN) IMT504 exhibits antifibrotic and pro-regenerative properties in the context of liver fibrosis. It also enhances the contribution of GLAST⁺ Wnt1⁺ bone marrow stromal progenitors (BMSPs) to liver regeneration in a mouse model of chronic liver disease. In this study, partial hepatectomy (PHx) was performed in CD1 mice. In parallel, Cre-loxP mice were used to identify GLAST⁺ Wnt1⁺ BMSPs and assess their contribution to liver cells populations. A combination of in vivo and in vitro assays was conducted. IMT504 significantly enhanced liver mass recovery following PHx by promoting both early and late induction of hepatocyte proliferation. The expression dynamics of genes associated with proliferation, liver function, and liver progenitor identity were analyzed. Moreover, IMT504 stimulated the pro-regenerative activity of GLAST⁺ Wnt1⁺ BMSPs by promoting their differentiation into liver cells. In summary, our findings identify IMT504 as a promising therapeutic candidate with strong pro-regenerative potential, particularly relevant in the setting of small-for-size syndrome. Additionally, our data suggest that GLAST⁺ Wnt1⁺ BMSPs represent a unique bone marrow-derived population capable of giving rise to liver cells, further supporting their pro-regenerative role in liver regeneration.

12. O2-03. IN VITRO EVALUATION OF BONE-RELATED BIOMATERIALS USING BONE TRAUMA-ASSOCIATED ADIPOSE TISSUE-DERIVED MESENCHYMAL STROMAL CELLS

- Loureyro María Albertina¹, Angelini Marquiani Gastón Ignacio², Valenzuela Alvarez Matías³, Ferraris Javier⁴, Reynoso Julián⁵, Camacho Nahuel Matías⁶, Farfalli Germán Luis⁷, Albergo José Ignacio⁸, Aponte Luis Alberto⁹, Bolontrade Marcela Fabiana¹⁰
1. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano (HI)-Universidad del Hospital Italiano (UHI), Buenos Aires, Argentina.; Laboratorio de Procesos Remodelativos y Nichos Celulares
 2. Instituto de Medicina Traslacional e Ingeniería Biomédica

ca (IMTIB) / CONICET-Hospital Italiano (HI)-Universidad del Hospital Italiano (UHI), Buenos Aires, Argentina.; Laboratorio de Procesos Remodelativos y Nichos Celulares
 3. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano (HI)-Universidad del Hospital Italiano (UHI), Buenos Aires, Argentina.; Laboratorio de Procesos Remodelativos y Nichos Celulares
 4. Hospital Italiano de Buenos Aires (HIBA); Servicio de Ortopedia y Traumatología
 5. InBiomed S.A.
 6. InBiomed S.A.; Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba
 7. Hospital Italiano de Buenos Aires (HIBA); Servicio de Ortopedia y Traumatología
 8. Hospital Italiano de Buenos Aires (HIBA); Servicio de Ortopedia y Traumatología
 9. Hospital Italiano de Buenos Aires (HIBA); Servicio de Ortopedia y Traumatología
 10. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano (HI)-Universidad del Hospital Italiano (UHI), Buenos Aires, Argentina.; Laboratorio de Procesos Remodelativos y Nichos Celulares
 maria.loureyro@hospitalitaliano.org.ar

To identify alternative sources of mesenchymal stromal cells (MSC) for regenerative medicine purposes, we evaluated anatomical localizations other than bone marrow. Subcutaneous adipose tissue adjacent to bones subjected to reconstructive surgery was selected to isolate MSC. Cells adhesion, viability and proliferation were evaluated in biocompatible osteoconductive biomaterials, to determine their potential for bone regeneration. Discarded adipose tissue from orthopaedic surgeries at HIBA was enzymatically disaggregated with Collagenase Type I (0,1%), and cultured with standard DMEM culture medium. Cell metabolic activity was measured by MTS assay at 24, 96 and 144 hours on cadaveric human bone chips from HIBA, bovine-derived hydroxyapatite mineral matrix, and resorbable porcine-derived collagen fibers provided by InBiomed laboratory. Absorbance (mean $\pm$ SD) for 24 hours were: human bone chips, 1.803 ± 0.968 ; bovine hydroxyapatite 1.108 ± 0.425 ; porcine collagen, 1.785 ± 0.442 ; and MSC controls, 0.39725 ± 0.266 . At 96 hours, values were: 1.492 ± 0.542 ; 1.140 ± 0.308 ; 1.780 ± 0.381 ; 1.019 ± 0.125 , respectively. At 144 hours, values increased to: 2.534 ± 0.547 ; 1.926 ± 0.477 ; 1.854 ± 0.609 ; and 1.712 ± 0.179 , respectively. Briefly, absorbance increased in all groups, with bovine hydroxyapatite and human bone chips showing highest osteoconductive potential. These results demonstrate scaffold-dependent differences in MSC metabolic activity over time and provide a foundation for further functional assays and in vivo evaluation toward clinical application in bone regeneration.

- 13. O2-04. METABOLIC MATURATION OF CARDIOMYOCYTES DIFFERENTIATED FROM STEM CELLS ENABLES MODELING CARDIOMYOPATHY OF P.GLU353DUP (C.1059_1061DUPGGA) DESMIN VARIANT**
 Sheila Lucia Castañeda¹, Constanza Confino Malecki², Guadalupe Amin³, Federico Zabalegui⁴, Santiago Gabriel Miriuka⁵, Ariel Waisman⁶, Lucia Natalia Moro⁷
 1. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)
 2. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)
 3. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)
 4. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)
 5. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)
 6. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)
 7. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)

Neurociencias (LIAN)

5. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)
 6. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)
 7. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)
 sheila.lucia.c@gmail.com

Desmin (DES) is the most abundant intermediate filament of adult cardiomyocytes (CMs) and maintains sarcomere alignment, mechanical contraction transmission and organelle disposition. DES mutations lead to cardiac conduction defects, arrhythmias and cardiomyopathies. By a single blood sample collection, we have previously generated pluripotent stem (PS) cell lines from a patient (DESY-HE, XY) with an heterozygous mutation in DES (c.1059_1061dupGGA; p.Glu353dup) and his healthy sister (DESS, XX). The aim of our work is to determine the most suitable in vitro model among immature (ICs, day 23 of differentiation), temporally mature (TMCs, 23+80 days in basal medium) and metabolically mature (MMC, 23+14 days in fatty acids enriched medium) CMs derived from PS cell lines to study the cardiomyopathy related to p.Glu353dup DES variant. Firstly, we characterized the cardiac differentiation to ICs and the temporal and metabolic maturation to TMCs and MMCs by RT-qPCR and immunofluorescence (IF). Then we determined higher DES expression by RT-qPCR, cTnT+ DES+ population by flow cytometry, and DES sarcomeric alignment by IF in MMCs with respect to ICs and TMCs. Moreover, we detected impairment of contraction by video analysis with ContractionWave software and glucose consumption by glucose oxidase assay in DESY-HE relative to DESS MMCs and this difference was milder in ICs and TMCs. We conclude that MMCs is our best model to emulate p.Glu353dup DES associated cardiomyopathy in vitro and our next goal is to study transcriptional, mitochondrial and intercellular variations between DESY-HE and DESS MMCs to model the disease and identify therapeutic targets.

- 14. O2-05. PRECISE GENE THERAPY FOR A DESMIN MUTATION CAUSING MUSCULAR DYSTROPHY USING CRISPR/CAS9 IN PATIENT-DERIVED IPSCS**
 constanza confino¹, Sheila Lucia Castañeda², Federico Zabalegui³, Guadalupe Amin⁴, Joaquin Smucler⁵, Julia Maria Halek⁶, Denisse Saulnier⁷, Santiago Gabriel Miriuka⁸, Lucia Natalia Moro⁹
 1. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)
 2. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)
 3. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)
 4. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)
 5. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)
 6. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)
 7. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)
 8. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)
 9. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

Neurociencias (LIAN)

7. Instituto de Neurociencias (INEU-CONICET), Fundacion para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

8. Instituto de Neurociencias (INEU-CONICET), Fundacion para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

9. Instituto de Neurociencias (INEU-CONICET), Fundacion para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

constanzaconfino@hotmail.com

Desminopathy comprises a heterogeneous group of disorders caused by mutations in the desmin (DES) gene, mainly expressed in striated muscle. It is a rare disease and manifests as skeletal myopathy and/or cardiomyopathy. No effective therapy has yet been developed, but gene editing offers a promising therapeutic strategy. This work aimed to develop a CRISPR/Cas9-based therapy to correct a heterozygous DES mutation (NM_001927.4: c.1059_1061dupGGA; p.Glu353dup) in patient-derived iPSCs (DES-Y line). Two CRISPR systems were designed using gRNA1/ssODN1 and gRNA2/ssODN2 with the gRNAs targeting the mutation site and the ssODNs homologous to that site but containing the correct DES sequence for homologous recombination. Following gRNA1/ssODN1 or gRNA2/ssODN2 transfection and puromycin selection, clonal iPSC cultures were established and analyzed by PCR and Sanger sequencing. All 25 clones from gRNA1/ssODN1 contained indels in both DES alleles, whereas 4 of 12 clones from gRNA2/ssODN2 were successfully corrected. Importantly, in all gRNA2/ssODN2 clones the wild-type allele remained unmodified, ensuring safety and precision. Two corrected clones were selected for further characterization. Both displayed normal karyotype (G-banding), retained the STR identity of the parental DES-Y line, and expressed pluripotency markers (OCT4, NANOG, SOX2) confirmed by RT-qPCR and immunofluorescence staining. Genomic qPCR demonstrated preservation of both alleles, ruling out large deletions. In conclusion, we established an efficient gRNA/ssODN pair that corrected the DES mutation in 33% of analyzed clones without affecting the wild-type allele. Our goal is to use this gene editing strategy in DES-Y derived cardiomyocytes as a new therapy, thus emulating an in vivo therapy in muscle

15. O2-06. THE HUMAN AMNIOTIC MEMBRANE CONDITIONED MEDIUM REGULATES CELL MIGRATION AND EMT IN HEPATOCELLULAR CARCINOMA CELLS

Luciano Perez¹, Diego Javier Brites Neira², Rodrigo Nicolas Riedel³, Antonio Perez - Perez⁴, Cecilia Varone⁵, Laura Todaro⁶, Julieta Maymó⁷

1. IQUIBICEN, CONICET- Biological Chemistry Department, FCEN, UBA, Ciudad Autónoma de Buenos Aires, Argentina; Fisiología Molecular Placentaria

2. Institute of Oncology "Angel H. Roffo" UBA; Research Department, Ciudad Autónoma de Buenos Aires, Argentina

3. IQUIBICEN, CONICET- Biological Chemistry Department, FCEN, UBA, Ciudad Autónoma de Buenos Aires, Argentina; Fisiología Molecular Placentaria

4. Seville University, Seville, Spain; Medical Biochemistry and Molecular Biology Department

5. IQUIBICEN, CONICET- Biological Chemistry Department, FCEN, UBA, Ciudad Autónoma de Buenos Aires, Argentina; Fisiología Molecular Placentaria

6. Institute of Oncology "Angel H. Roffo" UBA; Research Department, Ciudad Autónoma de Buenos Aires, Argentina

7. IQUIBICEN, CONICET- Biological Chemistry Department, FCEN, UBA, Ciudad Autónoma de Buenos Aires, Argentina; Fisiología Molecular Placentaria

lucianoangelp@gmail.com

Several studies have demonstrated the antitumor potential of the human amniotic membrane, attributing to it the ability to secrete molecules with antiproliferative, antiangiogenic, and immunomodulatory

effects in various tumor models. Hepatocellular carcinoma (HCC) represents the third most common cause of cancer-related mortality worldwide, which is primarily associated with late-stage diagnosis and high resistance to conventional therapies such as chemotherapy and radiotherapy. A large proportion of cancer patients die due to metastasis of the primary tumors. Previously, we have demonstrated the antiproliferative and pro-apoptotic capacity of the human amniotic membrane-conditioned medium (AM-CM). The present study aimed to evaluate the impact of AM-CM on cell motility and the expression of specific markers related to epithelial-mesenchymal transition (EMT). First, we assessed cell motility by the wound healing assay, observing that treatment with AM-CM reduced migration in HepG2 and Huh7 hepatocarcinoma cell lines. Then, using qRT-PCR and Western blot analysis, we measured the expression of genes associated with EMT. We observed that AM-CM treatment increased E-cadherin expression, along with a decrease in EpCAM and MMP-2 expression. MMP-9 expression did not show changes. Our results would suggest that AM-CM inhibits the migration of HCC tumor cells

16. O2-07. CROTALUS DURISSUS TERRIFICUS VENOM ADSORBED ONTO SILICA NANOPARTICLES FOR POTENTIAL USE IN SEROTHERAPY

Florencia Conti¹, Exequiel Giorgi², Juan Pablo Rodríguez³, Federico Baudou⁴, Mauricio De Marzi⁵

1. Universidad Nacional de Luján (UNLu); 1. Grupo de Investigaciones Básicas y Aplicadas en Inmunología y Bioactivos (GIBAIB), Instituto de Ecología y Desarrollo Sustentable (INEDES-CONICET); . FOCIS Center of Excellence-Vaccines and Immuno Therapies Against Infections and Cancers (VITIC).

2. Universidad Nacional de Luján (UNLu); 1. Grupo de Investigaciones Básicas y Aplicadas en Inmunología y Bioactivos (GIBAIB), Instituto de Ecología y Desarrollo Sustentable (INEDES-CONICET); . FOCIS Center of Excellence-Vaccines and Immuno Therapies Against Infections and Cancers (VITIC).

3. Universidad Nacional del Nordeste, Consejo Nacional de Investigaciones Científicas y Técnicas (UNNE-CONICET); . 3. Laboratorio de Investigaciones Bioquímicas, Facultad de Medicina (LIBIM), Instituto de Química Básica y Aplicada del Nordeste Argentino (QUIBA-NEA).

4. Universidad Nacional de Luján (UNLu); 1. Grupo de Investigaciones Básicas y Aplicadas en Inmunología y Bioactivos (GIBAIB), Instituto de Ecología y Desarrollo Sustentable (INEDES-CONICET); . Laboratorio de Glicomedicina, Instituto de Biología y Medicina Experimental, Consejo Nacional de Investigaciones Científicas y Técnicas (IBYME-CONICET).

5. Universidad Nacional de Luján (UNLu); 1. Grupo de Investigaciones Básicas y Aplicadas en Inmunología y Bioactivos (GIBAIB), Instituto de Ecología y Desarrollo Sustentable (INEDES-CONICET); . FOCIS Center of Excellence-Vaccines and Immuno Therapies Against Infections and Cancers (VITIC).

florencia.conti@yahoo.com.ar

Ophidism is a globally neglected health problem. In Argentina, *Crotalus durissus terrificus* (C.d.t.) is one of the species of greater medical importance since its venom (V) contains mainly crotoxin (CTX), a potent toxin responsible for its high lethality. The generation of antivenoms (AVs) is a costly and difficult task, and the possibility of using Silica nanoparticles (SiNPs) transporting snake toxins (complex called nanovenom-NV-) appears as a new tool to produce them. In this work, we study some physicochemical properties of NV complex formed by C.d.t. V and SiNPs with diameters of 150 nm and 330 nm. Proper C.d.t. V adsorption to both sizes of Stöber SiNPs was confirmed by TEM micrographs. The concentration of adsorbed V was determined using UV-visible spectrometry by measuring absorbance at 280 nm. As a result, more than 50% of different concentrations of V (0.0625 – 2 mg/ml) were adsorbed to the SiNPs. Adsorption isotherms were analyzed using Langmuir and Freundlich models to explain different forms of adsorption-NPs interaction. It was observed that the 150 nm NVs fit both models well (R² 0.98) whether 330 nm NVs presented a lower R² (0.88 for Freundlich and

0.87 for Langmuir). These results suggest that the proteins of the V assume the formation of multiple layers due to a heterogeneous surface with regions of high and low affinity. These findings demonstrate that SiNPs can effectively adsorb C.d.t. venom and may act as promising platforms for controlled antigen delivery. This approach opens the possibility of improving antivenom production strategies.

17. O2-08. GENERATION OF IPSC-DERIVED SKELETAL MYOCYTES AND SHRNA-MEDIATED SILENCING OF FHL1 FOR THERAPEUTIC APPLICATIONS

Federico Zabalegui¹, Sheila Lucia Castañeda², Guadalupe Amin³, Jazmin Agosti⁴, Ariel Waisman⁵, Gustavo Emilio Seivlever⁶, Santiago Gabriel Miriuka⁷, Lucia Natalia Moro⁸

1. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

2. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

3. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

4. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

5. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

6. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

7. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

8. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

federico_zabalegui@hotmail.com

The FHL1 gene, located on Xq26, encodes Four and a Half LIM domain protein 1, which is highly expressed in skeletal and cardiac muscle. This protein participates in cytoskeletal remodeling, myoblast differentiation, sarcomere assembly, and autophagy regulation. Pathogenic variants in FHL1 are associated with muscular dystrophies (MDs), leading to severe clinical manifestations and reduced life expectancy. We previously established patient-derived induced pluripotent stem cells (iPSCs) carrying the FHL1 c.377G>A, p.C126Y mutation (pFHL1). The aim of this study was to differentiate wild-type iPSCs into skeletal myocytes, thereby providing a platform to investigate FHL1-associated MD mechanisms and evaluate therapeutic strategies with patient-derived iPSCs in the future. For differentiation, iPSCs were induced toward the myogenic lineage using the STEMdiff™ Myogenic Progenitor Kit (STEMCELL Technologies). The resulting progenitors were expanded in MyoCult™-SF Expansion Medium and subsequently differentiated into myotubes with the MyoCult™ Differentiation Kit. iPSCs were successfully differentiated into skeletal myocytes, confirmed by expression of key markers including FHL1, dystrophin, desmin, myosin heavy chain and α -actinin, detected by RT-qPCR and immunofluorescence. To explore therapeutic strategies for FHL1-associated MD, we propose downregulating the endogenous mutant FHL1 while simultaneously overexpressing the wild-type gene. As an initial step, we tested four short hairpin RNAs (shRNAs) targeting FHL1 and achieved more than 50% knockdown with all of them.

In conclusion, we differentiated iPSCs into skeletal myocytes to later apply this protocol to patient-derived iPSCs. In parallel, we confirmed the effectiveness of four shRNAs in downregulating FHL1 expression as a first step toward a therapeutic strategy.

18. O2-09. SILICON DIOXIDE NANOPARTICLES: CHARACTERIZATION AND BONE BIOCOMPATIBILITY

Sabrina Cepeda¹, Pablo Cutin¹, Adrian Campelo¹, Marcos Lo Fiego², Mariela Sandova¹, Mariela Agotegaray², Virginia Massheimer¹

1. Instituto de Ciencias Biológicas y Biomédicas del Sur (INBIOSUR), CONICET-UNS, Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina; LIEByC

2. Instituto de Química del Sur (INQUISUR), CONICET-UNS, Departamento de Química, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina; NanoHiap
sabrina.cepeda@uns.edu.ar

This study investigates the bone biocompatibility of silica nanoparticles (SiO₂-NPs), with and without citrate coating (SiO₂-NPs/Cit), with a focus on osteoblast cells differentiation. SiO₂-NPs were synthesized using the Stöber method, and citrate coating was achieved by surface adsorption. Physicochemical analysis showed hydrodynamic diameters of 159.3 nm (SiO₂ NPs) and 189.6 nm (SiO₂ NPs/Cit), with surface charges of -31.3 and -26.7 mV, respectively. Fourier Transform Infrared (FTIR) spectroscopy study confirmed citric acid on SiO₂-NPs/Cit. In vitro studies using MC3T3 pre-osteoblast cell line, shown that after 24 hours treatment with SiO₂-NPs or SiO₂-NPs/Cit (10, 50 and 100 μ g/mL) cell viability was sustained. In MTT assays, citrate functionalization exhibited higher effect (14, 12 and 21% vs SiO₂-NPs, % cells viability above control 10, 50 and 100 μ g/mL respectively, $p < 0.05$). In agreement with these, the analysis of the cell cycle by flow cytometry evidenced no significant alterations in the cell cycle phases for both NP. After 8 days, NPs upregulated osteoblastic differentiation markers. A significant enhancement in alkaline phosphatase (ALP) activity and collagen synthesis was detected. The highest stimulation of ALP activity was observed with the 100 μ g/mL treatment (62.2 ± 14.5 UI $\times 10^{-3}$ /mg protein, 47.1 ± 9.5 UI $\times 10^{-3}$ /mg protein vs. $36.2 \pm$ UI $\times 10^{-3}$ /mg protein in controls, SiO₂-NPs, SiO₂-NPs/Cit vs control, respectively, $p < 0.05$). Collagen synthesis was also significantly enhanced (105%; 58% above control; 50 μ g/mL SiO₂-NPs or SiO₂-NPs/Cit, respectively, $p < 0.05$). These findings suggest that both NPs promote osteoblastic differentiation without cell viability alteration, suggesting their potential for applications in bone tissue engineering.

POSTERS 1 - AAFE - FARMACOLOGÍA 1

DATE & TIME: 17/11/2025 9:30 - 11:00 H

Chairs: Susana Gorzalczany, Santiago Zugbi

19. P1-01. ROLE OF BMP7 IN CISPLATIN CHEMORESISTANCE OF HELA CELL XENOGRAFTS

Cintia Birkenstok¹, Pedro Carriere², María Belén Novoa Díaz³, Graciela Gigola⁴, Luis Gómez⁵, Ariel Zwenger⁶, Claudia Gentili⁷, Natalia Calvo⁸

1. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)

2. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)

3. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)

4. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)

5. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina. Departamento de Ciencias de la Salud (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)

6. Grupo Oncológico Cooperativo del Sur (GOCS), Santiago de Chile, Chile.

7. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)

8. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)
cintia.birkenstok@uns.edu.ar

Bone morphogenetic protein 7 (BMP7) is a cytokine that is abnormally expressed in cervical cancer (CC). Although cisplatin is the first-line drug for treating CC, its effectiveness is limited due to tumor cell resistance. We previously observed, *in vitro*, that BMP7 is involved in CC chemoresistance to cisplatin that is promoted by endothelial cells from tumor microenvironment. Furthermore, we found that BMP7 overexpression in HeLa cells from CC regulates the resistance to cisplatin via PI3K/AKT pathway. This work aimed to evaluate the effect of BMP7 overexpression in the response of HeLa cells xenografts to cisplatin. First, HeLa cells overexpressing BMP7 or control cells were injected into N:NIH(S)_nu female mice to establish two xenograft models. Next, both models were treated with saline solution or cisplatin. We observed that tumor growth in the BMP7 group was accelerated and not suppressed by cisplatin compared to the control group. Furthermore, the observation of tissues stained with hematoxylin and eosin, reveals an increase of mitotic events in BMP7 overexpressing cells under cisplatin action suggesting that the greater tumor size in this group is due to an intense metabolic activity. Finally, by immunohistochemistry assay, we found that Ki-67 and CD31 protein levels are increased in HeLa cells overexpressing BMP7 and exposed to cisplatin. These findings suggest that BMP7 promotes tumor growth and also mediates HeLa cells resistance to cisplatin *in vivo*.

20. P1-02. LAVENDER ESSENTIAL OIL MITIGATE EMOTIONAL DISORDER INDUCED BY NEUROTRANSMITTER IMBALANCE: DEVELOPING A MICROENCAPSULATED SYSTEM

Sol Angulo¹, Franco Ambrosioni², Cristian Moya³, Alvaro Jimenez Kairuz¹, Claudia Bregonzio⁵

1. Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina. Departamento de Farmacología Experimental Otto Orsingher, Universidad Nacional de Córdoba, Córdoba, Argentina.; Dpto. de Farmacología Experimental Otto Orsingher, FCQ, UNC

2. Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina. Departamento de Ciencias Farmacéuticas, Universidad Nacional de Córdoba, Córdoba, Argentina.; Dpto de Farmacia, FCQ, UNC

3. Presidente de la Asociación Civil Foro de los Ríos, Córdoba, Argentina. Productor y responsable del grupo Cambio Rural INTA, Córdoba, Argentina.; -

4. Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina. Departamento de Ciencias Farmacéuticas, Universidad Nacional de Córdoba, Córdoba, Argentina. Unidad de Investigación y Desarrollo en Tecnología Farmacéutica (UNITEFA-CONICET), Córdoba, Argentina.; UNITEFA, FCQ, UNC

5. Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina. Departamento de Farmacología Experimental Otto Orsingher, Universidad Nacional de Córdoba, Córdoba, Argentina. Instituto de Farmacología Experimental de Córdoba (IFEC-CONICET), Córdoba, Argentina.; IFEC, FCQ, UNC
sol.angulo@unc.edu.ar

Schizophrenia is a psychiatric disorder characterized by positive, negative, and cognitive signs. It is associated with neurotransmitter imbalances—mainly dopamine and glutamate—and neuroinflammatory processes. Repeated ketamine administration constitutes a validated rodent model of schizophrenia that mimics the characteristic signs of the pathology. We previously found that *Lavandula burnatii* essential oil administra-

tion (30 mg/kg, 7 days) reduced anxiety-like behaviors in male Wistar rats. This species, cultivated in Córdoba, has a phytochemical profile similar to *Lavandula angustifolia*—traditionally used for medicinal purposes—with a yield 20 times higher than the European variety per plant. In this study, male Wistar rats (250–300 g) initially received saline or ketamine (30 mg/kg *i.p.*, 5 days), on day 6 *L. burnatii* essential oil/vehicle (30 mg/kg *i.p.*, 7 days). On day 7 from the ketamine withdrawal period and one hour after the last essential oil/vehicle administration the animals were tested in the plus maze. In the challenge group, an additional dose of ketamine (15 mg/kg, *ip*) was administered 45 minutes before the test. Results showed that *L. burnatii* reduced anxiety-like behavior across experimental groups. Data were analyzed using Two-way ANOVA followed by Tukey's test. Given the effectiveness of the essential oil and due to its volatility and chemical instability we focused on its encapsulation in micro-particulate systems based on biocompatible, safe interpolyelectrolyte complexes, aiming to stabilize its composition and enable future intranasal administration. This strategy may enhance therapeutic efficacy and position *L. burnatii* as an innovative alternative for managing negative symptoms associated with schizophrenia.

21. P1-03. IN VITRO ANTIOXIDANT EFFECT OF GUNNERA TINCTORIA LEAVES: COMPARISON OF INFUSION, DECOCTION AND ETHANOL EXTRACT

Agustín Jorge Peri¹, Marine Daniel², Laura Cogoi³, María Rosario Alonso⁴, Claudia Anesini⁵, Carla Marrasini⁶

1. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Instituto de Química y Metabolismo del Fármaco (IQUIMEFA); Farmacognosia, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina

2. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Instituto de Química y Metabolismo del Fármaco (IQUIMEFA); Farmacognosia, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina

3. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Instituto de Química y Metabolismo del Fármaco (IQUIMEFA); Farmacognosia, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina

4. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Instituto de Química y Metabolismo del Fármaco (IQUIMEFA); Farmacognosia, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina

5. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Instituto de Química y Metabolismo del Fármaco (IQUIMEFA); Farmacognosia, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina

6. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Instituto de Química y Metabolismo del Fármaco (IQUIMEFA); Farmacognosia, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina

agustinjorgep@hotmail.com

Gunnera tinctoria (Molina) Mirb. var. *tinctoria* (Gunneraceae) (Nalca) is an autochthonous plant of the southern hemisphere, used by Mapuches aborigines as food and medicine for pathologies related to oxidative stress. This study compares the antioxidant capacity of infusion(I), decoction (D) and ethanol extract (E) of Nalca's leaves, collected in Argentina, in regards to: DPPH scavenging (DPPHS), reducing (RC), metal chelating capacities (MCC), SOD like activities (SA) and the inhibition of lipid peroxidation (ILPX) and the total polyphenols, fla-

vonoids content (by spectrophotometric methods and HPLC-UV). D and E contained the highest level of polyphenols and flavonoids. Flavonoids rutin and catechin were quantified. Effective medium concentration (EC50) (mean $\pm$ ESM, n:6): DPPHS: I 38.90 $\pm$ 4a, D 22.38 $\pm$ 2 b, E 25.12 $\pm$ 2b,. ILPX: I 516.42 $\pm$ 50 a, D 288.40 $\pm$ 30b, E 363.9 $\pm$ 30 a,b. RC: I 69.40 $\pm$ 7,0 a, D 62.97 $\pm$ 6,0a, E 48.56 $\pm$ 5,0 a. MCC: I1336.59 $\pm$ 10a, D 1367.67 $\pm$ 68.385 a, E3090.295 $\pm$ 162b. SA activity: I 11.22 $\pm$ 1.2a, D 35.48 $\pm$ 3.6b, E16.98 $\pm$ 1.8a (different superscript letters indicate $p < 0.05$ ANOVA + Tukey). E and D exerted the highest potency in DPPHS and ILPX. E was most potent in RC. I and D showed the highest MCC, while I and E showed the highest SA. Polyphenols mainly enhanced DPPHS and ILPX but reduced SA. Flavonoids improved mainly DPPHS and RC while negatively affecting MCC. Catechin enhanced MCC, whereas rutin mainly improved DPPHS and ILPX. Both affected negatively SA. All these support future researches.

22. P1-04. COMPARISON OF THE TIME-KILL CURVES OF PSEUDOMONAS AERUGINOSA AGAINST TRADITIONAL ANTIMICROBIALS AND MELALEUCA ARMILLARIS ESSENTIAL OIL

Andrea Buchamer¹, Daniel Buldain², Alan Paris³, Karen Julca Lozano⁴, Eileen Scheinsohn⁵, Maria Laura Marchetti⁶

1. Facultad de Ciencias Veterinarias. Universidad Nacional de La Plata; Laboratorio de Estudios Farmacológicos y Toxicológicos (LEFyT)

2. Facultad de Ciencias Veterinarias. Universidad Nacional de La Plata; Laboratorio de Estudios Farmacológicos y Toxicológicos

3. Facultad de Ciencias Veterinarias. Universidad Nacional de La Plata; Laboratorio de Estudios Farmacológicos y Toxicológicos

4. Facultad de Ciencias Veterinarias. Universidad Nacional de La Plata; Laboratorio de Estudios Farmacológicos y Toxicológicos

5. Facultad de Ciencias Veterinarias. Universidad Nacional de La Plata; Laboratorio de Estudios Farmacológicos y Toxicológicos

6. Facultad de Ciencias Veterinarias. Universidad Nacional de La Plata; Laboratorio de Estudios Farmacológicos y Toxicológicos

avbuchamer@fcv.unlp.edu.ar

Pseudomonas aeruginosa is qualified as a priority opportunistic pathogen, highly prevalent in animal infections and frequently resistant to conventional antimicrobials. Essential oils (EOs) emerge as innovative therapeutic alternatives. This study evaluated the inhibitory (MIC), bactericidal (MBC) activity and time-kill curves (TKC) of *Melaleuca armillaris* essential oil (EO) compared to gentamicin (GEN) and enrofloxacin (ENR). Seventy-six isolates of *P. aeruginosa* from chronic canine otitis were tested by antibiogram. A total of 24 isolates resistant and sensitive to GEN and ENR, 1 mucoid phenotype and *P. aeruginosa* ATCC 27853 (as quality control), were selected to determine MIC and MBC against GEN, ENR, and the EO. TKC assays were performed on ATCC strain, a resistant isolate, and a mucoid exposed to increasing concentrations of antimicrobials. High resistance rates were observed for aminoglycosides (47.36%) and fluoroquinolones (34.2%) by antibiogram. GEN, ENR and EO showed bactericidal effect (MBC/MIC < 4). In TKC assays, the EO exhibited a concentration-dependent bactericidal effect, with rapid inoculum reduction and instantaneous killing at high concentrations against the mucoid strain. Subinhibitory concentrations of EO reduce bacterial growth. Compared with GEN and ENR, the EO achieved eradication at lower multiples of the MIC. *M. armillaris* EO demonstrated uniform bactericidal efficacy against sensitive, resistant, and mucoid *P. aeruginosa* isolates. Its multitarget action supports its potential use as topical monotherapy or as an adjuvant to reduce antibiotic doses. Although these are in vitro results, they highlight the EO as a promising alternative therapeutic approach against multidrug-resistant *P. aeruginosa* infections.

23. P1-05. ORAL SOY ISOFLAVONES REDUCE THE I/R INJURY

RY IN RATS: A MECHANISTIC STUDY

Juliana Fantinelli¹, Soledad Inés Matera², Alicia Consolini³

1. Consejo Nacional de Investigaciones Científicas y Técnicas; Centro de Investigaciones Cardiovasculares "Dr Horacio E Cingolani"

2. Facultad de Ciencias Exactas. Universidad Nacional de La Plata; Laboratorio de Farmacología Experimental y Energética Cardíaca (LaFEYEC)

3. Facultad de Ciencias Exactas. Universidad Nacional de La Plata; Laboratorio de Farmacología Experimental y Energética Cardíaca (LaFEYEC)

julianafantinelli@hotmail.com

Soy isoflavones (SI) are dietary supplements with a known phytoestrogenic effect associated to its main components: genistein and daidzein. Aim: This work studied the sex influence in the effects of the oral subacute treatment of SI in rat hearts exposed to ischemia/reperfusion (I/R), and evaluated whether they depend on activation of NO-synthases, PKC, mKATP channels, and/or induce antioxidant mechanisms. Methods: Wistar rats orally received SI 100mg/kg/day for a week. Hearts were isolated and arterially perfused inside a flow calorimeter, and stimulated at 5Hz. After stabilization, control (C), isoflavones treated (SI-T), or SI-T hearts perfused with aminoguanidine (AG), chelerythrine (Che) or 5HD were all exposed to 30'/60'R. Left intraventricular pressure (LVP) and total heat flow (Ht, mW/g) were measured. Maximal LVP of contraction (P) and muscle economy (Eco= P/Ht) were calculated. After R, reduced glutathione (GSH) and TBARS were determined in C and SI-T hearts. Statistics: 2-way ANOVA and post-tests ($p < 0.05$). Results: SI increased the post-ischemic contractile recovery (PICR, up to 55 $\pm$ 6% of pre-I vs 27 $\pm$ 6% in C*) and Eco-R in female (F), but not in male (M) rat hearts. Blocking with AG, Che, and 5HD reduced PICR of SI-T rat hearts (up to 35 $\pm$ 10%*, 5 $\pm$ 5%*, and 33 $\pm$ 7%* respectively). GSH was increased (198 $\pm$ 29% vs 100 $\pm$ 14% in C*) and TBARS were reduced (63 $\pm$ 8% vs 100 $\pm$ 4% in C*) in F reperused SI-T hearts, without changes in M with SI-T. Conclusions: SI cardioprotection occurs only in female rats and depends on NOS, PKC, and mKATP activations, and on increase in reduction equivalents of GSH.

24. P1-06. GAMBOGIC ACID AS A GIARDICIDAL AGENT: EVIDENCE OF EFFICACY AND MECHANISMS OF ACTION AGAINST GIARDIA LAMBLIA TROPHOZOITES

Jeronimo Laiolo¹, Gabriel, Luna Pizarro², Rocío G. Patolsky³, Maraiana Belén Joray⁴, María Laura Guantay⁵, Gastón Soria⁶, Constanza Feliziani⁷, Andrea S. Rópolo⁸, María Carolina Touz⁹

1. Instituto Ferreyra (INIMEC-CONICET-UNC) y Universidad Católica de Córdoba; Laboratorio de Microbiología

2. Instituto Ferreyra (INIMEC-CONICET-UNC); Laboratorio de Microbiología

3. Instituto Ferreyra (INIMEC-CONICET-UNC); Laboratorio de Microbiología

4. CIDIE-CONICET-UCC; Laboratorio de Química Fina y Productos Naturales

5. OncoPrecision

6. OncoPrecision

7. Instituto Ferreyra (INIMEC-CONICET-UNC); Laboratorio de Microbiología

8. Instituto Ferreyra (INIMEC-CONICET-UNC); Laboratorio de Microbiología

9. Instituto Ferreyra (INIMEC-CONICET-UNC); Laboratorio de Microbiología

jeronimolaiolo@ucc.edu.ar

Giardiasis is one of the most prevalent intestinal parasitic infections worldwide, and its treatment relies mainly on metronidazole (MTZ), whose effectiveness is often limited by adverse effects and the emergence of resistant strains. In the search for new therapeutic alternatives, gambogic acid—a xanthonoid isolated from *Garcinia hanburyi* and traditionally used in Chinese medicine—was evaluated. Initial screening of the Spectrum Collection library identified gambogic acid as a leading candidate due to its potent in vitro giardicidal activity, with a half-maximal inhibitory concentra-

tion (IC_{50}) of $3.25 \pm 0.33 \mu M$, approximately nine times more active than MTZ. Mechanistic studies revealed that the compound induced early apoptosis in 43% of trophozoites at the IC_{50} concentration, shifting toward late apoptosis and necrosis at higher doses. Confocal microscopy showed chromatin condensation and fragmentation, confirming programmed cell death. Additionally, treatment induced a significant increase in reactive oxygen species (ROS) production, showing a focal cytoplasmic distribution at the IC_{50} concentration and a dense accumulation at the membrane at higher doses, suggesting a role for oxidative stress in cytotoxicity. Transmission electron microscopy revealed progressive alterations in the plasma membrane, ventral disc, peripheral vacuoles, and cytoskeleton, ultimately leading to irreversible structural damage. Taken together, these findings highlight gambogic acid as a promising natural antiparasitic agent, acting through multifactorial mechanisms. Its potency and safety profile support further development as a therapeutic alternative against giardiasis.

25. P1-07. ANTIDEPRESSANT AND SEDATIVE EFFECTS OF VERBENA BONARIENSIS: ROLE OF NEUROTRANSMITTER SYSTEMS AND MAO-A INHIBITION

Heidenreich Brenda¹, Pastore Valentina², Rademacher, Mariana³, Ragone María Inés⁴

1. *Facultad de Ciencias Exactas UNLP; Laboratorio de Farmacología Experimental y Energética Cardíaca.*

2. *UBA-CONICET; Instituto de Química y Físicoquímica Biológicas Prof. Dr. Alejandro C. Paladini (IQUIFIB)*

3. *UBA-CONICET; Instituto de Química y Físicoquímica Biológicas Prof. Dr. Alejandro C. Paladini (IQUIFIB)*

4. *Facultad de Ciencias Exactas; Laboratorio de Farmacología Experimental y Energética Cardíaca*
brenda95@gmail.com

Depression is a common psychiatric disorder, and current antidepressants, although effective, often show limited efficacy and adverse effects, encouraging the search for new alternatives. *Verbena bonariensis* (Vb) (Verbenaceae), a South American species traditionally used in folk medicine, has neuropharmacological potential. This study aimed to evaluate the antidepressant and sedative effects of Vb extracts in mice. An infusion (VbW, 5% w/v) and a tincture (VbT, 20% w/v) were prepared from aerial parts. Antidepressant- and sedative-like effects were assessed using the tail suspension test (TST) and the open field test (OFT). In addition, MAO-A inhibitory activity was evaluated in vitro by a fluorometric method. VbW (30 mg/kg) significantly reduced immobility time (IT) compared with saline (60.8 ± 15.4 s vs. 128.7 ± 10.9 s, $p < 0.05$), similar to clomipramine (41.7 ± 5.0 s, $p < 0.05$). Likewise, VbT (5 mg/kg) significantly reduced IT (71.6 ± 12.4 s vs. 121.9 ± 14.8 s, $p < 0.05$). Pretreatment with ketanserin, haloperidol, propranolol, prazosin, or yohimbine reversed the antidepressant-like effect of VbW. Enzymatic assays showed that VbT (1 mg/mL) inhibited human MAO-A activity by $88.7 \pm 1.07\%$. Both VbW (15–30 mg/kg) and VbT (5–15 mg/kg) significantly decreased locomotor activity in the OFT similarly to diazepam. The results suggest that: a) *Verbena bonariensis* exerts an antidepressant-like effect, mediated in the tincture by MAO-A inhibition, while in the infusion serotonergic, dopaminergic, and adrenergic mechanisms are involved; b) *Verbena bonariensis* also exerts a sedative effect, evidenced by decreased locomotor activity in the OFT, similar to diazepam.

26. P1-08. IDENTIFICATION OF A COUMARIN-CHALCONE HYBRID AS A CANDIDATE FERROPTOSIS INHIBITOR IN NEURONS

Luz Stoessel¹, Micaela Dehumará², Ivana L. Casariego³, Darío C. Gerbino⁴, María Julia Castro⁵, Natalia Alza⁶

1. *INIBIBB (CONICET-UNS), Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur; Laboratorio de Neurobiología de Lípidos y Estrés Oxidativo*

2. *INIBIBB (CONICET-UNS), Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur; Laboratorio de Neurobiología de Lípidos y Estrés Oxidativo*

3. *INQUISUR (CONICET-UNS), Departamento de Química, Universidad Nacional del Sur; Grupo de Investigación en*

Síntesis Orgánica Medicinal

4. *INQUISUR (CONICET-UNS), Departamento de Química, Universidad Nacional del Sur; Grupo de Investigación en Síntesis Orgánica Medicinal*

5. *INQUISUR (CONICET-UNS), Departamento de Química, Universidad Nacional del Sur; Grupo de Investigación en Síntesis Orgánica Medicinal*

6. *INIBIBB (CONICET-UNS), Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur; Laboratorio de Neurobiología de Lípidos y Estrés Oxidativo*
luzstoesselb@gmail.com

Targeting ferroptosis with specific inhibitors has emerged as a promising strategy in drug discovery. Ferroptosis is an iron-dependent cell death modality driven by lipid peroxidation and implicated in degenerative pathologies, particularly in neurodegenerative diseases. In this study, we screened an in-house library of coumarins, including both natural and synthetic derivatives, for their potential to inhibit neuronal ferroptosis. The library comprised fifteen compounds predicted in silico to cross the blood–brain barrier. These compounds were subsequently evaluated for their activity in a neuronal model of ferroptosis, using N27 dopaminergic neurons challenged with two canonical ferroptosis inducers: RSL3 (a GPX4 inhibitor) and erastin (an inhibitor of cystine uptake via the system Xc⁻ antiporter). The effect of the coumarins on cell viability was assessed after 24 h using the MTT reduction assay. Remarkably, only one active compound was identified: a synthetic coumarin–chalcone hybrid, designed within the concept of molecular hybridization, which combines the coumarin scaffold with the chalcone moiety. This prototype provided significant protection against erastin-induced ferroptosis, restoring neuronal viability at 10 and 20 μM ($p < 0.01$ and $p < 0.001$, respectively). Preliminary results of this study showed that it promoted the upregulation of SLC7A11 expression under ferroptotic conditions. In conclusion, the coumarin–chalcone hybrid can be regarded as a lead candidate ferroptosis inhibitor with potential relevance to neurodegenerative processes. Future studies will further investigate the mechanisms underlying its protective effects and assessing its value as a prototype for further optimization.

27. P1-09. MONOTERPENES AS MODULATORS OF CYCLOOXYGENASE RECEPTORS: INSIGHTS INTO ANTHELMINTIC ACTIVITY IN CAENORHABDITIS ELEGANS

Alcibeth Pulido¹, Cecilia Bouzat², Guillermina Hernando³

1. *Instituto de Investigaciones Bioquímicas de Bahía Blanca, Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS)-CONICET, 8000 Bahía Blanca, Argentina.; Neurofisiología y Farmacología Molecular*

2. *Instituto de Investigaciones Bioquímicas de Bahía Blanca, Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS)-CONICET, 8000 Bahía Blanca, Argentina.; Neurofisiología y Farmacología Molecular*

3. *Instituto de Investigaciones Bioquímicas de Bahía Blanca, Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS)-CONICET, 8000 Bahía Blanca, Argentina.; Neurofisiología y Farmacología Molecular*
alcijosepulido@gmail.com

Growing resistance to conventional anthelmintics, coupled with the limited development of new compounds, has intensified the search for alternative therapeutic strategies. Among these, combination therapy—incorporating commercial drugs, new agents, or natural products—emerges as a promising approach to broaden treatment efficacy. Monoterpenes from essential oils are particularly attractive due to their reported anthelmintic activity. Here, we evaluated the effects of geraniol and citronellol on *Caenorhabditis elegans*, both individually and in combination with commercial anthelmintics. *C. elegans* is a well-established model system for anthelmintic drug discovery. Combining bioactive phytochemicals with synthetic drugs has been proposed as a strategy to enhance nematode control in both human and veterinary medicine. Behavioral assays showed that both terpenes significantly inhibited pharyngeal pumping in wild-type worms. In glutamate-gated chloride channel (GluCl)-deficient mutants, inhibition was reduced, suggesting GluCl channels as

relevant targets. In contrast, ACR-23 (betaine-gated cation channel) and MOD-1 (serotonin-gated chloride channel) mutants did not differ from wild-type. Paralysis assays were performed by exposing synchronized adult's worms to 0.600–0.750 mM geraniol or citronellol, respectively. Both compounds exhibited clear anthelmintic activity in a concentration-dependent manner. Combinations with anthelmintics were evaluated using the Chou–Talalay combination index. In addition, body length was measured and Cys-loop receptor mutant strains were employed to identify potential molecular targets. The results position Cys-loop receptors, particularly GluCl, as relevant molecular targets and highlight geraniol and citronellol as modulators of these channels, supporting their potential use in combined therapeutic strategies for helminth control in human and veterinary health.

28. P1-10. ROS OVERPRODUCTION IS THE CAUSE OF THE ABSENCE OF CARDIOPROTECTION WHEN AMIODARONE IS INTRAARTERIALY PERFUSED IN A STUNNING MODEL OF ISCHEMIA/REPERFUSION IN ISO-LATED RAT HEARTS

Matías Bayley¹, María Inés Ragone², Alicia Elvira Consolini³
 1. *Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP), CONICET; Laboratorio de Farmacología Experimental y Energética Cardíaca*
 2. *Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP), CONICET; Laboratorio de Farmacología Experimental y Energética Cardíaca*
 3. *Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP); Laboratorio de Farmacología Experimental y Energética Cardíaca*
 mbayley@biol.unlp.edu.ar

In previous communications, we showed that oral administration of amiodarone (Amd) improved post-ischemic recovery following ischemia/reperfusion (I/R) protocols in rat hearts. However, this effect was lost when the antiarrhythmic was directly perfused before ischemia. The aim of this study was to investigate the possible causes of the loss of protection when Amd was administered via arterial perfusion. Isolated Wistar rat hearts were perfused inside a flow calorimeter to simultaneously measure left intraventricular pressure (LVP) and total heat flow (Ht, mW·g⁻¹) before and during a 30-min ischemia / 45-min reperfusion protocol. Maximal contraction (P), diastolic contracture (ΔLVEDP) and muscle economy (P/Ht) were also calculated. Amd (5 μg/ml) was perfused for 20 minutes before zero-flow ischemia. The role of nitric oxide synthases (NOS) was evaluated by perfusing L-NAME (30 μM) for 20 minutes, while the role of reactive oxygen species (ROS) was assessed using the ROS scavenger MPG (0.2 mM). When L-NAME and Amd were co-administered, post-ischemic P and P/Ht did not differ significantly from hearts perfused with Amd alone (P= 17.9±9.3% of pre-I and P/Ht= 0.8±0.4mmHg.g/mW, NS vs Amd, n=4-6), although ΔLVEDP increased during reperfusion. When MPG and Amd were co-perfused and MPG also reperfusion, post-ischemic recovery improved compared to Amd-perfused hearts (55.1±7.5%, p<0.01 vs Amd, n=4-6), although P/Ht and ΔLVEDP remained unaffected. In conclusion: a) The lack of protection of perfused Amd is not related to NOS activation, while NO production contributes to prevent diastolic contracture during reperfusion; b) The reduced protection is associated with ROS overproduction. CONICET-PIP32141, UNLPX1003.

29. P1-11. COLLATERAL SENSITIVITY OF BETULIN DERIVATIVES IN MULTIDRUG RESISTANCE LEUKEMIC CELLS
 Ignacio Lopez Enrique¹, Jazmin Lavallen², Mariana Belén Joyray³, María Cecilia Carpinella⁴

1. *Centro de Investigacion y Desarrollo en Inmunología y Enfermedades Infecciosas (CIDIE), CONICET-UCC; Productos Naturales*
 2. *Centro de Investigacion y Desarrollo en Inmunología y Enfermedades Infecciosas (CIDIE), CONICET-UCC; Productos Naturales*
 3. *Centro de Investigacion y Desarrollo en Inmunología y Enfermedades Infecciosas (CIDIE), CONICET-UCC; Productos Naturales*
 4. *Centro de Investigacion y Desarrollo en Inmunología y Enfermedades Infecciosas (CIDIE), CONICET-UCC; Productos Naturales*

4. *Centro de Investigacion y Desarrollo en Inmunología y Enfermedades Infecciosas (CIDIE), CONICET-UCC; Productos Naturales*
 ignaciolopezhenrico@cidie.ucc.edu.ar

Multidrug resistance (MDR) is one of the main limitations of chemotherapy in cancer treatment, particularly in advanced stages. This phenomenon is often associated with ATP-binding cassette (ABC) transporters, such as P-glycoprotein (P-gp) and multidrug resistance-associated protein 1 (MRP1), which actively efflux chemotherapeutic agents, reducing their intracellular concentration and leading to therapeutic failure. Therefore, new strategies to overcome MDR are urgently needed. Collateral sensitivity (CS) is a promising approach based on the observation that resistant cells may become more sensitive to certain compounds than their drug-sensitive counterparts. Natural products and their derivatives represent an important source of molecules with potential to exploit this vulnerability. In this study, a panel of semisynthetic derivatives of betulin, a triterpene previously identified from *Ligaria cuneifolia* as a P-gp inhibitor, was evaluated in chronic myeloid leukemia cell lines: the drug-sensitive K562 and its resistant counterpart FEPS. Cytotoxicity was assessed using the MTT assay. Among the compounds tested, two derivatives exhibited activity consistent with CS, with one derivative showing IC₅₀ values of 6 μM in FEPS and 14 μM in K562. These results suggest that betulin derivatives may act as CS agents in leukemia, supporting the potential of natural products as sources of novel compounds for the development of therapeutic strategies aimed at counteracting MDR in cancer.

POSTERS 2 - SAIC - FIRST-TIME PRESENTERS 1
DATE & TIME: 17/11/2025 9:30 - 11:00 H
Chairs: Carlos Pomilio, Barbara Bueloni, Helena Sterle, Mariana Garces

30. P2-01. EVALUATE THE EFFECTS OF ALTERNATIVE POLYADENYLATION ON THE GENERATION OF DIFFERENT VARIANTS OF RAC1 mRNA

María Victoria Nápoli¹, Mercedes Montani², Sofía Chemes³, Omar Coso⁴, Julian Naipauer⁵
 1. *Instituto de Fisiología, Biología Molecular y Neurociencias (IFIByNE) - Universidad de Buenos Aires / CONICET; Laboratorio de Transducción de Señales del Dr. Omar Coso*
 2. *Instituto de Fisiología, Biología Molecular y Neurociencias (IFIByNE) - Universidad de Buenos Aires / CONICET; Laboratorio de Transducción de Señales del Dr. Omar Coso*
 3. *Instituto de Fisiología, Biología Molecular y Neurociencias (IFIByNE) - Universidad de Buenos Aires / CONICET; Laboratorio de Transducción de Señales del Dr. Omar Coso*
 4. *Instituto de Fisiología, Biología Molecular y Neurociencias (IFIByNE) - Universidad de Buenos Aires / CONICET; Laboratorio de Transducción de Señales del Dr. Omar Coso*
 5. *Instituto de Fisiología, Biología Molecular y Neurociencias (IFIByNE) - Universidad de Buenos Aires / CONICET; Laboratorio de Transducción de Señales del Dr. Omar Coso*
 mvickynapoli@gmail.com

Our main objective is to study the mechanisms that link extracellular signals with the control of gene expression, to understand the dysregulations that lead to pathogenic processes, particularly in Kaposi's sarcoma (KS) caused by Kaposi's sarcoma-associated herpesvirus (KSHV or HHV-8). Recent results from our laboratories show that both mRNA stability and alternative polyadenylation (APA) contribute to modulating the quantity and/or quality of molecules available for translation. APA is defined as the use of more than one functional polyadenylation signal in a primary transcript. Rac1, a member of the Rho family of small GTPases, regulates cytoskeletal organization, cell motility, and angiogenesis, and is implicated in KS tumorigenesis. In this work, we evaluated the effects of APA on the generation of different RAC1 mRNA variants, characterized by 3'UTRs of different lengths. Previous results in our laboratory showed the existence of a proximal polyadenylation signal (PAS Proximal) and a distal one downstream (PAS Distal), both corresponding to functional APA signals. With this knowledge, we

used reporter vectors to measure the relative strength of each site selected by the cleavage and polyadenylation machinery, as well as to explore possible regulatory mechanisms involved. Our results indicate that the distal signal is stronger than the proximal signal, suggesting an intrinsic preference of the cellular machinery. Moreover, we observed that the KSHV oncogene vGPCR modifies RAC1 polyadenylation site choice, weakening distal signal usage. These findings contribute to understanding the mechanisms that determine RAC1 isoform diversity, with potential implications for its functional regulation.

31. P2-02. REGULATION OF HUMAN AMNIOTIC EPITHELIAL STEM CELLS HEPATIC DIFFERENTIATION THROUGH WNT/ β -CATENIN SIGNALING PATHWAY

Camila Zárate¹, Mabel Bonardi², Luciano Pérez³, Antonio Pérez-Pérez⁴, Mariana Jaime⁵, Victor Sánchez-Margalet⁶, Cecilia Varone⁷, Rodrigo Riedel⁸, Julieta Maymó⁹

1. Biological Chemistry Department, School of Exact and Natural Sciences, University of Buenos Aires, City of Buenos Aires, Argentina; Placental Molecular Physiology

2. IQUIBICEN-CONICET, School of Exact and Natural Sciences, University of Buenos Aires, City of Buenos Aires, Argentina; Placental Molecular Physiology

3. Biological Chemistry Department, School of Exact and Natural Sciences, University of Buenos Aires, City of Buenos Aires, Argentina; Placental Molecular Physiology

4. Department of Medical Biochemistry and Molecular Biology and Immunology, School of Medicine, University of Seville, Seville, Spain; Medical Biochemistry and Molecular Biology and Immunology

5. Posadas Hospital, Buenos Aires, Argentina; 7AmniosBMA NGO, Buenos Aires, Argentina; Obstetrics Service

6. Department of Medical Biochemistry and Molecular Biology and Immunology, School of Medicine, University of Seville, Seville, Spain; Medical Biochemistry and Molecular Biology and Immunology

7. IQUIBICEN-CONICET, School of Exact and Natural Sciences, University of Buenos Aires, City of Buenos Aires, Argentina; Placental Molecular Physiology

8. Biological Chemistry Department, School of Exact and Natural Sciences, University of Buenos Aires, City of Buenos Aires, Argentina; Placental Molecular Physiology

9. IQUIBICEN-CONICET, School of Exact and Natural Sciences, University of Buenos Aires, City of Buenos Aires, Argentina; Placental Molecular Physiology
camila.zarate03@gmail.com

The human amniotic membrane is a valuable source of stem cells, particularly human amniotic epithelial cells (hAECs). These cells express embryonic stem cell markers, are pluripotent, non-tumorigenic, and exhibit immunomodulatory properties, positioning them as attractive candidates for regenerative medicine. Hepatic failure is a major global cause of morbidity and mortality, and current therapeutic strategies have significant limitations. Recently, hAECs have been highlighted as a key source of hepatocytes due to their potential for hepatic differentiation (HD). The Wnt/ β -catenin pathway is an evolutionarily conserved signalling cascade relevant for stem cell renewal, proliferation, and differentiation, including hepatogenesis. This work aimed to study the Wnt/ β -catenin pathway participation during the hepatic differentiation of hAECs. Cells were isolated from the amniotic membrane of the human term placenta and induced to undergo HD. Pharmacological modulation of the Wnt/ β -catenin pathway was performed using LiCl, a GSK-3 β inhibitor and XAV-939, a β -catenin inhibitor. Hepatocyte-specific markers (albumin, CYP3A4, CYP7A1), glycogen synthesis, and related hepatic microRNA expression, miR-221, were assessed by Western blot, PAS assay, and qRT-PCR, respectively. Up-regulation of the Wnt/ β -catenin pathway significantly increased albumin and CYP3A4 expression, and enhanced glycogen synthesis, improving HD. Additionally, we have found LiCl significantly induced an increment in miR-221 expression during HD. Conversely, inhibition with XAV-939 decreased albumin and CYP7A1 expression and reduced glycogen synthesis. Moreover, Wnt/ β -catenin pathway inhibition during HD decreased

miR-221 expression. These findings demonstrate that Wnt/ β -catenin signalling plays a central role in regulating hAEC hepatogenic differentiation and may represent a promising approach to optimizing hAEC-based strategies for liver regeneration.

32. P2-03. GLYCOSYLATION OF 4-METHYLBELLIFERONE COUMARIN ENHANCES ANTITUMOR EFFICACY IN AN EXPERIMENTAL NON-SMALL CELL LUNG CANCER MODEL

Mara Stinco¹, Alina González², Gisela Weiz³, Constanza Arriola Benítez⁴, Mariel Fusco⁵, Paula Rosello⁶, Maglio M. Rizzo⁷, Javier Breccia⁸, Flavia V. Piccioni⁹, Mariana Malvicini¹⁰

1. Instituto de Investigaciones en Medicina Traslacional (IIMT); Inmunobiología del Cáncer

2. Universidad de La Pampa; Laboratorio de Biocatálisis

3. Universidad de La Pampa; Laboratorio de Biocatálisis

4. Instituto de Investigaciones en Medicina Traslacional (IIMT-Universidad Austral-CONICET); Laboratorio de Inmunobiología del Cáncer

5. Instituto de Investigaciones en Medicina Traslacional (IIMT-Universidad Austral-CONICET); Laboratorio de Inmunobiología del Cáncer

6. Instituto de Investigaciones en Medicina Traslacional (IIMT-Universidad Austral-CONICET); Laboratorio de Inmunobiología del Cáncer

7. Servicio de Oncología, Hospital Universitario Austral.; Laboratorio de Inmunobiología del Cáncer

8. Universidad de La Pampa; Laboratorio de Biocatálisis

9. Instituto de Investigaciones en Medicina Traslacional (IIMT-Universidad Austral-CONICET); Laboratorio de Inmunobiología del Cáncer

10. Instituto de Investigaciones en Medicina Traslacional (IIMT-Universidad Austral-CONICET); Laboratorio de Inmunobiología del Cáncer
marastinco@gmail.com

Lung cancer is the leading cause of cancer-related mortality worldwide, with non-small cell lung cancer (NSCLC) accounting for more than two-thirds of cases. Current therapeutic strategies provide modest benefits, and selective eradication of tumor cells without affecting normal tissues remains a major challenge. Because tumor cells display increased glucose dependence and high glycolytic activity, glycosylation of therapeutic compounds represents a promising approach to enhance tumor selectivity and treatment efficacy. We evaluated the effects of glycosylated 4-methylumbelliferone (MuR; rutinoyl-4-Mu) in experimental NSCLC models. Murine LLC and human A549 cells exhibited significantly greater sensitivity to MuR compared with 4Mu, with IC50 values of 314 vs. 630 μ M in LLC and 460 vs. 2260 μ M in A549 cells, respectively. Human H1299 cells showed no differences between treatments and was also less responsive. Importantly, MuR did not affect the viability of non-tumor hepatic stellate cells (LX-2). In LLC cells, treatment with 250 μ M MuR induced a twofold increase in apoptosis relative to 4Mu at the same dose ($p < 0.05$). In vivo, MuR therapy reduced tumor volume by 44% compared with untreated controls ($p < 0.05$). Transcriptomic analysis of the TCGA Lung Adenocarcinoma (LUAD) dataset ($N = 706$) revealed that glucose transporter GLUT1 is upregulated in tumors from NSCLC patients, whereas the asialoglycoprotein receptors ASGR1 and ASGR2 are significantly downregulated relative to normal adjacent tissue ($p < 0.0001$). Notably, MuR treatment increased ASGR1 expression and reduced GLUT1 expression in LLC cells ($p < 0.05$). These findings indicate that glycosylation of 4Mu to generate MuR.

33. P2-04. SOLUBLE TUBULIN IN MOUSE SPERM: A NOVEL POOL ASSOCIATED WITH CAPACITATION AND METABOLIC PATHWAYS

Liza J. Schiavi-Ehrenhaus¹, Luna Magrotti Messa², Ana Romarowski³, Lucila R. Gómez Olivieri⁴, Cintia Stival⁵, Diego Krapf⁶, Darío Krapf⁷, Adán Guerrero⁸, Mariano G. Buffone⁹, Guillermina M. Luque¹⁰

1. Instituto de Biología y Medicina Experimental (IBYME-CONICET), Ciudad de Buenos Aires, Argentina; Biología Ce-

lular y Molecular de la Reproducción

2. Instituto de Biología y Medicina Experimental (IBYME-CO-NICET), Ciudad de Buenos Aires, Argentina; *Biología Celular y Molecular de la Reproducción*

3. Instituto de Biología y Medicina Experimental (IBYME-CO-NICET), Ciudad de Buenos Aires, Argentina.; *Biología Celular y Molecular de la Reproducción*

4. Instituto de Biología y Medicina Experimental (IBYME-CO-NICET), Ciudad de Buenos Aires, Argentina.; *Biología Celular y Molecular de la Reproducción*

5. Instituto de Biología Molecular y Celular de Rosario, CO-NICET-UNR, Rosario, Argentina.; *Cascadas de señalización celular*

6. Department of Electrical and Computer Engineering and School of Biomedical Engineering, Colorado State University, Fort Collins, United States.; *Krapf lab - Single Molecule Biophysics*

7. Instituto de Biología Molecular y Celular de Rosario, CO-NICET-UNR, Rosario, Argentina.; *Cascadas de señalización celular*

8. Instituto de Biotecnología, Universidad Nacional Autónoma de México (UNAM), Cuernavaca, Mexico.; *Laboratorio Nacional de Microscopía Avanzada*

9. Instituto de Biología y Medicina Experimental (IBYME-CO-NICET), Ciudad de Buenos Aires, Argentina.; *Biología Celular y Molecular de la Reproducción*

10. Instituto de Biología y Medicina Experimental (IBYME-CO-NICET), Ciudad de Buenos Aires, Argentina; *Biología Celular y Molecular de la Reproducción*
jlsehrenhaus@gmail.com

Tubulins are conserved cytoskeletal proteins best known for their role in microtubule formation. In mammalian sperm, α - and β -tubulin are classically associated with the axoneme, the flagellar structure essential for motility. However, evidence from somatic cells indicates that tubulin also exists in non-polymerized, soluble pools with regulatory roles, particularly through interactions with ion channels and signaling proteins. Whether such soluble tubulin populations exist in sperm and contribute to signaling during capacitation remains largely unexplored. Here, we report the presence of a small fraction (<10%) of tubulin in the detergent-soluble fraction of mouse sperm, behaving like a cytosolic or membrane-associated protein rather than a polymerized component. This soluble tubulin displayed a dynamic distribution dependent on capacitation conditions and required extracellular Ca^{2+} , soluble adenylyl cyclase (sAC), and PKA activity for its maintenance. Mass spectrometry identified 12 tubulin isoforms across sperm fractions, with distinct enrichment patterns: three isoforms were exclusive to the soluble pool, and two others were significantly enriched compared to the insoluble fraction. Moreover, soluble TUBB4B exhibited unique post-translational modifications, including Lys122 acetylation and Met147 oxidation, absent from insoluble counterparts. Proteomic analysis of soluble tubulin interactors revealed an enrichment of metabolic proteins, particularly those linked to carbohydrate metabolism and mitochondrial function, suggesting potential roles in energy sensing and signaling. Together, these findings uncover a previously unrecognized pool of soluble tubulin in sperm, regulated by capacitation-associated pathways, and suggest that it may contribute to the integration of metabolic and signaling networks required for fertilization competence.

34. P2-05. LOW-DOSE EARLY POSTNATAL ZEARELENONE EXPOSURE PROMOTES PRECOCIOUS PUBERTY, WEIGHT GAIN, AND IMPAIRED REPRODUCTIVE CAPACITY IN FEMALE RATS

Gabriela Anahí Bressan¹, Lucila Mijno², Ramiro Alarcón³, Enrique Hugo Luque⁴, Paola Inés Ingaramo⁵, María Laura Zenclussen⁶

1. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; *Fisiopatología Ambiental*

2. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional

del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; *Fisiopatología Ambiental*

3. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; *Fisiopatología Ambiental*

4. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; *Fisiopatología Ambiental*

5. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; *Fisiopatología Ambiental*

6. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; *Fisiopatología Ambiental*
gibressan98@hotmail.com

Exposure to environmental pollutants with estrogenic activity can cause problems such as precocious puberty and subfertility. One of the most widespread pollutants with estrogenic activity is zearalenone (ZEA), a mycotoxin that colonizes cereals and develops in humid conditions. Although its estrogenic activity was found at high doses, it is unknown whether the exposure to "safe" doses could cause any effect. To investigate this, we subcutaneously treated newborn female rat pups with either 0.25 $\mu\text{g/kg}$ of ZEA dissolved in sesame oil (ZEA group) or sesame oil alone (control group) on post-natal days (PND)1, 3, 5 and 7. The rats were then monitored and kept under normal household conditions until they reached a reproductive age. Females from both groups were analyzed for vaginal opening and weighed weekly from PND21 to PND90. Interestingly, rats exposed to ZEA ($n = 10$) showed vaginal opening at an earlier age than control rats ($n = 9$), indicating an earlier onset of puberty ($p < 0.05$). Additionally, ZEA-exposed rats had significantly higher weights from PND49 to PND77 ($p < 0.05$). From PND90 onwards, the rats were mated with males of proven fertility. The reproductive performance of these females was assessed on gestational day 15 (GD15). Notably, three out of ten ZEA-treated females showed severe pre-implantation failure. These findings demonstrate that neonatal exposure to low-dose ZEA accelerates puberty onset, increases body weight, and may impair implantation. Overall, the results highlight the need for further studies to confirm these observations and reassess the safety of low-dose ZEA exposure.

35. P2-06. DIAGNOSTIC ALGORITHM IN DUCHENNE MUSCULAR DYSTROPHY: FROM INDEX CASE TO PRENATAL TESTING

Micaela Ciepelinski¹, Carmen Llamas Massini², Micaela Carcione³, Agustina Bernardi⁴, Florencia Giliberto⁵

1. Laboratorio de Distrofinopatías, Cátedra de Genética, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Buenos Aires, Argentina; Instituto de Inmunología, Genética y Metabolismo INIGEM, (UBA-CONICET), Buenos Aires, Argentina.; Laboratorio de Distrofinopatías, FFyB (UBA); INIGEM (UBA-CONICET)

2. Laboratorio de Distrofinopatías, Cátedra de Genética, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Buenos Aires, Argentina; Instituto de Inmunología, Genética y Metabolismo INIGEM, (UBA-CONICET), Buenos Aires, Argentina.; Laboratorio de Distrofinopatías, FFyB (UBA); INIGEM (UBA-CONICET)

3. Laboratorio de Distrofinopatías, Cátedra de Genética, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Buenos Aires, Argentina; Instituto de Inmunología, Genética y Metabolismo INIGEM, (UBA-CONICET), Buenos Aires, Argentina.; Laboratorio de Distrofinopatías, FFyB (UBA); INIGEM (UBA-CONICET)

4. Laboratorio de Distrofinopatías, Cátedra de Genética, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Buenos Aires, Argentina; Instituto de Inmunología, Genética y Metabolismo INIGEM, (UBA-CONICET), Buenos Aires

res, Argentina.; Laboratorio de Distrofinopatías, FFyB (UBA); INIGEM (UBA-CONICET)

5. Laboratorio de Distrofinopatías, Cátedra de Genética, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Buenos Aires, Argentina.; Instituto de Inmunología, Genética y Metabolismo INIGEM, (UBA-CONICET), Buenos Aires, Argentina.; Laboratorio de Distrofinopatías, FFyB (UBA); INIGEM (UBA-CONICET)
micaciepe@gmail.com

Duchenne muscular dystrophy (DMD) is the most common and severe childhood-onset muscular dystrophy, classified as an X-linked neuromuscular disorder. It is caused by pathogenic variants in DMD gene, which encodes dystrophin protein essential for skeletal muscle function. Here we present a didactic case that illustrates the step-wise diagnostic algorithm implemented in our laboratory, to achieve definitive diagnosis and guide genetic counseling. We analyzed a family including an index case, a 5-year-old male patient with clinical features and elevated CK levels suggestive of DMD, his two sisters, and later a prenatal sample. The index case tested negative by MLPA, and subsequent WES revealed a nonsense variant in exon 21 (NM_004006.3: c.2626G>T; p.Glu876*), which was confirmed by Sanger sequencing. The variant, classified as pathogenic (ACMG-AMP: PVS1, PM2, PP4), is reported in ClinVar (ID 984110) and LOVD3, and affects all full-length isoforms (Dp427m, Dp427b, Dp427p), consistent with a classic Duchenne phenotype. Cascade testing confirmed the mother as a carrier and enabled risk assessment for her daughters. One of them, also a carrier, required urgent prenatal diagnosis during her third pregnancy. Chorionic villus sampling revealed the familial variant in a male fetus, with STR analysis specifically used to exclude significant maternal contamination. This case highlights the value of a comprehensive molecular workflow integrating MLPA, WES, and Sanger sequencing. Beyond diagnosis, molecular testing proved essential for carrier detection, family counseling, reproductive planning, and evaluating therapeutic eligibility. Presented as an educational example, it illustrates how genetic tools can be effectively applied in clinical practice for decision-making.

36. P2-07. EVIDENCE OF CELL FUSION EVENTS DURING CARDIAC DIFFERENTIATION OF HUMAN INDUCED PLURIPOTENT STEM CELL-DERIVED CARDIOMYOCYTES

Theo Fernández Long¹, Julia Halek², Joaquín Smucler³, Ariel Waisman⁴

1. INEU-FLENI; Laboratorio de Investigación Aplicada a Neurociencias (LIAN) - FLENI

2. INEU-FLENI; Laboratorio de Investigación Aplicada a Neurociencias (LIAN) - FLENI

3. INEU-FLENI; Laboratorio de Investigación Aplicada a Neurociencias (LIAN) - FLENI

4. INEU-FLENI; Laboratorio de Investigación Aplicada a Neurociencias (LIAN) - FLENI

theofernandezlong@gmail.com

The generation of cardiomyocytes (CMs) from human induced pluripotent stem cells (hiPSCs) is an essential model for cardiovascular research. Although widely used, the cellular and molecular mechanisms underlying differentiation are not fully understood. Less than 10% of adult cardiomyocytes are diploid, with the majority being polyploid or binucleated, thought to be mediated through alterations in karyokinesis and cytokinesis. Interestingly, we observed CMs with an odd number of nuclei, which may indicate cell fusion events during differentiation. This study aimed to experimentally investigate such fusion events. To demonstrate cell fusion between cardiomyocytes during hiPSC differentiation, we developed a dual nuclear reporter system using two hiPSC lines: a pre-existing line expressing H2B-Cerulean (green fluorescence) and a novel line engineered expressing H2B-emRFP670 (red fluorescence), by subcloning the transgene into a PiggyBac plasmid. The new reporter line was validated by confirming pluripotency markers (OCT4, NANOG, SOX2) and its capacity to differentiate into CMs,

evidenced by cardiac markers (TNNT2, NKX2.5, MYH6, MYL7). To detect fusion, both lines were co-cultured at 1:1 ratio and subjected to cardiac differentiation protocol over 37 days. During co-culture and differentiation, we observed cells containing nuclei positive for both fluorescent markers, providing direct evidence of cell fusion. These cells were efficiently quantified by epifluorescence microscopy and flow cytometry. Using a dual nuclear reporter system, we demonstrate that cell fusion events occur between hiPSC-derived CMs during cardiac differentiation. This finding provides a novel mechanistic explanation for multinucleated cardiomyocyte generation and opens new perspectives for understanding their biology and regenerative applications.

37. P2-08. IN VITRO STUDIES OF A NOVEL BORON-DE-RIVED ERLOTINIB FOR USE IN BORON NEUTRON CAPTURE THERAPY (BNCT) FOR THE TREATMENT OF REFRACTORY CANCERS

Candela Domínguez¹, Matías Svarzchtein², Maite Vallota³, Estanislao Pavlik⁴, Antonella Pastini⁵, Andrés Bechis⁶, Pablo Vallecorsa⁷, María Silvina Olivera⁸, Marcos Couto Sire⁹, Hugo Cerecetto¹⁰, Pablo Menéndez¹¹, Laura Todaro¹², Alejandro Urtreger¹³, Marina Carpano¹⁴, María Alejandra Dagrosa¹⁵

1. Escuela Ort (Sede Almagro). Especialidad de Química y Biotecnología. Ciudad Autónoma de Buenos Aires, Argentina; Centro Oncológico de Medicina Nuclear. Instituto de Oncología "Ángel Roffo. Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

2. Escuela Ort (Sede Almagro). Especialidad de Química y Biotecnología. Ciudad Autónoma de Buenos Aires, Argentina; Centro Oncológico de Medicina Nuclear. Instituto de Oncología "Ángel Roffo. Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

3. Escuela Ort (Sede Almagro). Especialidad de Química y Biotecnología. Ciudad Autónoma de Buenos Aires, Argentina; Centro Oncológico de Medicina Nuclear. Instituto de Oncología "Ángel Roffo. Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

4. Facultad de Ciencias Exactas y de la Ingeniería, Universidad Favaloro (UF). Ciudad Autónoma de Buenos Aires, Argentina; Centro Oncológico de Medicina Nuclear. Instituto de Oncología "Ángel Roffo. Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

5. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Ciudad Autónoma de Buenos Aires, Argentina; Centro Oncológico de Medicina Nuclear. Instituto de Oncología "Ángel Roffo. Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

6. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Ciudad Autónoma de Buenos Aires, Argentina; Área de Investigación Instituto de Oncología "Ángel Roffo". Facultad de Medicina, Universidad de Buenos Aires. Argentina

7. Comisión Nacional de Energía Atómica; Departamento Terapia por Captura Neutrónica en Boro. Centro Atómico Constituyentes. Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

8. Comisión Nacional de Energía Atómica; Departamento Terapia por Captura Neutrónica en Boro. Centro Atómico Constituyentes. Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

9. Instituto de Química Biológica. Facultad de Ciencias, Universidad de la República. Montevideo, Uruguay; Grupo de Química Orgánica Medicinal, Instituto de Química Biológica. Facultad de Ciencias, Universidad de la República. Montevideo, Uruguay

10. Instituto de Química Biológica. Facultad de Ciencias, Universidad de la República. Montevideo, Uruguay; Grupo de Química Orgánica Medicinal, Instituto de Química Biológica. Facultad de Ciencias, Universidad de la República. Montevideo, Uruguay

11. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Dirección de Terapia Radiante y Medici-

na Nuclear. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina

12. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Ciudad Autónoma de Buenos Aires, Argentina; Área de Investigación Instituto de Oncología "Ángel Roffo". Facultad de Medicina, Universidad de Buenos Aires. Argentina

13. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Ciudad Autónoma de Buenos Aires, Argentina; Área de Investigación Instituto de Oncología "Ángel Roffo". Facultad de Medicina, Universidad de Buenos Aires. Argentina

14. Comisión Nacional de Energía Atómica; Departamento de Radiobiología. Centro Atómico Constituyentes. Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

15. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Ciudad Autónoma de Buenos Aires, Argentina; Centro Oncológico de Medicina Nuclear. Instituto de Oncología "Ángel Roffo". Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina
alejandradagrosa@gmail.com

Introduction: Boron neutron capture therapy (BNCT) based on the ^{10}B (n, α) ^7Li nuclear reaction is a therapy for the treatment of tumors refractory to conventional therapies. Boron phenylalanine (BPA) is one of two boron compounds currently used in clinical trials with a low tumor selectivity (<3). Looking to improve the effectiveness of BNCT, a new boron drug derived from erlotinib, which is used in targeted therapy, was joined to organometallic carboranes containing boron. The aim of these studies was to evaluate the use of borated erlotinib for the treatment of advanced cutaneous melanoma and non-small cell lung (NSCLC). **Materials and Methods:** Proliferating human melanoma (Mel J) and NSCLC cisplatin-resistant (H125cpr) cell lines were incubated with borated erlotinib (Cmpd.3) at a concentration lower than their IC50 (15 μM) for 2, 4 and 24 hours. Boron content was measured by ICP-AES. Cells were incubated with 1 ppm boron-10 and irradiated in the RA-3 (neutron flux = 3.3×10^{11} n/cm ^{2} ·min), after cell survival by MTT and cell death by fluorescence microscopy were measured. **Results:** The Cmpd.3 uptake was 58 and 12.5 times higher than BPA uptake at 24 h for Mel J and H125cpr respectively. On the other hand the BPA uptake was significantly higher for lung cancer than for melanoma ($p < 0.01$). Cell survival post irradiation showed a tendency to decrease using cmpd.3 greater than with BPA and the percentage of death was mainly by necrosis with both drugs. **Conclusions:** Cmpd.3 showed to be a good candidate borated drug to BNCT in refractory cancers.

38. P2-09. METABOLIC REWIRING IN GLIOBLASTOMA: INHIBITION OF FATTY ACID β -OXIDATION FUELS THE WARBURG EFFECT AND COMPROMISES CELL SURVIVAL

Lola Martínez Ibarquén¹, Fiorella Orsini Zanetti², Juan Manuel Eggedman³, Catalina Lodillinsky⁴, Marcela Solange Villaverde⁵

1. Instituto de Oncología Ángel H. Roffo; Unidad de Transferencia Genética y Laboratorio de Metabolismo Tumoral

2. Instituto de Oncología Ángel H. Roffo, FMED, UBA; Unidad de Transferencia Genética y Laboratorio de Metabolismo Tumoral

3. Instituto de Oncología Ángel H. Roffo, FMED, UBA; Unidad de Transferencia Genética y Laboratorio de Metabolismo Tumoral

4. Instituto de Oncología Ángel H. Roffo, FMED, UBA; Departamento de Inmunobiología

5. Instituto de Oncología Ángel H. Roffo, FMED, UBA; Unidad de Transferencia Genética y Laboratorio de Metabolismo Tumoral, Área Investigación.

martinezibargurenloa@gmail.com

Metabolic reprogramming is a hallmark of tumor progression. Glioblastoma (GB), the most aggressive brain tumor, exhibits overexpression of fatty acid oxidation (FAO)-related genes, particularly carnitine palmitoyltransferase 1A (CPT1A). To investigate the rel-

evance of FAO in GB progression, we treated U251 human GB cells with etomoxir (ETO, 1–1000 μM), an inhibitor of CPT1A. After treatment (5 days in monolayers or 9 days in spheroids), U251 viability (assessed by crystal violet and APH assays, respectively) was significantly reduced ($p < 0.05$; IC50: 118 μM). Moreover, spheroid morphology was notably disrupted after only 2 days of treatment. However, U251 cell size and complexity remained conserved up to 72 h with 200 μM ETO (analyzed by FSC and SSC, flow cytometry). Interestingly, FAO inhibition promoted increased glucose consumption and lactate production ($p < 0.05$, determined using Glucose and Lactate Detection Kits, Wiener Lab and RANDOX, respectively), accompanied by extracellular acidification. We next examined whether 2-deoxyglucose (2DG, 1–2.5 mM), an inhibitor of the glycolytic enzyme hexokinase (HK), could enhance the cytotoxic effects of FAO inhibition. After 72 h, 2DG effectively potentiated the effects compared to each agent alone. Taken together, our results suggest that FAO represents a relevant energy source for GB cells, since its inhibition enhances glycolytic flux, likely as a compensatory mechanism. This study highlights a novel avenue to investigate the metabolic rewiring of GB, shifting between glycolysis and FAO.

39. P2-10. MATERNAL COENZYME Q10 SUPPLEMENTATION IMPROVES PREGNANCY OUTCOMES AND PRESERVES PLACENTAL MORPHOLOGY IN A RAT MODEL OF ADVANCED MATERNAL AGE

Alejandro Ranieri¹, María Laura Leonardi², Daniela Wainryb³, Lautaro Recchia⁴, Alicia Jawerbaum⁵, Romina Higa⁶

1. Centro de Estudios Farmacológicos y Botánicos, UBA-CO-NICET; Laboratorio de Reproducción y Metabolismo

2. Centro de Estudios Farmacológicos y Botánicos, UBA-CO-NICET; Laboratorio de Reproducción y Metabolismo

3. Centro de Estudios Farmacológicos y Botánicos, UBA-CO-NICET; Laboratorio de Reproducción y Metabolismo

4. Centro de Estudios Farmacológicos y Botánicos, UBA-CO-NICET; Laboratorio de Reproducción y Metabolismo

5. Centro de Estudios Farmacológicos y Botánicos, UBA-CO-NICET; Laboratorio de Reproducción y Metabolismo

6. Centro de Estudios Farmacológicos y Botánicos, UBA-CO-NICET; Laboratorio de Reproducción y Metabolismo
ranieriale77@gmail.com

Proper placental development is essential for sustaining pregnancy and supporting fetal growth. Pregnancies at advanced maternal age (AMA, more than 35 years in humans) are frequently associated with obstetric complications linked to placental dysfunction. We previously evaluated AMA rats at gestational day (GD) 12 and found increased decidual oxidative stress, a reduced embryonic growth and a disrupted balance between cellular proliferation and senescence in trophoblast, related to a reduction in the labyrinthine zone length. Here, we evaluated AMA rats at term (GD 21) and aimed to assess the effect of a maternal treatment with coenzyme Q10 (CoQ10, a mitochondrial antioxidant) on pregnancy outcomes and placental morphology. **Methods:** Three-months-old (Control) and 10-months-old (AMA) Wistar rats were mated with young males and orally treated with CoQ10 (100 mg/kg/day) or vehicle from GD1 to GD21. Pregnancy outcomes and histological placental morphology were assessed at GD21. **Results:** At term, AMA dams showed reduced fetal growth (-15%, $p < 0.05$), increased placental weight (+121%, $p < 0.001$), and decreased placental efficiency, as well as reduced area of labyrinthine zone (-11%, $p < 0.05$) compared to controls. In AMA dams, maternal CoQ10 treatment normalized placental weight ($p < 0.05$), increased placental efficiency, and restored fetal growth in females ($p < 0.05$). Histological analysis showed that CoQ10 prevented the reduction in the area of the labyrinthine zone (+116%, $p < 0.05$) in AMA dams. **Conclusion:** AMA induced fetal growth restriction probably due to impaired labyrinth development leading to a reduced placental efficiency in rats. Maternal CoQ10 treatment improved placental morphology and function highlighting its potential to ameliorate pregnancy outcomes at AMA.

40. P2-11. TOWARD AN OVARY-ON-CHIP: DEVELOPMENT OF A MICROFLUIDIC PLATFORM FOR IN VITRO FOLLICLE MATURATION AND OVULATION

Valeria Patricia Sanchez¹, Valentina Galliani², Julian Abud³, Claudio Berli⁴, Horacio Adolfo Rodríguez⁵

1. Instituto de Salud y Ambiente del Litoral (ISAL), Universidad Nacional del Litoral (UNL) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina; -

2. Instituto de Salud y Ambiente del Litoral (ISAL), Universidad Nacional del Litoral (UNL) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina; -

3. Instituto de Salud y Ambiente del Litoral (ISAL), Universidad Nacional del Litoral (UNL) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina; -

4. Instituto de Desarrollo Tecnológico para la Industria Química (INTEC), UNL-CONICET, Predio CCT CONICET Santa Fe, Argentina; -

5. Instituto de Salud y Ambiente del Litoral (ISAL), Universidad Nacional del Litoral (UNL) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina.; -

vale.sanchez.055@gmail.com

Traditional in vitro culture systems present significant limitations in reproducing the complex and dynamic microenvironment required for follicular development and ovulation. Microfluidics offers an innovative framework to overcome these constraints, enabling fine-tuned control of culture conditions and material interfaces. The aim of this work is to develop an Ovary-on-chip platform by adapting a conventional in vitro ovulation assay to microfluidic technology. In an exploratory stage, we systematically evaluated four different chip designs, testing variations in materials, lid and base structures, and overall chamber configuration. To optimize gas exchange, different configurations of gas-permeable membranes were incorporated and compared. Culture parameters were also challenged by modulating FSH concentrations across a wide range (0.1 IU/ml-10 mIU/ml). Functional assessment was performed using an average of 10 ovarian follicles from prepubertal Wistar rats per experiment. Follicles were encapsulated in 0.5% calcium alginate beads to recreate a 3D environment and cultured for 10–12 days. Cell viability and follicular diameter were monitored throughout. Under these conditions, 25%–40% of the follicles achieved sustained growth, with diameters increasing 1.5-2.5 fold relative to the baseline. Altogether, our findings highlight that the developed platform is not only functional but also versatile, supporting follicular survival and growth while allowing controlled testing of structural and hormonal variables. This work represents a key step toward a reproducible and physiologically relevant Ovary-on-chip model, with the next stage focused on establishing reliable induction and monitoring of in vitro ovulation.

41. P2-12. ANDROGEN RECEPTOR INHIBITION UNLOCKS PKA/OSTEOPONTIN ACTIVATION AND PROSTATE CANCER THERAPY RESISTANCE

Julia Lechuga¹, Agustina Sabater², Rocio Seniuk³, Elba Vazquez⁴, Estefania Labanca⁵, Nicolas Anselmino⁶, Geraldine Gueron⁷, Pablo Sanchis⁸

1. Laboratorio de Inflamación y Cáncer, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires C1428EGA, Argentina; CONICET-Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN), Buenos Aires C1428EGA, Argentina.; Laboratorio de Inflamación y Cáncer

2. Laboratorio de Inflamación y Cáncer, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires C1428EGA, Argentina; CONICET-Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN), Buenos Aires C1428EGA, Argentina; Universidad Argentina de la Empresa (UADE), Instituto de Tecnología (INTEC), Buenos Aires C1073AAO, Argentina; Department of Genitourinary Medical Oncology and The

David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA.; Laboratorio de Inflamación y Cáncer

3. Laboratorio de Inflamación y Cáncer, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires C1428EGA, Argentina; CONICET-Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN), Buenos Aires C1428EGA, Argentina; Laboratorio de Inflamación y Cáncer

4. Laboratorio de Inflamación y Cáncer, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires C1428EGA, Argentina; CONICET-Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN), Buenos Aires C1428EGA, Argentina; Laboratorio de Inflamación y Cáncer

5. Department of Genitourinary Medical Oncology and The David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA.

6. Prostate Cancer Research Group, Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, Barcelona, Spain

7. Laboratorio de Inflamación y Cáncer, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires C1428EGA, Argentina; CONICET-Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN), Buenos Aires C1428EGA, Argentina.; Laboratorio de Inflamación y Cáncer

8. Laboratorio de Inflamación y Cáncer, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires C1428EGA, Argentina; CONICET-Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN), Buenos Aires C1073AAO, Argentina; Universidad Argentina de la Empresa (UADE), Instituto de Tecnología (INTEC), Buenos Aires C1073AAO, Argentina; Department of Genitourinary Medical Oncology and The David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA.; Laboratorio de Inflamación y Cáncer

julialechu@gmail.com

SPP1 (osteopontin), a protein characterized for its role in bone physiology, has been tightly associated with prostate cancer (PCa). We have uncovered that bone-derived collagen I and fibronectin activate PKA which in turn regulates SPP1 expression in PCa. Here, we aimed at elucidating the role of the androgen receptor (AR) in the PKA/SPP1 axis. Using transcriptomics data from metastatic PCa patients (SU2C-PCF dataset), we observed that those with high AR-score had lower SPP1 expression and PKA activity ($P < 0.05$), suggesting a negative regulatory role of AR. In vitro, AR-positive C42B cells did not show SPP1 expression by RT-qPCR. This negative crosstalk was confirmed by transfecting PC3 cells (AR-negative) with pcDNA3-AR (sequence for AR). In this model, dihydrotestosterone (DHT; AR-inducer) 10nM reverted PKA/SPP1 axis upregulation induced by forskolin (FK; PKA-inducer; 10uM for 24h). In vivo, we injected C42B cells into the femurs of male CB17 SCID mice, which were sham or surgically castrated. Consistently, we observed an increase in both SPP1 staining and PKA activity in C42B bone xenotransplants after castration by IHC. Functionally, PKA activation with FK conferred resistance to the cytotoxic effect of enzalutamide (AR-inhibitor) in C42B cells ($P < 0.05$). In addition, H89 treatment (PKA inhibitor, 10uM, 7 days) significantly reduced colony formation in PC3 cells ($P < 0.05$). Overall, we demonstrated that AR exerts a negative regulation in the PKA/SPP1 axis, which is required for cell survival and clonogenic growth, indicating a potential role of this crosstalk as a contributor to therapy resistance.

42. P2-13. THE A7 NICOTINIC RECEPTOR IN RETINAL PIGMENT EPITHELIUM: EXPLORING A NEW PHARMACOLOGICAL TARGET

Nicolás Elías Castro¹, María Florencia Fernández Delias², Juan Facundo Chrestia³, Ignacio Bergé⁴, María del Carmen Esandi⁵, Cecilia Bouzat⁶

1. Instituto de Investigaciones Bioquímicas de Bahía Blanca, Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS)-CONICET; Neurofisiología y Farmacología Molecular

2. Instituto de Investigaciones Bioquímicas de Bahía Blanca, Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS)-CONICET; Neurofisiología y Farmacología Molecular

3. Instituto de Investigaciones Bioquímicas de Bahía Blanca, Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS)-CONICET; Neurofisiología y Farmacología Molecular

4. Instituto de Investigaciones Bioquímicas de Bahía Blanca, Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS)-CONICET; Neurofisiología y Farmacología Molecular

5. Instituto de Investigaciones Bioquímicas de Bahía Blanca, Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS)-CONICET; Neurofisiología y Farmacología Molecular

6. Instituto de Investigaciones Bioquímicas de Bahía Blanca, Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS)-CONICET; Neurofisiología y Farmacología Molecular
nicocastro299@gmail.com

The $\alpha 7$ nicotinic acetylcholine receptor is highly expressed in the brain and also found in non-neuronal cells, including epithelial and immune cells. It contributes to cognition, memory, neuroprotection, and inflammation regulation, and is increasingly studied as a therapeutic target in neurodegenerative and inflammatory disorders. The retinal pigment epithelium (RPE) supports photoreceptor function and maintains the outer blood-retinal barrier. RPE dysfunction is implicated in age-related macular degeneration (AMD), in which oxidative stress drives inflammation. Evidence suggests $\alpha 7$ is expressed in RPE, but its role remains unclear. We investigated $\alpha 7$ in the D407 cell line, a model of RPE cells. Using real-time PCR, immunofluorescence with anti- $\alpha 7$ antibody or alpha-bungarotoxin, confocal microscopy, and flow cytometry, we confirmed $\alpha 7$ expression. Notably, $\alpha 7$ cell distribution changed upon exposure to stressors such as ferric ammonium citrate (FAC) or β -amyloid. Functional activity was confirmed using fluo-4AM, showing a 3-fold increase in intracellular calcium following $\alpha 7$ stimulation. FAC-induced oxidative stress elevated reactive oxygen species (ROS), measured with DCFH-DA, but preincubation with an $\alpha 7$ agonist significantly reduced ROS levels. This study characterizes $\alpha 7$ in D407 cells and reveals its dynamic localization and protective role under oxidative stress. These findings support further exploration of $\alpha 7$ as a therapeutic target in retinal neurodegeneration.

43. P2-14. HO-1 NUCLEAR INTERACTORS DEFINE A NEUROENDOCRINE SIGNATURE IN PROSTATE CANCER REVEALED BY PDX MODELS AND SPATIAL TRANSCRIPTOMICS

Miranda Alfonsín¹, Magdalena Delfino², Pablo Sanchis³, Agustina Sabater⁴, Gastón Pascual⁵, Elba Vazquez⁶, Javier Cotignola⁷, Ayelén Toro⁸, Geraldine Gueron⁹, Rocio Seniuk¹⁰

1. IQUIBICEN - CONICET; Laboratorio de Inflamación y Cáncer

2. IQUIBICEN - CONICET; Laboratorio de Inflamación y Cáncer

3. IQUIBICEN - CONICET - MDACC - UADE; Department of Genitourinary Medical Oncology

4. IQUIBICEN - CONICET - MDACC - UADE; Department of Genitourinary Medical Oncology

5. IQUIBICEN - CONICET; Laboratorio de Inflamación y Cáncer

6. IQUIBICEN - CONICET; Laboratorio de Inflamación y Cáncer

7. IQUIBICEN - CONICET; Laboratorio de Inflamación y Cáncer

8. IQUIBICEN - CONICET; Laboratorio de Inflamación y Cáncer

9. IQUIBICEN - CONICET; Laboratorio de Inflamación y Cáncer

10. IQUIBICEN - CONICET; Laboratorio de Inflamación y Cáncer
alfonsinmiranda@gmail.com

Prostate cancer (PCa) progression towards neuroendocrine prostate cancer (NEPC) represents a lethal clinical scenario characterized by loss of androgen receptor signaling, cellular plasticity, and poor prognosis. Our group has previously defined the nuclear interactome of heme oxygenase-1 (HO-1), identifying factors such as BCLAF1, SAFB, DDX17, and ILF3 as potential transcriptional modulators associated with aggressive phenotypes. Transcriptomic analysis of patient-derived xenografts (PDXs) revealed that high expression of HO-1 interactors segregates with NEPC models in an unsupervised analysis, suggesting their role in lineage reprogramming. To validate these findings in clinical settings, we applied spatial transcriptomics to tumor samples from a patient harboring mixed histology, comprising adenocarcinoma and neuroendocrine regions. Spatially resolved expression confirmed the enrichment of canonical NE markers (CHGA, SYP, ENO2, EZH2) in NEPC foci, while HO-1 interactors displayed distinct expression patterns, clustering with neuroendocrine areas and diverging from adenocarcinoma regions. The integration of PDX-based transcriptomics and patient-derived spatial transcriptomics highlights HO-1 nuclear interactors as novel components of the NEPC transcriptional program. This dual approach underscores their potential as biomarkers for the identification of aggressive PCa subtypes and opens new avenues for targeted therapeutic strategies.

ORALES 3 - SAIC - NEUROCIENCIAS

DATE & TIME: 17/11/2025 13:00 - 14:30 H

Chairs: Diego Gelman, Lucía Moro

44. O3-01. DYSREGULATION OF MITOCHONDRIAL DYNAMICS-RELATED TRANSCRIPTS IN i3-NEURONS DERIVED FROM FAMILIAL ALZHEIMER'S DISEASE HUMAN INDUCED PLURIPOTENT STEM CELLS

Manuela Apecetche¹, Giulia Clas², Diego García Chialva³, Mercedes Vautier⁴, Sofía Mucci⁵, Gustavo Emilio Sevelever⁶, María E. Scassa⁷, Analía Czerniczyniec⁸, Leonardo Romorini⁹

1. FLENI; LIAN

2. FLENI; LIAN

3. FLENI; LIAN

4. FLENI; LIAN

5. FLENI; LIAN

6. FLENI; LIAN

7. FLENI; LIAN

8. FLENI; LIAN

9. FLENI; LIAN

manuapecetche@gmail.com

Mitochondrial dynamics, governed by the balance between fusion and fission, are crucial for neuronal health and have been implicated in Alzheimer's disease (AD) pathogenesis. Here, we investigated the expression of genes involved in mitochondrial fusion (OPA1, MFN2) and fission (DLP1/DRP1), as well as the mitophagy regulator PINK1, in Neurogenin-2 (NGN2)-induced cortical glutamatergic neurons (i3-neurons) derived from human induced pluripotent stem cells (hiPSCs) of patients with familial AD (fAD) carrying pathogenic variants in PSEN1 (p.T119I, p.A246E and p.M146L) and from non-demented controls. i3-neurons were generated by stable integration of a doxycycline-inducible NGN2 PiggyBac system (iF59 PB-TO-NGN2-puro) in hiPSCs, followed by a 14-day differentiation protocol on polyornithine-coated plates yielding rapid and homogeneous neuronal conversion. Neuronal identity was validated by RT-qPCR and immunofluorescence, confirming robust expression of pan-neuronal markers β III-tubulin (TUJ1), MAP2 and NEUN, as well as cortical lineage markers TBR2, TBR1, and CTIP2. RT-qPCR analysis revealed decreased transcript levels of DLP1, OPA1, and MFN2 in fAD i3-neurons compared to controls, suggesting a general down-regulation of mitochondrial dynamics at the transcriptional level. In contrast, PINK1 expression displayed heterogeneous results across patient lines, suggesting mutation-dependent heterogeneity in mito-

phagy regulation. Our findings highlight transcriptional dysregulation of mitochondrial fusion and fission machinery in PSEN1-mutant cortical neurons. These findings provide insights into how mitochondrial dysfunction may arise in the earliest stages of familial AD.

45. O3-02. IMMUNOMODULATORY OLIGONUCLEOTIDE IMT504 PRODUCES SIGNIFICANT IMPROVEMENTS IN LEARNING AND MEMORY IN AN ALZHEIMER'S DISEASE MODEL

Maria Victoria Oberholzer¹, Maria Belen Gonzalez², Mauro ezequiel Alfaro³, Martin Habif⁴, Luis Ignacio Brusco⁵, Jorge Zorzopulos⁶, Diana Alicia Jerusalinsky⁷

1. Fundación Favaloro (INECO- CONICET); Intituto de Neurociencia Cognitiva y Traslacional
 2. CONICET-UBA; Instituto de Biología Celular y Neurociencia Prof. Eduardo De Robertis (IBCN)
 3. CONICET-UBA; Instituto de Biología Celular y Neurociencia Prof. Eduardo De Robertis (IBCN)
 4. CONICET-UBA; Instituto de Biología Celular y Neurociencia Prof. Eduardo De Robertis (IBCN)
 5. Facultad de Ciencias Medicas - UBA; Centro de Neurología de la Conducta y Neurosiquiatría
 6. Fundación Jorge Cassará; Instituto Milstein
 7. CONICET - UBA; Instituto de Biología Celular y Neurociencia Prof. Eduardo de Robertis (IBCN)
- vic.ober@gmail.com

Alzheimer's disease (AD) is the most prevalent cause of dementia in the world and is characterized by a progressive decline in memory and other cognitive functions, posing a major public health challenge. Its neuropathological hallmarks include accumulation of β -amyloid plaques, tau neurofibrillary tangles, and neuroinflammation. Current treatments only modestly delay the onset and progression of symptoms, offering limited benefits for patients' quality of life. The McGill-R-Thy1-APP (TG) rat model of AD, which expresses the human amyloid precursor protein (hAPP) carrying two familial AD mutations (Leon et al., 2010), exhibits early deficits in the formation and consolidation of associative memories (Habif et al., 2021), making it a valuable model for exploring novel therapeutic strategies. The immunomodulatory oligonucleotide IMT504 (Franco et al., 2014) has demonstrated therapeutic efficacy in several animal models of human diseases with inflammatory profiles (Zorzopulos et al., 2017). Twelve-month-old transgenic rats were randomly assigned to a control group, which received physiological saline, or to an experimental group, which was treated subcutaneously with IMT504 (20 mg/kg) for five consecutive days. Seventy-two hours after treatment, animals were subjected to a battery of behavioral assessments, including open-field exploration, novel object recognition and discrimination, novel object location, and avoidance of an electrical stimulus associated with the environment. IMT504 administration produced significant improvements in object recognition and associative memory performance in the avoidance task. The proposed mechanism underlying these effects might involve the induction of B cells into a novel subtype with homeostatic properties (Rodriguez et al., 2025).

46. O3-03. METFORMIN RESTORES HIPPOCAMPAL VASCULAR INTEGRITY AND REDUCES AMYLOID PATHOLOGY IN A MOUSE MODEL OF ALZHEIMER'S DISEASE

Valentina Saud¹, Nicolas Gabriel Gonzalez Perez², Jessica Presa³, Melisa Bentivegna⁴, Melina Bellotto⁵, Facundo Dallo⁶, Martin Carrera⁷, Soledad Porte Alcon⁸, Juan Beauquis⁹, Carlos Javier Pomilio¹⁰, Flavia Eugenia Saravia¹¹

1. IBYME-CONICET, Departamento de Química Biológica FCEN-UBA; Neurobiología del Envejecimiento
2. IBYME-CONICET, Departamento de Química Biológica FCEN-UBA; Neurobiología del Envejecimiento
3. IBYME-CONICET, Departamento de Química Biológica FCEN-UBA; Neurobiología del Envejecimiento
4. IBYME-CONICET, Departamento de Química Biológica FCEN-UBA; Neurobiología del Envejecimiento
5. IBYME-CONICET, Departamento de Química Biológica FCEN-UBA; Neurobiología del Envejecimiento
6. IBYME-CONICET, Departamento de Química Biológica

FCEN-UBA; Neurobiología del Envejecimiento

7. IBYME-CONICET, Departamento de Química Biológica FCEN-UBA; Neurobiología del Envejecimiento
 8. Departamento de Química Biológica FCEN-UBA; Neurobiología del Envejecimiento
 9. IBYME-CONICET, Departamento de Química Biológica FCEN-UBA; Neurobiología del Envejecimiento
 10. IBYME-CONICET, Departamento de Química Biológica FCEN-UBA; Neurobiología del Envejecimiento
 11. IBYME-CONICET, Departamento de Química Biológica FCEN-UBA; Neurobiología del Envejecimiento
- valentinasaud00@gmail.com

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by the accumulation of amyloid and vascular damage in specific brain structures, being the hippocampus – critical for learning and memory – a vulnerable region affected by AD. Drug repurposing is a promising strategy that allows established medications to be evaluated for new uses. In this context, metformin, a commonly prescribed anti-diabetic medication, has recently emerged as a potential treatment for neurodegenerative diseases. Here, we evaluated the effects of metformin on cognition, amyloid deposition and vascular integrity in the hippocampus of PDAPP-J20 mouse, model of AD. Nine-month-old male mice received intraperitoneal injections of metformin (350 mg/kg, three times per week for three weeks). Behavioral assessment using the Barnes maze test revealed improved spatial memory in metformin-treated AD mice. Histological analyses showed a significant reduction in hippocampal amyloid deposits in metformin-treated mice compared to vehicle controls ($p < 0.01$). Focusing on the vasculature of the hippocampus, the percentage of area occupied by vessels, as assessed by tomato lectin, decreased by 42.9% in transgenic mice compared to non-transgenic controls ($p < 0.01$), a reduction that was reversed by metformin treatment ($p < 0.05$). Furthermore, vascular morphological alterations per mm² were restored towards control levels with metformin treatment ($p < 0.05$). Perivascular amyloid deposits -evaluated using 4G8 immunofluorescence- were reduced by 71.5% in metformin-treated transgenic mice ($p < 0.001$). These results indicate that metformin improves cognitive performance and hippocampal vascular structure while reducing both parenchymal and perivascular amyloid accumulation, supporting its potential as a repurposed therapeutic candidate for AD.

47. O3-04. EFFECT OF LPS-INDUCED MATERNAL IMMUNE ACTIVATION ON MICE PLACENTAL AND BRAIN OXYTOCINERGIC SYSTEM

Marisol Murillo Murillo¹, Ayelén Mirón Granese², Fernando Correa³, Andrea De Laurentiis⁴

1. Centro de Estudios Farmacológicos y Botánicos, Universidad de Buenos Aires-Consejo Nacional de Investigaciones Científicas y Técnicas; Neuroinmunoendocrinología
 2. Centro de Estudios Farmacológicos y Botánicos, Universidad de Buenos Aires-Consejo Nacional de Investigaciones Científicas y Técnicas; Neuroinmunoendocrinología
 3. Centro de Estudios Farmacológicos y Botánicos, Universidad de Buenos Aires-Consejo Nacional de Investigaciones Científicas y Técnicas; Neuroinmunoendocrinología
 4. Centro de Estudios Farmacológicos y Botánicos, Universidad de Buenos Aires-Consejo Nacional de Investigaciones Científicas y Técnicas; Neuroinmunoendocrinología
- mmurillomurillo@fmed.uba.ar

Maternal immune activation (MIA) adversely impacts fetal brain development and has been associated with an increased risk of neurodevelopmental disorders, including deficits in memory, attention, and learning, as well as autism spectrum disorders. While no effective pharmacological interventions currently mitigate these impairments, oxytocin (OXT) has emerged as a potential modulator. The placenta, a critical maternal-fetal interface, protects against adverse exposures; however, maternal inflammation may compromise this protective function, probably by disrupting the oxytocinergic system, which is essential for regulating inflammatory processes, especially

during parturition. This study examined the effects of MIA on the oxytocinergic system in fetal brain and placenta. LPS was administered to pregnant CD1 mice at gestational day 15 to induce MIA. LPS significantly increased inflammatory markers (Il1b and mcp1) in brain and placental tissues, while oxotocin was significantly increased in placentas of both sexes. MIA significantly reduced oxytocin receptor (OXTR) protein levels in male fetal brains, whereas a non-significant increase was observed in females. OXT showed a trend toward higher protein levels only in male brains. OXTR mRNA expression was decreased in both brain and placenta, and OXT mRNA was significantly reduced in fetal brains, but unchanged in placentas, regardless of sex. In conclusion, MIA induces a pronounced inflammatory response in the maternal–fetal unit and disrupts transcription of OXT and OXTR in brain and placenta. The sexually dimorphic alteration of OXTR protein expression in the brain suggests that males and females may differ in their vulnerability to maternal inflammation, with implications for sex-specific risk of neurodevelopmental disorders.

48. O3-05. SECRETOME PROFILING OF CORTICAL NEURONS DERIVED FROM HIPSCS CARRYING THE NOVEL PSEN1 T119I VARIANT ASSOCIATED WITH FAMILIAL ALZHEIMER'S DISEASE

Mercedes Florencia Vautier¹, Manuela Apecetche², Sofía Mucci³, Micaela Nieves⁴, Diego García Chialva⁵, Gustavo Sevelever⁶, Ezequiel Surace⁷, Mariela Marazita⁸, Maria Élica Scassa⁹, Leonardo Romorini¹⁰

1. Instituto de Neurociencias FLENI-CONICET; Laboratorio de Investigación Aplicada a Neurociencias
 2. Instituto de Neurociencias FLENI-CONICET; Laboratorio de Investigación Aplicada a Neurociencias
 3. Instituto de Neurociencias FLENI-CONICET; Laboratorio de Investigación Aplicada a Neurociencias
 4. Instituto de Neurociencias FLENI-CONICET; Laboratorio de Investigación Aplicada a Neurociencias
 5. Instituto de Neurociencias FLENI-CONICET; Laboratorio de Investigación Aplicada a Neurociencias
 6. Instituto de Neurociencias FLENI-CONICET; Laboratorio de Investigación Aplicada a Neurociencias
 7. Instituto de Neurociencias FLENI-CONICET; Laboratorio de Investigación Aplicada a Neurociencias
 8. Instituto de Neurociencias FLENI-CONICET; Laboratorio de Investigación Aplicada a Neurociencias
 9. Instituto de Neurociencias FLENI-CONICET; Laboratorio de Investigación Aplicada a Neurociencias
 10. Instituto de Neurociencias FLENI-CONICET; Laboratorio de Investigación Aplicada a Neurociencias
- mechivautier@gmail.com

Familial Alzheimer's disease (fAD) is an autosomal dominant form of dementia commonly caused by mutations in PSEN1, a gene that encodes a protein involved in the proteolytic cleavage of multiple substrates, including the amyloid precursor protein. Alterations in presenilin function may impact not only amyloid processing but also the broader repertoire of proteins secreted by neurons. Here, we differentiated human induced pluripotent stem cells (hiPSCs) into cortical neurons using a 70-day protocol based on dual SMAD inhibition. Two lines were employed: one derived from an Argentine patient with fAD carrying the novel PSEN1 T119I variant and a control line, PSEN1 wild type. Given the central role of presenilin in proteolytic pathways, we hypothesized that the mutation might alter the composition of secreted proteins. To test this, we collected conditioned media from neuronal cultures and profiled the secretome by label-free LC-MS/MS. Raw spectra were processed with Proteome Discoverer and differential abundance was modeled in R with limma (FDR ≤ 0.10; fold-change ≥ 2). In total, we quantified 506 proteins, many linked to synaptic function, extracellular matrix organization, and vesicle-mediated transport, all pathways expected in mature neuronal cultures. Although no significant differences were observed between the PSEN1 T119I and the control line under basal conditions, our findings confirm that the approach captures biologically relevant features of neuronal secretion. This workflow, therefore, might be useful for future studies exploring how different genetic variants may

modulate the neuronal secretome in Alzheimer's disease.

49. O3-06. SEX-SPECIFIC EFFECTS OF PSYCHOACTIVE DRUGS ON COGNITIVE DYSFUNCTION IN AN ADHD MOUSE MODEL: IMPLICATIONS FOR CLINICAL PHARMACOTHERAPY

Florencia Dadam¹, Franco Haehnel², Osvaldo Martin Bas-madjian³, Berardo Gimena⁴, Varayoud Jorgelina⁵, Gabriela Paglini⁶

1. Instituto de Investigación Médica Mercedes y Martín Ferreyra, INIMEC-CONICET-UNC. Facultad de Odontología. Universidad Nacional de Córdoba; Neurobiología funcional
 2. Instituto de Investigación Médica Mercedes y Martín Ferreyra, INIMEC-CONICET-UNC.; Neurociencia funcional
 3. Instituto de Investigación Médica Mercedes y Martín Ferreyra, INIMEC-CONICET-UNC.; Neurobiología funcional
 4. Instituto de Investigación Médica Mercedes y Martín Ferreyra, INIMEC-CONICET-UNC.; Neurobiología funcional
 5. Instituto de Salud y Ambiente del Litoral ISAL-CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral. Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral; Cátedra de Fisiología Humana
 6. Instituto de Investigación Médica Mercedes y Martín Ferreyra, INIMEC-CONICET-UNC. Instituto de Virología "Dr. José María Vanella", In.Vi.V.-CONICET-UNC.; Neurobiología funcional
- fdadam@unc.edu.ar

Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most frequently diagnosed neuropsychiatric conditions in childhood and adolescence, often persisting into adulthood. A consistent cognitive hallmark of ADHD is working memory (WM) impairment, an executive function essential for goal-directed behavior. Treatment typically involves psychostimulants such as methylphenidate (MPH), while fluoxetine (FLX) may be incorporated when depressive comorbidities are present. p35KO mice display ADHD-like traits, including hyperactivity and dopaminergic dysfunction, serving as a relevant model for the disorder. We investigated the role of the Cdk5/p35 complex in WM and neuronal activation, as well as the effects of acute MPH and FLX treatments, considering potential sex differences. Juvenile WT and p35KO mice (PND 21–25) received saline, MPH, FLX, or combined treatment. WM was assessed using the Y-maze, and neuronal activity was evaluated via c-FOS immunolabeling. Both male and female p35KO mice showed WM impairments, while recognition memory remained intact. Deficits were more pronounced in males, with reduced prefrontal and increased hippocampal (CA1, CA3) activation, indicating a dysregulated pattern. Females preserved prefrontal activation but showed increased activity in CA1, CA3, and the dentate gyrus, suggesting sex-specific functional reorganization. Behaviorally, MPH and FLX improved WM in p35KO males, though their combination yielded no added benefit. WT females showed reduced WM performance under all treatments, and p35KO females did not respond. These findings highlight the role of the Cdk5/p35 complex in WM and neuronal activation, emphasizing sex- and genotype-specific effects of psychoactive drugs and the importance of considering biological sex and genetic background in ADHD pharmacotherapy.

50. O3-07. SILENT MESSENGERS: THE ROLE OF CIRCULATING EXTRACELLULAR VESICLES IN HUNTINGTON'S DISEASE

Julietta Saba¹, Facundo Ortuzar², María Friser Frederiksen^{1,3}, Federico López Couselo^{1,4}, Carla Caruso⁵, Daniela Durand⁶, Mercedes Lasaga⁷

1. CONICET-Universidad de Buenos Aires. Instituto de Investigaciones Biomédicas (INBIOMED). Buenos Aires, Argentina; Mecanismos protectores en la neurodegeneración
2. CONICET-Universidad de Buenos Aires. Instituto de Investigaciones Biomédicas (INBIOMED). Buenos Aires, Argentina; Mecanismos protectores en la neurodegeneración
3. CONICET-Universidad de Buenos Aires. Instituto de In-

vestigaciones Biomédicas (INBIOMED). Buenos Aires, Argentina; *Mecanismos protectores en la neurodegeneración*

4. CONICET-Universidad de Buenos Aires. Instituto de Investigaciones Biomédicas (INBIOMED). Buenos Aires, Argentina; *Mecanismos protectores en la neurodegeneración*

5. CONICET-Universidad de Buenos Aires. Instituto de Investigaciones Biomédicas (INBIOMED). Buenos Aires, Argentina; *Mecanismos protectores en la neurodegeneración*

6. CONICET - Universidad de Buenos Aires. Instituto de Investigaciones Biomédicas Universidad de Buenos Aires - CONICET (INBIOMED). Buenos Aires, Argentina.; *Neuro protección y Neurobiología de la glía*

7. CONICET-Universidad de Buenos Aires. Instituto de Investigaciones Biomédicas (INBIOMED). Buenos Aires, Argentina; *Neurobiología*
jsaba@fmed.uba.ar

Huntington's disease (HD) is an autosomal dominant disorder caused by the expansion of CAG repeats in the gene that codes for huntingtin (HTT), resulting in a mutated version (mHTT). This leads to the progressive death of striatal neurons and later spreads to other areas of the brain. Extracellular vesicles (EVs) are small membranous structures released by cells, including neurons, astrocytes, microglia, and oligodendrocytes in the central nervous system, and can be found in biofluids such as blood. In this study, we characterized circulating EVs in the serum of wild-type (WT) and zQ175 (HD) mice and evaluated their potential neuroprotective and antioxidant effects in in vitro models of HD. We used immortalized mouse striatal neurons, STHdh-Q7 with normal HTT (Q7) and STHdh-Q111 (Q111) expressing mHTT with 111 CAG repeats. The EVs were characterized by western blot and transmission electron microscopy. We observed the uptake of calcein-labeled EVs by Q111 neurons. From a functional standpoint, both WT-derived serum EVs (WT-EVs) and HD-derived serum EVs (HD-EVs) protected Q7 cells from toxicity induced by 3-nitropropionic acid (3NP), a toxin widely used to model HD in vitro ($p < 0.0001$). However, only WT-EVs showed an antioxidant effect against the production of reactive oxygen species (ROS) induced by 3NP ($p < 0.05$). In neurons expressing mHTT (Q111), only WT-EVs protected against toxicity and reduced 3NP-induced ROS production ($p < 0.05$), whereas HD-EVs did not modify the effect of 3NP. Therefore, treatment with HD-EVs in Q111 cells loses the protective effect observed in Q7 cells, suggesting that the functionality of HD-EVs is compromised.

51. O3-08. USED-DEPENDENT REGULATION OF GABAA RECEPTORS INDUCED BY PERSISTENT EXPOSURE OF CEREBROCORTICAL NEURONS TO DIAZEPAM

L. Carolina González Gómez¹, María Clara Gravielle²

1. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires-CONICET; Instituto de Investigaciones Farmacológicas (ININFA)

2. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires-CONICET; Instituto de Investigaciones Farmacológicas (ININFA)

lcarolina.gonzalez@udea.edu.co

Despite their high therapeutic index and low toxicity, the clinical utility of benzodiazepines is limited by the development of tolerance to most of the behavioral effects produced by long-term administration. In previous work, we analyzed the modulation of GABAA receptors induced by a sustained exposure of rat primary cerebrocortical cultures to diazepam. Our results demonstrated that a 48-hour treatment of cultured neurons with diazepam produces uncoupling between GABA and benzodiazepine sites, as measured by a decrease in the potentiation of flunitrazepam binding by GABA. Uncoupling depends on the diazepam binding to its specific site on the GABAA receptor and on the activation of the receptor and L-type voltage-gated calcium channels (L-VGCCs). This regulatory process was accompanied by the transcriptional repression of the $\alpha 1$ subunit gene through a mechanism involving the activation of L-VGCCs, protein kinase A, and two transcription factors, CREB and ICER. Here, we examined the relationship between $\alpha 1$ subunit downregulation and uncoupling produced by diazepam treatment. We

knocked down $\alpha 1$ subunit expression by transfecting cultured neurons with small interfering RNAs corresponding to the $\alpha 1$ sequence. Flunitrazepam binding experiments revealed that the reduction of $\alpha 1$ subunit levels induced by these transfection assays resulted in a small but non-statistically significant decrease in the coupling between GABA and benzodiazepine sites. These results suggest that additional regulatory mechanisms other than $\alpha 1$ downregulation are responsible for uncoupling. Together, our results contribute to uncovering the mechanisms triggered by the persistent stimulation of GABAA receptors by benzodiazepines that underlie tolerance.

52. O3-09. DYNAMIC CHANGES IN MITOCHONDRIAL FUNCTION IN BRAIN CORTEX SYNAPTOSOMES DURING AGING

Paulina Lombardi¹, Analía G. Karadayian², Juan I. Guerra³, Silvia Loes Arnaiz⁴

1. Instituto de Bioquímica y Medicina Molecular (IBIMOL, UBA-CONICET), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.; Laboratorio IV, Catedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.

2. Instituto de Bioquímica y Medicina Molecular (IBIMOL, UBA-CONICET), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.; Laboratorio IV, Catedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.

3. Instituto de Bioquímica y Medicina Molecular (IBIMOL, UBA-CONICET), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.; Laboratorio IV, Catedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.

4. Instituto de Bioquímica y Medicina Molecular (IBIMOL, UBA-CONICET), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.; Laboratorio IV, Catedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.

paulina.lombardi@gmail.com

Alterations in mitochondrial function and reactive oxygen species (ROS) generation have been associated with physiological aging. Here, we investigated age-related changes in synaptic mitochondria using mice aged 3, 10, 17, 20, and 24 months. Mitochondrial membrane potential was reduced by 21% at 20 months but showed a 24% increase at 24 months compared with young animals. Respiratory complex activities exhibited age-dependent variations without a clear linear trend in complexes I–III, II–III, and IV. Superoxide anion levels increased at 10, 20, and 24 months, whereas a transient decrease was observed at 17 months. These findings suggest that changes in respiratory complex activity and ROS modulation may contribute to preserving mitochondrial integrity in synaptic terminals up to 20 months of age. In synaptosomes from 24-month-old mice, basal and maximal respiration remained unaffected, but proton leak was elevated, while ATP-linked respiration, coupling efficiency, and ATP synthesis were significantly reduced compared with young controls. At advanced ages, compensatory mechanisms may emerge to counteract mitochondrial dysfunction and oxidative stress, potentially contributing to the selective survival of aged animals.

ORALES 4 - SAIC - METABOLISMO Y NUTRICIÓN 1

DATE & TIME: 17/11/2025 13:00 - 14:30 H

Chairs: Adriana Burgueño, Romina Hermann

53. O4-01. SPX IMPROVES LIPID METABOLISM AND INFLAMMATION IN HYPERTROPHIC AND INSULIN RESISTANT ADIPOCYTES IN VITRO

Sabrina E. Gambaro¹, Catalina Latina², Carolina Garraza³, Ana Alzamendi⁴, Guillermina M. Zubiria⁵, Andrés Giovambattista⁶

1. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP, La Plata, Buenos Aires, Argentina; Laboratorio de metabolismo y tejido adiposo

2. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP, La Plata, Buenos Aires, Argentina

na; Laboratorio de metabolismo y tejido adiposo

3. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP, La Plata, Buenos Aires, Argentina; Laboratorio de metabolismo y tejido adiposo

4. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP, La Plata, Buenos Aires, Argentina; Laboratorio de metabolismo y tejido adiposo

5. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP, La Plata, Buenos Aires, Argentina; Laboratorio de metabolismo y tejido adiposo

6. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP, La Plata, Buenos Aires, Argentina; Laboratorio de metabolismo y tejido adiposo
sabriganbaro@gmail.com

Spexin (SPX), a novel peptide, regulates metabolic processes, including food intake, gastrointestinal motility, and lipid and carbohydrate metabolism. In this study we aimed to evaluate, in vitro, the direct effect of SPX on hypertrophic or insulin-resistant adipocytes. Experimental models were developed using differentiated 3T3L1 cells treated with either lauric acid (hypertrophic model) or high concentrations of insulin and glucose (IR model). We assessed gene expression, lipolysis/lipogenesis, lipid content and degree of adipocytes maturation (Papanicolaou stain). Although leptin expression was not altered in these models, SPX reduced its levels. In the hypertrophic model, adiponectin expression returned to normal ($p < 0.05$). SPX treatment restored Irs1 expression ($p < 0.05$), which was decreased in both models, as well as Glut4 expression in the IR model ($p < 0.05$). In the hypertrophic adipocytes, SPX induced hsl expression ($p < 0.01$) and tended to normalize fas levels. Functional analysis (two-way ANOVA) showed that SPX decreased lipid accumulation in both models (SPX $p < 0.05$). Lipogenesis, measured by triglycerides content, was reduced by SPX in the hypertrophic model (SPX $p < 0.001$). Lipolysis was evaluated through glycerol release under basal and stimulated conditions using forskolin (FSK). SPX promoted lipolysis in the IR model ($p < 0.05$), whereas a synergistic effect between SPX and FSK ($p < 0.001$) was observed in the hypertrophic model. The degree of adipocyte maturation increased in the hypertrophic model and SPX could not return them to control. In conclusion, SPX improves the gene expression involved in metabolism, insulin sensitivity and inflammation. Also, it promotes lipid metabolism toward lipolysis in basal and stimulated conditions improving adipocyte metabolic function.

54. O4-02. BONE EFFECTS OF PREBIOTICS IN DIETS WITH VARYING CALCIUM AND VITAMIN D CONTENT. EXPERIMENTAL MODEL OF LOW BONE MASS DUE TO ESTROGEN DEFICIENCY

Marina Bonanno¹, Estefanía Magali Zeni Coronel², Mascias Hernán³, Longo Morena⁴, Diego Vázquez⁵, Ailín Gómez⁶, Mariana Seijo⁷

1. Instituto de Inmunología, Genética y Metabolismo (INIGEM), CONICET-UBA-Hospital de Clínicas; Laboratorio de Osteopatías Metabólicas

2. Instituto de Inmunología, Genética y Metabolismo (INIGEM), CONICET-UBA-Hospital de Clínicas; Laboratorio de Osteopatías Metabólicas

3. Instituto de Inmunología, Genética y Metabolismo (INIGEM), CONICET-UBA-Hospital de Clínicas; Laboratorio de Osteopatías Metabólicas

4. Instituto de Inmunología, Genética y Metabolismo (INIGEM), CONICET-UBA-Hospital de Clínicas; Laboratorio de Osteopatías Metabólicas

5. Facultad de Odontología-Universidad de Buenos Aires; Cátedra de Diagnóstico por Imágenes

6. Facultad de Odontología-Universidad de Buenos Aires; Cátedra de Diagnóstico por imágenes

7. Instituto de Inmunología, Genética y Metabolismo (INIGEM), CONICET-UBA-Hospital de Clínicas; Laboratorio de Osteopatías Metabólicas

marinita.honanno@gmail.com

while vitamin D (VD) supports Ca absorption and mineralisation. We evaluated the effect of a prebiotic mixture (MP) under VD and Ca deficiency, in an OVX-induced low bone mass model. Adult Wistar rats were fed AIN'93-M diets differing in VD (100 vs. 0 IU%), Ca (0.5% vs. 0.3%) and prebiotic mixture (MP, 2.5% GOS/FOS vs. none), resulting in 8 groups: +D0.5; -D0.5; +D0.3; -D0.3; MP+D0.5; MP-D0.5; MP+D0.3; MP-D0.3. At the end of the study, the following were measured: body weight gain (Δ PC), faecal Lactobacillus colony counts (LCC); caecal pH; Ca absorption (Abs); femoral Ca content (ContCa). In serum, osteocalcin (OCN), β -crosslaps (CTX) and 25-hydroxyVD (25OHD). Femoral bone quality was assessed by fracture strength [Fmax (N)], bone mineral density by DEXA (BMDf), and bone volume (BV/TV), trabecular separation (Tb.Sp) and trabecular number (Tb.N) by micro-CT. RCL, Abs and ContCa increased, while cecal pH decreased in MP+D0.5 and MP+D0.3 ($p < 0.05$). 25OHD was lower in -D groups, and CTX was elevated in -D0.3. No changes in OCN. BMDf, BV/TV and Tb.N improved with MP, whereas Tb.Sp was elevated in -D groups and decreased with MP. Fmax was higher in MP+D0.5 ($p < 0.05$). According to our results, the effect of low Ca and/or VD intake is partially corrected by MP consumption.

55. O4-03. COMPARISON BETWEEN THE INTAKE OF AN OAT MALTED BREAD AND A WHEAT BREAD ON LIPID PROFILE AND BONE MINERAL CONTENT IN AN EXPERIMENTAL MODEL IN GROWING WISTAR RATS

Adriana Weisstaub¹, María Laura Gómez Castro², Ethel Coscarello³, Silvana Fleischman⁴, Liliana Zago⁵, Magali Barchuk⁶, Gabriela Berg⁷, Angela Zuleta⁸, Claudia Larregain⁹

1. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires; Cátedra de Nutrición.

2. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires; Cátedra de Nutrición.

3. Facultad de Agronomía y Ciencias Agroalimentarias, Universidad de Morón; Laboratorio de Investigación de Agroalimentos

4. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires; Cátedra de Nutrición

5. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires; Cátedra de Nutrición

6. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires; INFIBIOC

7. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires; INFIBIOC, CONICET

8. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Argentina; Cátedra de Bromatología

9. Facultad de Agronomía y Ciencias Agroalimentarias, Universidad de Morón; Laboratorio de Investigación de Agroalimentos

arweiss@ffyba.uba.ar

High consumption of wheat bread has been correlated with chronic diseases and whole oats can be malted, obtaining a flour with greater amount of soluble fibers that, in addition to the beta-glucan content, are a good choice for preparing baked goods with a healthier profile. The aim of this study was to compare the effect of the intake of bread made with whole oat malted flour (BOM) and bread made with wheat flour (BW) on lipid profile and bone mineral content during 60 days, in a rat model. A total of 24 newly weaned male Wistar rats (8/group) were fed with control diet (C) and two semisynthetic diets BOM and BW diets. Rats were anesthetized and right tibia was excised to assess Ca/P ratio. Total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-c) were measured in serum and NonHDL cholesterol (NonHDL-c) was calculated. BOM and C had a higher Ca/P ratio than BW (2.57 ± 0.28 vs 2.55 ± 0.19 vs 1.50 ± 0.09 ; $p < 0.0001$). TC was lower in BOM and C than BW (mg/dL) (77.4 ± 12.7 vs 62.3 ± 8.8 vs 124.6 ± 16.4 ; $pBOM > C$ (mg/dL) (89.8 ± 12.7 vs 39.7 ± 11.9 vs 18.4 ± 5.2 ; $p < 0.0001$). Conclusions: oat bread showed a prebiotic effect improving Ca/P bone ratio and a better lipid profile comparing with white bread, considering a food for carrying out a diet with healthier characteristics. Financed by UBA-CyT N° 20020220100205BA.

NOPEPTIDES FROM SPENT BREWER'S YEAST IN A RODENT MODEL OF METABOLIC SYNDROME INDUCED BY A HIGH-SUCROSE DIET

Maria Del Rosario Ferreira¹, Matias Rodrigo Vargas², Marilin Estefania Aquino³, Raúl Esteban Cian⁴, Silvina Rosa Drago⁵, Maria Eugenia D'Alessandro⁶

1-*Facultad de Bioquímica y Cs. Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina; -Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición.*

2-*1-Facultad de Bioquímica y Cs. Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición.*

3-*1-Facultad de Ingeniería Química, Universidad Nacional del Litoral, Santa Fe, Argentina; -Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Instituto de Tecnología de Alimentos.*

4-*1-Facultad de Ingeniería Química, Universidad Nacional del Litoral, Santa Fe, Argentina; -Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Instituto de Tecnología de Alimentos.*

5-*1-Facultad de Ingeniería Química, Universidad Nacional del Litoral, Santa Fe, Argentina; -Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Instituto de Tecnología de Alimentos.*

6-*1-Facultad de Bioquímica y Cs. Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina; -Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición, Facultad de Bioquímica y Cs. Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina. mrferreira@fbcb.unl.edu.ar*

Mannopeptides derived from Brewer's spent yeast, a by-product of the brewing industry, have shown in vitro bioactivity. However, their in vivo effects are not yet known. This study aimed to evaluate the potential bioactive properties of mannopeptides in an experimental model of Metabolic Syndrome induced by a high-sucrose diet (HSD). Male Wistar rats received from weaning and for 100 days either a Control diet (C), HSD or a HSD plus a daily supplement of mannopeptides (400 mg/kg body weight/day, administered orally) (HSD+MP). We analyzed: a- Biometric parameters: body weight (BW), body length (BL), thoracic (TC) and abdominal circumferences (AC), body mass index (BMI) b- Energy intake, c- Visceral adiposity index (VAI), d- Glucose (G), triglycerides (TG), free fatty acids (FFA), cholesterol (Ch), and uric acid (UA) serum levels, e- Liver TG and Ch content, f- Blood pressure, g- Cognitive performance, by conducting the novel object recognition test (NORT) and the T-Maze memory tasks. Data were analyzed by one-way ANOVA and Newman Keuls post-hoc. Compared with HSD-fed rats, HSD+MP group shown: a- a significant reduction ($P<0.05$) in BW gain, energy intake, CT, VAI, serum G, FFA and Ch, and systolic blood pressure. b- an improved cognitive performance in the T-Maze memory task. BL, AC and BMI were similar in the 3 dietary groups. TG and UA serum levels, and TG and Ch liver levels were increased in HSD and HSD+MP groups. The results show that mannopeptides can attenuate several cardiometabolic risk factors and spatial memory deficits developed in HSD-fed rats.

57. O4-05. ANTI-INFLAMMATORY EFFECTS OF NITRONE SPIN TRAP DMPO IN A MURINE MODEL OF DIET-INDUCED OBESITY

Carla Florencia Guzman¹, Inalen Del V. Chacon², Florencia S. Barrera³, Riveros L.⁴, Morales, I.⁵, Barberis, S.⁶, Santillan, Ld⁷, Ramirez Dc⁸, Sandra E. Gomez Mejiba⁹

1. *IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis,*

Argentina.

2. *IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.*

3. *IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.*

4. *IMIBIO-CCT-SL-CONICET; Laboratory of Bromatology, CONICET-San Luis & National University of San Luis, San Luis, Argentina*

5. *IMIBIO-CCT-SL-CONICET; Laboratory of Bromatology, CONICET-San Luis & National University of San Luis, San Luis, Argentina*

6. *IMIBIO-CCT-SL-CONICET; Laboratory of Bromatology, CONICET-San Luis & National University of San Luis, San Luis, Argentina*

7. *IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.*

8. *IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.*

9. *IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.*

florguzman56@gmail.com

Obesity induced by a chronic positive energy balance is associated with metabolic alterations such as insulin resistance (IR), hypertension, and low-grade systemic inflammation. Activation of the antioxidant Nrf2 pathway should modulate these effects by improving free fatty acid storage as triglycerides. The compound 5,5-dimethyl-1-pyrroline N-oxide (DMPO) is a nitron with antioxidant and anti-inflammatory properties that can activate the Nrf2 pathway. In this study, we aimed to evaluate the effect of DMPO in a mouse model of diet-induced obesity (DIO). Male C57BL/6J mice were fed a control diet (CoD) or an obesogenic diet (ObD; 22% bovine fat + 10% fructose in the drinking water) for 24 weeks. One week before the end of the diet regimen, the animals received daily intraperitoneal injections of DMPO (2.5 μ mol/mouse/day) or saline. The parameters evaluated included weight gain, adiposity, blood pressure, fasting blood glucose, glucose tolerance test (GTT), metabolic markers, hepatic and adipose TNF α expression, and serum concentrations of IL-6 and IL-1 β . The ObD-fed mice presented increased adiposity, blood pressure, fasting glucose, insulin resistance, and concentrations of TNF α , IL-6, and IL-1 β in the serum. Compared with saline control treatment, treatment of ObD-fed mice with DMPO significantly reduced IR, blood pressure, and the expression of TNF α , IL-6, and IL-1 β . However, it improved adipogenesis. These results suggest that DMPO may have a protective effect against obesity-associated metabolic and inflammatory alterations, potentially by improving adipogenesis through the activation of the Nrf2 pathway.

58. O4-06. MECHANISTIC INSIGHTS INTO CPDA-MEDIATED PROTECTION OF B-CELLS UNDER GLUCOLIPOTOXIC STRESS

Miranda Sol Orellano¹, Ingrid Pensado Evans², Andrea Scelza-Figueroa³, Carolina Sétula⁴, Marcelo Javier Perone⁵, Luz Andreone⁶

1. *Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIIMT), CONICET - Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo (IIIMT, CONI-*

CET-Univ. Austral)

2. Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo (IIMT, CONICET-Univ. Austral)

3. Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo (IIMT, CONICET-Univ. Austral)

4. Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo (IIMT, CONICET-Univ. Austral)

5. Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo (IIMT, CONICET-Univ. Austral)

6. Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo (IIMT, CONICET-Univ. Austral)

morellano-conicet@austral.edu.ar

Diabetes mellitus type 2 (DM2) is an endocrine-metabolic disease characterized by progressive loss of β -cell function due to chronic hyperglycemia and elevated free fatty acids —a phenomenon known as glucolipotoxicity (GLT)—, involving oxidative and endoplasmic reticulum (ER) stress. We previously demonstrated that Compound A (CpdA), a dissociative GR-ligand, improves glucose tolerance, enhances insulin sensitivity, and preserves pancreatic islet histophysiology in a murine model of DM2. Here, we aim to delve into the molecular mechanisms by which CpdA mitigates the toxic effects of GLT. INS-1E β -cell line was exposed or not for 4-24h to 30mM glucose and 500 μ M palmitate, and co-treated with or without 10 μ M CpdA. Cell viability was analyzed by flow cytometry, mRNA by RT-qPCR, protein by WB and insulin by ELISA. GSIS (glucose-stimulated insulin secretion) index was calculated as the ratio of insulin released during 1h under stimuli of 20mM/2mM glucose. CpdA treatment protected β -cells from ER stress by downregulating ATF4 pathway and stimulating XBP1 and ATF6 pathways, thereby promoting ER-chaperone expression (e.g., GRP94, PDI, BIP $p < 0.05$ GLT vs GLT+CpdA). In addition, CpdA enhanced antioxidant defense through Nrf2 pathway activation and upregulation of its targets (e.g., NQO1, HO1, TXNRD1 $p < 0.05$ GLT vs GLT+CpdA). Consequently, CpdA reduced GLT-induced cell death while maintaining β -cell identity gene expression (e.g., MafA, FoxO1 $p < 0.05$ GLT vs GLT+CpdA) and preserving GSIS ($p < 0.05$ GLT vs GLT+CpdA). These findings demonstrate that CpdA mitigates ER and oxidative stress, enhances survival and preserves β -cell identity and function under GLT insult, supporting its potential as a therapeutic strategy in DM2.

59. O4-07. A COMBINED DIETARY AND CHEMICAL APPROACH TO RAPIDLY INDUCE MASLD PROGRESSION AND FIBROSIS IN MICE

Brian Martínez Ruiz¹, Lucía Lameroli², Bárbara Bueloni³, María José Cantero⁴, Mailin Casadei⁵, Martina Malaspina⁶, Esteban Fiore⁷, Guillermo Mazzolini⁸, Juan Bayo Fina⁹, Catalina Atorrasagasti¹⁰

1. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Universidad Austral; Programa de Hepatología Experimental y Terapia Génica

2. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Universidad Austral; Programa de Hepatología Experimental y Terapia Génica

tología Experimental y Terapia Génica

3. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Universidad Austral; Programa de Hepatología Experimental y Terapia Génica

4. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Universidad Austral; Programa de Hepatología Experimental y Terapia Génica

5. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Universidad Austral; Programa de Hepatología Experimental y Terapia Génica

6. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Universidad Austral; Programa de Hepatología Experimental y Terapia Génica

7. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Universidad Austral; Programa de Hepatología Experimental y Terapia Génica

8. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Universidad Austral; Programa de Hepatología Experimental y Terapia Génica

9. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Universidad Austral; Programa de Hepatología Experimental y Terapia Génica

10. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET - Universidad Austral; Programa de Hepatología Experimental y Terapia Génica

bmartinezruiz-iimt@austral.edu.ar

Metabolic dysfunction-associated steatotic liver disease (MASLD) affects ~25% of the population and can progress from steatosis to steatohepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). About 85% of HCC cases arise in fibrotic or cirrhotic livers. Existing murine models fail to recapitulate the full spectrum of human MASLD. We aimed to establish a murine model that rapidly induces steatohepatitis with metabolic alterations and advanced fibrosis. Male C57BL/6N mice (8 weeks-old) were fed a high-fat, high-sucrose diet (HFD) or control diet (CD) for 12 weeks and received thioacetamide (TAA, i.p.) under three regimens: 50 mg/kg since diet initiation (TAA-50 group), or 100/200 mg/kg starting at week 6 of feeding (TAA-100 or TAA-200). At sacrifice, livers were analyzed by histology (H&E, Oil Red O, Sirius Red), triglyceride quantification, and qPCR. Serum was assessed for biochemical markers. After 12 weeks, HFD-fed mice gained 78 $\pm$ 6% body weight versus 23 $\pm$ 9% in CD. TAA reduced weight gain (38 $\pm$ 10% in HFD-TAA-50, 55 $\pm$ 10% HFD-TAA-100, 40 $\pm$ 7% in HFD-TAA-200), though HFD-TAA-100 group still showed significantly higher weight than CD. HFD induced hyperglycemia and glucose intolerance, whereas HFD+TAA groups maintained normoglycemia and glucose tolerance. HFD induced hepatic steatosis, whereas TAA reduced the number of steatotic hepatocytes; however, HFD-TAA-100 still retained lipid droplets. TAA induced fibrosis in both CD and HFD mice, with severity increasing with prolonged TAA exposure. HFD-TAA-100 showed extensive fibrosis with porto-portal septa, yielding a balanced steatosis-fibrosis phenotype. This combined model rapidly induces steatohepatitis with fibrosis, offering a reliable platform to study the liver microenvironment in preclinical orthotopic HCC models.

60. O4-08. ALCOHOL METABOLITES, OXIDATIVE STRESS, AND THEIR ASSOCIATION WITH ALCOHOL HANGOVER SEVERITY

Analia Karadayian¹, Laura A Tijs², Evi C van Oostrom³, Aurora JAE van de Loo⁴, Silvia Lores-Arnaiz⁵, Joris C Verster⁶

1. Institute for Biomedical Research (BIOMED), Laboratory of Cellular and Molecular Biology, National Scientific and Technical Research Council (CONICET), Argentina. School of Medical Sciences, Pontifical Catholic University of Argentina (UCA), Buenos Aires, Argentina.; Laboratory of Cellular and Molecular Biology

2. Utrecht University, Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacology, Utrecht, The Netherlands.; Division of Pharmacology

3. Utrecht University, Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacology, Utrecht, The Netherlands.; Division of Pharmacology

4. Utrecht University, Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacology, Utrecht, The Netherlands.; Division of Pharmacology
5. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Fisiología, Buenos Aires, Argentina. CONICET-Universidad de Buenos Aires, Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBI-MOL) Buenos Aires, Argentina.; Cátedra de Fisiología
6. Utrecht University, Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacology, Utrecht, The Netherlands. Swinburne University of Technology, Centre for Mental Health and Brain Sciences, Melbourne, Australia. Cognitive Neurophysiology, Department of Child and Adolescent Psychiatry, Faculty of Medicine, TU Dresden, Germany; Division of Pharmacology
analiakarayian@uca.edu.ar

Accumulating acetaldehyde has been proposed as a key factor in alcohol hangover pathology. This study evaluated associations between biomarkers of alcohol metabolism, oxidative stress, and hangover severity. A naturalistic study was conducted in 15 healthy social drinkers (18–30 years), including an alcohol day and an alcohol-free control day. On both days, saliva and urine samples were collected at 09:30, and hangover severity was assessed hourly until 15:30 on a 0–10 scale. Biomarkers of alcohol metabolism measured were ethanol, acetaldehyde, and acetate; oxidative stress biomarkers included nitrite (NO_2^-), nitrate (NO_3^-), and the $\text{NO}_3^-/\text{NO}_2^-$ ratio. Spearman's correlations were calculated between the change in biomarker concentrations (alcohol minus control day) and hangover severity, with bootstrapping ($B = 10,000$) to compute bias-corrected and accelerated 95% confidence intervals (BCa 95% CI). In urine, acetaldehyde correlated with hangover severity at 12:30 ($r = 0.675$, $CI = 0.418\text{--}0.798$) and 14:30 ($r = 0.536$, $CI = 0.008\text{--}0.804$). Acetate showed a significant negative correlation at 15:30 ($r = -0.709$, $CI = -0.922$ to -0.234). Urinary NO_2^- correlated with severity at 12:30 ($r = 0.518$, $CI = 0.037\text{--}0.814$). In saliva, acetaldehyde correlated strongly with hangover severity across multiple timepoints, peaking at 12:30 ($r = 0.711$, $CI = 0.458\text{--}0.850$). Salivary NO_2^- correlated with severity at 09:30 ($r = 0.500$, $CI = 0.001\text{--}0.888$). No significant associations were found for NO_3^- or the $\text{NO}_3^-/\text{NO}_2^-$ ratio. These findings support a role for acetaldehyde and oxidative stress in alcohol hangover pathology.

POSTERS 3 - SAIC - BIOLOGÍA CELULAR Y MOLECULAR 1

DATE & TIME: 17/11/2025 13:00 - 14:30 H

Chairs: María Gabriela Lombardi, Florencia Cayrol, Yanina Benzo

61. P3-13. **LRRK2 KINASE ON PROTEIN CO-TRANSLATIONAL CONTROL**
Ana J. Fernández-Alvarez¹, Francisco Corvetto Aristarain², Pablo La Spina³, Graciela L. Boccaccio⁴
1. Fundación Leloir - IIBBA Conicet - Universidad Argentina de la Empresa (UADE); Laboratorio de Biología celular del ARN
2. Fundación Leloir - IIBBA CONICET; Laboratorio de Biología Celular del ARN
3. Fundación Leloir - IIBBA CONICET; Laboratorio de Biología Celular del ARN
4. Fundación Leloir - IIBBA CONICET - FCEN Universidad de Buenos Aires; Laboratorio de Biología Celular del ARN
ajfernandez@uade.edu.ar

Mutations in the human LRRK2 protein, mainly gain-of-function on its kinase activity, are the leading cause of both familial and sporadic Parkinson's disease, and they also give rise to immune system disorders, including Crohn's disease. LRRK2 is a very large multidomain protein with a wide range of downstream effectors. Functionally, LRRK2 has been linked to multiple cellular processes such as autophagy, endolysosomal pathways, and synaptic vesicle trafficking, among others. Several ribosomal proteins are targets of LRRK2, and translational alterations associated with changes in its

kinase activity have been reported. In our laboratory, we found that LRRK2 participates in Ribosome-associated Quality Control (RQC), an essential mechanism that monitors protein synthesis and triggers the degradation of defective polypeptides. Using mammalian cell cultures and RQC reporters, we demonstrated that silencing LRRK2 leads to the accumulation of defective polypeptides normally recognized by RQC. Microscopy analysis of cells treated with Lrrk2-specific siRNAs suggests that these abortive polypeptides accumulate as ubiquitinated species in cytosolic condensates. We propose that LRRK2 specifically operates in the degradation of aberrant polypeptides by RQC, whose accumulation contributes to cellular damage by stimulating the cellular stress response. Since cellular stress plays a crucial role in the development and perpetuation of inflammation, the role of LRRK2 in co-translational control may contribute to pathophysiological mechanisms associated with its dysregulation. Our findings further contribute to the understanding of the consequences of pharmacological inhibition of LRRK2, currently being considered as a therapeutic strategy.

62. P3-14. **A MULTIDIMENSIONAL PLATFORM TO RANK AND CLASSIFY CHEMOTHERAPEUTIC DRUGS**

Florencia Hernandez¹, Yiovana Verónica Okrainne², Martina Vazquez³, Sara Miranda⁴, Ariel Isaac Abramovici Blasco⁵, María Candelaria Mares Ahlers⁶, Ginette Moyano⁷, Vanesa Gottifredi⁸, Nicolás Luis Calzetta⁹

1. Fundación Instituto Leloir - IIBBA; Ciclo Celular y Estabilidad Genómica
2. Fundación Instituto Leloir - IIBBA; Ciclo Celular y Estabilidad Genómica
3. Fundación Instituto Leloir - IIBBA; Ciclo Celular y Estabilidad Genómica
4. Fundación Instituto Leloir - IIBBA; Ciclo Celular y Estabilidad Genómica
5. Fundación Instituto Leloir - IIBBA; Ciclo Celular y Estabilidad Genómica
6. Fundación Instituto Leloir - IIBBA; Ciclo Celular y Estabilidad Genómica
7. Fundación Instituto Leloir - IIBBA; Ciclo Celular y Estabilidad Genómica
8. Fundación Instituto Leloir - IIBBA; Ciclo Celular y Estabilidad Genómica
9. Fundación Instituto Leloir - IIBBA; Ciclo Celular y Estabilidad Genómica
fernandez@leloir.org.ar

Cancer is the leading cause of death worldwide. In an effort to cure or control this disease, more than a hundred chemotherapeutic drugs have been tested, and thousands more are still undergoing clinical trials. Currently, ranking of these drugs is done only considering its ability to destroy cancerous cells (cytotoxicity). Taking into account not only cancer's complexity but also its recognized hallmarks (Hanahan, 2000, 2011, 2022) we have decided to evaluate multiple parameters in order to compare the effects different drugs generate in tumoral cells and rank them in a more strict and precise manner. As a result, we designed a platform that evaluates the effect each drug has, using an automatized fluorescent microscope and open access software for its analysis. These tools allowed us to automate the acquisition of images and analysis of results. For the setting up, we used as a model the osteosarcoma cell line U2OS, which is widely used in the DNA damage field, and as a positive control we used the Checkpoint Kinase 1 inhibitor (iChk1), extensively used in our laboratory. With the objective of evaluating the classification and ranking capacity of our platform, we put it to the test using four known chemotherapeutic drugs, where each has its own action mechanism, which in turn generates different effects on the cancerous cells. Altogether, this proves that it is possible to rank a list of drugs considering more than one parameter simultaneously, and that the result is different from the one obtained in a unidimensional manner.

63. P3-15. **MITOCHONDRIAL DISFUNCTION IN ENDOTOXEMIA IN AR42J ACINAR CELLS**

Wendy Quilumbaquin¹, Juan S. Adan Arean², Tamara Vico³, Guadalupe Roo⁴, María Ines Vaccaro⁵, Silvia Alvarez⁶, Virgi-

nia Vanasco⁷

1. Instituto de Bioquímica y Medicina Molecular "Profesor Alberto Boveris" (UBA-CONICET); Cátedra de Fisicoquímica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956-C1113 AAD, Buenos Aires-Argentina.

2. Instituto de Bioquímica y Medicina Molecular "Profesor Alberto Boveris" (UBA-CONICET); Cátedra de Fisicoquímica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956-C1113 AAD, Buenos Aires-Argentina.

3. Instituto de Bioquímica y Medicina Molecular "Profesor Alberto Boveris" (UBA-CONICET); Cátedra de Fisicoquímica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956-C1113 AAD, Buenos Aires-Argentina.

4. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956-C1113 AAD, Buenos Aires-Argentina; Cátedra de Fisicoquímica

5. Instituto de Bioquímica y Medicina Molecular "Profesor Alberto Boveris" (UBA-CONICET); Cátedra de Fisiopatología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956-C1113 AAD, Buenos Aires-Argentina.

6. Instituto de Bioquímica y Medicina Molecular "Profesor Alberto Boveris" (UBA-CONICET); Cátedra de Fisicoquímica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956-C1113 AAD, Buenos Aires-Argentina.

7. Instituto de Bioquímica y Medicina Molecular "Profesor Alberto Boveris" (UBA-CONICET); Cátedra de Fisicoquímica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956-C1113 AAD, Buenos Aires-Argentina.

wendyquilumbaquin@gmail.com

Sepsis and endotoxemia represent systemic inflammatory syndromes driven primarily by the host response to infection. Molecular mechanisms within the exocrine pancreas cells have gained attention, as these cells represent an early and important target during endotoxemia and sepsis. Their high metabolic demand, dependence on mitochondrial function, and sensitivity to inflammatory stress position acinar cells as a relevant model for studying how systemic inflammation translates into dysfunction at the cellular level in the pancreas. Our aim was to analyze the cellular oxidative and nitrosative status and mitochondrial function both as the main source of ATP and reactive oxygen species in a cellular model of pancreatic endotoxemia. AR42J rat pancreatic acinar cells were treated with serum from rats previously injected ip with 8 mg/kg LPS or vehicle (control). We assessed mitochondrial function by measuring ATP production, mitochondrial membrane potential, and mitochondrial mass. In addition, we analyzed the ROS production and NO levels. NO and H₂O₂ (H₂O₂ control value: 0.068±0.002 nmoles/min mg protein) levels increased from 2 to 24 hours after serum-LPS-treatment. For the other hand mitochondrial membrane potential was found to decrease from 2 hours, while the mitochondrial ATP production rate decreased from 6 hours (control value: 3.3±0.3 nmol/min mg protein). Our results show that in the pancreatic cell model of endotoxemia, mitochondrial function becomes impaired in association with elevated NO levels. This model approach provides a valuable complement to vivo studies and may help to further elucidate the molecular mechanisms activated in the pancreas during endotoxemia and sepsis.

64. P3-16. INTERPLAY BETWEEN FOXA2, FOXO1 AND AKT1 IN THE REGULATION OF NANOG EXPRESSION IN EMBRYONIC STEM CELLS

Santiago Cavedo¹, Sabrina Roberti², Melanie Aranovich³, Federico Rovner⁴, María Candelaria Díaz⁵, Lucas Cozza⁶, Lucila Boto⁷, Valeria Levi⁸, Alejandra Guberman⁹

1. IQIBICEN CONICET-UBA; Laboratorio de Regulación Génica en Células Madre

2. IQIBICEN CONICET-UBA; Laboratorio de Regulación Génica en Células Madre

3. IQIBICEN CONICET-UBA; Laboratorio de Regulación Génica en Células Madre

4. IQIBICEN CONICET-UBA; Laboratorio de Regulación Génica en Células Madre

5. IQIBICEN CONICET-UBA; Laboratorio de Regulación

Génica en Células Madre

6. IQIBICEN CONICET-UBA; Laboratorio de Regulación Génica en Células Madre

7. IQIBICEN CONICET-UBA; Laboratorio de Regulación Génica en Células Madre

8. IQIBICEN CONICET-UBA; Laboratorio de Dinámica Intracelular

9. IQIBICEN CONICET-UBA y FBMC, FCEN, UBA; Laboratorio de Regulación Génica en Células Madre
santicavedo@gmail.com

The maintenance of the naïve state in mouse embryonic stem cells (mESCs) depends on a complex network of transcription factors (TFs). Nanog is a central naïve pluripotency TF and its downregulation constitutes a critical milestone at the onset of differentiation. We have found that the TF FOXA2, which is expressed in undifferentiated mESCs and increases at early differentiation, represses Nanog expression. We hypothesize that AKT1 interferes with this repression in the naïve state by promoting FOXA2 nuclear exclusion. Here, we studied the effect of AKT1 overexpression on FOXA2 localization both in fixed cells through endogenous FOXA2 immunofluorescence and on living cells by confocal microscopy. Surprisingly, we found FOXA2 into the nucleus in all conditions, suggesting that AKT1 effect on FOXA2 involves different mechanisms and/or additional factors. FOXA2 interacts with the TF FOXO1, an AKT1 target that undergoes phosphorylation-dependent nuclear exclusion in multiple systems. We therefore propose that these TFs form complexes in mESCs and that this interaction regulates FOXA2 localization and/or activity. At the onset of differentiation, AKT1 activity decline would reduce phosphorylation of the FOXO1/FOXA2 complex, promoting its nuclear retention, which could be involved in the repression of pluripotency genes like Nanog. We are currently studying the relationship between FOXA2, FOXO1, AKT1 and Nanog gene regulation at different levels by transfection in mESCs, live cell confocal microscopy, immunofluorescence, RT-qPCR, RNA-FISH and reporter assays. Elucidating these mechanisms will contribute to a deeper understanding of the mechanisms involved at the onset of differentiation, providing valuable insights for regenerative medicine.

65. P3-17. GENERATION OF A DUAL-REPORTER PLURIPOTENT STEM CELL LINE VIA HOMOLOGOUS RECOMBINATION TO MONITOR ENDOGENOUS EXPRESSION OF OCT6 AND BRACHYURY DURING DIFFERENTIATION

Agustin Aguzzi¹, Denisse Saulnier², Renata Blanco³, Juan Puracchio⁴, Federico Sevlever⁵, Lucía Moro⁶, Ariel Waisman⁷

1. FLENI, Instituto de Neurociencias (INEU), CONICET, Buenos Aires, Argentina; Laboratorio de Investigación Aplicada a Neurociencias (LIAN)

2. FLENI, Instituto de Neurociencias (INEU), CONICET, Buenos Aires, Argentina; Laboratorio de Investigación Aplicada a Neurociencias (LIAN)

3. FLENI, Instituto de Neurociencias (INEU), CONICET, Buenos Aires, Argentina; Laboratorio de Investigación Aplicada a Neurociencias (LIAN)

4. FLENI, Instituto de Neurociencias (INEU), CONICET, Buenos Aires, Argentina; Laboratorio de Investigación Aplicada a Neurociencias (LIAN)

5. FLENI, Instituto de Neurociencias (INEU), CONICET, Buenos Aires, Argentina; Laboratorio de Investigación Aplicada a Neurociencias (LIAN)

6. FLENI, Instituto de Neurociencias (INEU), CONICET, Buenos Aires, Argentina; Laboratorio de Investigación Aplicada a Neurociencias (LIAN)

7. FLENI, Instituto de Neurociencias (INEU), CONICET, Buenos Aires, Argentina; Laboratorio de Investigación Aplicada a Neurociencias (LIAN)

aaguzzi@uade.edu.ar

Mouse embryonic stem cells (mESCs) are a powerful model to study mammalian embryonic development and pluripotency mechanisms. Oct6 is a transcription factor present in "primed" pluripotent state, while Brachyury is involved in primitive streak and mesodermal lineage formation. Understanding their expression dynamics in live

cells is essential to assess how pluripotent cells exit undifferentiated state and commit to specific identities.

We aimed to construct a dual-reporter mESC line to simultaneously monitor Oct6 and Brachyury expression during differentiation. CRISPR-Cas9 was employed to introduce fluorescent reporters mScarlet3 and mEmerald into endogenous loci via homology-directed repair (HDR).

We first characterized mESC pluripotency and differentiation capacity. Pluripotency markers (Oct4, Nanog) were analyzed by immunofluorescence on D0, while Oct6 and Brachyury were assessed at D2-D3. Additional markers were evaluated by RT-qPCR, confirming correct differentiation protocol. Reporter lines were generated sequentially, starting with Oct6. CRISPR guides targeting Oct6 stop codon and HDR-mScarlet3 donors were transfected into mESCs. After antibiotic selection, we observed high recombination rate (40%) upon differentiation, as judged by mScarlet3 nuclear fluorescence. Using this pool, we generated the Brachyury reporter by transfecting CRISPR guides targeting Brachyury stop codon with HDR mEmerald plasmid. Although nuclear mEmerald fluorescence was detected after differentiation, signal was weak and infrequent, indicating low recombination efficiency despite strong Cas9 cutting activity.

To address this, we generated a new Brachyury HDR donor with longer right homology arm and mStayGold fluorescent protein for higher fluorescence. We will assess recombination efficiency, establish clonal lines, and validate via genomic PCR for fluorescence time-lapse microscopy studies.

66. P3-18. PAPER-BASED MICROFLUIDIC DETECTION OF PYROPHOSPHATE AS A READOUT FOR LOOP MEDIATED ISOTHERMAL AMPLIFICATION (LAMP)

Sandra G. Vlachovsky¹, Lucas R. Sousa², Fabiana Stolicz³, Wendell K. T. Coltro⁴, Adrian Vojnov⁵, Eduardo Cortón⁶, Federico Figueredo⁷

1. Departamento de Química Biológica e IQUIBICEN - CONICET, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (UBA), CABA, Argentina; Laboratorio de Biosensores y Bioanálisis

2. Departamento de Química Biológica e IQUIBICEN - CONICET, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (UBA), CABA, Argentina/ Instituto de Química, Universidad Federal de Goiás, 74690-900, Goiânia, GO, Brazil; Laboratorio de Biosensores y Bioanálisis

3. Fundación Pablo Cassará, Buenos Aires, Argentina- CONICET; Instituto de Ciencia y Tecnología Dr. Cesar Milstein

4. Universidad Federal de Goiás, 74690-900, Goiânia, GO, Brazil; Instituto de Química

5. Fundación Pablo Cassará, Buenos Aires, Argentina- CONICET; Instituto de Ciencia y Tecnología Dr. Cesar Milstein

6. Departamento de Química Biológica e IQUIBICEN - CONICET, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (UBA), CABA, Argentina; Laboratorio de Biosensores y Bioanálisis

7. Departamento de Química Biológica e IQUIBICEN - CONICET, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (UBA), CABA, Argentina; Laboratorio de Biosensores y Bioanálisis
sandragvla@gmail.com

Loop-mediated isothermal amplification (LAMP) is a powerful tool for nucleic acid amplification due to its high specificity and speed, as well as its operation at a constant temperature. Its application in the diagnosis of infectious diseases has grown significantly in recent years. The characteristics of LAMP enable its use in point-of-care (POC) diagnostic devices, allowing rapid testing without the need to transport the sample to a laboratory. However, current LAMP detection methods, often based on visual turbidity or color changes in microtubes, present a certain degree of subjectivity and require relatively large reaction volumes. Our group has developed a paper-based microfluidic analytical device (μ PAD), which allows LAMP amplification results to be determined either by naked-eye observation or through a smartphone application. μ PADs are considered among the most suitable tools for integrating sensors into POC applications and performing molecular diagnostics.

The target analyte is pyrophosphate (PPi), a product of amplification reactions. PPi can be detected through a colorimetric reaction with ammonium molybdate. This compound has been primarily used for the determination of orthophosphate in environmental samples, but this reaction can be specifically optimized for PPi detection in μ PADs. In the device, ammonium molybdate reacts with pyrophosphate under acidic conditions, forming a deep blue color in the detection zone. Positive and negative LAMPs for various infectious disease agents such as tuberculosis were tested and compared with the traditional electrophoresis method, showing a linear response at PPi concentrations of 0 to 2.5 mmol L⁻¹, with a limit of detection of 0.15 mmol L⁻¹.

67. P3-19. EXTRACELLULAR VESICLES FROM POMEGRANATE (PUNICA GRANATUM L.) JUICE INHIBIT LPS-INDUCED MAMMARY INFLAMMATION IN LACTATING MICE

Agustina Manzella¹, Marcos Palavecino², Christian M. Sánchez López³, Pedro Javier Salaberry⁴, Noemi Jordanovski⁵, Silvia Vornetti⁶, Antonio Marcilla⁷, Angela Lara Montero⁸, Edith Kordon⁹

1. Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE, UBA-CONICET), Buenos Aires, Argentina.

2. Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE, UBA-CONICET), Buenos Aires, Argentina.

3. Parasites and Health Group, Área de Parasitología, Departament de Farmàcia i Tecnologia Farmacèutica i Parasitologia, Facultat de Farmàcia i Ciències de l'Alimentació Universitat de València Valencia Spain. Joint Research Unit on Endocrinology, Nutrition and Clinical Dietetics Health Research IIS La Fe-Universitat de València Valencia Spain.

4. Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE, UBA-CONICET), Buenos Aires, Argentina.

5. Hospital de Oncología Marie Curie, Buenos Aires, Argentina.

6. Hospital de Oncología Marie Curie, Buenos Aires, Argentina.

7. Parasites and Health Group, Área de Parasitología, Departament de Farmàcia i Tecnologia Farmacèutica i Parasitologia, Facultat de Farmàcia i Ciències de l'Alimentació Universitat de València Valencia Spain. Joint Research Unit on Endocrinology, Nutrition and Clinical Dietetics Health Research IIS La Fe-Universitat de València Valencia Spain.

8. Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE, UBA-CONICET), Buenos Aires, Argentina.

9. Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE, UBA-CONICET), Buenos Aires, Argentina.

agustinamanzella@gmail.com

Pomegranate-derived extracellular vesicles (PgEVs) have demonstrated a notable anti-inflammatory effect by inhibiting lipopolysaccharide (LPS) induced NF- κ B in human monocytes. Given that mastitis is a prevalent inflammatory disease of the mammary gland during lactation, we aim to evaluate the therapeutic potential of PgEVs in a mouse model of LPS-induced mastitis. Ten days after delivery, mouse pups (C57/bl6) were weaned and their mothers were inoculated subcutaneously (sc) with LPS or vehicle (PBS). Then, 24h later, both groups were treated with a sc injection of PgEVs or PBS (n=3 each group). All mice were sacrificed 48h after pups' removal. Mammary tissue was obtained and either fixed in formalin for histological analysis using Hematoxylin-Eosin (H&E) staining and Immunohistochemistry (IHC), or frozen for protein extraction and Western Blot (WB) analysis. LPS treatment successfully induced significant immune infiltration in the mammary tissue, as evidenced by H&E staining and S100A9 IHC, an effect that was significantly reversed by PgEV treatment, primarily by affecting myeloid cells. No significant differences were detected in P-STAT3 levels by IHC, possibly because the removal of the pups caused mammary involution and the activation of this transcription factor in all groups. WB analysis showed no significant differences in CC3 levels in mammary epithelial cells, suggesting that PgEVs did not affect mammary involution. Our results suggest that PgEVs are a promising pharmacological strategy for mitigating mammary inflammation by attenuating im-

mune infiltration. However, further research is needed to fully elucidate their mechanisms of action and confirm their possible clinical application.

68. P3-20. TARGETED MODULATION OF ENDOTHELIAL INFLAMMATION USING MIRNA-LOADED EXTRACELLULAR VESICLES: A STRATEGY TO COUNTERACT VASCULAR SENESCENCE

Sofía Masuelli¹, Diego Croci², Nadia Bannoud³

1. *Facultad de Ciencias Médicas, Universidad Nacional de Cuyo. Instituto Tecnológico de Buenos Aires. Instituto de Histología y Embriología de Mendoza.; Laboratorio de Glicobiología y Biología Vascular*

2. *Instituto de Histología y Embriología de Mendoza. Instituto Tecnológico de Buenos Aires.; Laboratorio de Glicobiología y Biología Vascular*

3. *Facultad de Ciencias Médicas, Universidad Nacional de Cuyo. Instituto de Histología y Embriología de Mendoza.; Laboratorio de Glicobiología y Biología Vascular*
sofiamasuelli@gmail.com

As the global population ages, vascular diseases have emerged as leading contributors to morbidity, disability, and death. A central mechanism in their progression is endothelial dysfunction, driven in part by inflammaging—a chronic, low-grade inflammatory state. Despite its clinical relevance, there are no therapies capable of simultaneously modulating the multiple molecular circuits that sustain this systemic and vascular inflammatory state. Extracellular vesicles (EVs) are natural carriers for proteins, lipids, and nucleic acids to facilitate intercellular communication and regulate biological processes. We established a representative ex vivo model of vascular inflammation by obtaining HUVECs and treating them with 5ng/ml TNF- α 24hs to induce an inflammatory phenotype (ICAM+high, high β -Gal activity, and high PBMC attachment to HUVEC). We performed in-silico analyses on human senescent endothelial tissue from public datasets, finding specific miRNAs and genes differentially expressed compared to non-senescent counterparts as potential targets. To epigenetically and synergistically regulate different cellular pathways associated with vascular deterioration, we designed a synthetic miRNA cassette capable of encoding multiple functional miRNAs. HEK293T cells were transfected with miR146-5p constructs and successfully secreted EVs containing the selected miRNA cargo. Current experiments are focused on validating the expression and functionality of EVs loaded with the full synthetic cassette in our inflammatory endothelial model. Conclusion: Our findings support the hypothesis of the use of modified EVs to epigenetically modulate senescence-related pathways in endothelial cells. This strategy also represents a promising and scalable approach to counteract vascular aging and inflammation, opening new avenues for the treatment of chronic age-associated diseases.

69. P3-21. DETERMINATION OF SALIVARY BIOMARKERS IN BRUXISM, ITS RELATIONSHIP WITH STRESS

Judith Palomino¹, Juliana Sesma², Edgardo Hugo Lopez D'allesandro³, Ada Karina Molinas⁴

1. *CIC- UNR.- Facultad de Odontología de Rosario. Maestranda Maestría Biología Molecular Medica. Facultad de Bioquímica y Farmacia. UBA.; Facultad Odontología de Rosario*

2. *IDICER CONICET- Facultad de Ciencias Médicas. Hospital Provincial de Rosario; Facultad Odontología de Rosario. Hospital Provincial de Rosario*

3. *Facultad Odontología de Rosario. Cátedra Estomatología II.; Facultad Odontología de Rosario*

4. *CIC- UNR.- Facultad de Odontología de Rosario. Cátedra de Microbiología y Parasitología.; Facultad Odontología de Rosario*
palominoj@intramed.net

Bruxism is a parafunctional muscular activity, characterised by clenching or grinding of the teeth, which can occur during sleep or wakefulness. Its aetiology is multifactorial and includes biological, psychological and behavioural components, with stress being one

of the most frequently associated variables. Empirical evidence supporting this association is conflicting. The present study aimed to evaluate the relationship between bruxism and different indicators of stress, psychological profile, using a multimodal strategy. Fifty patients with a diagnosis of bruxism and 100 control subjects were included. Validated questionnaires were administered and saliva samples were taken for biomarker determination, cortisol and dopamine were determined by biochemical methods. The instruments used included HADS, Levenstein and EPQ-RVA questionnaires. Comparative statistical analysis between groups was performed using Student's t-tests with Welch's correction for unequal variances. The results showed no statistically significant differences between groups in any of the variables analysed. No differences were observed in cortisol levels (morning, evening, or delta), nor in dopamine levels. Nor were differences found in anxiety scores, depression, perceived stress or in the personality traits assessed (neuroticism, extroversion, psychoticism and sincerity). These findings suggest that, in the sample analysed, bruxism is not associated with biological markers of stress, emotional state or personality structure. The importance of continuing research with more robust methodological designs that consider other intervening variables and complementary diagnostic tools is highlighted.

70. P3-22. EVALUATION OF BONE STRUCTURE IN DEVELOPING APICAL PROCESSES: A MODEL IN HYPERCHOLESTEROLEMIC RATS

Romina Loiacono¹, Ariel F Gualtieri², Leonardo Cacciagui³, Pablo A Rodríguez¹, Romina C De Lucca⁵

1. *FOUBA; Cátedra de Histología y embriología - FOUBA*

2. *FOUBA; Cátedra de Odontología Legal y Forense - FOUBA*

3. *FOUBA; Cátedra de Bioquímica - FOUBA*

4. *FOUBA; Cátedra de Endodoncia - FOUBA*

5. *FOUBA; Cátedra de Histología y Embriología - FOUBA*

romina.loiacono@odontologia.uba.ar

The relationship between lipid metabolism and bone microstructure represents an emerging field of research in experimental dentistry. CICUAL ODon/FOUBA 004/2023. UBACYT 2023 20020220400037BA Objective: To evaluate the bone structure of developing periapical processes in hypercholesterolemic Wistar rats. Materials and Methods: Fourteen adult Wistar rats (average weight 190 g) were randomly divided into two groups: HCD (high-cholesterol diet) and CD (control diet). The HCD group received a cholesterol-enriched diet for 5 weeks, while the CD group was fed a standard diet. After this period, both groups underwent access cavity preparation of the first mandibular molars, which were left exposed to the oral environment for 10 days. Following euthanasia, micro-computed tomography (micro-CT) was performed to determine bone volume in the studied regions (apical, crest, furcation, and periapical process). Results were analyzed using Student's t-test ($p < 0.05$). Results: Differences were observed in bone volume in the crest and apical regions. In both cases, the CD group showed greater volume, indicating a higher amount of mineralized bone tissue within the total volume (mineralized bone and bone marrow). Conversely, furcation and periapical process regions showed no significant differences in bone volume, although a trend toward higher values was observed in the CD group. Conclusion: Developing apical processes exhibit distinct alterations in bone structure depending on the evaluated region and serum cholesterol levels.

POSTERS 4 - SAIC - GENÉTICA 1

DATE & TIME: 17/11/2025 13:00 - 14:30 H

Chairs: Ariel Pablo López, Andrea Liliana Millán, Liliana Carmen Rossetti

71. P4-01. EXPANDING THE SPECTRUM OF DMD PATHOGENIC VARIANTS: PSEUDOEXON INCLUSION TRIGGERED BY A NOVEL ULTRARARE INTRONIC DELETION

María Eugenia Foncuberta¹, Soledad Monges², Emma Prieto³, Abel Ismael Gómez⁴, Sofía Corbaz⁵, Silvina Gómez Montoya⁶, Fabiana Lubieniecki⁷, Luis Pablo Gravina⁸

1. *Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Laboratorio de Biología Molecular-Genética*

2. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Servicio de Neurología
3. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Laboratorio de Inmunología Molecular
4. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Laboratorio de Biología Molecular-Genética
5. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Servicio de Neurología
6. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Servicio de Neurología
7. Laboratorio de Biología Molecular-Genética; Servicio de Patología
8. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Laboratorio de Biología Molecular-Genética
eufoncu@gmail.com

Dystrophinopathies are X-linked recessive neuromuscular disorders caused by pathogenic variants in the DMD gene. Although copy number variation analysis and sequencing of the DMD gene identify most causative variants, approximately 1% of patients remain unsolved. In such cases, muscle-derived mRNA analysis is critical to detect deep intronic variants that escape conventional DNA-based assays. We report a 15-year-old male with Becker muscular dystrophy in whom routine genetic testing failed to identify a causative variant. Muscle biopsy revealed a dystrophic pattern, with preserved staining for DYS1, irregular staining for DYS2, and markedly reduced expression for DYS3. RNA analysis from muscle biopsy revealed the inclusion of a pseudoexon (PE) derived from intron 47 in the DMD transcript. To investigate the genomic basis of PE47 activation, primers flanking PE47 were designed; PCR amplification failed in the patient but succeeded in controls, suggesting a deletion within the intronic segment adjacent to PE47. On the basis of this evidence, additional probes targeting intron 47 were included into a custom neuromuscular NGS-panel. One targeted region showed absence of sequencing reads, narrowing the candidate interval upstream of PE47. Long-range PCR confirmed a deletion, and Sanger sequencing precisely defined the breakpoints (NM_004006.3:c.6913-8360_6913-4040del). This variant has not been previously reported in LOVD, ClinVar, or gnomAD, confirming it as a novel pathogenic variant. This case illustrates an ultrarare mutational mechanism and highlights the importance of integrating RNA and DNA analyses to achieve definitive diagnoses and expand the mutational spectrum of dystrophinopathies.

72. P4-02. UPDATED CATALOG OF GENES AND VARIANTS ASSOCIATED WITH CONGENITAL HYPOGONADOTROPIC HYPOGONADISM: SYSTEMATIC REVIEW, NOVEL AUTOMATED RECLASSIFICATION PIPELINE AND FUNCTIONAL NETWORK ANALYSIS

Franco G. Brunello¹, Sebastián Castro², Jonathan Zaiat³, Gabriela Sansó⁴, Agustín Izquierdo⁵, Mariela Urrutia⁶, Rodolfo A. Rey⁷, Marcelo Martí⁸, Romina P. Grinspon⁹, Mariana L. Tellechea* (*Equal contribution)¹⁰

1. Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (FCEyN-UBA); Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN) CONICET, C1428E-GA Buenos Aires, Argentina.
2. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina; Fisiopatología y Clínica del Desarrollo Gonadal
3. Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (FCEyN-UBA); Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN) CONICET, C1428E-GA Buenos Aires, Argentina.
4. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina; Unidad de Medicina Traslacional
5. Centro de Investigaciones Endocrinológicas "Dr. César

Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina.; Unidad de Medicina Traslacional.

6. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina.; Fisiopatología y Clínica del Desarrollo Gonadal
7. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina.; Fisiopatología y Clínica del Desarrollo Gonadal.
8. Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (FCEyN-UBA); Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN) CONICET, C1428E-GA Buenos Aires, Argentina.
9. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina.; Fisiopatología y Clínica del Desarrollo Gonadal.
10. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina.; Biología de la tiroides y trastornos del metabolismo
fgbrunello@gmail.com

Genetic variant classification represents a major challenge in disorders exhibiting genetic heterogeneity. To advance the understanding of Congenital Hypogonadotropic Hypogonadism (CHH), we aimed to refine the catalog of causal genes and variants. We systematically collected variants reported in the literature and created CHH_vd, a curated database. In parallel, we developed CHH_vip, a custom-built computational pipeline for variant annotation and classification, integrating data from CHH_vd and multiple sources. Gene network and term enrichment analyses were applied to generate disease-specific gene panels. Our systematic review retrieved 352 curated scientific studies, documenting 1,937 patients carrying a total of 2,603 variants, of which 1,518 were unique, distributed across 143 genes. All variants were incorporated into CHH_vd (publicly available) and reclassified using CHH_vip. Major classification changes with medically significant impact (InterVar vs. CHH_vip) were identified for 227 variants: 159 were downgraded and 68 upgraded (from/to P/LP/High_VUS). Among the downgrades, genes such as GNRHR, RELN, and SEMA7A were particularly implicated. Importantly, this reclassification decreased the proportion of total VUS by 10% and Medium_VUS by 5%. Through CHH_vd, we provide an updated view of the genes impacted by variation in CHH, highlighting the genetic heterogeneity underlying this condition. The implementation of curated "Green" and "Yellow" gene panels, together with CHH_vip, establishes a reproducible platform for compiling and interpreting variation data. These resources will optimize the filtering and classification processes, reduce the diagnostic turnaround time, and partially fill an existing gap in CHH.

73. P4-03. BUILDING A GENOMICS UNIT IN A PUBLIC HOSPITAL: THE EL CRUCE EXPERIENCE

Carolina Victoria Ramirez¹, Gisela Zolezzi², Gaston Montecino³, Ana Damia⁴, Paloma Brun⁵, Cristian Calandra⁶, Gisela Streitenberger⁷, Agostina Llarens⁸, Viviana Fanessi⁹

1. Area de Investigación, Hospital de alta complejidad en red el Cruce - HNK SAMIC; Unidad Genómica
2. CEMET, Hospital de alta complejidad en red el Cruce - HNK SAMIC; Unidad Genómica
3. Laboratorio Central, Hospital de alta complejidad en red el Cruce - HNK SAMIC; Sector Biología Molecular
4. CEMET, Hospital de alta complejidad en red el Cruce - HNK SAMIC; Consultorio de genética médica
5. CEMET, Hospital de alta complejidad en red el Cruce - HNK SAMIC; Consultorio de genética médica

6. *Servicio de Neurociencias, Hospital de alta complejidad en red el Cruce - HNK SAMIC; Consultorio de neurología*
7. *Unidad Coronaria, Hospital de alta complejidad en red el Cruce - HNK SAMIC; Consultorio de cardiogenética*
8. *Servicio de Inmuno Reumatología, Hospital de alta complejidad en red el Cruce - HNK SAMIC; Consultorio de inmunología pediátrica*
9. *CEMET, Hospital de alta complejidad en red el Cruce - HNK SAMIC; Coordinación*
carolinavramirez@gmail.com

Background: The Genomics Unit, located within the Center for Translational Medicine (CEMET) of Hospital El Cruce, was established to incorporate molecular and genomic technologies into clinical practice, with the dual aim of improving patient care and supporting biomedical research. **Objective:** To describe the implementation, diagnostic applications, and main achievements of the Genomics Unit during its first two years of activity. **Methods:** The Unit implemented targeted next-generation sequencing (NGS) for the diagnosis of myeloid malignancies, Sanger sequencing for the analysis of known variants in hereditary diseases, and molecular testing for somatic markers in solid tumors. Additionally, whole-exome sequencing (WES) was introduced for the study of patients with rare diseases. Sequencing and bioinformatics support were also provided to external research groups. **Results:** Over a two-year period, the Unit established robust diagnostic workflows. A total of 48 patients were analyzed using targeted NGS panels for myeloid malignancies, enabling the detection of pathogenic and clinically relevant variants. Sixty cases underwent Sanger sequencing for known hereditary variants, 12 solid tumor samples were tested for somatic molecular markers, and exome sequencing was performed in selected rare disease cases. This work was carried out in close collaboration with geneticists, oncologists, and other specialists who actively integrated genomic findings into clinical decision-making. **Conclusion:** The experience of the CEMET-Hospital El Cruce demonstrates the feasibility of implementing genomic diagnostics in a public hospital setting. Integrating NGS, Sanger, exome sequencing, and somatic marker analysis—alongside interdisciplinary collaboration—has strengthened clinical-research ties and advanced precision medicine in Argentina's public health system.

74. P4-04. MOLECULAR DIAGNOSIS OF FMR1 GENE DISORDERS IN THE PUBLIC HEALTH SYSTEM IN CORDOBA, ARGENTINA

Carla Deporte¹, Florencia Celeste Salazar², Silene Silvera³, Julia Mugnaini⁴, Ruth Schumiachkin⁵, Gonzalo Castro⁶, María Gabriela Barbas⁷

1. *Ministerio de Salud de la provincia de Córdoba; Departamento Laboratorio Central*
2. *Ministerio de Salud de la provincia de Córdoba; Departamento Laboratorio Central*
3. *Ministerio de Salud de la provincia de Córdoba; Departamento Laboratorio Central*
4. *Subsecretaría de Discapacidad, Rehabilitación e Inclusión, Ministerio de Salud de la provincia de Córdoba; Área de Genética Médica*
5. *Subsecretaría de Discapacidad, Rehabilitación e Inclusión, Ministerio de Salud de la provincia de Córdoba; Área de Genética Médica*
6. *Ministerio de Salud de la provincia de Córdoba; Departamento Laboratorio Central*
7. *Ministerio de Salud de la provincia de Córdoba; Departamento Laboratorio Central*
carlodeporte-07@hotmail.com

The FMR1 gene (Fragile X Mental Retardation 1) encodes the FMRP protein, which is essential for neuronal development and synaptic plasticity. Its 5'UTR contains a CGG repeat region; expansions beyond 200 repeats are associated with hypermethylation, gene silencing, loss of FMRP, and development of fragile X syndrome (FXS). Premutation alleles are associated to fragile X-associated primary ovarian insufficiency (FXPOI) a leading cause of ovarian dysfunction in women, and fragile X-associated tremor/ataxia syndrome (FXTAS).

This study reports our experience implementing FMR1 molecular testing within the public health system of Córdoba, highlighting its value for diagnosis, prevention and genetic counseling. DNA extracted from peripheral blood was analyzed by PCR with a commercial kit followed by capillary electrophoresis, and results were interpreted using the AmpliX® FMR1 Reporter software (Asuragen). Between October 2022 and July 2025, 137 patients were tested (40 females, 97 males; median age 12 years). Most subjects were referred due to behavioral disorders or intellectual disability. Overall, 4.4% (6/137) showed a pathological number of CGG repeats, half within the premutation range and half with full mutations consistent with FXS. The incorporation of the FMR1 testing into the public health system represents a significant advance, enabling accurate diagnosis of previously undiagnosed patients. This allows them access to appropriate treatment and genetic counseling. Furthermore, negative results are equally valuable, as they contribute to the differential diagnosis of FXS, reduce clinical uncertainty, and guide the search for other causes.

75. P4-05. ABCB6: ARE GENETIC VARIANTS RELATED TO HEPATIC PORPHYRIAS ONSET?

Mateo De Jorge¹, Catalina Bruguera², Laura Varela³, Victoria Parera⁴, Viviana Melito⁵, Johanna Zuccoli⁶, Ana María Buza-leh⁷

1. *Escuela Técnica ORT, Buenos Aires; Laboratorio del metabolismo del hemo. Porfirias humanas y en animales. CIPYP*
2. *Escuelas Técnicas ORT, Buenos Aires; Laboratorio del metabolismo del hemo. Porfirias humanas y en animales. CIPYP*
3. *Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín, Buenos Aires; Laboratorio del metabolismo del hemo. Porfirias humanas y en animales.*
4. *Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín, Buenos Aires; Laboratorio del metabolismo del hemo. Porfirias humanas y en animales.*
5. *1-Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín, Buenos Aires; -Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, UBA, Buenos Aires; Laboratorio del metabolismo del hemo. Porfirias humanas y en animales. CIPYP*
6. *Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín, Buenos Aires; Laboratorio del metabolismo del hemo. Porfirias humanas y en animales. CIPYP*
7. *1-Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín, Buenos Aires; -Universidad Favaloro, Buenos Aires; Laboratorio del metabolismo del hemo. Porfirias humanas y en animales. CIPYP*
mateodejorge07@gmail.com

ABCB6 variants have been associated with cytotoxics resistance, iron homeostasis, and porphyrin transport. Porphyrins are due to heme enzymes deficiencies: Porphobilinogen deaminase in Acute Intermittent Porphyria (AIP), and Uroporphyrinogen decarboxylase in Porphyria Cutanea Tarda (PCT). Heme biosynthesis takes place between mitochondria and cytosol. Variants in heme metabolites transporters could contribute to Porphyria onset altering the translocation from cytosol to mitochondria. The aim was to evaluate ABCB6 variant (rs149202834; NM_005689.4:c.574C>T) role in hepatic Porphyrias triggering and/or clinical manifestations. Six cohorts were included (n=15/each): Control (non-porphyric); AIP patients carrying PBGD mutation: symptomatic (S-AIP) or non-symptomatic (L-AIP); acquired PCT infected (PCT-HIV) or not with HIV (PCT) and HIV non-porphyric (HIV). All have given their informed consent. PCR-RFLP was performed for genotyping rs149202834 variant. No differences in T allele frequency were found among AIP groups vs Control. Regarding PCT cohorts, allelic frequency was higher in PCT-HIV (0.14) than Control and PCT (frequency=0), and lower than HIV (0.28, p<0.05). Differential proportion of genotypic

frequencies were found in HIV (CC:55.55%; CT:33.34%; TT:11.11%) and PCT-HIV (CC:71.43%; CT:28.57%; TT:0%), being CC:100% in the other groups. rs149202834 has low frequency independently of ethnicity (gnomAd and ClinVar); we found similar values in the Argentinian population. Considering the low frequency, it is remarkable the values found in HIV groups. In our experience, PCT-HIV patients show more severe clinical picture than PCT, probably due to variations in genotype distribution, potentially related to altered porphyrin homeostasis and impaired distribution between mitochondria, liver, and skin. Further studies are needed to clarify variant biological.

76. P4-06. ANALYSIS OF THE WHOLE EXOME SEQUENCING (WES) STUDY IN PATIENTS FROM ARGENTINA, PERIOD 2023-2025

Julieta Laiseca¹, Melisa Taboas², Aldana Claps³, Tania Castro⁴, Vanesa Lotersztejn⁵, Cinthia Martinez⁶, Andrea Solari⁷, Florencia Rebagliati⁸, Florencia Vazquez⁹, Talia Dos Santos¹⁰, Pedro Stockdale¹¹, Carolina Dellamea¹², Celeste Martinoli¹³, María Paz Bidondo¹⁴, Pablo Barbero¹⁵, Paloma Brun¹⁶, Natalia Jaen Oliveri¹⁷, Viviana Cosentino¹⁸, Lucia Vago¹⁹, Marilena Antinori²⁰, Mailen Costa²¹, María de los Ángeles Albarracín²², Marcelo Marti²³, Jonathan Zaia²⁴, Agustín Izquierdo²⁵, Julian Sanchez Loria²⁶, Liliana Dain²⁷

1. Centro Nacional de Genética Médica (CNGM), Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina.; Diagnóstico Molecular

2. Centro Nacional de Genética Médica (CNGM), Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina.; Diagnóstico Molecular

3. Centro Nacional de Genética Médica (CNGM), Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina.; Diagnóstico Molecular

4. Centro Nacional de Genética Médica (CNGM), Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina.; Diagnóstico Molecular

5. Centro Nacional de Genética Médica (CNGM), Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina.; -

6. Centro Nacional de Genética Médica (CNGM), Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina.; -

7. Centro Nacional de Genética Médica (CNGM), Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina.; -

8. Centro Nacional de Genética Médica (CNGM), Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina.; -

9. Centro Nacional de Genética Médica (CNGM), Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina.; -

10. Centro Nacional de Genética Médica (CNGM), Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina.; -

11. Centro Nacional de Genética Médica (CNGM), Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina.; -

12. Hospital Castelan. Chaco, Argentina.; -

13. Hospital Interzonal Especializado en Pediatría, Sor María Ludovica de la Plata.; Sala de Genética.I

14. Red Nacional de Anomalías Congénitas (RENAC-INE-CNGM), ANLIS "Carlos Malbrán", Buenos Aires, Argentina.;

15. Red Nacional de Anomalías Congénitas (RENAC-INE-CNGM), ANLIS "Carlos Malbrán", Buenos Aires, Argentina.;

16. Hospital de Alta Complejidad en Red El Cruce "Dr. Néstor Carlos Kirchner"; -

17. Hospital de Alta Complejidad en Red El Cruce "Dr. Néstor Carlos Kirchner"; -

18. Hospital Interzonal General de Agudos Luisa C. de Gandulfo, Buenos Aires, Argentina.; -

19. Servicio de Genética, Hospital de Dependencia Provincial de Rosario y Hospital de Niños Zona Norte de Rosario, Santa Fe, Argentina.; -

20. Hospital de la madre y el niño, Sector Genética, Formosa, Argentina.; Genética

21. Hospital Provincial Neuquén, Neuquén, Argentina.; -

22. Servicio de Neonatología, Hospital Público Materno Infantil, Salta Capital, Salta.; -

23. CONICET, Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales IQUIBICEN, Buenos Aires, Argentina.; -

24. CONICET, Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales IQUIBICEN, Buenos Aires, Argentina.; -

25. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) - CONICET, FEI; División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, CABA, Argentina. y Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, CABA, Argentina.; -

26. Unidad Operativa Centro Nacional de Genómica y Bioinformática, Administración Nacional de Laboratorios e Institutos de Salud "Dr. Carlos G. Malbrán", Ciudad Autónoma de Buenos Aires, Argentina.; -

27. Centro Nacional de Genética Médica (CNGM), Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina.; y Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires.; Diagnóstico Molecular

julieta_laiseca@yahoo.com.ar

Whole Exome Sequencing (WES) enables the identification of genetic variants (GVs) in coding regions of the genome. In this study, we reviewed the results by WES during 2023-2025 period performed at CNGM. WES was performed using the Twist human core exome and the DNA Prep with Exome 2.5 Enrichment (Illumina) in 77 samples. An in-silico selection of candidate genes was developed in-house. Variants were interpreted using ACMG guidelines and Clingen recommendations. From the total of patients, 57.1% (n=44) had a previous study and almost 50% arrived with a defined clinical suspicion (n=38). A total of 57/77 samples were concluded: 31 with clinical suspicion, while from the remaining 20 samples that are still in analysis, 13 were without a defined phenotype. Among the 57 concluded samples, 66.7% had Pathogenic (P)/likely pathogenic (LP) variants (n=38), 10.5% had variants of uncertain significance (VUS) (n=6) and in 22.8% no causal variants were observed (n=13) from which 11 had no defined phenotype. In 25/31 patients, their diagnostic suspicion was confirmed, while in 4/31 cases, the diagnosis changed. A total of 46 GV's were observed: 17 loss of function, 26 missense, 1 in-frame deletion and 2 CNVs; 2 patients had 2 variants. Among the most represented genes, 3 patients had variants in PTPN11, 3 in NF1, 2 in PIEZO2 and 2 in CHD7. In summary, the percentage of patients with clinically relevant variants found was 77.2%. This emphasizes the importance of using this technology in patients with rare diseases.

77. P4-07. DETECTION AND CHARACTERIZATION OF TWO POLYMORPHIC STRUCTURAL VARIANTS IN XQ28 USING SHORT-READ GENOME SEQUENCING FROM RESTRICTION DNA-CIRCLES

Miguel M. Abelleiro¹, Patricio Yankilevich², Betiana M. Ziegler³, Claudia P. Radic¹, Florencia Giliberto⁵, Liliana C. Rossetti⁶, Carlos D. De Brasi⁷

1. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM); Genética Molecular de la Hemofilia (GMH)

2. Instituto de Investigación en Biomedicina de Buenos Aires (IBIOBA), CONICET-Partner Institute of the Max Planck Society.; Plataforma Bioinformática

3. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM); Genética Molecular de la Hemofilia (GMH)

4. Instituto de Medicina Experimental (IMEX), CONICET-Aca-

demia Nacional de Medicina (ANM); Genética Molecular de la Hemofilia (GMH)

5. Instituto de Inmunología, Genética y Metabolismo (INIGEM), CONICET-Universidad de Buenos Aires (UBA); Distrofinopatías

6. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM); Genética Molecular de la Hemofilia (GMH)

7. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM); Genética Molecular de la Hemofilia (GMH)

martinabelleyro@gmail.com

Structural variants (SVs) may drive chromosomal evolution and are often associated with human diseases. SVs comprise copy number variants (CNVs) (e.g., deletions, duplications), non-CNV rearrangements (e.g., perfect inversions, balanced translocations) and complex SV combining different classes. SV identification for short and long-read high-throughput DNA sequencing technology remains challenging to implement in clinical settings, especially in those cases involving the detection of perfect inversions mediated by highly-homologous inverted-repeats (IR). Applying a novel experimental and bioinformatics pipeline with short-read whole-genome sequencing (2nd-gen-WGS) (HiSeq Illumina) from circularized BclI restriction-fragments, we detected and characterized two polymorphic SV on Xq28, which were verified by direct molecular testing: -an 1.4kb-deletion (DEL) with an allelic frequency AF(CI95%) of 0.83(0.71-0.91) in 41 individuals from the general population with a moderate excess of heterozygotes (observed vs expected, 0.47 vs 0.29) in Hardy-Weinberg (HW) equilibrium, NC_000023.11:g.148428177_148429716del and, notably, -a perfect inversion (INV) otherwise invisible for 2nd-gen-WGS, mediated by recombination between 99% homologous 8.4kb-long IRs, which were studied in 11 individuals with AF(CI95%) of 0.31(0.08-0.54) with an observed/expected heterozygosity of 0.6/0.43, in HW equilibrium, g.(153066014_153074418)_ (153075613_153084041)inv. The novel approach led to an improved identification of these two polymorphic SVs and predicts that a massive genomic exploration of SVs could detect many other non-CNV SVs particularly those mediated by IRs otherwise invisible. These findings may have a positive clinical impact and will contribute to a better understanding of the dynamics of the human genome.

78. P4-08. DEVELOPMENT AND VALIDATION OF A RAPID AND EFFICIENT NEXT GENERATION SEQUENCING (NGS) PROTOCOL FOR MECP2 GENE SEQUENCING IN THE MOLECULAR DIAGNOSIS OF RETT SYNDROME

Hector Martin Cifuentes¹, Fabian Alberto Crespo², Sanchez Loria Julian³, Maria Eugenia Foncuberta⁴, Victoria Huckstadt⁵, Sofia De La Fuente⁶, Camila Ximena Peñalva⁷, Belén Fiamma Figueredo⁸, Tomás J. Poklepovich Caride⁹, Gonzalo Raúl Acevedo¹⁰, Guillermo Corró¹¹, Bruque Carlos David¹², Marisol Delea¹³

1. Unidad de Conocimiento Traslacional Hospitalaria Patagónica-CONCIET, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Diagnostico molecular

2. Fundacion sin Rett Argentina; -

3. ANLIS Malbrán, Buenos Aires, Argentina.; Unidad Operativa Centro Nacional de Genómica y Bioinformática (UOC-NGB)

4. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Laboratorio de Biología Molecular-Genética

5. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; -

6. Unidad de Conocimiento Traslacional Hospitalaria Patagónica-CONCIET, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Diagnostico molecular

7. Unidad de Conocimiento Traslacional Hospitalaria Patagónica-CONCIET, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Diagnostico molecular

8. Unidad de Conocimiento Traslacional Hospitalaria Patagónica-CONCIET, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Diagnostico molecular

gónica-CONCIET, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Diagnostico molecular

9. ANLIS Malbrán, Buenos Aires, Argentina.; Unidad Operativa Centro Nacional de Genómica y Bioinformática (UOC-NGB)

10. Unidad de Conocimiento Traslacional Hospitalaria Patagónica-CONCIET, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Diagnostico molecular

11. Unidad de Conocimiento Traslacional Hospitalaria Patagónica-CONCIET, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Diagnostico molecular

12. Unidad de Conocimiento Traslacional Hospitalaria Patagónica-CONCIET, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Diagnostico molecular

13. Unidad de Conocimiento Traslacional Hospitalaria Patagónica-CONCIET, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Diagnostico molecular

h.martin.cifuentes@gmail.com

Rett syndrome (RS) is a severe neurodevelopmental disorder that mostly affects females, it's a rare disease with an incidence of 1 in 10,000 live births characterized by a period of normal early development followed by loss of acquired motor and communication skills, stereotypic hand movements, seizures, and intellectual disability. Pathogenic variants in MECP2 account for the majority of cases, making molecular testing essential for diagnosis, genetic counseling. This study aimed to develop and validate a rapid and cost-effective NGS-based protocol for sequencing MECP2 in patients with suspicion of RS. PCRs for all coding exons of both canonical and alternative MECP2 transcripts were designed and performed. Libraries were prepared using the COVIDSeq-kit (Illumina) and the sequencing was performed on the Illumina MiSeq platform. Sequence mapping and variant calling were performed with BWA and the GATK Best Practices pipeline. Annotation and prioritization were performed using Franklin (Genoox). Candidate variants were confirmed by Sanger, and segregation studies were performed whenever relatives were available. The analysis of an initial cohort of 10 patients revealed 6 pathogenic or likely pathogenic variants, including one possible mosaicism. Additionally, three cases referred from Hospital Garrahan with suspected mosaic pathogenic variants detected by Sanger were analyzed. We developed and validated a new NGS protocol for MECP2 analysis with excellent performance in variant detection, including mosaicism. This approach provides a faster, more sensitive, and cost-effective diagnostic technique for RS. This protocol provides a faster, more sensitive, and cost-effective diagnostic tool for RS, improving detection of mosaic and non-mosaic variants.

79. P4-09. NOVEL VARIANTS IN THE THYROGLOBULIN GENE DISCOVERED IN ARGENTINIAN CHILDREN PRESENTING WITH CONGENITAL HYPOTHYROIDISM

Valentina Ricci^{*1}, Valeria F. Garzón^{*} (*Equal contribution)², Paula A. Scaglia³, Mauricio Gomes Pio⁴, María E. Masnata⁵, María Esnaola Azcoiti⁶, Agustín Izquierdo⁷, Gabriela E. Sansó⁸, Carina M. Rivolta⁹, María G. Ropelato¹⁰, Ana E. Chiesa¹¹, Héctor M. Targovnik^{**12}, Mariana L. Tellechea^{**} (**Equal contribution)¹³

1. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez (HNRG), Buenos Aires, Argentina.; Biología de la tiroides y trastornos del metabolismo

2. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires. Hospital de Clínicas "José de San Martín", Buenos Aires, Argentina.; Cátedra de Genética. Departamento de Microbiología, Inmunología, Biotecnología y Genética.

3. Centro de Investigaciones Endocrinológicas "Dr. César

Bergadá" (CEDIE) CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez (HNRG), Buenos Aires, Argentina.; Unidad de Medicina Traslacional.

4. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires. Hospital de Clínicas "José de San Martín", Buenos Aires, Argentina.; Cátedra de Genética. Departamento de Microbiología, Inmunología, Biotecnología y Genética.

5. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez (HNRG), Buenos Aires, Argentina.; Biología de la tiroides y trastornos del metabolismo.

6. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez (HNRG), Buenos Aires, Argentina.; Unidad de Medicina Traslacional.

7. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez (HNRG), Buenos Aires, Argentina.; Unidad de Medicina Traslacional.

8. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez (HNRG), Buenos Aires, Argentina.; Unidad de Medicina Traslacional.

9. Cátedra de Genética. Departamento de Microbiología, Inmunología, Biotecnología y Genética. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires. Hospital de Clínicas "José de San Martín", Buenos Aires, Argentina.; Instituto de Inmunología, Genética y Metabolismo (INIGEM). CONICET-Universidad de Buenos Aires.

10. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez (HNRG), Buenos Aires, Argentina.; Laboratorio de Endocrinología.

11. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez (HNRG), Buenos Aires, Argentina.; Biología de la tiroides y trastornos del metabolismo.

12. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires. Hospital de Clínicas "José de San Martín", Buenos Aires, Argentina.; Cátedra de Genética. Departamento de Microbiología, Inmunología, Biotecnología y Genética.

13. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez (HNRG), Buenos Aires, Argentina.; Biología de la tiroides y trastornos del metabolismo.

vr Ricci@cedie.org.ar

Thyroglobulin (TG) is a homodimeric secretory glycoprotein synthesized by the thyroid gland. Thyroid dysmorphogenesis (TDH) due to TG gene disease-causing variants (TDH3, MIM:274700) has an estimated incidence of ~1:100,000 newborns. The clinical spectrum ranges from euthyroid to mild or severe hypothyroidism. To contribute to the phenotypic and genetic landscape of TDH, we use next-generation sequencing (NGS) in cases diagnosed at the HNRG, a tertiary pediatric public hospital. All patients underwent clinical, biochemical, and imaging evaluation. Sanger validation and family segregation, as well as bioinformatics analysis, were performed for causative variants. The pathogenicity of the variants was established using the ACMG/AMP, and ClinGen SVI WG recommendations. In a cohort of 28 patients, we found 2 novel variants in 2 compound heterozygous cases: NM_003235.5:c.1375C>T(p.Gln459Ter) and c.7880A>G(p.Asp2627Gly); and 2 previously reported variants: c.378C>A(p.Tyr126Ter) and c.5509_5518del(p.Lys1837Cysfs*12). c.1375C>T was classified as Pathogenic. This variant was predicted to cause loss of normal protein function, was not present in population databases, was confirmed in trans with a Pathogenic variant in our patient, and the patient's phenotype was specific for TDH3. c.7880A>G was classified as of Uncertain Significance with a tendency toward Pathogenicity. Our results confirm the phenotypic and genetic heterogeneity of TG defects. Clinically

relevant variants, particularly missense variants at the cholinesterase-like domain, have been found to impede the export of mutant TG, causing an endoplasmic reticulum storage disease. Nonsense variants give rise to premature stop codons in the TG coding sequences, resulting in a truncated protein with limited functional capacity for thyroid hormone synthesis.

80. P4-10. QF-PCR FOR CHROMOSOMAL ANEUPLOIDY: FIRST EXPERIENCE IN CÓRDOBA'S PUBLIC HEALTH SYSTEM

Florencia Celeste Salazar¹, Carla Deporte², Silene Silveira-Ruiz³, Cecilia Panero⁴, Mónica Antuña⁵, Viviana Arroyo Paiges⁶, Melina Gigena⁷, Gonzalo Castro⁸, María Gabriela Barbas⁹

1. Ministerio de Salud de Córdoba; Departamento Laboratorio Central

2. Ministerio de Salud de Córdoba; Departamento Laboratorio Central

3. Ministerio de Salud de Córdoba; Departamento Laboratorio Central

4. Ministerio de Salud de Córdoba; Nueva Maternidad Provincial

5. Ministerio de Salud de Córdoba; Nueva Maternidad Provincial

6. Ministerio de Salud de Córdoba; Nueva Maternidad Provincial

7. Ministerio de Salud de Córdoba; Nueva Maternidad Provincial

8. Ministerio de Salud de Córdoba; Departamento Laboratorio Central

9. Ministerio de Salud de Córdoba; Departamento Laboratorio Central

florenciacsalazar@gmail.com

Chromosomal aneuploidy is a major cause of pregnancy loss, congenital anomalies, and developmental disorders. Although conventional karyotyping is the gold standard for diagnosis, its time-consuming and often limited by sample quality or culture failure. Quantitative Fluorescent PCR (QF-PCR) offers a rapid and robust alternative for detecting common chromosomal abnormalities, making it a valuable addition to public healthcare settings. This work reports the first implementation of QF-PCR in Córdoba's public health system. A total of 50 samples (amniotic fluid, chorionic villi, fetal tissue) collected between February and August of 2025 were analyzed. Most referrals were due to ultrasound-detected malformations or abnormal first-trimester screening results. DNA was extracted and amplified using the Devyser Compact kit targeting chromosomes 13, 18, 21, X, and Y. Products were separated by capillary electrophoresis, analyzed with Microsatellite Analysis Software (Applied Biosystems), and the copy number inferred from allele peak area ratios. The QF-PCR results revealed a spectrum of chromosomal abnormalities in 11/50 (22%) cases: Trisomy 21 (4 cases), Trisomy 13 (2 cases, one 30% mosaic), Triploidy (2 cases), and Monosomy X (3 cases). Maternal cell contamination was also detected in 5 samples (10%). When conventional karyotyping was available, molecular results were 100% concordant, confirming the accuracy of the method. Notably, in 14 cases where karyotyping was inconclusive or failed, QF-PCR provided essential diagnostic information. Our findings demonstrate the high sensitivity and diagnostic utility of QF-PCR as a complementary tool to conventional karyotyping, enabling rapid detection of common aneuploidies and improving diagnostic efficiency and clinical decision-making.

ORALES 5 - SAIC - BIOLOGÍA CELULAR Y MOLECULAR 1

DATE & TIME: 17/11/2025 15:00 - 16:30 H

Chairs: Carolina Ghanem, Pablo Sanchis

81. O5-01. CLINICAL PARAMETERS AND GENETIC VARIANTS LINKING RHEUMATOID ARTHRITIS AND PERIODONTAL DISEASE

Angélica Castro Escalante¹, Pablo A. Salgado², Hector M,

Cifuentes³, Débora A. Gonzalez⁴, Paula Pedreira⁵, Betina Orman⁶, Teresita Ferrary⁷, Carlos David Bruque⁸

1. Facultad de Odontología, Universidad de Buenos Aires; Cátedra de Farmacología

2. Facultad de Odontología, Universidad de Buenos Aires; Cátedra de Microbiología

3. Hospital de Alta Complejidad SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica

4. Facultad de Odontología, Universidad de Buenos Aires; Cátedra de Biofísica

5. Facultad de Odontología, Universidad de Buenos Aires; Cátedra de Periodoncia

6. Facultad de Odontología, Universidad de Buenos Aires; Cátedra de Farmacología

7. Facultad de Odontología, Universidad de Buenos Aires; Cátedra de Medicina interna

8. Hospital de Alta Complejidad SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica

angelica_castro_123@hotmail.com

Rheumatoid arthritis (RA) is a chronic autoimmune disorder affecting connective tissue. Previous findings from our group demonstrated that RA patients show higher prevalence and severity of periodontal disease (PD) compared with the general population. They share pathogenic pathways, with TNFAIP3 and FCGR2A genes involved in cytokine regulation and immune responses. The aim of this study was to evaluate the relationship between clinical and serological parameters and PD severity in RA patients and healthy controls (C), and to analyze the association of single nucleotide polymorphisms (SNPs) rs1801274 (FCGR2A) and rs6920220 (TNFAIP3). We recruited 40 RA patients and 21 controls. Periodontal assessment included dental, gingival, and plaque indices, with resting and stimulated salivary flow rates. RA activity was determined by DAS28. Genotyping of rs1801274 and rs6920220 was performed by endpoint PCR, and sequenced by Sanger and NGS. Results: RA patients exhibited higher gingival and plaque indices ($p=0.003$ $p=0.009$), lower salivary flow rates ($p=0.036$ $p=0.016$), and more severe and generalized PD ($p<0.003$ $p=0.005$). Advanced stages of PD were associated with active RA ($p=0.04$). A differential distribution of the wild type allele (GG) was observed in relation to the severity of PD $p=0.008$. The presence of rs1801274 variants was associated with the prevalence of PD, $p=0.024$. Conclusion: Patients with RA exhibit poorer periodontal health, higher Löe and Silness and Silnes and Löe indices, more severe and extensive PD, and reduced salivary flow. DAS28, is associated with the severity of PD. We identified associations between specific SNPs and both the presence and severity of PD.

82. O5-02. TARGETING HO-1 TO REVERT THE NEUROENDOCRINE PHENOTYPE OF PROSTATE CANCER

Rocio Alejandra Seniuk¹, Pablo Sanchis², Agustina Sabater³, Gaston Pascual⁴, Juan Bizzotto⁵, Julia Lechuga⁶, Nicolas Anselmino⁷, Elba Vazquez⁸, Javier Cotignola⁹, Pia Valacco¹⁰, Estefania Labanca¹¹, Geraldine Gueron¹², Ayelén Toro¹³

1. IQUIBICEN - CONICET; Laboratorio de Inflamación y Cáncer

2. IQUIBICEN-CONICET-UADE-MDACC; Department of Genitourinary Medical Oncology

3. IQUIBICEN-CONICET-UADE-MDACC; Department of Genitourinary Medical Oncology

4. IQUIBICEN-CONICET; Laboratorio de Inflamación y Cáncer

5. IQUIBICEN-CONICET-UADE; Laboratorio de Inflamación y Cáncer

6. FCEyN-UBA; Laboratorio de Inflamación y Cáncer

7. MDACC; Department of Genitourinary Medical Oncology

8. IQUIBICEN-CONICET; Laboratorio de Inflamación y Cáncer

9. IQUIBICEN-CONICET; Laboratorio de Inflamación y Cáncer

10. CEQUIBIEM-CONICET; Centro de Estudios Químicos y

Biologicos por Espectrometría de Masas

11. MDACC; Department of Genitourinary Medical Oncology

12. IQUIBICEN-CONICET; Laboratorio de Inflamación y Cáncer

13. IQUIBICEN-CONICET; Laboratorio de Inflamación y Cáncer

rocioseniuk@gmail.com

Previous work has demonstrated the anti-tumor role of Heme-oxygenase-1 (HO-1), encoded by the gene HMOX1, in prostate cancer (PCa). This study tests the hypothesis that HO-1 exerts a regulatory role in PCa through its protein nuclear interactome. For this purpose, PCa cells were treated with hemin (80 μ M-24h), a specific HO-1 inducer, underwent HO-1 immunoprecipitation and LC-ESI MS/MS analysis, identifying 42 interactors. We focused on analyzing 11 interactors unique to the nucleus of hemin-treated cells. ChIP-Atlas analysis indicated that 4/11 interactors—ILF3, DDX17, BCLAF1, and SAFB—are DNA-binding factors associated with neurological diseases. To explore their role in PCa, we analyzed RNA-seq data from the PCa Patient-Derived Xenografts (MD Anderson Cancer Center). Unsupervised clustering revealed high expression of these interactors in neuroendocrine PCa (NEPC). Bioinformatics analysis of a NEPC samples dataset confirmed that HO-1 interactors expression distinctly grouped NEPC samples with high ILF3, DDX17, SAFB, BCLAF1, and low HMOX1 levels. We also developed a protocol to transdifferentiate PCa cells into neuroendocrine (NE)-like cells using Forskolin (10 μ M-48h). Forskolin-treated cells showed increased expression of NE-markers NSE ($p<0.05$), EZH2 ($p<0.01$), and SOX2 ($p<0.05$), alongside morphological changes consistent with an NE-like phenotype. Furthermore, HMOX1 expression was significantly downregulated in PCa cells treated with forskolin ($p<0.01$). Notably, combined hemin-forskolin treatment reversed this NE-like phenotype at both morphological and transcriptional levels, suggesting that HO-1 modulation disrupts transdifferentiation. Overall, these findings propose that HO-1 may play a protective role in PCa blocking the transition to more aggressive phenotypes.

83. O5-03. A FLAVONOID-ENRICHED FRACTION FROM LIGARIA CUNEIFOLIA IMPROVES 5-FLUOROURACIL TUMOR TREATMENT IN COLORECTAL CANCER

Lucía Quiroz¹, Ariadna Birocco², Sol Cargnel³, Rafael Ricco⁴, Cecilia Dobrecky⁵, Graciela C. Calabrese⁶

1. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra Biología Celular y Molecular. (IQUIFIB, UBA/CONICET). Junín 954, CABA.; Matriz Extracelular

2. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra Biología Celular y Molecular. (IQUIFIB, UBA/CONICET). Junín 954, CABA.; Matriz Extracelular

3. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra Biología Celular y Molecular. (IQUIFIB, UBA/CONICET). Junín 954, CABA.; Matriz Extracelular

4. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. Departamento de Farmacología. Junín 954, CABA.; Cátedra de Farmacobotánica

5. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. Departamento de Farmacología. Junín 954, CABA.; Cátedra de Farmacobotánica.

6. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra Biología Celular y Molecular. (IQUIFIB, UBA/CONICET). Junín 954, CABA.; Matriz Extracelular

lquiroz1008@gmail.com

5-Fluorouracil (5-FU) is the gold-standard chemotherapeutic agent in colorectal cancer (CRC). However, the development of 5-FU resistance significantly limits its clinical effectiveness, particularly during long-term treatment. The aim of this work is to evaluate a flavonoid-enriched fraction (FEF) from *Ligaria cuneifolia* (Ruiz & Pav.) Tiegh. (Loranthaceae) (LC), the 'Argentine mistletoe', as a natural alternative to sensitize CRC cells to 5-FU. FEF (5-25 μ g/

ml) cytotoxicity was evaluated by MTT assay, both on human CRC cell line HCT116 and human endothelial cell line EAhy926. HCT116 cell cycle was studied by flow cytometry, with 5-FU (5 μ M, 48h) and with or without FEF pretreatment (20 μ g/ml; 4h). Also, immunofluorescence studies were conducted to analyze subcellular distribution of transcriptional factor NF κ B, a key player in 5-FU resistance. A decrease of 21% of viability was registered after adding FEF (20 μ g/ml; $p < 0.05$, control vs FEF). FEF pretreatment (20 μ g/ml) decreased cell viability in the presence of 5-FU (5 μ M) after 24 hs ($p < 0.0001$; 5FU vs FEF+5FU); accompanied by an increase of cells in subG1 phase; exerting cell sensibilization to 5-FU. Then, an improvement of sensitivity to 5-FU in HCT116 was registered in association with the inhibition of NF- κ B nuclear translocation. No cytotoxic effects were detected for healthy human endothelial cells, however, experiments on endothelium during hypoxia are required to simulate tumoral microenvironment. These *in vitro* results support the potential use of a FEF pretreatment as a strategy to modulate pharmacological stress tolerance to 5-FU related to NF κ B signaling pathway.

84. O5-04. BEYOND PARP INHIBITION: TARGETING MITOTIC VULNERABILITIES IN BRCA2-DEFICIENT TUMORS

Abramovici Blasco, Ariel¹, Siri, Sebastián Omar², Mares Ahlers, María Candelaria³, Miranda, Sara⁴, Vázquez, Martina⁵, Okraine, Yiovana Verónica⁶, Caimi, Lilien Ivonne⁷, Gotifredi, Vanesa⁸

1. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires (IBBA)- CONICET. CP:1405.; Ciclo Celular y Estabilidad Genómica.
 2. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires (IBBA)- CONICET. CP:1405.; Ciclo Celular y Estabilidad Genómica.
 3. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires (IBBA)- CONICET. CP:1405.; Ciclo Celular y Estabilidad Genómica.
 4. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires (IBBA)- CONICET. CP:1405.; Ciclo Celular y Estabilidad Genómica.
 5. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires (IBBA)- CONICET. CP:1405.; Ciclo Celular y Estabilidad Genómica.
 6. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires (IBBA)- CONICET. CP:1405.; Ciclo Celular y Estabilidad Genómica.
 7. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires (IBBA)- CONICET. CP:1405.; Ciclo Celular y Estabilidad Genómica.
 8. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires (IBBA)- CONICET. CP:1405.; Ciclo Celular y Estabilidad Genómica.
- aabramovici@leloir.org.ar

Rationally exploiting synthetic lethality has transformed cancer therapy, exemplified by the clinical success of PARP inhibitors (PARPi) in BRCA-deficient tumors. However, resistance to PARPi frequently arises, limiting their long-term benefit and underscoring the need for alternative vulnerabilities. Building on our previous work showing that mitotic kinases such as ROCK, Citron kinase, and PLK1 are synthetic lethal (SL) targets in BRCA2-deficient cells, we investigated whether mitotic control could serve more broadly as a therapeutic vulnerability in this context. Using isogenic BRCA2-proficient and -deficient models, we evaluated inhibitors of multiple M-phase regulators. Several compounds triggered SL in BRCA2-deficient cells, marked by aberrant mitotic progression and increased anaphase defects, but independent of replication stress or micronuclei formation, distinguishing their mechanism from PARPi. Importantly, this SL interaction persisted in cells with acquired PARPi resistance through depletion of the chromatin remodeler EZH2, confirming that mitotic inhibitors act through distinct mechanisms. While combinations with PARPi produced heterogeneous effects—ranging from synergistic to antagonistic—all mitotic inhibitors consistently maintained efficacy in resistant models. These findings position mitotic regulators as promising therapeutic targets in BRCA2-deficient tumors, with potential applications both as frontline strategies and

as effective treatments for patients who relapse after PARPi therapy.

85. O5-05. ALTERATION IN BREAST CANCER CELL METABOLISM BY THE METASTASIS PROMOTING FACTOR AKR1B1

Sabrina Velasquez¹, Nabila Cocordano², Carola Di Benedetto³, Carla Borini Etichetti⁴, Alejo Cantoia⁵, Evelyn Arel Zalazar⁶, Germán Rosano⁷

1. Instituto de Inmunología Clínica y Experimental de Rosario; Inmuno oncología molecular
 2. Instituto de Inmunología Clínica y Experimental de Rosario; Inmuno oncología molecular
 3. University of California; Department of Radiation Oncology
 4. Instituto de Fisiología Experimental de Rosario; Laboratorio de Biología Celular
 5. Instituto de Biología Molecular y Celular de Rosario; Unidad de espectrometría de masa
 6. Instituto de Inmunología Clínica y Experimental de Rosario; Inmuno oncología molecular
 7. Instituto de Biología Molecular y Celular de Rosario; Unidad de espectrometría de masa
- velasquez@idicer-conicet.gob.ar

AKR1B1 catalyzes the reduction of aldehydes to alcohols and has been implicated in tumor progression, although its precise role in cancer remains insufficiently explored. Our group has shown that AKR1B1 promotes tumor growth and metastasis *in vivo*. While it catalyzes the rate-limiting step of the polyol pathway, reducing glucose to sorbitol, AKR1B1 also reduces diverse substrates such as glyceraldehyde, methylglyoxal, prostaglandin H, and lipid peroxides. This broad substrate specificity complicates the understanding of its pathological contribution. To dissect the molecular mechanisms underlying the pro-oncogenic activity of AKR1B1, we performed a proteomic analysis. Using liquid chromatography–mass spectrometry, we examined the effects of AKR1B1 overexpression in murine triple-negative breast cancer 4T1 cells. We found a strong impact on the proteomic landscape, with several differentially expressed proteins detected. Functional enrichment analysis identified “metabolic pathways” as the most significantly enriched category, highlighting alterations in the mitochondrial electron transport chain and lipid metabolism. To assess the clinical significance of AKR1B1, we analyzed breast cancer patient datasets. Elevated AKR1B1 mRNA expression was significantly associated with reduced survival, especially in patients with lymph node invasion ($p = 7.7 \times 10^{-4}$, log-rank test). We also investigated factors affecting AKR1B1 expression. In cell lines, glucose restriction decreased AKR1B1 expression, as shown by qPCR, and luciferase assays. In summary, our study indicates that AKR1B1 overexpression has a profound impact on the expression of proteins associated with mitochondrial function and lipid metabolism. Moreover, it provides evidence suggesting a significant effect of AKR1B1 overexpression on breast cancer patient survival.

86. O5-06. ATP13A2-MEDIATED SPERMINE EXPORT MODULATES ACID HYDROLASE ACTIVITY IN SH-SY5Y CELLS

Agustina Lujan Suárez¹, Alejandra Lucía Marcos², Felicitas de Tezanos Pinto³

1. Health Sciences Institute, Arturo Jauretche National University, Argentina.; Institute of Biochemistry and Biophysics, Consejo Nacional de Investigaciones Científicas y Tecnológicas (IQUIFIB-CONICET), Buenos Aires, Argentina.
 2. Department of Biological Chemistry, School of Pharmacy and Biochemistry, University of Buenos, Buenos Aires, Argentina; Institute of Biochemistry and Biophysics, Consejo Nacional de Investigaciones Científicas y Tecnológicas (IQUIFIB-CONICET), Buenos Aires, Argentina.
 3. Department of Biological Chemistry, School of Pharmacy and Biochemistry, University of Buenos, Buenos Aires, Argentina. Health Sciences Institute, Arturo Jauretche National University, Argentina.; Institute of Biochemistry and Biophysics, Consejo Nacional de Investigaciones Científicas y Tecnológicas (IQUIFIB-CONICET), Buenos Aires, Argentina.
- agustinalujan00@hotmail.com

P-type ATPases are membrane transporters energized by ATP hydrolysis. Among them, ATP13A2 has attracted attention, as mutations in this gene have been linked to several neurodegenerative disorders, such as Parkinson's disease, neuronal ceroid lipofuscinosis (CLN12), hereditary spastic paraplegia (SPG78), amyotrophic lateral sclerosis, and, more recently, colorectal cancer. ATP13A2 localizes to lysosomes and late endosomes, where its dysfunction leads to a broad impairment of endolysosomal function. We previously showed that ATP13A2 expression reduces the levels of bis(monoacylglycero)phosphate (BMP) while increasing the expression of α/β -hydrolase domain-containing 6 (ABHD6), the enzyme responsible for BMP catabolism. Given that BMP is an anionic phospholipid essential for lipid breakdown in acidic compartments, these findings suggest that ATP13A2 may influence lysosomal lipid catabolism. By using SH-SY5Y cells overexpressing the human P5-ATP13A2 (ATP13A2), we found that ATP13A2-expressing cells show higher activity of acid glucocerebrosidase (GCase), which is involved in the degradation of glucosylceramide inside the endolysosome system. Besides, the polyamine inhibited GCase activity in intact cells and this effect was more pronounced in ATP13A2-expressing cells. Acid ceramidase (ACase) activity was not altered by ATP13A2 expression; however, it was reduced by spermine in a concentration-dependent manner. Interestingly, spermine induced a transient increase in ACase activity within the first 3 hours of incubation, followed by an inhibitory effect that was more pronounced in ATP13A2-expressing cells. Altogether, these findings suggest that ATP13A2-mediated spermine export may influence the lipid digestion capacity of the endolysosomal system and favors the idea of an interconnection between polyamines and lipid metabolism in these organelles.

87. O5-07. IN SILICO AND FUNCTIONAL CHARACTERIZATION OF THE KANSL2 PROMOTER REGION

Agustín Ezequiel Morellato¹, Nicolás Budnik², Ken Kobayashi³, Carolina Perez-Castro⁴

1. Instituto de Investigación en Biomedicina de Buenos Aires (IBioBA) - CONICET - Partner Institute of the Max Planck Society. Buenos Aires, Argentina; Células Madre Tumorales y Plasticidad Celular

2. Instituto de Investigación en Biomedicina de Buenos Aires (IBioBA) - CONICET - Partner Institute of the Max Planck Society. Buenos Aires, Argentina; Células Madre Tumorales y Plasticidad Celular

3. Instituto de Biodiversidad y Biología Experimental Aplicada (IBBEA-CONICET-UBA), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina; Laboratorio de Agrobiotecnología

4. Instituto de Investigación en Biomedicina de Buenos Aires (IBioBA) - CONICET - Partner Institute of the Max Planck Society. Buenos Aires, Argentina; Células Madre Tumorales y Plasticidad Celular

morellatoagustin@gmail.com

KANSL2 is an integral subunit of the non-specific lethal (NSL) chromatin modifier complex. It is critical for sustaining tumorigenesis and maintaining the stem cell population in glioblastoma stem cells (GSCs). However, the transcriptional network involving KANSL2 that maintains tumor cell identity remains undefined. We postulate that the expression levels of KANSL2 may regulate cellular heterogeneity as indicated by its association with YAP1-mediated signaling pathways. By using the UCSC Genome Browser and the Gene Transcription Regulation Database (GTRD) portals, we identified several transcription factors (TFs) with binding sites in the KANSL2 promoter region. Of these, 22 are specific to GSCs (Piccolo et al, 2021). To determine whether these TFs modulate KANSL2, their expression was analyzed after KANSL2 silencing, revealing alterations in JUN, TEAD1, and YAP1. Next, we searched for TFs that might mediate regulatory mechanisms between KANSL2 and YAP1 by cross-referencing known YAP1-mediated TFs (Piccolo et al, 2021). We found FOXO1, FOS, BCL6, FOXO3, and ERF. These results indicate that the TFs that regulate KANSL2 expression are part of a regulatory circuit

that modulates YAP1 and KANSL2 itself in GSCs. Finally, a segment of the KANSL2 promoter region was cloned into the pLOX-GFP reporter vector, and its expression was detected in glioblastoma cells. This construct will be used to characterize the regulatory mechanism ruling KANSL2 expression.

88. O5-08. MITOCHONDRIAL COMPLEX I INHIBITION DRIVES NEURAL STEM CELL AGING

Micaela Nievas¹, Morena Mogetti², Sol Quevedo Prol³, Analía Czerniczyniec⁴, Ezequiel Surace⁵, María Elida Scassa⁶, Mariela Marazita⁷

1. INEU-FLENI-CONICET; Laboratorio de Investigaciones Aplicadas a Neurociencias

2. INEU-FLENI-CONICET; Laboratorio de Investigaciones Aplicadas a Neurociencias

3. INEU-FLENI-CONICET; Laboratorio de Investigaciones Aplicadas a Neurociencias

4. INEU-FLENI-CONICET; Laboratorio de Investigaciones Aplicadas a Neurociencias

5. INEU-FLENI-CONICET; Laboratorio de Investigaciones Aplicadas a Neurociencias

6. INEU-FLENI-CONICET; Laboratorio de Investigaciones Aplicadas a Neurociencias

7. INEU-FLENI-CONICET; Laboratorio de Investigaciones Aplicadas a Neurociencias

micnievas@gmail.com

Brain aging is a multifactorial process characterized by a progressive decline in cognitive function and represents the main risk factor for neurodegenerative disorders such as Alzheimer's and Parkinson's disease. Neural stem cells, responsible for sustaining adult neurogenesis, gradually lose their functionality with age, limiting self-renewal and tissue repair. Among the cellular factors underlying this decline, mitochondrial dysfunction plays a central role by promoting oxidative stress, structural damage, and disruption of cellular homeostasis. Understanding its contribution to NSC aging is therefore critical to identify potential therapeutic targets. Here, we investigated the effect of mitochondrial Complex I (CI) inhibition on human neural stem cells (hNSC-H9) derived from embryonic pluripotent stem cells. Cells were exposed to a non-lethal concentration of rotenone (200 nM), a CI inhibitor, for 72 hours to induce mitochondrial dysfunction. We then assessed temporal changes in aging-associated markers. CI inhibition triggered a sustained increase in both total and mitochondrial reactive oxygen species (ROS), accompanied by downregulation of the SIRT1/NRF2/SOD2 antioxidant pathway. Persistent DNA and nuclear damage was observed, evidenced by elevated γ H2AX and reduced Lamin B1 levels, along with nuclear morphological alterations. Moreover, hNSCs displayed decreased proliferative capacity and an increase in β -galactosidase activity, a hallmark of cellular senescence. Collectively, our findings demonstrate that CI inhibition induces persistent functional decline and the emergence of cellular aging markers in hNSCs. This model provides a valuable tool to investigate the molecular mechanisms linking mitochondrial dysfunction and NSC aging, as well as to explore therapeutic strategies aimed at restoring their regenerative potential.

89. O5-09. CANNABIDIOL AS AN ADJUNCT TO BIODENTINE IN VITAL PULP THERAPY: EXPERIMENTAL IN VIVO FINDINGS

Chaintiou Piorno Romina¹, Rodríguez Pablo Alejandro², Fernández Solari Javier³, Mohn Claudia Ester⁴

1. Universidad de Buenos Aires. Facultad de Odontología.; Cátedra de Endodoncia

2. Universidad de Buenos Aires. Facultad de Odontología.; Cátedra de Endodoncia

3. Universidad de Buenos Aires, Facultad de Odontología. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Buenos Aires, Argentina; FOUBA Cátedra de Fisiología

4. Universidad de Buenos Aires, Facultad de Odontología. Consejo Nacional de Investigaciones Científicas y Técnicas

(CONICET). Buenos Aires, Argentina; FOUBA Cátedra de Fisiología
rominachp@hotmail.com

Objectives: To investigate the pulpal response to the incorporation of cannabidiol (CBD) into Biodentine as a potential material for vital pulp therapy (VPT). **Methods:** Female Wistar rats weighing 250 gr (n=27) were used. Moderate pulpitis was induced in the mandibular first molars prior to performing VPT. Group 1 (n=9): Biodentine; Group 2 (n=9) Biodentine plus 2.5µm CBD; Group 3 (n=9): Biodentine plus 25µm CBD. Coronal sealing was performed with composite. The animals were euthanized 7-, 14-, and 25-days post-treatment following CICUAL-FOUBA guidelines. The hemimandibles were processed for histopathologic examination. **Results:** At 7 days, Group 1 showed no inflammation, while Groups 2 and 3 presented exacerbated chronic inflammation with abscesses and hyaline matrix deposition along canal walls. By 14 days, all groups demonstrated dentin/osteodentin bridge formation and osteodentin deposition against the root canal walls. Inflammation was absent in Group 1 but persisted in Groups 2 and 3. After 25 days, all groups exhibited a continuous dentin–osteodentin bridge which continued along the root canal wall; notably, Group 3 showed a well-organized structure containing dentinal tubules. At this time point, some cases also revealed osteochondral-like tissue along canal walls. No inflammation was observed at this time point in any group. **Conclusions:** Addition of CBD to Biodentine produced an initial inflammatory response, which appeared to activate pulp cells and enhance tissue repair. The higher concentration of CBD in Biodentine promoted the formation of a dentin bridge with organized dentinal tubules, resembling primary dentin.

POSTERS 5 - SAIC - ONCOLOGÍA 1

DATE & TIME: 17/11/2025 15:00 - 16:30 H

Chairs: Veronica Trivillin, Mariana Malvicini,
Noelia Di Giorgio

90. P5-13. GALECTIN-1 PROMOTES STEM-LIKE PROPERTIES IN HEPATOCELLULAR CARCINOMA

Lorena Rocío García¹, Daniela Romina Montagna², Fátima Ferragut³, Luciana Sarrias⁴, Karina Gómez⁵, María Teresa Elola⁶, María Victoria Espelt⁷, Johanna Gabriela Miquet⁸, María Fernanda Troncoso⁹

1. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Instituto de Química y Fisicoquímica Biológicas (IQUIFIB), Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Laboratorio de Glicobiología Tumoral

2. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Instituto de Química y Fisicoquímica Biológicas (IQUIFIB), Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Laboratorio de Glicobiología Tumoral

3. Instituto de Investigaciones en Ingeniería Genética y Biología Molecular (INGEBI), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina; Laboratorio de Inmunología de las Infecciones por Tripanosomátidos

4. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Instituto de Química y Fisicoquímica Biológicas (IQUIFIB), Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Laboratorio de Glicobiología Tumoral

5. Instituto de Investigaciones en Ingeniería Genética y Biología Molecular (INGEBI), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina; Laboratorio de Inmunología de las Infecciones por Tripanosomátidos

6. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Instituto

de Química y Fisicoquímica Biológicas (IQUIFIB), Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Laboratorio de Glicobiología Tumoral

7. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Instituto de Química y Fisicoquímica Biológicas (IQUIFIB), Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Laboratorio de Glicobiología Tumoral

8. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Instituto de Química y Fisicoquímica Biológicas (IQUIFIB), Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Laboratorio de Endocrinología Molecular y Carcinogénesis

9. Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Instituto de Química y Fisicoquímica Biológicas (IQUIFIB), Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Laboratorio de Glicobiología Tumoral

loreena.rocio@gmail.com

Cancer stem cells (CSCs) are a small subpopulation of tumor cells with enhanced pro-malignant properties. In hepatocellular carcinoma (HCC), CSCs are associated with tumor recurrence, metastasis, resistance to radio- and chemotherapy, and poor prognosis. We previously showed that galectin-1 (GAL1) promotes HCC progression, metastasis and chemoresistance, and identified CD13, a liver CSC marker, as a novel GAL1 receptor on HCC cells. This work aimed to explore GAL1's role in promoting CSC features (stemness) in HCC. CSC subpopulations were isolated from human HCC HepG2 and PLC/PRF/5 cells based on their ability to form non-adherent spheres (NAS). Wild type (WT), GAL1-overexpressing (ΔGAL1), and mock (M) cells were cultured in anti-adherent wells in serum-free DMEM with B27 and epidermal growth factor. Under these growth differentiation-inhibiting conditions, spheres formed after 7 and 11 days were photographed, quantified, and their area were measured. GAL1 and CD13 protein levels in NAS and parental cells (PC) were assessed by Western blotting and flow cytometry. P<0.05 was considered significant. After 7 days of culture, NAS from WT, M and ΔGAL1 HCC cells showed significant increases in GAL1 and CD13 compared with the corresponding PC (Student's t-test). The elevated expression of the hepatic CSC marker CD13 confirmed the CSC-like nature of NAS isolated from HCC cells. NAS from ΔGAL1 were significantly larger and more numerous than those from WT and M at both 7 and 11 days (ANOVA followed by Tukey's test). These findings indicate that GAL1 promotes HCC stemness, highlighting its potential as a liver CSC marker.

91. P5-14. MAGE-A9 AS A MODULATOR OF AGGRESSIVENESS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

Melisa Suberbordes¹, Micaela Escalada², Candela Vidal³, Rocío Topino⁴, Ana Raimondi⁵, Philippe Soubeyran⁶, Martin Monte⁷

1. Dpto. Química Biológica, FCEN-UBA e Instituto IQUIB-CEN, UBA-CONICET; Laboratorio de Oncología Molecular

2. Dpto. Química Biológica, FCEN-UBA e Instituto IQUIB-CEN, UBA-CONICET; Laboratorio de Oncología Molecular

3. Dpto. Química Biológica, FCEN-UBA e Instituto IQUIB-CEN, UBA-CONICET; Laboratorio de Oncología Molecular

4. Dpto. Química Biológica, FCEN-UBA e Instituto IQUIB-CEN, UBA-CONICET; Laboratorio de Oncología Molecular

5. Instituto de Fisiología, Biología Molecular y Neurociencias IFIBYNE, UBA-CONICET

6. Centre de Recherche en Cancérologie de Marseille, Inserm UMR1068, Marseille France.

7. Dpto. Química Biológica, FCEN-UBA e Instituto IQUIB-CEN, UBA-CONICET; Laboratorio de Oncología Molecular

melisasuber@gmail.com

MAGE-A9 is a cancer-testis antigen of the MAGE-I family, normally silenced in somatic tissues but aberrantly re-expressed in tumors and associated with poor clinical prognosis. To investigate the mechanisms by which MAGE-A9 may contribute to this unfavorable profile, we generated cellular models and applied multi-omic approaches. Human head and neck squamous cell carcinoma (HNSCC) lines HN12 (p53 null), HN13 (p53 mutated), and HN30 (p53 wild-type) were engineered with a doxycycline-inducible MAGE-A9 expression system. Using the HN30 inducible model treated with the chemotherapeutic oxaliplatin, we performed RNA sequencing (RNA-seq). Statistically significant data sets were interrogated using KEGG, GO, and Reactome. The analysis revealed that MAGE-A9 negatively regulates the p53 pathway under genotoxic stress. In untreated cells, MAGE-A9 expression correlated with upregulation of VEGFA, a key pro-angiogenic factor. Furthermore, we carried out two proteomic-based studies in inducible HN30 cells: the interactome and the ubiquitinome (proteins with altered ubiquitination). These analyses, performed in triplicate and filtered for statistical significance, revealed associations of MAGE-A9 with "Regulation of TP53 Activity," "VEGF-A-related sets," and "Autodegradation of Cdh1" pathways in KEGG and Reactome databases. Wet experiments indicated that MAGE-A9 inhibits p53 transcriptional activity, while Annexin V and MTT assays demonstrated anti-apoptotic effects and increased chemoresistance in a p53-dependent fashion. RT-qPCR confirmed elevated VEGFA and MMP2 expression across all models (HN12, HN13, HN30, and HEK293T), independently of p53 status. Moreover, wound healing assays revealed that MAGE-A9 expression significantly enhances cell migration. Collectively, our findings unveil novel mechanisms of MAGE-A9 that could be associated with poor clinical prognosis.

92. P5-15. NOTCH RECEPTOR SIGNAL MODULATES THE RESPONSE TO ANTIANDROGEN DRUGS

Agustina Chimento¹, Sofía Belén Herrera², Fernanda Parenti³, Carolina Cristina⁴

1. Centro de Investigaciones Básicas y Aplicadas (CIBA) - Universidad Nacional del Noroeste de la Provincia de Buenos Aires - Argentina; Comisión de Investigaciones Científicas de la Provincia de Buenos Aires, CIC, La Plata, Buenos Aires, Argentina.; Laboratorio de Neuroendocrinología/Fisiopatología de la Hipófisis; Centro de Investigaciones Básicas y Aplicadas (CIBA) - Universidad Nacional del Noroeste de la Provincia de Buenos Aires - Argentina.

2. Centro de Investigaciones Básicas y Aplicadas (CIBA) - Universidad Nacional del Noroeste de la Provincia de Buenos Aires - Argentina. Comisión de Investigaciones Científicas de la Provincia de Buenos Aires, CIC, La Plata, Buenos Aires, Argentina.; Laboratorio de Neuroendocrinología/Fisiopatología de la Hipófisis; Centro de Investigaciones Básicas y Aplicadas (CIBA) - Universidad Nacional del Noroeste de la Provincia de Buenos Aires - Argentina.

3. Centro Médico Famy, Junín, provincia de Buenos Aires.

4. Centro de Investigaciones Básicas y Aplicadas (CIBA) - Universidad Nacional del Noroeste de la Provincia de Buenos Aires - Argentina; Centro de Investigaciones y Transferencia CITNOBA, Consejo Nacional de Investigaciones Científicas y Técnicas (UNNOBA-UNSA-CONICET).; Laboratorio de Neuroendocrinología/Fisiopatología de la Hipófisis; Centro de Investigaciones Básicas y Aplicadas (CIBA) - Universidad Nacional del Noroeste de la Provincia de Buenos Aires - Argentina.

agustinachimento13@gmail.com

Prostate cancer is the most common cancer in men in Argentina. Its high probability of progressing to aggressive stages poses major challenges for conventional antiandrogen therapies. Testosterone activates the androgen receptor (AR), promoting its nuclear translocation and the expression of target genes PSA and TMPRSS2. There is strong evidence that involves Notch pathway in prostate development but its role in prostate cancer generation and progression is poorly understood. The present objective was to evaluate the re-

ciprocal activation of the AR and Notch pathways in androgen-sensitive LNCaP cells, by modulating these signals in vitro either individually or sequentially. Treatment with the androgen Testosterone (T, 10⁻⁸ M) reduced cytoplasmic AR expression, as assessed by flow cytometry; interestingly, inhibition of the Notch pathway with DAPT (30 μM) appeared to retain AR in the cytoplasm. The Notch target gene HES1 showed increased expression under androgen stimulation when Notch signalling was inhibited previously (p = 0,005). DAPT reduced PSA expression when compared to Testosterone stimulation (p = 0,044), and this effect was reversed when cells were first exposed to androgens (p = 0,005). Altogether, our in vitro findings demonstrate a reciprocal activation of AR and Notch, pointing the important crosstalk between these pathways in prostate cancer treatment.

93. P5-16. ROLE OF THE STEM CELL MARKER CD44 IN REGULATING THE PHENOTYPE OF ORAL SQUAMOUS CELLS DERIVED FROM 4NQO-INDUCED TONGUE TUMORS IN C57BL/6 MICE

GÓMEZ NOELIA¹, Alberto Penas-Steinhard², Fiorella Belforte³, Flavia Piccioni⁴, María José Cantero⁵, Mariel Fusco⁶, Paula Roselló⁷, Manglio Miguel Rizzo⁸, Paula Constanza Arriola Benitez⁹, Mariana Malvicini¹⁰

1. Instituto de Investigaciones en Medicina Traslacional (IIMT-Universidad Austral CONICET), Pilar, Argentina.; Laboratorio de Inmunobiología del Cáncer

2. Departamento de Ciencias Básicas, Universidad Nacional de Luján, Luján 6700, Argentina.; Laboratorio de Genómica Computacional (GeC-UNLu)

3. Universidad Nacional de Luján, Luján 6700, Argentina.; Instituto de Ecología y Desarrollo Sustentable (INEDES-CO-NICET-UNLu), Departamento de Ciencias Básicas, Universidad Nacional de Luján, Luján 6700, Argentina.; Carrera Nutrición, Facultad de Ciencias Biomédicas, Universidad Austral; Laboratorio de Genómica Computacional (GeC-UNLu), Departamento de Ciencias Básicas

4. Instituto de Investigaciones en Medicina Traslacional (IIMT-Universidad Austral CONICET), Pilar, Argentina.; Laboratorio de Inmunobiología del Cáncer

5. Instituto de Investigaciones en Medicina Traslacional (IIMT Universidad Austral-CONICET), Pilar, Argentina.; Programa de Hepatología Experimental y Terapia Génica

6. Instituto de Investigaciones en Medicina Traslacional (IIMT-Universidad Austral CONICET), Pilar, Argentina.; Laboratorio de Inmunobiología del Cáncer

7. Instituto de Investigaciones en Medicina Traslacional (IIMT-Universidad Austral CONICET), Pilar, Argentina.; Laboratorio de Inmunobiología del Cáncer,

8. Instituto de Investigaciones en Medicina Traslacional (IIMT-Universidad Austral CONICET), Pilar, Argentina.; Servicio de Oncología, Hospital Universitario Austral, Pilar, Argentina.; Laboratorio de Inmunobiología del Cáncer

9. Instituto de Investigaciones en Medicina Traslacional (IIMT-Universidad Austral CONICET), Pilar, Argentina.; Laboratorio de Inmunobiología del Cáncer

10. Instituto de Investigaciones en Medicina Traslacional (IIMT-Universidad Austral CONICET), Pilar, Argentina.; Laboratorio de Inmunobiología del Cáncer

nugomez9@gmail.com

Introduction: Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide and represents a heterogeneous and complex disease. Resistance to therapy is partly driven by cancer stem cells (CSCs), often marked by CD44 expression. Objective: This study aimed to investigate the role of CD44 in the phenotype and tumorigenic capacity of murine HNSCC cell lines. Methodology: Cell lines were established from primary 4-nitroquinoline-1-oxide (4NQO)-induced tongue tumors in wild-type (WT; denominated C57OC) and CD44-knockout (CD44KO; denominated H1 and 2M) C57Bl/6 mice. Results: Whole-exome sequencing of C57OC revealed multiple mutations, including 38 INDELs, 1061 SNPs, and 19 MNPs. RT-qPCR analysis showed higher expression of CSC markers OCT4 and KLF4 and lower expression of SOX2

in C57OC cells compared to CD44KO lines ($p < 0.05$). Additionally, C57OC cells expressed more Cytokeratin 18 (CK18), and less CK16 and CK14 than CD44KO cells ($p < 0.01$). Both WT and CD44KO cells formed colonies in anchorage-dependent assays. However, only C57OC cells were able to form spheroids and colonies in soft agar, indicating anchorage-independent growth capacity. To assess tumorigenicity, C57Bl/6 mice were subcutaneously injected with C57OC, H1 or 2M cell lines. Only C57OC cells formed squamous carcinomas when implanted in immunocompetent mice; Remarkably, CD44KO cells failed to grow and form tumors in vivo. Discussion: These findings suggest that CD44 contributes to key malignant features of HNSCC cells, including stemness, invasion, and tumor-initiating capacity.

94. P5-17. RAC1 ACTIVATION AND ITS ROLE IN RADIORESISTANCE IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

Maximiliano Aparicio¹, Yasmany Gonz lez Garc es², Ariana Miconi³, Mirco Mian⁴, Karina E J Tr podi⁵

1. Facultad de Ciencias M dicas. Universidad Nacional de Rosario.; Centro de Investigaci n del C ncer de Rosario y Centro de Investigaci n y Producci n de Reactivos Biol gicos (CIC-R; CIPReB).

2. Facultad de Ciencias M dicas. Universidad Nacional de Rosario. IDICER (CONICET-UNR); Centro de Investigaci n del C ncer de Rosario y Centro de Investigaci n y Producci n de Reactivos Biol gicos (CIC-R; CIPReB).

3. Facultad de Ciencias M dicas. Universidad Nacional de Rosario.; Centro de Investigaci n del C ncer de Rosario y Centro de Investigaci n y Producci n de Reactivos Biol gicos (CIC-R; CIPReB).

4. Facultad de Ciencias M dicas. Universidad Nacional de Rosario.; Centro de Investigaci n del C ncer de Rosario y Centro de Investigaci n y Producci n de Reactivos Biol gicos (CIC-R; CIPReB).

5. CONICET-UNR; Centro de Estudios Fotosint ticos y Bioqu micos (CEFOBI)

max.r.aparicio@gmail.com

The Rho GTPase Rac1 regulates key cellular functions such as migration, proliferation, and cytoskeletal dynamics. In head and neck squamous cell carcinoma (hNSCC), Rac1 has been implicated in epithelial-mesenchymal transition (EMT), promoting invasiveness and resistance to therapy. This study aimed to characterize Rac1's involvement in hNSCC progression and radioresistance. Through bioinformatic analysis of GEO datasets (GSE173855, GSE235223, GSE304200) and TCGA patient samples, gene set enrichment revealed overrepresentation of Rho GTPase signaling, including Rac1 pathways, in radiotherapy-resistant tumors. Resistant phenotypes also showed enrichment in extracellular matrix remodeling, chemotaxis, and immune checkpoint pathways, whereas sensitive phenotypes were enriched in immune activation and antioxidant metabolism pathways. In vitro, human hNSCC cell lines (HN13 and CAL27) were subjected to repeated gamma radiation (2 Gy, 10 rounds) to induce radioresistance, confirmed by clonogenic assays ($p < 0.05$). Fluorescence microscopy with DAPI and phalloidin staining demonstrated increased nuclear and cellular size ($p < 0.001$) and cytoskeletal reorganization consistent with a migratory phenotype. Immunocytochemistry and Western blot showed significantly increased Rac1 expression and EMT marker modulation associated with resistance development. These findings support a role for Rac1 activation in hNSCC progression and radioresistance, paralleling observations in chemoresistant colorectal cancer. Ongoing biobanking of oral lesion and saliva samples aims to identify prognostic biomarkers and liquid biopsy markers. Further studies are required to confirm Rac1 as a therapeutic target to overcome resistance in hNSCC.

95. P5-18. TARGETING RAC1 AS A THERAPEUTIC VULNERABILITY IN T-CELL LYMPHOMAS

Lucero Alvarado¹, Mercedes Debernardi², Florencia Cayrol³, Georgina Cardama⁴, Silvina Palmer⁵, Valeria S nchez⁶, Sof a Rivarola⁷

1. Instituto de Investigaciones Biom dicas (BIO-MED-UCA-CONICET), Buenos Aires, Argentina.; Laboratorio de Neuroinmunomodulaci n y Oncolog a Molecular

2. Instituto de Investigaciones Biom dicas (BIO-MED-UCA-CONICET), Buenos Aires, Argentina.; Laboratorio de Neuroinmunomodulaci n y Oncolog a Molecular

3. Instituto de Investigaciones Biom dicas (BIO-MED-UCA-CONICET), Buenos Aires, Argentina.; Laboratorio de Neuroinmunomodulaci n y Oncolog a Molecular

4. Universidad Nacional de Quilmes, Bernal, Argentina. Consejo Nacional de Investigaciones Cient ficas y T cnicas (CONICET), Argentina; Centro de Oncolog a Molecular y Traslacional (COMTra)

5. Hospital Brit nico, Buenos Aires, Argentina; Servicio de Hematolog a

6. Instituto de Investigaciones Biom dicas (BIO-MED-UCA-CONICET), Buenos Aires, Argentina.; Laboratorio de Histolog a e Histopatolog a

7. Hospital Brit nico, Buenos Aires, Argentina; Servicio de Hematolog a

luceroalvarado@uca.edu.ar

T-cell lymphomas (TCL) are aggressive and heterogeneous neoplasms with limited therapeutic options and poor prognosis, underscoring the need for novel targeted strategies. Here, we evaluated Rac1, a member of the Rho GTPase family, as a molecular target in TCL. We tested the Rac1 inhibitor 1A-116 in a panel of TCL cell lines (EL4, OCI-Ly12, OCI-Ly13.2, HuT78, MJ, Karpas299) and observed a significant reduction in cell viability across all models ($p < 0.05$), with IC_{50} values ranging from 20 to 250 μ M. HuT78 and Karpas299 displayed the highest IC_{50} values, consistent with a more resistant phenotype. Additionally, 1A-116 significantly induced apoptosis after 48 hours of treatment in all cell lines, evidenced by a 60–200% increase in caspase 3/7 activity ($p < 0.05$ vs vehicle). Basal expression of Rac1 and its downstream effector pPAK, assessed by western blot, revealed heterogeneous levels among cell lines, with reduced expression in the more resistant HuT78 and Karpas299 models. Analysis of three public RNA-seq datasets of TCL patients (GSE113113, GSE168508, GSE58445) revealed that the expression of eleven Rac1 downstream effectors, including PAK2, FMNL1, and GSK3, is increased in advanced disease stages and/or correlates with lower overall survival ($p < 0.05$). Furthermore, immunohistochemical analysis of 14 TCL patient samples demonstrated Rac1 expression in all cases evaluated. All together, these results identify Rac1 as a promising therapeutic vulnerability in TCL and support the preclinical evaluation of Rac1 inhibitors, either as monotherapy or in rational combinations, for the development of new therapeutic protocols in TCL.

96. P5-19. IN SILICO EVALUATION OF RAC1 EXPRESSION IN CERVICAL CANCER SAMPLES AND EFFECTS OF RAC1 INHIBITOR 1A-116 IN HIGH RISK HPV-RELATED CELL LINE MODELS

Jes s Lemos¹, Paula Buccic , Lara L. Scialfa³, Sandra E. Gof i⁴, Hern n G. Farina⁵, Daniel F. Alonso⁶, Georgina A. Cardama⁷

1. Universidad Nacional de Quilmes (UNQ); Centro de Oncolog a Molecular y Traslacional (COMTra)

2. Universidad de Valladolid; Instituto de Procesos Sostenibles (ISP)

3. Universidad Nacional de Quilmes (UNQ); Laboratorio de Virus Emergentes (LVE)

4. Universidad Nacional de Quilmes (UNQ); Laboratorio de Virus Emergentes (LVE)

5. Universidad Nacional de Quilmes (UNQ); Centro de Oncolog a Molecular y Traslacional (COMTra)

6. Universidad Nacional de Quilmes (UNQ); Centro de Oncolog a Molecular y Traslacional (COMTra)

7. Universidad Nacional de Quilmes (UNQ); Centro de Oncolog a Molecular y Traslacional (COMTra)

jesusselemos@gmail.com

Human papillomavirus (HPV) is responsible for several epithelial neoplasms, including cervical cancer (CC), which remains a major

public health concern with limited therapeutic options in advanced stages. Of the 14 high-risk HPV (HR-HPV) types, 16, 18, and 31 are the most prevalent, playing a central role in cervical carcinogenesis and being implicated in tumor chemoresistance, underscoring the need for more effective and less toxic treatments. The small GTPase RAC1 regulates key processes related to tumor growth, invasion, and therapy resistance, and has emerged as a potential therapeutic target. The aim of this study was to investigate the role of the RAC1 pathway in CC HPV-positive. First, RAC1 and selected RAC1-GEFs were analyzed in cervical cancer clinical samples using the OncoDB platform. RAC1 expression was significantly elevated in CC compared with normal tissue, with particularly high levels in tumors associated with HR-HPV. Second, we evaluated the effect of 1A-116, a RAC1 inhibitor developed by our group, in HR-HPV-related cell models. Treatment with 1A-116 (5–50 μ M) impaired cell growth in HPV-positive CC cell lines HeLa and CaSki. In addition, in non-tumor epithelial HaCaT cell model transfected with HPV16 E6/E7 (p1321) or HPV31 (pBR322) plasmids, 1A-116 significantly reduced cell viability. Importantly, 1A-116 significantly decreased RAC1 activation in HPV-transfected models, without a comparable effect on the closely-related GTPase CDC42. Together, these findings support RAC1 inhibition by 1A-116 as a promising therapeutic strategy for HPV-associated neoplasms.

97. P5-20. MicroRNAs, D2R AND CABERGOLINE RESPONSE IN PITUITARY TUMORS

Evelyn N. Prodan¹, Emilia Maticich², Erika Werner³, Miguel Mural⁴, Nelson Picard⁵, Andrés Cervio⁶, Gustavo Sevelever⁷, Pablo E. Espil⁸, Silvia Berner⁹, Carolina Cristina¹⁰

1. Centro de Investigaciones y Transferencia del Noroeste de la Provincia de Buenos Aires (CITNOBA) - UNNOBA-UNSAAdA-CONICET.; Laboratorio de Neuroendocrinología/Fisiopatología de la Hipófisis; Centro de Investigaciones Básicas y Aplicadas (CIBA), Universidad Nacional del Noroeste de la Pcia. de Bs. As. Junín B6000, Argentina.

2. Centro de Investigaciones Básicas y Aplicadas (CIBA), Universidad Nacional del Noroeste de la Pcia. de Bs. As. Junín B6000, Argentina.; Laboratorio de Neuroendocrinología/Fisiopatología de la Hipófisis

3. Centro de Investigaciones Básicas y Aplicadas (CIBA), Universidad Nacional del Noroeste de la Pcia. de Bs. As. Junín B6000, Argentina.; Laboratorio de Neuroendocrinología/Fisiopatología de la Hipófisis

4. Hospital El Cruce Dr. Néstor Carlos Kirchner, CABA, Buenos Aires.

5. Hospital La Pequeña Familia, Junín, Buenos Aires.

6. Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI), CABA, Buenos Aires.

7. Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI), CABA, Buenos Aires.

8. Servicio Neurocirugía, Clínica Santa Isabel, CABA, CP1406, Argentina

9. Servicio Neurocirugía, Clínica Santa Isabel, CABA, CP1406, Argentina

10. Centro de Investigaciones y Transferencia del Noroeste de la Provincia de Buenos Aires (CITNOBA) - UNNOBA-UNSAAdA-CONICET.; Laboratorio de Neuroendocrinología/Fisiopatología de la Hipófisis; Centro de Investigaciones Básicas y Aplicadas (CIBA), Universidad Nacional del Noroeste de la Pcia. de Bs. As. Junín B6000, Argentina.
prodanevelyn@gmail.com

Pituitary tumors (PT) represent ~15% of intracranial neoplasms and, despite being non-metastatic, they might become invasive, recurrent or resistant to therapy. MicroRNAs (miRNAs) may contribute to tumor behavior/drug response. We aimed to investigate in silico preselected miRNAs associated with drug response in human PT samples, and in the GH3 cell line treated with CAB. The study included 28 NF, 8 GH-, 4 ACTH-, and 6 PRL-secreting PT. miR-Cab1 and miR-Cab2 were analyzed by Stem-loop RT-PCR, and D2R by RT-qPCR. miRNA levels were normalized to 5S or SNORD44, and D2R expression to GAPDH. Parametric and non-parametric data were analyzed with ANOVA and Kruskal-Wallis tests, respectively.

We found lower expression levels of D2R in ATCH-secreting tumors compared to non-functioning (*p=0,0572). Macroadenomas exhibited increased D2R expression compared to giant tumors (Macroadenomas, n=34; giant, n=7; ns). Somatotropinomas showed significantly higher expression of miR-Cab1 compared with other histotypes (*p=0,0433). Macroadenomas showed higher levels of miR-Cab2 expression compared with giant tumors, which positively correlated with tumor size (*p=0.05). In NF tumors, D2R positively correlated with miR-Cab1 (p=0.0314), whereas tumors expressing miR-Cab2 had lower D2R expression (p=0.0433). As expected, in GH3 cells, CAB reduced prolactin and growth hormone mRNA levels and inhibited viability. These effects were accompanied by increased expression of both miRNAs, suggesting that CAB modulation of miR-Cab1 and miR-Cab2, together with D2R signaling, may contribute to hormone regulation, tumor growth, and cabergoline responsiveness in PT, thus providing insight into resistance mechanisms and treatment.

98. P5-21. TUMOR MicroRNAs: POTENTIAL BIOMARKERS OF TEMOZOLOMIDE RESISTANCE IN AGGRESSIVE PITUITARY TUMORS

Maticich, Emilia¹, Prodan, Evelyn N.², Werner, Erika³, Mural, Miguel⁴, Espil, Pablo Ezequiel⁵, Picard, Nelson⁶, Cervio, Andres⁷, Sevelever, Gustavo⁸, Berner, Silvia⁹, Cristina, Carolina¹⁰

1. 1) Centro de Investigaciones Básicas y Aplicadas (CIBA), Universidad Nacional del Noroeste de la Pcia. de Bs. As. Junín B6000, Argentina. 2) Comisión de Investigaciones Científicas de la Provincia de Buenos Aires, CIC, La Plata, Buenos Aires, Argentina.; Laboratorio de Neuroendocrinología/Fisiopatología de la Hipófisis

2. 1) Centro de Investigaciones Básicas y Aplicadas (CIBA), Universidad Nacional del Noroeste de la Pcia. de Bs. As. Junín B6000, Argentina.;) Centro de Investigaciones y Transferencia del Noroeste de la Provincia de Buenos Aires (CITNOBA) - UNNOBA-UNSAAdA-CONICET.; Laboratorio de Neuroendocrinología/Fisiopatología de la Hipófisis

3. Centro de Investigaciones Básicas y Aplicadas (CIBA), Universidad Nacional del Noroeste de la Pcia. de Bs. As. Junín B6000, Argentina.; Laboratorio de Neuroendocrinología/Fisiopatología de la Hipófisis

4. Hospital El Cruce Dr. Néstor Carlos Kirchner, CABA, Buenos Aires.

5. Servicio Neurocirugía, Clínica Santa Isabel, CABA, CP1406, Argentina

6. Hospital La Pequeña Familia, Junín, Buenos Aires.

7. Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI), CABA, Buenos Aires.

8. Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI), CABA, Buenos Aires.

9. Servicio Neurocirugía, Clínica Santa Isabel, CABA, CP1406, Argentina

10. 1) Centro de Investigaciones Básicas y Aplicadas (CIBA), Universidad Nacional del Noroeste de la Pcia. de Bs. As. Junín B6000, Argentina.;) Centro de Investigaciones y Transferencia del Noroeste de la Provincia de Buenos Aires (CITNOBA) - UNNOBA-UNSAAdA-CONICET.; Laboratorio de Neuroendocrinología/Fisiopatología de la Hipófisis
ematiach@comunidad.unnoba.edu.ar

Pituitary tumors (PTs) represent a frequent type of intracranial neoplasms with heterogeneous clinical behavior. In aggressive or treatment-resistant cases, Temozolomide (TMZ) is used as a salvage therapy, and predictive biomarkers of response are still lacking. In this context, microRNAs (miRNAs) have emerged as potential candidates due to their specific expression patterns. The Wnt/ β -Catenin pathway, frequently hyperactivated in cancer, regulates proliferation, differentiation, and survival, and its dysregulation has been linked to tumor aggressiveness and drug resistance. Our objective was to identify intratumoral miRNAs capable of predicting the TMZ response. In silico analyses pointed to a set of miR-TMZ as potential regulators of TMZ-resistance genes such as MPG and MGMT, and components of the Wnt pathway as well. Validation was performed using surgically resected PT samples (n=24)

and the GH3 pituitary adenoma cell line. miR-R1TMZ expression was quantified by Stem Loop RT-qPCR (normalized to SNORD44) and mRNA expression by RT-qPCR (normalized to GAPDH). In patients, miR-R1TMZ correlated positively with MPG ($p=0.001$), and higher levels of MGMT were observed in invasive PTs compared to non-invasive ones ($p=0.03$). Regarding Wnt pathway, Cyclin D1 correlated positively with miR-R1TMZ ($p=0.04$), while Axin correlated positively with MPG ($p=0.03$) and MGMT ($p=0.07$). In GH3 cells, exposure to 200 μ M TMZ for 72 h induced a significant increase in MGMT mRNA ($p=0.0025$), while it reduced both viability and clonogenic capacity. These findings suggest that miR-R1TMZ may contribute to TMZ resistance in invasive PTs, potentially through modulation of the Wnt pathway, and highlight the potential of miRNAs as predictive biomarker

POSTERS 6 - SAIC - INFECTOLOGÍA Y PARASITOLOGÍA

DATE & TIME: 17/11/2025 15:00 - 16:30 H

Chairs: Emmanuel Angeli, Maria Victoria Ramos, Maria Priscilla Saracino

99. P6-17. ELECTROCARDIOGRAPHIC AND TRANSCRIPTOMIC ANALYSIS OF THE EFFECTS OF FENOFIBRATE IN AN EXPERIMENTAL MODEL OF ACUTE CHAGAS MYOCARDITIS

Aleli Silva Del Puerto¹, Javier Ruiz Luque², Ignacio Mazzitelli³, Lucía Bleichmar⁴, Cecilia Monzani⁵, Ignacio Barbieri⁶, Bruno Buchholz⁷, Nora Goren⁸, Ágata Cevey⁹, Federico Penas¹⁰

1. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires.; Fisiopatología de la Inflamación

2. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires.; Fisiopatología de la Inflamación

3. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires.; Fisiopatología de la Inflamación

4. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires.; Fisiopatología de la Inflamación

5. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires.; Fisiopatología de la Inflamación

6. Instituto de Fisiopatología Cardiovascular (INFICA), UBA. Facultad de Medicina-Universidad de Buenos Aires.; Fisiopatología Cardiovascular

7. Instituto de Fisiopatología Cardiovascular (INFICA), UBA. Facultad de Medicina-Universidad de Buenos Aires.; Fisiopatología Cardiovascular

8. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires.; Fisiopatología de la Inflamación

9. Departamento de Química y Bioquímica. Facultad de Ciencias Exactas y Naturales-Universidad Nacional de Mar del Plata; Laboratorio de Fisiopatología Cardíaca de Enfermedades Infecciosas

10. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires.; Fisiopatología de la Inflamación
alelisilvadelpuerto@gmail.com

Chagas disease remains one of the most neglected parasitic infections in Latin America. During the acute phase, the parasite spreads hematogenously and invades multiple tissues, with a tropism for the myocardium, where it triggers an intense inflammatory response. Although most immunocompetent individuals experience mild or asymptomatic infections, acute cases can evolve into severe manifestations such as acute myocarditis. This condition is characterized by inflammatory cell infiltration, tissue damage, and cardiac electrical disturbances. These features not only serve as early clinical markers, but also provide a better understanding of the molecular mechanisms responsible for myocardial injury. In this context, analysis by

RNA sequencing (RNAseq) enables complete profiling of gene expression in cardiac tissue. Fenofibrate (fen), PPAR α agonist, modulates genes involved in inflammation, lipid metabolism, and oxidative stress. Here, we evaluated the effects of fen in an experimental model of acute chagasic myocarditis through electrocardiographic assessment and cardiac transcriptomic analysis. C57BL/6 mice infected with *T. cruzi* (RA strain) were treated with fen. At 14 dpi, electrocardiographic recordings and RNAseq analysis of cardiac tissue were performed. Fen normalized intraventricular conduction (QRS complex) and action potential duration (QT interval) in infected mice ($p<0.05$). RNAseq revealed differentially expressed genes associated with immune function and inflammatory responses during infection ($p<0.05$). Fen downregulated proinflammatory gene sets while upregulating genes related to cardiac contraction, potassium channels, and purine metabolism, among others ($p<0.05$). This study demonstrates the protective effect of fen on cardiac electrical function and highlights novel therapeutic targets identified through RNAseq in the context of Chagas disease

100. P6-18. HOST GENETIC VARIANTS AND THEIR INFLUENCE ON PEDIATRIC DENGUE DISEASE OUTCOMES

Florencia Bonnin¹, Agustín Herrera², Sofía S Carril³, María S Tineo⁴, Antonella S Antonelli Sanz⁵, Agustina Denardi⁶, Andrea Marin⁷, Carolina Ordoñez⁸, Elisa Espinosa Charris⁹, Christian Vergara¹⁰, Patricio L Acosta¹¹, Eduardo L López¹², Laura B Talarico¹³

1. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina. Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Buenos Aires, Argentina.; Laboratory of Infectious Diseases and Molecular Biology, Department of Medicine, Hospital de Niños Dr. Ricardo Gutiérrez, Buenos Aires, Argentina.

2. Department of Medicine, Hospital de Niños Dr. Ricardo Gutiérrez, Buenos Aires, Argentina.; Laboratory of Infectious Diseases and Molecular Biology

3. Infectious Diseases Program, Hospital de Niños Dr. Ricardo Gutiérrez, Universidad de Buenos Aires, Argentina.; Department of Medicine

4. Infectious Diseases Program, Hospital de Niños Dr. Ricardo Gutiérrez, Universidad de Buenos Aires, Argentina.; Department of Medicine

5. Infectious Diseases Program, Hospital de Niños Dr. Ricardo Gutiérrez, Universidad de Buenos Aires, Argentina.; Department of Medicine

6. Infectious Diseases Program, Hospital de Niños Dr. Ricardo Gutiérrez, Universidad de Buenos Aires, Argentina.; Department of Medicine

7. Infectious Diseases Program, Hospital de Niños Dr. Ricardo Gutiérrez, Universidad de Buenos Aires, Argentina.; Department of Medicine

8. Infectious Diseases Program, Hospital de Niños Dr. Ricardo Gutiérrez, Universidad de Buenos Aires, Argentina.; Department of Medicine

9. Infectious Diseases Program, Hospital de Niños Dr. Ricardo Gutiérrez, Universidad de Buenos Aires, Argentina.; Department of Medicine

10. Infectious Diseases Program, Hospital de Niños Dr. Ricardo Gutiérrez, Universidad de Buenos Aires, Argentina.; Department of Medicine

11. Department of Medicine, Hospital de Niños Dr. Ricardo Gutiérrez, Buenos Aires, Argentina. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina.; Laboratory of Infectious Diseases and Molecular Biology

12. Infectious Diseases Program, Hospital de Niños Dr. Ricardo Gutiérrez, Universidad de Buenos Aires, Argentina.; Department of Medicine

13. Department of Medicine, Hospital de Niños Dr. Ricardo Gutiérrez, Buenos Aires, Argentina. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina.; Laboratory of Infectious Diseases and Molecular

Biology

florenciabonn616@gmail.com

Background: This work aimed to study the influence of specific single-nucleotide polymorphisms (SNPs) in genes associated with antiviral innate immunity on dengue disease outcomes. **Methods:** Retrospective study including children <18 years diagnosed with dengue virus (DENV) infection at Ricardo Gutiérrez Children's Hospital during the 2023 and 2024 outbreaks. Diagnosis was confirmed by PCR or NS1 immunoassay, viremia was determined by RT-qPCR, while anti-DENV antibodies in acute-phase or convalescent sera were measured using PanBio Dengue IgG-Capture ELISA. Genotyping for SNPs in macrophage receptor with collagenous structure (MARCO rs1318645), interferon-alpha/beta receptor 1 (IFNAR1 rs2257167), and interferon-induced transmembrane protein 3 (IFITM3 rs34481144) was performed by qPCR in PBMCs. **Results:** One-hundred and thirty patients were studied, median age 12 years [2-17]; 50 (39%) developed dengue with warning signs (DWWS) and 33 (25%) required hospitalization. DWWS cases had significantly lower platelet counts ($P<0.0001$) and viremia ($P=0.0014$), and increased transaminases ($P=0.023$), although antibody levels did not vary with disease severity. Genetic analysis revealed that children with the SNP in MARCO exhibited an increased risk of developing leukopenia (odds ratio [OR]=3.94, $P=0.0090$), whereas patients with the SNP in IFITM3 had an augmented risk of developing nausea (OR=2.37, $P=0.023$), vomiting (OR=2.86, $P=0.006$) and thrombocytopenia (OR=2.48, $P=0.041$). The presence of simultaneous SNPs in MARCO and IFNAR1 was associated with a higher risk of myoarthralgia (OR=2.91, $P=0.047$), while co-occurring SNPs in MARCO and IFITM3 were linked to increased susceptibility to thrombocytopenia (OR=2.64, $P=0.032$). **Conclusions:** Genetic polymorphisms in MARCO, IFNAR1, and IFITM3 were associated with dengue disease outcomes in children.

101. P6-19. NEUROIMMUNE CONSEQUENCES OF IFN- γ -DRIVEN MULTIORGAN RESPONSE TO CORONAVIRUS

Agustina Sabater¹, Paula Perbolianachis², Rocio Seniuk³, Gaston Pascual⁴, Ana Paula Arévalo⁵, Pablo Sanchis⁶, Jimena Rada⁷, Jorge Pórfido⁸, Juan Manuel Carballeda⁹, Martina Crispo¹⁰, Gonzalo Moratorio¹¹, Geraldine Gueron¹², Ayelen Toro¹³

1. *Laboratorio de Inflamación y Cáncer, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN-CONICET); 2Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina; 3Instituto de Tecnología (INTEC), Universidad Argentina de la Empresa (UADE), Buenos Aires, Argentina; 4Department of Genitourinary Medical Oncology and The David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; Laboratorio de Inflamación y Cáncer*

2. *5Laboratorio de Evolución Experimental de Virus, Institut Pasteur de Montevideo, Montevideo, Uruguay; 6Laboratorio de Virología Molecular, Centro de Investigaciones Nucleares, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; Laboratorio de Evolución Experimental de Virus/Laboratorio de Virología Molecular*

3. *1Laboratorio de Inflamación y Cáncer, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN-CONICET); 2Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer*

4. *1Laboratorio de Inflamación y Cáncer, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN-CONICET); 2Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer*

5. *7Unidad de Biotecnología en Animales de Laboratorio, Institut Pasteur de Montevideo, Montevideo, Uruguay; Unidad de Biotecnología en Animales de Laboratorio*

6. *1Laboratorio de Inflamación y Cáncer, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN-CONICET); 2Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina; 3Instituto de Tecnología (INTEC), Universidad Argentina de la Empresa (UADE), Buenos Aires, Argentina; 4Department of Genitourinary Medical Oncology and The David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; Laboratorio de Inflamación y Cáncer*

7. *1Laboratorio de Inflamación y Cáncer, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN-CONICET); 2Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer*

8. *7Unidad de Biotecnología en Animales de Laboratorio, Institut Pasteur de Montevideo, Montevideo, Uruguay; Unidad de Biotecnología en Animales de Laboratorio*

9. *Laboratorio de Virología Molecular, Universidad Nacional de Hurlingham; Laboratorio de Virología Molecular*

10. *7Unidad de Biotecnología en Animales de Laboratorio, Institut Pasteur de Montevideo, Montevideo, Uruguay; Unidad de Biotecnología en Animales de Laboratorio*

11. *5Laboratorio de Evolución Experimental de Virus, Institut Pasteur de Montevideo, Montevideo, Uruguay; 6Laboratorio de Virología Molecular, Centro de Investigaciones Nucleares, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; Laboratorio de Evolución Experimental de Virus/Laboratorio de Virología Molecular*

12. *1Laboratorio de Inflamación y Cáncer, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN-CONICET); 2Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer*

13. *1Laboratorio de Inflamación y Cáncer, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (QUIBICEN-CONICET); 2Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer*
agustinasabater@gmail.com

Despite the end of the public health emergency, the World Health Organization warns that COVID-19 remains a global threat. In this context, understanding the molecular and cellular mechanisms of Coronavirus infections, as well as the host determinants that shape its pathogenesis, is essential for developing effective intervention strategies. We previously demonstrated dysregulation of genes involved in the IFN- γ response in COVID-19 patients, in association with both age and viral load, positioning IFN- γ as a critical mediator of host defense against SARS-CoV-2. In this work, we employed a preclinical murine model of Coronavirus MHV infection, widely validated for the study of SARS-CoV-2, to assess IFN- γ relevance by leveraging a transgenic IFN- γ KO model. Viral assessment by probed-qPCR and viral titration (TCID₅₀) revealed increased viral load and infectious particles in liver, spleen, heart and muscle of IFN- γ KO mice ($p<0.05$), in contrast to significantly reduced levels in the brain ($p<0.01$). Further analysis of different regions of the brain showed significant reductions in viral load of IFN- γ KO prefrontal cortex and hippocampus ($p<0.05$). Consistently, plasma proteomics revealed positive enrichment of multiorgan-damage categories, while negative enrichment of pathways related to neurological diseases and neuroinflammation was observed in the absence of IFN- γ . Together, these findings indicate that IFN- γ signalling shapes the multiorgan impact of Coronavirus infection, orchestrating an antiviral response that may ultimately exert detrimental effects on the brain. This work opens the possibility for therapeutic strategies based on IFN- γ modulation to prevent or mitigate neurological complications associated with the disease.

102. P6-20. SYNTHESIS AND FUNCTIONALIZATION OF MAGNETIC PARTICLES WITH IgG-ANTI-STX2 AS A TOOL TO IMPROVE THE DIAGNOSIS OF HEMOLYTIC UREMIC SYNDROME

Claudia Guerrero^{1,2}, Elisa de Sousa⁶, Luciana Juncal⁶, Claudio Daniel Girón Reyes^{1,2}, Diego Chiappetta^{2,3,4}, Marcela Morretton^{2,3,4}, Sheila Ons⁵, Carla Layana⁵, Carolina B. Otonelo⁵, Pedro Mendoza Zélis⁶, Claudia Rodríguez Torres⁶, Flavia Sacerdoti^{1,2}.

1. Universidad de Buenos Aires, Facultad de Ciencias Médicas, Departamento de Ciencias Fisiológicas. Laboratorio de Fisiopatología. Buenos Aires, Argentina.

2. CONICET - Universidad de Buenos Aires. Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO Houssay). Buenos Aires, Argentina.

3. Cátedra de Tecnología Farmacéutica I, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Argentina

4. Universidad de Buenos Aires, Instituto de Tecnología Farmacéutica y Biofarmacia (InTecFyB), Argentina

5. CONICET-Universidad Nacional de La Plata. CENE-XA-CREG.

6. CONICET-Universidad Nacional de La Plata-Instituto de Física La Plata, IFLP, La Plata, Argentina.

claudiogironr@gmail.com

Shiga toxin-producing *Escherichia coli* (STEC) is a foodborne pathogen that may trigger hemolytic uremic syndrome (HUS). Rapid and accurate diagnosis of STEC infection is critical for proper clinical treatment and patient management. We aimed to develop and characterize magnetic particles (MP) associated to IgG-anti-Stx2 to propose an innovative tool for the detection of Stx2 and diagnosis of STEC-HUS. MP of magnetite (Fe₃O₄) were synthesized and coated with amine-silane groups (MP@Si@NH₂) by a co-precipitation method and associated with IgG-anti-Stx2 (1 mg/ml) activated or not with N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDC). The percentage of IgG-anti-Stx2 associated to MP (MP-anti-Stx2) was calculated measuring proteins by Bradford method. The hydrodynamic diameter of MP and MP-anti-Stx2 was evaluated by Dynamic Light Scattering. Then, MP-anti-Stx2 were incubated 1 h with pure Stx2 (4 µg/ml) at room temperature and Stx2 binding was analyzed by ELISA. MP (18.6 g Fe₃O₄/ml) had a dry mass of 25.58 mg/ml with a % of SiO₂ of 27%. The hydrodynamic size of MP alone showed peaks of 2769 ± 1858 (61.5 %) and 5509 ± 73 nm (38.5%). MP-anti-Stx2 with and without EDC showed a peak of 3147 ± 794 or 2811 ± 119 nm, respectively. EDC-treated IgG associated in 71% to MP (318 µg/ mg Fe) while non-EDC-treated IgG associated in 49% (280 µg/mg Fe). Only non-EDC treated IgG associated to MP was able to bind Stx2 (0.215 µg/ml). These preliminary results open the perspective to use MP-anti-Stx2 for sample enrichment of Stx2 and introduce this method to improve diagnosis STEC-HUS.

103. P6-21. USE OF BACCHARIS SALICIFOLIA AQUEOUS EXTRACTS AS ANTHELMINTIC AGAINST TRICHINELLA SPIRALIS

Maria Priscila Saracino¹, Cecilia Vila², Cecilia B. Dobrecky³, Rafael Ricco⁴, Pablo C. Baldi⁵, Ignacio Agudelo⁶

1. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Inmunología; CONICET-Universidad de Buenos Aires, Instituto de Estudios de la Inmunidad Humoral (IDEHU), Buenos Aires, Argentina.; Laboratorio de Respuesta Inmune a Enfermedades Infecciosas Endémicas

2. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Inmunología; CONICET-Universidad de Buenos Aires, Instituto de Estudios de la Inmunidad Humoral (IDEHU), Buenos Aires, Argentina.; Laboratorio de Inmunología Molecular y Estructural

3. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Tecnología Farmacéutica; Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Tecnología Farmacéutica y Biofarmacia (InTecFyB), Buenos Aires, Argentina; Cátedra de Tecnología

Farmacéutica

4. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Farmacobotánica, Buenos Aires, Argentina.; Cátedra de Farmacobotánica

5. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Inmunología; CONICET-Universidad de Buenos Aires, Instituto de Estudios de la Inmunidad Humoral (IDEHU), Buenos Aires, Argentina.; Laboratorio de Respuesta Inmune a Enfermedades Infecciosas Endémicas

6. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Farmacobotánica; Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Tecnología Farmacéutica y Biofarmacia (InTecFyB), Buenos Aires, Argentina; Cátedra de Farmacobotánica mpsaracino@ffyb.uba.ar

Baccharis salicifolia (Ruiz y Pav.) has been employed as an anti-inflammatory and vermifuge agent in traditional herbal medicine. Helminth infections remain an international concern since these infections may become chronic and even public health emergencies. This study seeks to evaluate the anthelmintic efficacy of *B. salicifolia* aqueous extracts on *Trichinella spiralis*, a nematode parasite whose life cycle consists of three phases: intestinal, muscle larvae (ML) and adult worms (AW); migrant, newborn larvae (NBL) and muscular, ML. Phytochemical analysis of *B. salicifolia* extract via HPLC identified quercetin, apigenin, sakuranetin, naringenin and scopoletin. In vivo anthelmintic properties of pure *B. salicifolia* extracts were tested in mice infected with *T. spiralis* employing a treatment scheme on days 3-5 p.i. with one-dose/day of the plant extract (220 mg/kg body weight/per dose), ML and AW burden was determined as well as fecundity index (NBL/female AW). *B. salicifolia* treatment significantly reduced the AW burden on days 4 and 6 p.i. (vs. PBS, P<0.001) and ML burden (vs. PBS, P<0.001) whereas the fecundity index was also reduced (vs. PBS, P<0.0001). Antibodies presence in lung and intestinal extracts, obtained by PERFEXT method, anti-ML/AW excretory-secretory products (ESP) was analyzed by ELISA: on day 6 p.i., intestinal extracts showed increased anti-ML-ESP IgG1 and IgG2a, while lung extracts showed elevated IgA and IgG1 (vs. PBS, P<0.05). Conversely, anti-AW-ESP IgG1 and IgG2a decreased in intestinal extracts (vs. PBS, P<0.01). This study provides evidence for the anthelmintic efficacy of *B. salicifolia* extract, validating its traditional use and highlighting its potential as a cost-effective source for novel natural anthelmintics.

104. P6-22. STRATEGIES FOR THE LIGHT-MEDIATED TREATMENT OF BACTERIAL INFECTIONS

Mamone, Leandro¹, Tomás, Roberto Sebastián², Di Venosa, Gabriela³, Casas, Adriana⁴, Sáenz, Daniel⁵

1. Centro de Investigaciones sobre porfirinas y porfirias (CIPYP), Hospital de Clínicas José de San Martín, UBA, CONICET. Buenos Aires, Argentina.; Laboratorio de Terapias Fotoasistidas

2. Centro de Investigaciones sobre porfirinas y porfirias (CIPYP), Hospital de Clínicas José de San Martín, UBA, CONICET. Buenos Aires, Argentina.; Laboratorio de Terapias Fotoasistidas

3. Centro de Investigaciones sobre porfirinas y porfirias (CIPYP), Hospital de Clínicas José de San Martín, UBA, CONICET. Buenos Aires, Argentina.; Laboratorio de Terapias Fotoasistidas

4. Centro de Investigaciones sobre porfirinas y porfirias (CIPYP), Hospital de Clínicas José de San Martín, UBA, CONICET. Buenos Aires, Argentina.; Laboratorio de Terapias Fotoasistidas

5. Centro de Investigaciones sobre porfirinas y porfirias (CIPYP), Hospital de Clínicas José de San Martín, UBA, CONICET. Buenos Aires, Argentina.; Laboratorio de Terapias Fotoasistidas

leandro_mamone@hotmail.com

Antimicrobial photodynamic therapy (aPDT) with 5-aminolevulinic acid (ALA) and photobiomodulation (PBM) with light represent novel strategies for treating bacterial infections. aPDT relies on

the generation of reactive oxygen species (ROS) that kill bacteria, whereas PBM is proposed to enhance mitochondrial function. Three different light sources, including a 635 nm laser, red–yellow LEDs, and solar light, were employed against *Staphylococcus aureus* RN6390. Biofilms of *S. aureus* were treated with ALA-aPDT using a light dose of 250 mW/cm², achieving reductions of 6, 4, and 0.7 log CFU/mL with solar light, LEDs, and laser, respectively ($P < 0.05$ vs. control). Light alone did not reduce bacterial counts under any condition. In a murine model of *S. aureus* cutaneous abscesses (CF-1 mice), untreated lesions required 27 days to heal. Laser PBM accelerated wound closure by 7 days, while LEDs reduced healing time by 5 days. ALA-aPDT with laser further shortened healing time by 12 days. In incisional non-infected wound models, all three light sources accelerated tissue repair, indicating that PBM alone has a significant contribution to wound healing. Taken together, our findings support the therapeutic potential of both ALA-aPDT and PBM as effective approaches for the treatment of cutaneous infections.

105. P6-23. VALIDATION OF NEXT-GENERATION SEQUENCING FOR THE DETECTION OF HIV-1 DRUG RESISTANCE VARIANTS: IMPLICATIONS FOR PRECISION MEDICINE

Sofía de la Fuente¹, María Cecilia Monzani², Cifuentes Héctor Martín³, Figueredo Belén Fiamma⁴, Peñalba Camila Ximena⁵, Bellazzi Mónica Paola⁶, Machado Gimena Alejandra⁷, Sánchez Loria Julián⁸, Poklépovich Caride Tomas⁹, Delea Marisol¹⁰, Bruque Carlos David¹¹, Corró Guillermo¹²

1. Hospital de Alta Complejidad El Calafate SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica
2. INSTITUTO DE INVESTIGACIONES BIOMEDICAS EN RETROVIRUS Y SIDA; Laboratorio de Secuenciación
3. Hospital de Alta Complejidad El Calafate SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica
4. Hospital de Alta Complejidad El Calafate SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica
5. Hospital de Alta Complejidad El Calafate SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica
6. Hospital de Alta Complejidad El Calafate SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica
7. Hospital de Alta Complejidad El Calafate SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica
8. Unidad Operativa Centro Nacional de Genómica y Bioinformática (UOCNGB); ANLIS Malbrán
9. Unidad Operativa Centro Nacional de Genómica y Bioinformática (UOCNGB); ANLIS Malbrán
10. Hospital de Alta Complejidad El Calafate SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica
11. Hospital de Alta Complejidad El Calafate SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica
12. Hospital de Alta Complejidad El Calafate SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica

sofidelaf98@gmail.com

HAART resistance associated variants reduce treatment efficacy increasing the therapeutic failure odds. Next generation sequencing (NGS) has emerged as a powerful tool for HIV drug resistance testing, as it can detect minority variants within the viral quasispecies that are often missed by conventional Sanger sequencing (SS). Early detection of these subpopulations may optimize therapeutic strategies. This study aimed to validate NGS for the detection of antiretroviral resistance variants, and compare its sensitivity with SS. We analyzed samples from 48 people living with HIV (CV>=1000copies/mL). Fragments of Integrase, Protease and Reverse Transcriptase were sequenced using MiSeq Illumina and Sanger technology. Sequences were aligned to the HXB2 reference genome and analyzed with the Stanford HIV-Drug-Resistance Database. Our preliminary results showed an excellent correlation between methodologies, having a higher sensitivity with NGS ($n=2033$) than with SS ($n=1827$). We observed that NGS detects variants at low frequencies (89% for protease and integrase inhibitors associated mutations, while 64% agreement was observed for reverse transcriptase inhibitors due to variants observed only by NGS, mainly throughout the RT-RNase-H type-1 domain.

NGS showed superior sensitivity, enabling detection of minority variants, supporting its use as an early warning tool for resistance emergence. These findings highlight the advantage of NGS in capturing low-frequency variants missed by SS, reinforcing its utility for HIV resistance monitoring and its potential role in optimizing therapeutic decision making. Larger studies are required to validate its role in routine HIV-1 resistance monitoring.

106. P6-24. EVALUATION OF CIRCULATING MIRNAS AS POTENTIAL BIOMARKERS OF THERAPEUTIC RESPONSE IN PATIENTS WITH TRYPANOSOMA CRUZI INFECTION

María Laura Hulaniuk Wolaniuk¹, Paula Finamore², Amanda Fair³, Nicolás González⁴, Samanta Moroni⁵, Guillermo Moscatelli⁶, Jaime Altcheh⁷, Otacilio Moreira⁸, Juan Carlos Ramírez Gómez⁹

1. Instituto Multidisciplinario de Investigaciones en Patologías Pediátricas (IMIPP), CONICET-GCBA, Buenos Aires, Argentina; Laboratorio de Parasitología Molecular
2. Instituto Oswaldo Cruz, Fundação Oswaldo Cruz, Rio de Janeiro, Brasil; Laboratório de Virologia e Parasitologia Molecular
3. Instituto Oswaldo Cruz, Fundação Oswaldo Cruz, Rio de Janeiro, Brasil; Laboratório de Virologia e Parasitologia Molecular
4. Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina; Servicio de Parasitología y Chagas
5. Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina; Servicio de Parasitología y Chagas
6. Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina; Servicio de Parasitología y Chagas
7. Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina; Servicio de Parasitología y Chagas
8. Instituto Oswaldo Cruz, Fundação Oswaldo Cruz, Rio de Janeiro, Brasil; Laboratório de Virologia e Parasitologia Molecular
9. Instituto Multidisciplinario de Investigaciones en Patologías Pediátricas (IMIPP), CONICET-GCBA, Buenos Aires, Argentina; Laboratorio de Parasitología Molecular

marialaurahulaniuk@gmail.com

The gold standard for evaluating treatment efficacy in patients with Chagas disease is the seroconversion of conventional serological tests, which may take more than 10 years in chronic cases. Circulating microRNAs (miRNAs) have been proposed as potential biomarkers for the diagnosis and prognosis of several pathologies, including infectious diseases. In this context, we aimed to evaluate the potential use of miRNAs as biomarkers of therapeutic response in patients with vertical *Trypanosoma cruzi* infection as well as to compare the expression levels of miRNAs in neonates with and without Chagas disease. A total of 28 neonates were included, 14 with and 14 without vertical transmission of *T. cruzi* infection. RNA extraction was performed from blood samples collected at diagnosis, end of treatment, and end of follow-up visits. RT-qPCR was conducted using specific stem-loop primers and probes for endogenous (snRNA U6 and miR-16-5p) and exogenous (cel-miR-39-3p and cel-miR-54-5p) controls, and candidate targets (hsa-miR-146b-5p and hsa-miR-210-3p). For miRNAs expression analysis the comparative Ct method was used. Statistical analysis was performed using Tukey's test, ANNOVA and Student's t-test. Nearly 50% of newborns showed a decrease in miR-146b-5p and miR-210-3p baseline expression levels at the end of treatment and follow-up. No differences in miRNAs expression were found between infected and uninfected neonates. Further studies with a larger number of patients and miRNAs will be necessary to confirm the usefulness of miRNAs as biomarkers of therapeutic response for patients with *T. cruzi* infection.

107. P6-25. RECOMBINANT FAB MONOCLONAL ANTIBODIES PARTIALLY NEUTRALIZE THE CYTOTOXICITY OF SHIGA TOXIN-PRODUCING ESCHERICHIA COLI (STEC) IN HUMAN RENAL ENDOTHELIAL CELLS (HGEC)

Fernando Gomez¹, Daniela Luz Hessel Da Cunha², Carolina Carbonari³, Claudio Daniel Girón⁴, Wanderson Marques Da Silva⁵, Flavia Sacerdoti⁶, Elizabeth Miliwebsky⁷, Roxane Ma-

ria Fontes Piazza⁸, María Marta Amaral⁹

1. (1) Universidad de Buenos Aires, Facultad de Ciencias Médicas, Departamento de Ciencias Fisiológicas. Laboratorio de Fisiopatogenia. (2) CONICET - Universidad de Buenos Aires. Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO Houssay).; Laboratorio de Fisiopatogenia
 2. Instituto Butantan, São Paulo, Brasil.; Laboratório de Bacteriologia.
 3. Instituto Nacional de Enfermedades Infecciosas ANLIS "Dr. Carlos G. Malbrán", Buenos Aires.; Servicio Fisiopatogenia, Departamento Bacteriología.
 4. (1) Universidad de Buenos Aires, Facultad de Ciencias Médicas, Departamento de Ciencias Fisiológicas. (2) CONICET - Universidad de Buenos Aires. Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO Houssay).; Laboratorio de Fisiopatogenia.
 5. (1) Universidad de Buenos Aires, Facultad de Ciencias Médicas, Departamento de Ciencias Fisiológicas. (2) CONICET - Universidad de Buenos Aires. Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO Houssay).; Laboratorio de Fisiopatogenia
 6. (1) Universidad de Buenos Aires, Facultad de Ciencias Médicas, Departamento de Ciencias Fisiológicas. (2) CONICET - Universidad de Buenos Aires. Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO Houssay).; Laboratorio de Fisiopatogenia.
 7. Instituto Nacional de Enfermedades Infecciosas ANLIS "Dr. Carlos G. Malbrán", Buenos Aires.; Servicio Fisiopatogenia, Departamento Bacteriología.
 8. Instituto Butantan, São Paulo, Brasil.; Laboratório de Bacteriologia.
 9. (1) Universidad de Buenos Aires, Facultad de Ciencias Médicas, Departamento de Ciencias Fisiológicas. (2) CONICET - Universidad de Buenos Aires. Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO Houssay).; Laboratorio de Fisiopatogenia.
- gomezfernandod@gmail.com

Hemolytic Uremic Syndrome (HUS) associated with STEC infections is one of the most important causes of acute renal injury in pediatric age groups in Argentina. Neither a licensed vaccine nor an effective therapy for HUS is available for humans. We previously showed that FabC11 and FabF8 neutralized Stx2 cytotoxicity in HGEC cultures. Here, we assessed the neutralizing capacity of FabF8:Stx2, FabC11:Stx1/Stx2, FabC8:Stx1, and FabB6:Stx1 against STEC supernatants in HGEC cultures. Cells were exposed to Fab (10 µg/mL) pre-incubated with STEC supernatants (1/50) for 72 h, and viability was determined by neutral red uptake. Cytotoxicity of Stx1a, Stx1a/Stx2a, Stx2a and Stx2c-producing serotypes in HGEC ranged from 70-85%; 70-80%; 70-85% and 70-77%, respectively, n=3, p<0.05. The maximum percentage of neutralization obtained was: for Stx1a serotypes: 47% for O26:H11 with FabB6 and 29% for O151:H2 with FabC8. For Stx1a/Stx2a serotypes: 48% for O103:H2 with FabC8, 42% for O111:H8 and 44% for O179:H8 with FabF8. For Stx2a serotypes: 44% for O157:H7, 40% for O145:H28, 23% for O121:H19 and 41% for OgN31:H49, all with FabF8; and for O115:H25, 60% was obtained with FabC11. For Stx2c serotypes: 36% for O157:H7 with FabF8 and 40% for O174:H24 with FabC11. Despite unadjusted variation in Shiga toxin release, most tested Fab fragments neutralized STEC supernatant cytotoxicity in human renal cells by ~40%. Therefore, these findings demonstrate that Fab fragments can partially neutralize the cytotoxicity of diverse STEC isolates in human renal cells, supporting their potential as a therapeutic strategy to mitigate kidney injury and treat HUS.

108. P6-26. CARDIAC AUTOPHAGY DISRUPTION IN EXPERIMENTAL ACUTE CHAGAS DISEASE: PRELIMINARY TRANSCRIPTOMIC EVIDENCE AND MODULATION BY FENOFIBRATE

Maia Chop¹, Alelí Silva del Puerto², Ignacio Mazzitelli³, Lucía Bleichmar⁴, Cecilia Monzani⁵, Verena Franco Riveros⁶, Ignacio Barbieri⁷, Bruno Buchholz⁸, Christian Rodríguez Rodríguez⁹, Nora Goren¹⁰, Federico Penas¹¹, Ágata Cevey de

Laforé¹²

1. CONICET, Universidad Nacional de Mar del Plata; Lab 1
 2. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires.; Laboratorio de Fisiopatología de la Inflamación
 3. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires.; INBIRS
 4. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires.; INBIRS
 5. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires.; INBIRS
 6. Instituto de Fisiopatología Cardiovascular, UBA. Facultad de Medicina-Universidad de Buenos Aires; Laboratorio de Fisiopatología Cardiovascular
 7. Instituto de Fisiopatología Cardiovascular, UBA. Facultad de Medicina-Universidad de Buenos Aires; Laboratorio de Fisiopatología Cardiovascular
 8. Instituto de Fisiopatología Cardiovascular, UBA. Facultad de Medicina-Universidad de Buenos Aires; Laboratorio de Fisiopatología Cardiovascular
 9. CONICET. Departamento de Química y Bioquímica. Facultad De Cs. Exactas y Naturales. Universidad Nacional de Mar del Plata; Lab 1
 10. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires; Laboratorio de Fisiopatología de la Inflamación
 11. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA, UBA-CONICET. Facultad de Medicina-Universidad de Buenos Aires; Laboratorio de Fisiopatología de la Inflamación
 12. CONICET. Departamento de Química y Bioquímica. Facultad De Cs. Exactas y Naturales. Universidad Nacional de Mar del Plata.; Lab 1
- maia chop@gmail.com

Chagas disease, caused by *Trypanosoma cruzi*, leads to chronic cardiomyopathy through multifactorial mechanisms that include inflammation, oxidative stress, and metabolic deregulation. Emerging evidence suggests that autophagy may play a critical role in host defense and cardiac homeostasis. However, its precise role in the pathophysiology of Chagas disease remains controversial. Here, we performed an exploratory RNA-seq analysis of cardiac tissue from mice infected with *T. cruzi* (RA strain, 14 dpi) to investigate transcriptomic signatures of autophagy dysregulation. This model recapitulates acute myocarditis with evidence of ventricular dysfunction and QRS interval prolongation (p<0.05). We observed a coordinated downregulation of master regulators of autophagy, including *Ppara*, *Foxo3*, and *Tfeb*, accompanied by decreased expression of key components involved in phagophore initiation (*Ulk1*), nucleation (*Atg14*), and elongation (*Atg16l1*, *Atg10*) (p<0.05). Interestingly, genes associated with later steps of the autophagic process (*Atg3*, *Atg4b*, *Sqstm1/p62*, *Lamp2*) were upregulated, suggesting a possible accumulation of immature autophagic vesicles and impaired flux. These transcriptional alterations are consistent with a functional inhibition of autophagy at early stages. Preliminary results from infected mice treated with fenofibrate, a PPARα agonist, show a partial restoration of autophagy-related gene expression. Notably, *Ppara*, *Foxo3*, *Atg14*, and *Atg10* returned to levels comparable to uninfected controls (p<0.05), supporting the hypothesis that fenofibrate may counteract *T. cruzi*-induced autophagic inhibition. This improved autophagic flux correlates with cardioprotection in vivo (p<0.05). These findings provide early evidence that pharmacological activation of PPARα can modulate the cardiac autophagy transcriptome in Chagas disease. This work opens a potential therapeutic strategy in Chagas cardiomyopathy.

POSTERS 6 - SAIC - INMUNOLOGÍA E INFLAMACIÓN
DATE & TIME: 17/11/2025 15:00 - 16:30 H

Chairs: Emmanuel Angeli, Maria Victoria Ramos, Maria Priscilla Saracino

109. P6-27. OCCURRENCE OF THE “DEFENSIVE LIPID DROPLETS” IN ECHINOCOCCUS GRANULOSUS EVIDENCE INNATE IMMUNITY IN THE PARASITE

Sofía Blanco^{1*}, Luciano Lausero^{1*2}, Noelia Foresi²³, Andrea Cumino^{1,3*}

1. *Facultad de Ciencias Exactas y Naturales, Universidad Nacional de Mar del Plata.; BIPaM-IIPROSAM1*

2. *Facultad de Ciencias Exactas y Naturales, Universidad Nacional de Mar del Plata.; BIPaM-IIPROSAM 1*

3. *Facultad de Ciencias Exactas y Naturales, Universidad Nacional de Mar del Plata.; IIB- Conicet 2*

4. *Facultad de Ciencias Exactas y Naturales, Universidad Nacional de Mar del Plata1, Departamento de Química y Bioquímica 3; BIPaM-IIPROSAM 1*

sofiambianco@gmail.com

Lophotrochozoa is a clade of bilateral animals which includes the cestode *Echinococcus granulosus*, a zoonotic parasite whose larval stage is the causative agent of cystic echinococcosis. Although they lack adaptive immunity, lophotrochozoans possess innate immune response mechanisms, still unknown in other parasitic species. Previously, we identified evolutionarily conserved innate immune surveillance mechanisms in this parasite, such as UPR induction, endoplasmic reticulum-stress responses, and the expression of autophagy-related defense genes under transcriptional control of FOXO and TFEB. Genomic analyses suggest functional and molecular divergence of pattern recognition receptors, signaling adaptors and cytokine receptors. We isolated lipid droplets (LDs) from metacystodes by density gradient ultracentrifugation, followed by delipidation and proteomic analysis of LD-associated proteins. The proteome showed enrichment in uncharacterized proteins containing domains involved in antiviral and antibacterial defense functions and in NF- κ B signaling such as: TIR (Toll/Interleukin-1 Receptor) domains; tumor necrosis factor receptor family, pore-forming proteins, immunity-related GTPases, guanylate-binding proteins, smc complex proteins, Pur- α homolog protein and several iron-metabolism proteins, suggesting that parasite LDs could serve as a suitable checkpoint harnessed to organize a front-line defense. Moreover, we identified a putative gene encoding a nitric oxide synthase (NOS) and immunodetected the enzyme in LPS-, -PI:C and arginine-treated parasites, accompanied by enhanced NO release (DAF-FM-DA) which was reduced with competitive NOS inhibitors, suggesting a key hallmark of phagocytic-like cells. Further experiments should determine whether the parasite, which coexists with a beneficial microbiome within the host tissue environment, establishes a parasite-microbiome interaction or, alternatively, generates an immune defense against tissue-resident viruses and bacteria.

110. P6-28. MUTAGENESIS CAUSED BY HOCL IS PREVENTED BY THE NITRONE COMPOUND 5,5-DIMETHYL-1-PYRROLINE N-OXIDE

Cristofer M. Lopez¹, Dario C. Ramirez², Sandra E. Gomez Mejiba³

1. *IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.*

2. *IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.*

3. *IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.*

cristofermlopez.1@gmail.com

When neutrophils are activated, they release myeloperoxidase (MPO) into the extracellular compartment through the neutrophil extracellular traps, from where it can be taken up by bystander cells.

Inside these cells, HOCl produced by MPO can cause oxidative damage to the genome, that if is not repaired, can cause cell transformation. Under pathological conditions, the microenvironmental concentration of HOCl is 200 μ M, and under neutrophilic inflammation, it can reach 8 mM. Hypochlorite is a nonradical oxidant that can react with macromolecules, including DNA. When HOCl reacts with DNA, it can generate DNA chloramines, which subsequently decompose into DNA (nitrogen)-centered radicals. Upon reaction with oxygen, DNA-centered radicals decay into mutagenic DNA oxidation products (e.g., 8-oxo-dGuo) that, if unrepaired, cause mutations and cellular transformation. Herein, we aimed to test whether HOCl-induced DNA-centered radicals precede DNA oxidation and mutagenesis in MPO-loaded A549 human lung epithelial cells treated with non-cytotoxic concentrations of H₂O₂—an in vitro model resembling pulmonary neutrophilic inflammation in irritated airways. Intracellularly produced HOCl can oxidize DNA with the intermediacy of DNA-centered radicals. The nitron spin trap 5,5-dimethyl-1-pyrroline N-oxide (DMPO) traps HOCl-induced DNA-centered radicals, forming DNA-DMPO nitron adducts and reducing 8-oxo-dGuo accumulation, and blocking mutation of the hypoxanthine phosphoribosyl transferase gene. Scavenging DNA-centered radicals to reduce the accumulation of mutagenic, HOCl-induced end-oxidation products in the genome of bystander cells will provide new therapeutic avenues to reduce genotoxic damage at sites of neutrophilic inflammation, such as irritated airways.

111. P6-29. ADHERENCE AND INTERNALIZATION OF ESCHERICHIA COLI IN BOVINE ENDOMETRIAL CELLS

Sofía Cainelli¹, Ma. Emilia Odriozola², Carolina Engler³, Enzo R. Cabaña⁴, Ma. Sol Renna⁵, Pilmaiquen A. Miño⁶, Hugo H. Ortega⁷, Melisa M. L. Velázquez⁸, Antonela F. Stassi⁹

1. *Instituto de Ciencias Veterinarias del Litoral (ICiVet-Litoral), Universidad Nacional del Litoral (UNL) / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Laboratorio de Biología Celular y Molecular Aplicada.*

2. *Instituto de Ciencias Veterinarias del Litoral (ICiVet-Litoral), Universidad Nacional del Litoral (UNL) / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Laboratorio de Biología Celular y Molecular Aplicada.*

3. *Instituto de Ciencias Veterinarias del Litoral (ICiVet-Litoral), Universidad Nacional del Litoral (UNL) / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Laboratorio de Biología Celular y Molecular Aplicada.*

4. *Instituto de Ciencias Veterinarias del Litoral (ICiVet-Litoral), Universidad Nacional del Litoral (UNL) / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Laboratorio de Biología Celular y Molecular Aplicada.*

5. *Instituto de Ciencias Veterinarias del Litoral (ICiVet-Litoral), Universidad Nacional del Litoral (UNL) / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Laboratorio de Biología Celular y Molecular Aplicada.*

6. *Instituto de Ciencias Veterinarias del Litoral (ICiVet-Litoral), Universidad Nacional del Litoral (UNL) / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Laboratorio de Biología Celular y Molecular Aplicada.*

7. *Instituto de Ciencias Veterinarias del Litoral (ICiVet-Litoral), Universidad Nacional del Litoral (UNL) / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Laboratorio de Biología Celular y Molecular Aplicada.*

8. *Universidad Católica de Santa Fe / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Instituto de Ecología Humana y Desarrollo Sustentable.*

9. *Instituto de Ciencias Veterinarias del Litoral (ICiVet-Litoral), Universidad Nacional del Litoral (UNL) / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Laboratorio de Biología Celular y Molecular Aplicada.*

sofiacainelli64@gmail.com

During uterine involution, the endometrium initiates an innate immune response to defend against and eliminate bacterial contaminants. This response is mediated not only by professional immune cells but also by endometrial epithelial cells (EpC) and stromal cells (StC). A better understanding of the interactions between endome-

trial cells and *Escherichia coli* may contribute to the design of therapeutic strategies that improve the resolution of inflammation and thereby, enhanced conception efficiency in dairy cattle. This study aimed to investigate the adherence and internalization capacity of the bovine endometrium EpC and StC in vitro. For this purpose, we established primary bovine endometrial cell cultures (BECC) composed of EpC and StC. Two replicates of each culture system (n=4) were incubated with FITC-labeled *E. coli* for 2h at either 4°C or 37°C in the dark. Cells recovered from each replicate were independently labelled with Alexa Fluor 750 anti-cytokeratin antibody or Alexa Fluor 680 anti-vimentin antibody, specific for EpC or StC respectively. Samples were acquired by flow cytometry, and statistical analyses were performed using IBM SPSS Statistic 22. Results demonstrated that, unlike StC (P=0.883), EpC cultured at 37°C showed significantly greater adherence and/or internalization of *E. coli* compared with those at 4°C (P=0.013). To confirm these findings, cytological preparations of BECC incubated with FITC-labeled *E. coli* were examined by immunofluorescence, showing bacterial fluorescence associated with endometrial EpC. Given that *E. coli* is typically considered an extracellular bacterium, these findings provide the first evidence suggesting that bovine endometrial EpC are capable of adhering and internalizing *E. coli*.

ORALES 6 - SAIC - NEFROLOGÍA Y SISTEMA GENITOURINARIO

DATE & TIME: 18/11/2025 9:00 - 10:30 H

Chairs: Monica Majowicz, Ana Maria Puyo

112. O6-01. AFFORDABLE MAGNETIC CAPTURE OF EXOSOMES: A PROMISING TOOL FOR CLINICAL BIOMARKER STUDIES

Pablo Javier Azurmendi¹, Maria Lucia Rosenberg², Vanesa Torbidoni³, Marcelo Vasquez Mansilla⁴, Enio Enio Lima Jr⁵, Elisabet Mónica Oddo⁶, Elin Winkler⁷, Roberto Zysler⁸, Mariana Raineri⁹, Roxana Noemí Peroni¹⁰

1. Instituto de Investigaciones Médicas Alfredo Lanari, Facultad de Medicina, UBA; IDIM (UBA - CONICET), Buenos Aires, Argentina.; Div. Nefrología Experimental y Bioquímica Molecular

2. Instituto de Investigaciones Médicas Alfredo Lanari, Facultad de Medicina, UBA; IDIM (UBA - CONICET), Buenos Aires, Argentina.; Div. Nefrología Experimental y Bioquímica Molecular

3. Instituto Argentino de Veterinaria, Ambiente y Salud (IAVAS), Universidad Juan Agustín Maza (UMaza). Guaymallén, Mendoza, Argentina.; Laboratorio de Biología Celular y Molecular

4. Instituto de Nanociencia y Nanotecnología (INN, CNEA-CONICET), Bariloche, Río Negro. Argentina.; Laboratorio de Resonancias Magnéticas

5. Instituto de Nanociencia y Nanotecnología (INN, CNEA-CONICET), Bariloche, Río Negro. Argentina.; Laboratorio de Resonancias Magnéticas

6. Instituto de Investigaciones Médicas Alfredo Lanari, Facultad de Medicina, UBA; IDIM (UBA - CONICET), Buenos Aires, Argentina.; Div. Nefrología Experimental y Bioquímica Molecular

7. Instituto de Nanociencia y Nanotecnología (INN, CNEA-CONICET). Instituto Balseiro, Bariloche, Río Negro, Argentina.; Laboratorio de Resonancias Magnéticas

8. Instituto de Nanociencia y Nanotecnología (INN, CNEA-CONICET). Instituto Balseiro, Bariloche, Río Negro, Argentina.; Laboratorio de Resonancias Magnéticas

9. Instituto de Nanociencia y Nanotecnología (INN, CNEA-CONICET), Bariloche, Río Negro. Argentina.; Laboratorio de Resonancias Magnéticas

10. Instituto de Investigaciones Farmacológicas (ININFA, UBA-CONICET), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Cátedra de Farmacología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Buenos Aires, Argentina.; Laboratorio de Farmacología de Transportadores de Drogas II. azurmendi.pablo@lanari.uba.ar

Urinary exosomes are promising biomarkers in kidney diseases, but their isolation is costly and complex. Developing simpler and more accessible methods is essential. To evaluate the feasibility and performance of a low-cost magnetic method for the selective capture of urinary exosomes, using magnetite particles functionalized with an anti-CD63 aptamer. Magnetite particles were obtained by milling local mineral sources, coated with silica, and conjugated with an anti-CD63 aptamer. Functionalization was verified by transmission electron microscopy (TEM), zeta potential analysis, and attenuated total reflection infrared spectroscopy. Exosomes were isolated from urine and cell culture supernatants by ultracentrifugation and characterized by TEM, scanning electron microscopy (SEM), and atomic force microscopy (AFM). Aptamer functionality was tested via aptafluorescence in U87 cells and with isolated exosomes. Magnetic capture efficiency was evaluated using supernatants from MDA-MB-231 cells. Ultracentrifugation-isolated exosomes exhibited spherical morphology ranging from 22 – 150 nm. Aptamer-functionalized particles showed a surface charge shift from negative to positive upon incubation with exosomes, confirming specific interaction. No such shift was observed in control particles lacking aptamer or bearing random sequences. Magnetic capture achieved 36 – 43% efficiency relative to ultracentrifugation and recovered vesicles with comparable size profiles. This low-cost magnetic approach allows for the selective isolation of urinary exosomes with moderate efficiency and high specificity. It represents a promising, simple, and accessible alternative for clinical implementation in biomarker discovery.

113. O6-02. CHRONIC ADMINISTRATION OF CARBIDOPA IN MALE WISTAR KYOTO AND SPONTANEOUSLY HYPERTENSIVE RATS: ITS IMPACT ON BLOOD PRESSURE AND RENAL INFLAMMATORY RESPONSE

Nicolás Martín Kouyoumdzian¹, Gustavo Daniel Risso², Paula Denise Prince³, María Julieta Rudi⁴, Beatriz Perazzi⁵, Hyun Jin Lee⁶, Natalia Lucía Rukavina Mikusic⁷, Marcelo Roberto Choi⁸

1. Universidad de Buenos Aires (UBA). Facultad de Farmacia y Bioquímica (FFyB). Departamento de Ciencias Biológicas, Cátedra de Anatomía e Histología. Buenos Aires, Argentina. CONICET-UBA, Instituto Alberto C. Taquini de Investigaciones en Medicina Traslacional (IATIMET). Buenos Aires, Argentina.; Laboratorio de Fisiopatología Cardiometaabólica y Renal (LAFCAR)

2. CONICET-UBA, Instituto Alberto C. Taquini de Investigaciones en Medicina Traslacional (IATIMET). Buenos Aires, Argentina.; Laboratorio de Fisiopatología Cardiometaabólica y Renal (LAFCAR)

3. CONICET-UBA, Instituto Alberto C. Taquini de Investigaciones en Medicina Traslacional (IATIMET). Buenos Aires, Argentina.; Laboratorio de Fisiopatología Cardiometaabólica y Renal (LAFCAR)

4. Universidad de Buenos Aires (UBA). Facultad de Farmacia y Bioquímica (FFyB). Departamento de Ciencias Biológicas, Cátedra de Anatomía e Histología. Buenos Aires, Argentina.; Laboratorio de Fisiopatología Cardiometaabólica y Renal (LAFCAR)

5. UBA. FFyB. Departamento de Análisis Clínicos, Cátedra de Química Clínica. Buenos Aires, Argentina. UBA. FFyB, Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC). Buenos Aires, Argentina.; Laboratorio de Fisiopatología Cardiometaabólica y Renal (LAFCAR)

6. Universidad de Buenos Aires (UBA). Facultad de Farmacia y Bioquímica (FFyB). Departamento de Ciencias Biológicas, Cátedra de Anatomía e Histología. Buenos Aires, Argentina. UBA. FFyB, Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC). Buenos Aires, Argentina.; Laboratorio de Fisiopatología Cardiometaabólica y Renal (LAFCAR)

7. Universidad de Buenos Aires (UBA). Facultad de Farmacia y Bioquímica (FFyB). Departamento de Ciencias Biológicas, Cátedra de Anatomía e Histología. Buenos Aires, Argentina. CONICET-UBA, Instituto Alberto C. Taquini de

Investigaciones en Medicina Traslacional (IATIMET). Buenos Aires, Argentina.; Laboratorio de Fisiopatología Cardio-metabólica y Renal (LAFCAR)

8. *Universidad de Buenos Aires (UBA). Facultad de Farmacia y Bioquímica (FFyB). Departamento de Ciencias Biológicas, Cátedra de Anatomía e Histología. Buenos Aires, Argentina. CONICET-UBA, Instituto Alberto C. Taquini de Investigaciones en Medicina Traslacional (IATIMET). Buenos Aires, Argentina.; Laboratorio de Fisiopatología Cardio-metabólica y Renal (LAFCAR)*
nicokouy214@gmail.com

Given the natriuretic and antiinflammatory actions of renal dopamine, our objective was to evaluate if chronic inhibition of peripheral aromatic L-amino acid decarboxylase with carbidopa (Cb) could lead to renal inflammation and increased blood pressure. 16 male Wistar Kyoto (WKY) and 16 spontaneously hypertensive rats (SHR) were divided into four groups (n=8/group): WKY (tap water), WKY+Cb (Cb 25 mg/kg/day in the drinking water), SHR and SHR+Cb. Systolic blood pressure (SBP) was measured weekly by the tail-cuff method. After three weeks, we determined 24-hour fractional and urinary sodium excretion. We performed renal histology and measured renal expressions of Na⁺,K⁺-ATPase pump (NKA), dopaminergic receptors (D1R and D2R), and nuclear factor kappa B (NF-κB) by Western Blot. (p<0.05: *versus WKY; #versus SHR). Cb administration increased SBP in SHR+Cb group versus SHR (mmHg: 240±3#; 210±10) after one week, with no changes after three weeks. A significant reduction in fractional and urinary sodium excretion was accompanied by an increase in renal NKA expression in SHR and WKY rats (arbitrary units, AU: WKY:1.00±0.08; WKY+Cb:1.30±0.14*; SHR:1.30±0.23*; SHR+Cb:1.78±0.13*#). D1R expression was decreased in the WKY+Cb group versus WKY (AU: WKY:1.00±0.17; WKY+Cb:0.65±0.10*), with no changes D2R expression. NF-κB expression was higher in SHR+Cb versus WKY group (AU: WKY:1.00±0.11; WKY+Cb:1.12±0.16; SHR:1.22±0.07; SHR+Cb:1.36±0.18*). Carbidopa alters tubular sodium handling, by increasing Na⁺,K⁺-ATPase expression and promoting greater sodium reabsorption. In hypertensive rats, carbidopa led to increased tubulointerstitial spaces in the renal stroma, and these changes were accompanied by an augmented expression of NFκB in renal cortex.

114. O6-03. ESTROGEN AND PROGESTERONE REPLACEMENT MODULATES PROTEIN EXPRESSION IN PERIPHERAL BLOOD LYMPHOCYTES IN AN ANIMAL MODEL OF SALT-SENSITIVE HYPERTENSION

Sandra G Vlachovsky¹, Romina S. Rodríguez², Pablo J. Azurmendi³, Elisabet M. Oddo⁴, Claudia Silberstein⁵, Fernando R. Ibarra⁶

1. *Universidad de Buenos Aires, Facultad de Medicina, Instituto de Investigaciones Médicas A. Lanari / 2Universidad de Buenos Aires, Facultad de Medicina, Instituto de Investigaciones Médicas, Consejo Nacional de Investigaciones Científicas y Técnicas (IDIM UBA-CONICET), Buenos Aires, Argentina./4Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, UBA-CONICET.; Laboratorio de Nefrología Experimental y Bioquímica Molecular / Laboratorio de Biosensores y Bioanálisis.*

2. *Universidad de Buenos Aires, Facultad de Medicina, Instituto de Investigaciones Médicas A. Lanari; Laboratorio de Nefrología Experimental y Bioquímica Molecular*

3. *Universidad de Buenos Aires, Facultad de Medicina, Instituto de Investigaciones Médicas A. Lanari / Universidad de Buenos Aires, Facultad de Medicina, Instituto de Investigaciones Médicas, Consejo Nacional de Investigaciones Científicas y Técnicas (IDIM UBA-CONICET), Buenos Aires, Argentina; Laboratorio de Nefrología Experimental y Bioquímica Molecular*

4. *Universidad de Buenos Aires, Facultad de Medicina, Instituto de Investigaciones Médicas A. Lanari / 2Universidad de Buenos Aires, Facultad de Medicina, Instituto de Investigaciones Médicas, Consejo Nacional de Investigacio-*

nes Científicas y Técnicas (IDIM UBA-CONICET), Buenos Aires, Argentina; Laboratorio de Nefrología Experimental y Bioquímica Molecular

5. *Universidad de Buenos Aires, Facultad de Medicina, Departamento de Ciencias Fisiológicas. Instituto de Fisiología y Biofísica B. Houssay (IFIBIO-Houssay) UBA-CONICET.; Laboratorio de Investigaciones en Fisiología Renal*

6. *Universidad de Buenos Aires, Facultad de Medicina, Instituto de Investigaciones Médicas A. Lanari / 2Universidad de Buenos Aires, Facultad de Medicina, Instituto de Investigaciones Médicas, Consejo Nacional de Investigaciones Científicas y Técnicas (IDIM UBA-CONICET) / 3Universidad de Buenos Aires, Facultad de Medicina, Departamento de Ciencias Fisiológicas. Instituto de Fisiología y Biofísica B. Houssay (IFIBIO-Houssay) UBA-CONICET. Laboratorio de Investigaciones en Fisiología Renal. Buenos Aires, Argentina.; Laboratorio de Nefrología Experimental y Bioquímica Molecular / Laboratorio de Investigaciones en Fisiología Renal. Buenos Aires, Argentina.*
sandragvla@gmail.com

Previously, we presented a salt-sensitive hypertension (SSH) model in which ovariectomized (oVx) Wistar rats increased systolic blood pressure (SBP) after consuming a high sodium intake (HS) for more than 5 days. Animals exhibited altered renal expression of Na⁺-K⁺-ATPase (NKA) impairing ion handling. Immune system is also implicated in SSH development, so we studied NKA expression in peripheral blood lymphocytes (PBL) of oVx rats, supplemented with estrogen (E2) or progesterone (P4). Female rats were studied. At 60 days of age, half of the rats were oVx, and at 145 days, intact female (IF) and oVx rats were divided into NS (0.24% NaCl) or HS (1% NaCl in drinking water) subgroups. Simultaneously, oVx rats were supplemented with 17β-estradiol-3-benzoate (oVxNSE2 and oVxHSE2, 60 µg/kg), progesterone (oVxNSP4 and oVxHSP4, 10 mg/kg), or vehicle for three weeks. E2 supplementation, but not P4, normalized SBP and increased urinary sodium excretion in oVxHS. Blood counts showed an increase of total leukocytes and lymphocytes in oVx rats, and neutrophils only in oVx HS, which were reversed by E2. NKA expression was evaluated in lymphocytes (LTCD4+) by flow cytometry. The percentage of LTCD4+NKA+ decreased in oVxNS compared with IFNS, IFHS, and oVxHS. Reduction of NKA mean fluorescence intensity was observed in IFHS and oVx NS compared to IFNS, which was reversed by E2, but not by P4. In PBLs, the expression and activity of NKA are strongly regulated by female sex hormones. E2 supplementation stabilizes NKA expression in oVx groups, whereas P4 reduces NKA expression in oVxHS.

115. O6-04. NITRIC OXIDE INHIBITION IMPAIRED AQUAPORIN 4 EXPRESSION AND SHIGA TOXIN-2 INDUCED-TUBULAR CELL PROLIFERATION IN THE KIDNEY OF PREGNANT RATS

Lilian Karina Fischer Sigel¹, Agustina Presta², Elsa Zotta³, Claudia Silberstein⁴

1. *Universidad de Buenos Aires - CONICET. Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO Houssay), Facultad de Medicina, Departamento de Ciencias Fisiológicas. Buenos Aires, Argentina.; Laboratorio de Fisiología Renal.*

2. *Universidad de Buenos Aires - CONICET. Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO Houssay), Facultad de Medicina, Departamento de Ciencias Fisiológicas. Buenos Aires, Argentina.; IFIBIO*

3. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas. Cátedra de Fisiopatología. Universidad de Buenos Aires - CONICET. Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO Houssay), Facultad de Medicina, Departamento de Ciencias Fisiológicas. Buenos Aires, Argentina.; Laboratorio de Patología.*

4. *Universidad de Buenos Aires - CONICET. Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO Houssay),*

Facultad de Medicina, Departamento de Ciencias Fisiológicas. Buenos Aires, Argentina.; Laboratorio de Fisiología Renal.
kfischersigel@gmail.com

Previously we showed that a sublethal dose of Shiga toxin 2 (Stx2) caused minor renal injury in pregnant rats than in non-pregnant rats, and transient increased tubular cell proliferation, mainly in collecting ducts. Adaptive mechanisms during pregnancy involve increased nitric oxide (NO) production. The treatment of pregnant rats with L-NAME, a NO inhibitor, aggravated the tubular damage caused by Stx2. Besides, collecting ducts expresses Aquaporin 4 (AQP4), which participates in cell proliferation regulation in other tissues. Therefore, our work aimed to study whether NO and AQP4 are implicated in Stx2 induced-renal tubule cell proliferation in the kidney of pregnant rats. Pregnant Sprague-Dawley rats, at day 8 of gestation, were intraperitoneally injected with a sublethal dose of Stx2 (0.5ng/g body weight) (PS) or eluent (PC). Some rats were treated with L-NAME (1 mg/ml) in drinking water from 1 day prior to 4 days post-injection with Stx2 (PSL) or eluent (PCL). At 4 days post-injection, renal tubular AQP4 and Ki67 (proliferation marker) expression and NO serum levels were evaluated. Stx2 caused Ki67 increase and AQP4 down-regulation in renal tubules of PS compared to PC rats ($p < 0.05$). L-NAME treatment decreased NO serum levels of PCL and PSL rats compared to both PC and PS rats ($p < 0.05$). NO inhibition significantly potentiated AQP4 reduction caused by Stx2 and impaired Stx2-induced Ki67 tubular expression in collecting tubules of PSL rats. In conclusion, NO and AQP4 may participate in the renal collecting duct epithelial proliferation and repairing in response to the injury caused by Stx2.

116. O6-05. RENAL EFFECT OF CONCOMITANT ADMINISTRATION OF LITHIUM AND AMILORIDE

Gabriel Casas¹, Ana Uceda², Verónica D'Annunzio³, Elsa Zotta⁴, Néstor Lago⁵, Diego Martino⁶, Georgina Ossani⁷

1. University of Buenos Aires; Department of Pathology, School of Medicine

2. University of Buenos Aires; Department of Pathology, School of Medicine

3. University of Buenos Aires; Institute of Cardiovascular Physiopathology, Department of Pathology and Institute of Biochemistry and Molecular Medicine (IBIMOL UBA-CONICET), School of Medicine

4. University of Buenos Aires; Faculty of Pharmacy and Biochemistry. Department of Biological Sciences, Chair of Pathophysiology

5. University of Buenos Aires; Department of Pathology, School of Medicine

6. Favaloro University; Institute of Cognitive and Translational Neuroscience (INCYT), INECO Foundation

7. University of Buenos Aires; Department of Pathology, School of Medicine
gcasas@fmed.uba.ar

Lithium (Li) remained the gold standard in the treatment of bipolar disorder. There is evidence that the prevalence of CKD is higher in patients treated with Li than in general population. Cortical collecting tubules appear to be the primary target of Li-toxicity. Principal cells have the epithelial sodium channel (ENaC), which has high affinity for sodium and even greater for Li. Amiloride acts by blocking ENaC. The aim of this study was to evaluate whether concomitant administration of lithium and amiloride can attenuate Li-induced renal damage. Twenty-four rats were randomized into three groups: control group (CoG) fed powered standard diet (PSD) for 3 months; and two experimental groups (LiG and LiAG), fed PSD supplemented with lithium-carbonate (60 mmol of Li/kg diet) for 3 months; LiAG was also supplemented with amiloride in drinking water. Lithemias were within therapeutic range throughout the entire experiment. Serum creatinine (SCr) was significantly higher ($p < 0.011$) in LiG (0.72 ± 0.18) than in CoG (0.55 ± 0.06) and LiAG (0.53 ± 0.07) after 3 months of treatment, and Creatinine Clearance (CrCl) was significantly lower ($p < 0.007$) in LiG (1.43 ± 0.46) versus CoG (2.44 ± 0.43); with no significant differences between LiAG (1.98 ± 0.62) and the

other groups. LiG and LiAG showed damage of cortical collecting tubules, evidenced as dilatation and hypertrophy of the lining epithelium compared to controls. We found no significant differences in hypertrophy between LiG and LiAG, but dilatation was greater in LiAG. Coadministration of lithium and amiloride improves renal function, with no significative morphological differences.

117. O6-06. RELATIONSHIP BETWEEN THE NUMBER OF URINARY EXTRACELLULAR VESICLES (UEV) AND THEIR CYCLIC ADENOSINE MONOPHOSPHATE (cAMP) CONTENT IN THE PROGRESSION OF AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD)

Maria Lucia Rosenberg¹, Agustín Yaneff², Bruno Ezequiel Branca³, Natalia Elizabeth Riera⁴, Juan Ignacio Tortoriello⁵, Jorge Eduardo Toledo⁶, Carlos Alberto Davio⁷, Elisabet Mónica Oddo⁸, Roxana Noemí Peroni⁹, Pablo Javier Azurmendi¹⁰

1. Instituto de Investigaciones Médicas Alfredo Lanari, Facultad de Medicina, UBA; IDIM (UBA - CONICET), Buenos Aires, Argentina; Div. Nefrología Experimental y Bioquímica Molecular

2. Instituto de Investigaciones Farmacológicas (ININFA, UBA-CONICET), Buenos Aires, Argentina; Laboratorio de Farmacología y Oncología Molecular

3. Instituto de Investigaciones Médicas Alfredo Lanari, Facultad de Medicina, UBA; IDIM (UBA - CONICET), Buenos Aires, Argentina; Div. Nefrología Experimental y Bioquímica Molecular

4. Instituto de Investigaciones Médicas Alfredo Lanari, Facultad de Medicina, UBA; IDIM (UBA - CONICET), Buenos Aires, Argentina; Div. Nefrología Experimental y Bioquímica Molecular

5. Instituto de Investigaciones Médicas Alfredo Lanari, Facultad de Medicina, UBA; IDIM (UBA - CONICET), Buenos Aires, Argentina; Div. Nefrología Experimental y Bioquímica Molecular

6. Instituto de Investigaciones Médicas Alfredo Lanari, Facultad de Medicina, UBA; IDIM (UBA - CONICET), Buenos Aires, Argentina; Div. Nefrología Experimental y Bioquímica Molecular

7. Instituto de Investigaciones Farmacológicas (ININFA, UBA-CONICET), Buenos Aires, Argentina; Laboratorio de Farmacología y Oncología Molecular

8. Instituto de Investigaciones Médicas Alfredo Lanari, Facultad de Medicina, UBA; IDIM (UBA - CONICET), Buenos Aires, Argentina; Div. Nefrología Experimental y Bioquímica Molecular

9. Instituto de Investigaciones Farmacológicas (ININFA, UBA-CONICET), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Cátedra de Farmacología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Buenos Aires, Argentina.; Laboratorio de Farmacología de Transportadores de Drogas II.

10. Instituto de Investigaciones Médicas Alfredo Lanari, Facultad de Medicina, UBA; IDIM (UBA - CONICET), Buenos Aires, Argentina; Div. Nefrología Experimental y Bioquímica Molecular

luciarosenberg@gmail.com

ADPKD progression has been associated with increased cAMP in uEV. However, it remains unclear whether this reflects higher intravesicular concentration or increased uEV quantity. This analysis explores both variables and their relationship with ADPKD progression. As cAMP is stimulated by ADH, we also assessed their potential influence on uEV content. Ten midstream first morning urine samples were analysed. The uEV was isolated by ultracentrifugation method. cAMP was quantified by the radioligand binding method. Nanotracking particle analysis assessed uEV size and concentration. Cr and osmolality (Osm) were measured via standard methods. Copeptin, surrogate ADH biomarker, was quantified by ELISA. Estimated glomerular filtration rate (eGFR) was determined by the MDRD-4 formula, and total kidney volume (TKV) was obtained through imaging studies. The uEV concentration was 2.2×10^8 ($3 \times 10^7 - 9 \times 10^8$) particles/mL.

eGFR averaged 59 ± 11 ml/min/1.73 m², and TKV was 1.0 ± 0.2 L/m. uEV/mL correlated with both uEV/mg Cr ($R=0.89$, $p=0.001$) and uEV/mOsm/KgH₂O ($R=0.86$, $p=0.001$). It also showed an association with eGFR ($R=0.75$, $p=0.013$) and a negative trend with TKV. The cAMP content did not correlate with the uEV number, nor with Cr or Osm excretion. The cAMP was 4.5 ± 1.9 pmol/10⁶uEV, showing a tendency to correlate with TKV ($R=0.71$, $p=0.075$), but not with eGFR. Copeptin was not associated with cAMP in uEV or the amount of uEV. These findings suggest that uEV amount is associated with GFR, as well as Cr and osmolyte excretion. Increasing renal volume may be accompanied by elevated intravesicular cAMP alongside decreased uEV excretion. Further research is needed to verify these observations.

POSTERS 7 - SAIC - ONCOLOGÍA 2

DATE & TIME: 18/11/2025 9:00 - 10:30 H

Chairs: Romina Armando, Luciana Cañonero, Giselle Ripoll

118. P7-01. OXALIPLATIN RESISTANCE INDUCED BY PTHrP IN COLORECTAL CANCER: STUDY IN CELL AND ANIMAL MODELS

Cintia Birkenstok¹, Pedro Carriere², María Belén Novoa Diaz³, Graciela Gigola⁴, Luis Gómez⁵, Ariel Zwenger⁶, Claudia Gentili⁷

1. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)
 2. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)
 3. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)
 4. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)
 5. Departamento de Biología, Bioquímica y Farmacia, UNS, Bahía Blanca, Argentina. Departamento de Ciencias de la Salud, UNS, Bahía Blanca.; INBIOSUR (CONICET-UNS)
 6. Grupo Oncológico Cooperativo del Sur (GOCS), Santiago de Chile, Chile.
 7. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)
- cintia.birkenstok@uns.edu.ar

The tumor microenvironment (TM) participates in the chemoresistance in colorectal cancer (CRC). We previously observed that parathyroid hormone-related peptide (PTHrP), present in the TM, induces events associated with the aggressive behavior of CRC cells. The aim of this work is to study through in vitro and in vivo models whether PTHrP mediates the communication between CRC cells and their TM to promote chemoresistance to oxaliplatin, a drug used in CRC. Employing viability assays, we observed that PTHrP, directly or indirectly through endothelial cells from TM, induces chemoresistance to oxaliplatin in HCT-116 cells, derived from human CRC. Next, we evaluated the effect of PTHrP on resistance to oxaliplatin in HCT-116 cell xenografts generated in N:NIH(S)_nu mice. In contrast to our in vitro observations, no statistical differences were observed between control and PTHrP groups under oxaliplatin treatment, at least during the time of the assay. Furthermore, we found that PTHrP decreases the sensitivity to oxaliplatin of CT-26 murine intestinal tumor cells. Based on these results, we decided to conduct an in vivo assay using Balb/c mice with CT-26 cell tumors. In this syngeneic model we found that PTHrP not only attenuates the effect of oxaliplatin but also increases the levels of the pro-tumor factor β -catenin even under the action of the cytostatic, according to immunohistochemistry analysis. Taken together, these results provide evidence that PTHrP may promote resistance to oxaliplatin both in vitro and in vivo models.

119. P7-02. A THEORETICAL MODEL OF TUMOR GROWTH

AND REJECTION: DIFFERENTIAL IMMUNE CELL DYNAMICS IN CBI AND CBI- MOUSE STRAINS

Antonela Del Giudice¹, Matías Fusini², M. Celeste³, O. Graciela⁴, Viviana R. Rozados⁵, Rico María José⁶, Mainetti Leandro E⁷

1. Facultad de Ciencias Médicas Universidad Nacional de Rosario; Instituto de Genética Experimental, CONICET
 2. Facultad de Ciencias Médicas Universidad Nacional de Rosario.; Instituto de Genética Experimental
 3. Facultad de Ciencias Médicas Universidad Nacional de Rosario; Instituto de Genética Experimental
 4. Facultad de Ciencias Médicas Universidad Nacional de Rosario. CIC-UNR. CONICET; Instituto de Genética Experimental
 5. Facultad de Ciencias Médicas Universidad Nacional de Rosario. CONICET; Instituto de Genética Experimental
 6. Facultad de Ciencias Médicas Universidad Nacional de Rosario. CONICET; Instituto de Genética
 7. Facultad de Ciencias Médicas Universidad Nacional de Rosario. CONICET; Instituto de Genética Experimental
- adelgiudice.papaolo@gmail.com

M-406 is a triple-negative mammary adenocarcinoma that arose spontaneously in a female CBI mouse. CBI mice share the heterozygous haplotype H2/H2, while CBI- mice were obtained by artificial selection based on body conformation. Subcutaneous inoculation of M-406 in CBI induces exponential tumor growth in 100% of animals, whereas in CBI- the tumor shows brief growth and is subsequently eliminated in all cases. To investigate the immune mechanisms involved, CBI and CBI- females (N=6) were inoculated with M-406. Tumor and blood samples were collected during the growth phase in both strains and during escape (CBI) or elimination (CBI-). Histomorphological analyses were performed, and circulating and intratumoral CD4+, CD8+, Treg, and Th17 cells were quantified by flow cytometry. During growth in CBI-, a higher number of intratumoral eosinophils, macrophages, mast cells, and greater vascularization were observed compared with CBI. Circulating Treg cells were higher in CBI ($P=0.0005$), while CD8+ cells were reduced ($P=0.0172$). In tumor infiltrates, Treg cells were lower in CBI- ($P=0.0043$), whereas CD4+ ($P=0.0022$) and CD8+ ($P=0.0260$) were higher. During elimination in CBI-, more intratumoral histiocytes were found, with lower Treg ($P=0.0043$) and higher CD4+ ($P=0.0087$) and CD8+ cells ($P=0.0043$) compared with CBI. These findings indicate that increased infiltration of eosinophils, macrophages, mast cells, and CD8+ lymphocytes, along with reduced Treg cells, promotes an immune microenvironment that facilitates tumor rejection in CBI-. This model provides valuable insight into tumor susceptibility and rejection mechanisms, supporting future therapeutic strategies against triple-negative breast cancer.

120. P7-03. TUMOR MICROENVIRONMENT AND STROMAL CONTRIBUTION TO CHEMORESISTANCE IS MODULATED BY DYNAMIC TUMOR-STROMAL CELLS INTERACTION

Jimena Soledad Dominguez¹, Matias Eduardo Rizzo², Gastón Ignacio Angelini Marquiani³, Matias Valenzuela Alvarez⁴, Marcela Fabiana Bolontrade⁵

1. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB); Laboratorio de Procesos Remodelativos y Nichos Celulares
 2. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB); Laboratorio de Procesos Remodelativos y Nichos Celulares
 3. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB); Laboratorio de Procesos Remodelativos y Nichos Celulares
 4. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB); Laboratorio de Procesos Remodelativos y Nichos Celulares
 5. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB); Laboratorio de Procesos Remodelativos y Nichos Celulares
- jimena.jsd@gmail.com

Osteosarcoma (OS) is a malignant bone tumor most frequent in children, adolescents and young adults with stagnant five-year survival rates of 15-30% for patients with lung metastases. While advances in chemotherapy have improved overall outcomes, resistance mechanisms remain poorly understood. We previously demonstrated that fibroblast secretome increased OS cells sensitivity to doxorubicin in both metastatic (LM7) and non-metastatic (SAOS2) cells. Identifying the modulatory effects exerted by tumor cells on their own microenvironment, will be helpful since non-tumoral stromal cells play a critical role in shaping the response to chemotherapeutic treatment. To this end, we determined the IC50 of stromal cells against doxorubicin, under naive or modulated conditions, simulating the tumor microenvironment. Fibroblasts exposed to doxorubicin showed resistance after 2hs (4,52 $\times$ 10⁻⁶mM), and 24hs (6,10 $\times$ 10⁻⁵mM) of treatment. However, after 48hs of exposure (7,06 $\times$ 10⁻⁷mM), fibroblasts became markedly more sensitive to doxorubicin, with IC50 values decreasing by almost one order of magnitude compared to 24 hs. Interestingly, when fibroblast cells were challenged to doxorubicin under OS cells modulation, the IC50 increased 4,73 (LM7) and 5,79 (SAOS2) times after 2hs, and 2,93 (LM7) and 2,21 (SAOS2) times after 24hs, in comparison to naive fibroblasts exposed to doxorubicin. However, at 48hs a significant decrease in the IC50 was observed (~9-fold, LM7 and 5-fold, SAOS2), suggesting that tumor-derived factors may initially induce adaptive mechanisms that protect fibroblasts from drug toxicity but, over time, could trigger delayed vulnerability, ultimately enhancing their susceptibility to doxorubicin.

121. P7-04. CHARACTERIZATION OF THE HYPOXIC TUMOR MICROENVIRONMENT CONDITIONS DURING EARLY GROWTH OF THE TRIPLE-NEGATIVE MURINE MAMMARY ADENOCARCINOMA M-406

Martínez, M. Itati¹, Fusini, Matías E.², Lanternier, Marina³, Sand, Lucio⁴, Rozados, Viviana R.⁵, Scharovsky O. Graciela⁶, Mainetti, Leandro E.⁷, Rico, María José⁸

1. Instituto de Genética Experimental - FCM - UNR; Instituto de Genética Experimental
 2. Cátedra de Histología y Embriología - Instituto de Genética Experimental - FCM - UNR; Instituto de Genética Experimental
 3. Cátedra de Histología y Embriología - Instituto de Genética Experimental - FCM - UNR; Instituto de Genética Experimental
 4. Instituto de Genética Experimental - FCM - UNR; Instituto de Genética Experimental
 5. Instituto de Genética Experimental - FCM - UNR; Instituto de Genética Experimental
 6. Instituto de Genética Experimental - FCM - UNR; Instituto de Genética Experimental
 7. Instituto de Genética Experimental - FCM - UNR. CONICET; Instituto de Genética Experimental
 8. Instituto de Genética Experimental - FCM - UNR. CONICET; Instituto de Genética Experimental
- itatimartmart22@gmail.com

Hypoxia is one of the hallmarks of tumorigenesis and shapes the tumor microenvironment (TME). Eosinophil granulocytes (Eo) have been reported to exert emerging antitumor activity. M-406 is a spontaneous tumor derived from the CBI mouse inbred line. To characterize hypoxia-related conditions within the TME during its early growth phase, female CBI mice were challenged s.c. (n=15) with M-406 tumor (day 0). Tumors were sampled on days 3, 5, and 7 (n=5/day), fixed in 10% formalin, and embedded in paraffin. The number of HIF-1 α cells, percentage area (%) of α -SMA+ cells, Collagen deposition, Tumor Vascular Mimicry (TVM), and a histomorphological features of vascular architecture were determined. M-406 exhibited exponential tumor volume growth and, from day 3 to day 7, showed a significant increase in the n° of tumor Mitosis/field, HIF-1 α cells, % of α -SMA+ cells and Collagen (P<0.01). In contrast, a significant decrease was observed in the n° of Eo (P<0.05) and CD8+ T cells/field (P<0.01). On day 3, tumor vasculature exhibited continuous endothelial lining and pericyte coverage, on day 7 it displayed a thin,

discontinuous endothelium lacking pericytes. An increase in TVM was observed across all comparison days (P<0.0001). HIF-1 α expression was positively correlated with α -SMA+ area (P<0.01), Mitosis, Collagen content and, TVM density (P<0.0001) while correlating negatively with Eo (P<0.01) and CD8+ T cells (P<0.0001). In conclusion, M-406 tumor is characterized by an early proliferative state with reduced antitumor activity, accompanied by a hypoxic TME with stromal fibrosis, primitive and unstable vasculature, and a compensatory increase in TVM.

122. P7-05. CHARACTERIZATION OF THE LT1 LUNG TUMOR MODEL AND ESTABLISHMENT OF ITS LLT1 CELL LINE
Marianela Abrigo¹, María de las Nieves Pelagatti², Marianela Vence³, Noelia Paola Cardozo⁴, Erica Rojas Bilbao⁵, Yanina Verónica Langle⁶

1. Instituto de Oncología Ángel H. Roffo, Facultad de Medicina, Universidad de Buenos Aires.; Departamento de Bioterapia y Cáncer Experimental, Área Investigación.
 2. Instituto de Oncología Ángel H. Roffo, Facultad de Medicina, Universidad de Buenos Aires.; Departamento de Bioterapia y Cáncer Experimental, Área Investigación.
 3. Instituto de Oncología Ángel H. Roffo, Facultad de Medicina, Universidad de Buenos Aires.; Departamento de Bioterapia y Cáncer Experimental, Área Investigación.
 4. Instituto de Oncología Ángel H. Roffo, Facultad de Medicina, Universidad de Buenos Aires.; Departamento de Bioterapia y Cáncer Experimental, Área Investigación.
 5. Instituto de Oncología Ángel H. Roffo, Facultad de Medicina, Universidad de Buenos Aires.; Departamento de Anatomía-Patológica, Área Diagnóstica.
 6. Instituto de Oncología Ángel H. Roffo, Facultad de Medicina, Universidad de Buenos Aires.; Departamento de Bioterapia y Cáncer Experimental, Área Investigación.
- marianela.abrigo@gmail.com

Background: Lung cancer is the leading cause of cancer-related mortality worldwide and remains a major health burden. Reliable animal and cellular models are essential to study its biology. Methods: A spontaneous lung tumor (LT1) was detected in a 14-month-old male BALB/c mouse from the Roffo Institute colony (2023). LT1 was characterized through serial syngeneic transplants, assessment of tumor growth, histopathology, hematology, and immunohistochemistry. A derived cell line (LLT1) was established by mechanical dissociation under sterile conditions. Results: Subcutaneous transplants in male and female mice achieved a 97% tumor incidence with a latency of 12.15 $\pm$ 5 days. Tumors exceeding 500 mm³ displayed necrosis, hemorrhage, and serous content; therefore, the experimental endpoint was set at 171.5 mm³. No sex-related differences were observed in tumor size, kinetics, or metastasis rate (4%). Hematological parameters (cell counts and differential leukocyte formula) remained unchanged between baseline and endpoint. Histological analysis identified LT1 as a well-differentiated adenocarcinoma. Immunohistochemistry confirmed pulmonary origin (TTF1 positive, PAX8 negative). LLT1 cells showed stable and homogeneous growth over multiple passages, confirming successful establishment of the cell line. Conclusion: LT1 constitutes a reproducible murine model of well-differentiated lung adenocarcinoma. The derived LLT1 cell line offers a complementary in vitro platform for molecular and functional studies. Together, these models expand the available tools for preclinical lung cancer research.

123. P7-06. CHARACTERIZATION OF A NEW CISPLATIN-RESISTANT CELL LINE DERIVED FROM NON-SMALL LUNG CANCER (NSCLC) CELL LINE NCI-H125

Andrés Bechis¹, Brítez Neira, Diego Javier², Lizeth Aixa Ariza Bareño³, Cañonero Luciana⁴, Antonella Clara Pastini⁵, María Alejandra Dagrosa⁶, Alejandro Jorge Urtreger⁷, Laura Beatriz Todaro⁸

1. Instituto de Oncología "Ángel H. Roffo"; Departamento de Biología Celular
2. Instituto de Oncología "Ángel H. Roffo"; Departamento de Biología Celular

3. Instituto de Oncología "Ángel H. Roffo"; Departamento de Biología Celular
 4. Instituto de Oncología "Ángel H. Roffo"; Departamento de Biología Celular
 5. Instituto de Oncología "Ángel H. Roffo"; Centro Oncológico de Medicina Nuclear
 6. Instituto de Oncología "Ángel H. Roffo"; Centro Oncológico de Medicina Nuclear
 7. Instituto de Oncología "Ángel H. Roffo"; Departamento de Biología Celular
 8. Instituto de Oncología "Ángel H. Roffo"; Departamento de Biología Celular
- andy_bechis@hotmail.com

Cisplatin (CDDP) is a non-small cell lung cancer (NSCLC) standard therapy. The frequent resistance acquisition to this treatment would be associated with the presence of cancer stem cells (CSC). The aim of this study is to develop a CDDP-resistant cell line as an important tool to study the mechanisms involved in resistant human lung tumors. To generate the H125 CDDP-resistant cell line (H125cpr), we treated parental H125 with CDDP 1 μ M in 72h weekly pulses for 12 weeks. Then, we escalate the treatment dose to 2 μ M. After 32 weeks, H125cpr showed an IC50 of 6 μ M vs 1.5 μ M IC50 of H125ct (control cell line without treatment). We observed that CDDP treatment induces cell cycle arrest in G2-M phase as well as an increase in cell size and complexity only in H125ct. Besides, we observed that H125cpr has a lower migratory capability and CDDP treatment causes a decrease in their adhesive capacity. Regarding CSC, H125cpr shows not only higher clonogenicity but also a higher growth rate of their oncospheres respect H125ct. Finally, we performed an in vivo experiment in nude mice. We found that only H125ct subcutaneous tumors were sensitive to CDDP treatment, reducing tumoral volume. The latency was 5 days and 100% of the mice developed tumors in both experimental models. Taking all together, we hypothesize that H125cpr has higher proportion cells with a phenotype more stem-like than H125ct. Besides, we propose this new model to evaluate mechanisms involved in CDDP-resistance not only in vitro but also in vivo.

124. P7-07. DISRUPTING TUMOR STEMNESS AND BONE ARCHITECTURE IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER VIA FGFR INHIBITION

Agustina Sabater¹, Pablo Sanchis², Juan Bizzotto³, Jun Yang⁴, Peter Shepherd⁵, Jiabin Dong⁶, Elba Vazquez⁷, Christopher Logothetis⁸, Paul Corn⁹, Geraldine Gueron¹⁰, Estefania Labanca¹¹

1. 1Department of Genitourinary Medical Oncology and the David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center; Laboratorio de Inflamación y Cáncer, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), CONICET-Universidad de Buenos Aires; Instituto de Tecnología (INTEC), Universidad Argentina de la Empresa (UADE); Laboratorio de Inflamación y Cáncer
2. 1Department of Genitourinary Medical Oncology and the David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center; Laboratorio de Inflamación y Cáncer, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), CONICET-Universidad de Buenos Aires; Instituto de Tecnología (INTEC), Universidad Argentina de la Empresa (UADE); Laboratorio de Inflamación y Cáncer
3. 2Laboratorio de Inflamación y Cáncer, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), CONICET-Universidad de Buenos Aires; Instituto de Tecnología (INTEC), Universidad Argentina de la Empresa (UADE); Laboratorio de Inflamación y Cáncer

4. 1Department of Genitourinary Medical Oncology and the David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center.; Laboratorio of Prostate Cancer Models
 5. 1Department of Genitourinary Medical Oncology and the David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center.; Laboratorio of Prostate Cancer Models
 6. 1Department of Genitourinary Medical Oncology and the David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center.; Laboratorio of Prostate Cancer Models
 7. 2Laboratorio de Inflamación y Cáncer, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), CONICET-Universidad de Buenos Aires.; Laboratorio de Inflamación y Cáncer
 8. 1Department of Genitourinary Medical Oncology and the David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center.; Laboratorio of Prostate Cancer Models
 9. 1Department of Genitourinary Medical Oncology and the David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center.; Laboratorio of Prostate Cancer Models
 10. 2Laboratorio de Inflamación y Cáncer, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), CONICET-Universidad de Buenos Aires.; Laboratorio de Inflamación y Cáncer
 11. 1Department of Genitourinary Medical Oncology and the David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center.; Laboratorio of Prostate Cancer Models
- asabater@qb.fcen.uba.ar

There are no curative therapies for castration-resistant prostate cancer (CRPC) bone metastases. Fibroblast growth factor receptor (FGFR) is overexpressed upon arrival of tumor cells to the bone, promoting cancer stemness and therapy resistance. We previously showed that Dovitinib, a non-specific FGFR inhibitor, disrupts tumor-bone crosstalk. Here we evaluated erdafitinib, an FDA approved pan-FGFR inhibitor, for bone metastatic prostate cancer (PCa). In vitro, erdafitinib altered PCa spheroids stem-like morphology (area, circularity, solidity, Feret's diameter; $p < 0.05$). Cell viability assays of PCa cells revealed differential sensitivity to erdafitinib: C42b were highly resistant (IC50: 4336nM), 22Rv1 and DU145 moderately responsive (1950nM and 1899nM, respectively), and PC3 more sensitive (585.5nM), with increased resistance upon FGFR1-isoforms overexpression (α : 2508nM; β : 4896nM). MC3T3, pre-osteoblasts, exhibited the highest sensitivity (49.75nM), independent of FGFR1 modulation. In tumor-free mice, erdafitinib (12.5mg/kg BID, 21 days) altered bone architecture (μ CT, bone histomorphometry). In mice with intrafemoral PCa patient-derived xenografts (MDA-PCa-PDX), bone mineral density and volume were significantly reduced in treated contralateral tumor-free and FGFR1-low tumor-bearing femurs. MRI revealed a 40% tumor reduction in FGFR1-high tumors ($p < 0.05$), without significant osseous changes. Lastly, our pilot clinical study (NCT04754425) showed bone metastasis reductions in 20% of erdafitinib-treated CRPC patients, with decreased alkaline phosphatase but unchanged PSA, indicating bone-microenvironment targeting. Overall, FGFR inhibition may disrupt the tumor-bone interplay by modulating tumor stemness and bone remodeling, creating a less permissive metastatic niche. These findings support erdafitinib as a promising therapeutic strategy for PCa bone metastasis. Future work will identify responsive PCa patient subsets and explore combination therapies.

125. P7-08. EFFECT OF CDK2 INHIBITORS TREATMENT ON CELL PROLIFERATION AND CELL CYCLE IN AN EXPERIMENTAL LUMINAL BREAST CANCER MODEL

Pedro Villagra Delgado¹, Lucía Vottero², Claudia Lanari³, Victoria Fabris⁴

1. Instituto de Biología y Medicina Experimental; Carcinogénesis Hormonal

2. Instituto de Biología y Medicina Experimental; Carcinogénesis Hormonal

3. Instituto de Biología y Medicina Experimental; Carcinogénesis Hormonal

4. Instituto de Biología y Medicina Experimental; Carcinogénesis Hormonal

pjoaquinvilla@gmail.com

Seventy percent of breast cancers express hormonal receptors and are treated with endocrine therapy, mainly targeting the estrogen receptor (ER) pathway. Progesterone receptor (PR) has also been explored as a therapeutic target and antiprogestins have been proposed to treat luminal breast carcinomas expressing higher levels of isoform A of PR (PRA) than isoform B (PRB). CDK4/6 inhibitors are used in combination with anti-estrogen therapy to treat metastatic ER+/HER2- tumors. However, cell cycle therapy resistance may appear mainly through the activation of CDK2 pathway. Thus, CDK2 inhibitors in combination with the standard therapy may be a therapeutic option. The aim of our study is to evaluate the effect of the CDK2 inhibitors Roscovitine (Rosco) and Dinacliclib (Dina) in T47D cells and variants that express PRA (T47D-YA) or PRB (T47D-YB) isoforms. Both inhibitors diminish cell proliferation of the three T47D lines (IC50 Rosco 11-12 μ M; IC50 Dina 5-11 nM) and decrease RB1 phosphorylation ($p < 0.05$). Preliminary studies show a tendency of increased phospho-CDK2 in T47D-YA treated cells, while a decrease was observed in T47D-YB cells. Rosco 5 μ M and Dina 10 nM inhibited progesterone-induced cell proliferation in PRA expressing cells ($p < 0.05$; $p < 0.01$). The combined treatment of both inhibitors with the antiprogesterone mifepristone was more efficient to inhibit cell proliferation only in T47D-YA cells ($p < 0.05$). We conclude that Rosco and Dina would be effective in treating luminal breast carcinomas and the combination with mifepristone may be a therapeutic option in tumors expressing higher levels of PRA than PRB.

126. P7-09. STUDY OF S100A9 PROTEIN AS A POTENTIAL PROGNOSTIC AND PREDICTIVE BIOMARKER IN METASTATIC PROSTATE CANCER: PRELIMINARY RESULTS OF A PROSPECTIVE TRANSLATIONAL CLINICAL STUDY

Carolina Belén Iglesias¹, María Florencia Guerra², Alejandra Gabriela Bruke³, Francisco Stefano⁴, Eduardo Omar Sandes⁵, Yanina Verónica Langle⁶

1. Instituto de Oncología Ángel H. Roffo; Facultad de Medicina; Universidad de Buenos Aires.; Departamento de Bioterrio y Cáncer Experimental, Área Investigación.

2. Instituto de Oncología Ángel H. Roffo; Facultad de Medicina; Universidad de Buenos Aires.; Departamento de Clínica Oncológica, Área Médica.

3. Instituto de Oncología Ángel H. Roffo; Facultad de Medicina; Universidad de Buenos Aires.; Departamento de Laboratorio Central y Bacteriología, Área Diagnóstica.

4. Instituto de Oncología Ángel H. Roffo; Facultad de Medicina; Universidad de Buenos Aires.; Departamento de Bioterrio y Cáncer Experimental, Área Investigación.

5. Instituto de Oncología Ángel H. Roffo; Facultad de Medicina; Universidad de Buenos Aires.; Departamento de Biología Celular, Área Investigación.

6. Instituto de Oncología Ángel H. Roffo; Facultad de Medicina; Universidad de Buenos Aires.; Departamento de Bioterrio y Cáncer Experimental, Área Investigación.

iglesiascarolinab@gmail.com

Background: S100A9 is a calgranulin physiologically expressed in myeloid cells (granulocytes and monocytes). Its overexpression has been associated with several carcinomas, including prostate cancer (PCa). Prognostic and staging tools for PCa remain limited. We propose S100A9 as a potential biomarker to identify patients with poorer prognosis and/or treatment response. Objective: To evaluate S100A9 expression in peripheral blood myeloid cells from metastatic PCa (mPCa) patients and healthy controls. Methods:

Peripheral blood samples were collected from 20 mPCa patients (20 baseline, 9 at 3 months treatment assessment) and 7 controls. Serum, plasma, and buffy coat fractions were obtained. Flow cytometry assessed S100A9 expression in granulocytes (CD15+S100A9+) and monocytes (CD14+S100A9+). Results: S100A9+ monocytes ranged from 1.2–5.6% in both, patients and controls, while most granulocytes expressed S100A9. Two distinct S100A9+ granulocyte subpopulations were identified: Middle High and Very High. Some individuals showed one subpopulation, while others showed both. S100A9+ monocytes appear to be increased in patients vs. controls. S100A9+ granulocytes Middle High subpopulation was significantly higher in patients compared to controls ($p = 0.026$). In patients, the Very High subpopulation displayed significantly increased S100A9 expression intensity at treatment assessment compared to baseline ($p = 0.003$). A decreasing trend in the percentage of S100A9+ granulocyte was observed after treatment. Conclusion: We established a method to evaluate S100A9 in monocytes and granulocytes from mPCa patients. For the first time, two S100A9+ granulocyte subpopulations were identified, potentially associated with disease presence and treatment. Larger cohorts will be required to validate these promising preliminary findings.

127. P7-10. RAC3-ASSOCIATED MICROBIOME SUPPORTS CANCER STEMNESS AND POOR COLORECTAL CANCER OUTCOMES

Juliana Lourdes Bernacchia¹, Alejandra Graciela Palma², Francisco Damián Rosa³, María Florencia Quintanilla⁴, Juan Nicolas Arán Bedia⁵, Ana Ludueña⁶, Adriana Noemí De Paulis⁷, Eugenia Bertona⁸, Melisa Fernández⁹, Oscar Laudano¹⁰, Mónica Vázquez-Levin¹¹, María Fernanda Rubio¹², Mónica Alejandra Costas¹³

1. IDIM - UBA - CONICET; Biología molecular y apoptosis

2. IDIM - UBA - CONICET; Biología molecular y apoptosis

3. IDIM - UBA - CONICET; Biología molecular y apoptosis

4. IDIM - UBA - CONICET; Biología molecular y apoptosis

5. IDIM - UBA - CONICET; Biología molecular y apoptosis

6. Instituto de Investigaciones Médicas A. Lanari; Unidad de breve estadía

7. Instituto de Investigaciones Médicas A. Lanari - Facultad de Medicina, UBA; Unidad de Microbiología

8. Instituto de Investigaciones Médicas A. Lanari - Facultad de Medicina, UBA; Unidad de Microbiología

9. Instituto de Investigaciones Médicas A. Lanari - Facultad de Medicina, UBA; Unidad de Microbiología

10. Instituto de Investigaciones Médicas A. Lanari - Facultad de Medicina, UBA; Unidad de Gastroenterología

11. Instituto de Biología y Medicina Experimental (IBYME), CONICET; Reproducción y Cáncer

12. IDIM - UBA - CONICET; Biología molecular y apoptosis

13. IDIM - UBA - CONICET; Biología molecular y apoptosis

jubernacchia@hotmail.com

We found that fecal bacteria from colorectal cancer (CRC) patients induced the increase in RAC3 expression (required to maintain de CSC population), NF- κ B nuclear translocation factor and tumor-spheres formation in HCT116 (high RAC3) and LoVo cells (low RAC3) respect to healthy samples ($p = 1.6$ (107 samples) medium -0.6 (205 samples) or low RAC3 < -0.6 log fold change values (117 samples). The community profile assessed through alpha and beta diversities, using Chao1, Shannon diversity measures, and Bray-Curtis index, respectively, shown that non-tumoral, and tumoral high, low and medium RAC3 corresponds to 4 different populations (PERMANOVA F-value: 2.93; R-squared: 0.017; p-value: 0.001 at genus taxa level, pairwise high vs. low $p < 0.008$). Core microbiome analysis ($\geq 20\%$ prevalence, $\geq 0.01\%$ abundance) showed the phylum Verrucomicrobia (Akkermansia genus) as the most increased in high RAC3 samples, that were associated with reduced disease-free survival (HR = 3.8, $p = 0.0132$), increased tumor burden, aneuploidy, genomic alterations, advanced metastasis stage ($p < 0.05$), upregulated Toll-like receptors and CSC markers and reduced mucin expression (MUC1, 2, 4, 5B and 6) ($p < 0.001$). Therefore, some microorganism signals may modulate the RAC3

levels in CRC cells and contribute to the change of microbiome diversity, CRC progression and a worse prognosis.

128. P7-11. BIOINFORMATIC STUDY OF PHENOMENA ASSOCIATED WITH RESISTANCE TO TARGETED THERAPIES IN MELANOMA

Yasmany González Garcés¹, Aylén Avila², Juliana Osorio³, Flavia Molinas⁴, Mauricio Menacho Márquez⁵

1. Facultad de Ciencias Médicas. Universidad Nacional de Rosario. CONICET.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB). IDICER.

2. Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).

3. Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).

4. Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).

5. Facultad de Ciencias Médicas. Universidad Nacional de Rosario. CONICET.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB). IDICER.
yasmagarcés@gmail.com

Cutaneous melanoma is among the most common and aggressive skin cancers in Argentina. A major challenge in clinical management is tumor resistance to targeted therapies, including BRAF, MEK, and MAPK inhibitors, which limits treatment efficacy. This study employed a bioinformatics approach to investigate mechanisms underlying resistance to these therapies in melanoma. Expression datasets GSE65185, GSE196434, and GSE214473 were obtained from the Gene Expression Omnibus, analyzed independently and combined into a single matrix. Differentially expressed genes (DEGs) were identified using the EdgeR package in R/Bioconductor. Over-representation analyses were conducted with Enrichplot and ClusterProfiler, followed by gene set enrichment analysis (GSEA) using GSEA software v4.0.2. Pathways enriched in the resistant phenotype included muscle contraction, actin filament and filopodia formation, and MET signaling, indicative of epithelial-mesenchymal transition and invasive potential. Immune activation pathways predominated in the sensitive phenotype, suggesting immune susceptibility of these tumors. GSEA further highlighted enrichment of Rho GTPase and cell division pathways in resistant cells. These results point to complex resistance mechanisms involving cytoskeletal remodeling and signaling adaptations. Importantly, RAC1, a Rho GTPase, emerged as a key player in resistance-associated pathways. Given these findings, future studies could explore RAC1 inhibition as a strategy to overcome resistance to targeted therapies in melanoma.

POSTERS 8 - SAIC - FIRST-TIME PRESENTERS 2

DATE & TIME: 18/11/2025 9:00 - 10:30 H

Chairs: Pablo Sanchis, Soledad Porte Alcon, Mariel Fusco, Rocío Seniuk

129. P8-01. CHARACTERIZATION OF TRANSCRIPTIONAL HETEROGENEITY OF THERAPEUTIC TARGETS FOR THE IDENTIFICATION OF PREDICTIVE BIOMARKERS IN B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA USING LONG-READ SEQUENCING

Lucila Viappiani¹, Marina Luz Ingravidi², Javier Cotignola³, Geraldine Gueron⁴, María Sol Ruiz⁵

1. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Buenos Aires C1428E-GA, Argentina; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química

Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina

2. Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina; Instituto de Biociencias, Biotecnología y Biología Translacional, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires

3. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Buenos Aires C1428E-GA, Argentina; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina

4. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Buenos Aires C1428E-GA, Argentina; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina

5. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Buenos Aires C1428E-GA, Argentina; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Laboratorio de Inflamación y Cáncer, Buenos Aires, Argentina

lucilaviappiani@outlook.com

Introduction: Immunotherapies targeting CD19, CD20, and CD22 have improved treatment outcomes in B-cell acute lymphoblastic leukemia (B-ALL). However, resistance can arise from isoform variations or epitope loss. Resolving full-length isoforms is crucial, as short-read RNA-seq only infers transcript structures indirectly. In this pilot study we characterized and quantified CD19, CD20, and CD22 isoforms using long-read sequencing (LRS). Materials and Methods: RNAs from two pediatric B-ALL patients were analyzed using whole-transcriptome (WTS) and amplicon sequencing (CD19, MS4A1 coding CD20) using Oxford Nanopore Technologies (ONT) and compared to Illumina RNA-seq. Bioinformatics: quality control (NanoPlot), filtering (Seqkit), alignment (Minimap2), quantification (Salmon, Oarfish, Minnow) and isoform discovery (FLAIR, IsoQuant). Results: We observed a moderate correlation ($r=0.53-0.59$) between ONT and Illumina quantification (20.335 and 14.341 transcripts, respectively). Despite 6–11x lower ONT depth, molecular classification based on gene-level quantification was concordant. Using Salmon, Illumina identified 9 MS4A1 isoforms, 5 for CD19, and 15–20 for CD22, while ONT detected 1–3 major isoforms per gene. Amplicon sequencing uncovered >10 novel MS4A1 isoforms with low frequencies (<2.8%), including isoforms skipping the exon coding for the antibody-binding domain. These isoforms were not identified by WTS, probably due to the low abundance. For CD19, we observed a short-isoform amplification bias in amplicon sequencing, limiting the sensitivity for identifying novel isoforms. Conclusion: LRS effectively detects full-length transcriptional isoforms with potential relevance for immunotherapy resistance in pediatric B-ALL. However, variability in quantification across technologies, tools and amplicon approaches highlights the need for further standardization and validation for translation to the clinics.

130. P8-02. ANTIMICROBIAL ACTIVITY OF FUNGAL EXTRACTS AGAINST FOODBORNE PATHOGENS

María Florencia Larroque¹, Gabriel A. de Diego², Laura B. C. Duverne³, Gabriela F. Rocha⁴, María José Formoso⁵, Jimena Mazieres⁶, Mauricio De Marzi⁷, María Eugenia Díaz⁸

1. Departamento de Ciencias Básicas, Universidad Nacional de Luján; Inmunología

2. Departamento de Ciencias Básicas, Universidad Nacional de Luján; Inmunología

3. Departamento de Tecnología, Universidad Nacional de Luján; Microbiología

4. Departamento de Ciencias Básicas, Universidad Nacional de Luján; Inmunología
 5. Departamento de Tecnología, Universidad Nacional de Luján; Microbiología
 6. Departamento de Tecnología, Universidad Nacional de Luján; Microbiología
 7. Departamento de Ciencias Básicas, Universidad Nacional de Luján; Inmunología
 8. Departamento de Ciencias Básicas, Universidad Nacional de Luján; Inmunología
- florlarroque15@gmail.com

Background: Given the increasing development of drug resistance in foodborne human pathogens, and in order to ensure food safety, the search for natural sources of antimicrobial compounds becomes essential. Fungi present great potential due to their diversity and unique bioactivity. **Aim:** To obtain aqueous extracts from edible fungi and evaluate their antibacterial activity against bacteria responsible for foodborne diseases. **Materials and Methods:** In order to prepare the aqueous extracts, fruiting bodies of *Agaricus bisporus*, *A. bisporus* var. *brunnescens*, *Pleurotus ostreatus*, and *Ganoderma lucidum* were lyophilized and homogenized in 50 mM phosphate buffer (pH 7) for one hour under cold or heat (100 °C) conditions. The antimicrobial activity of the extracts against the bacterial strains *Bacillus cereus*, *Escherichia coli* O157:H7, *Staphylococcus aureus*, and *Klebsiella pneumoniae* was assessed using the disk diffusion method. **Results** The growth of *S. aureus* was inhibited only by the cold extract of *A. bisporus*. Regarding *E. coli*, both cold extracts of *A. bisporus* and *A. bisporus* var. *brunnescens* showed inhibitory activity, with a larger inhibition halo observed for the *brunnescens* variety. Cold extracts of *A. bisporus*, *A. bisporus* var. *brunnescens*, and *P. ostreatus* inhibited the growth of *B. cereus*, with the strongest effect observed for *P. ostreatus*. Finally, the growth of *K. pneumoniae* was not inhibited by any of the extracts tested. **Conclusions:** The inhibitory activity observed in the fungal extracts against foodborne pathogens represents a promising advance for combating antimicrobial resistance and enhancing food safety.

131. P8-03. ANTICANCER ACTIVITY OF A NOVEL SERIES OF COPPER-HYDRAZONES COMPOUNDS OVER 2D AND 3D HUMAN OSTEOSARCOMA MODELS

Espindola Moreno Olivia¹, Santa Maria de la Parra Lucia², Fagner da Silva Moura³, Llanquileo Martin⁴, Lucia M. Balsa⁵, Nicolás A. Rey⁶, León Ignacio E.⁷

1. CEQUINOR (UNLP, CCT-CONICET La Plata, Asociado a CIC), Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata; Metalofármacos y Biología Tumoral
 2. CEQUINOR (UNLP, CCT-CONICET La Plata, Asociado a CIC), Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata; Metalofármacos y Biología Tumoral
 3. LABSO-Bio (CTC, PUC-Rio), Departamento de Química, Pontifícia Universidade Católica do Rio de Janeiro; Química Inorgânica
 4. CEQUINOR (UNLP, CCT-CONICET La Plata, Asociado a CIC), Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata; Metalofármacos y Biología Tumoral
 5. CEQUINOR (UNLP, CCT-CONICET La Plata, Asociado a CIC), Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata; Metalofármacos y Biología Tumoral
 6. LABSO-Bio (CTC, PUC-Rio), Departamento de Química, Pontifícia Universidade Católica do Rio de Janeiro; Química Inorgânica
 7. CEQUINOR (UNLP, CCT-CONICET La Plata, Asociado a CIC), Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata; Metalofármacos y Biología Tumoral
- espindolaoliviam00@gmail.com

Osteosarcoma is a frequent bone cancer, affecting largely chil-

dren and young adults. Cisplatin (CDDP) has been efficacious in the treatment of different types of cancer. However, platinum toxicity and acquired resistance to treatment promote the interest of researchers to explore new compounds. Copper-based drugs have been found to possess promising anti-tumor and anti-metastatic properties for many solid tumors, including osteosarcoma. This work aims to evaluate the antitumoral activity of a new series of copper(II) compounds with acylhydrazones in 2D and 3D human osteosarcoma models derived from the cell line MG-63. Using MTT assay, we demonstrated that all complexes significantly reduced MG-63 cell viability (IC50: Cu1: 1,76±0,11µM; Cu2L1: 0,81±0,09µM; CuL2: 2,23±0,11µM; Cu2L2: 1,20±0,02µM), while uncoordinated ligands (L1 and L2) were essentially inactive (IC50: L1>50 µM; L2>30µM), indicating that copper coordination is essential for the observed anticancer activity. Moreover, it is important to highlight that binuclear Cu complexes showed stronger antitumor effects than mononuclear complexes suggesting the importance of nuclearity of Cu in the design of new compounds with potential anticancer activity. Reactive oxygen species (ROS) generation was determined by oxidation of fluorescence dye DHR-123, evidenced that all complexes caused an increment in ROS production. MG-63 spheroids were cultured by the hanging drop technique and cell viability was determined via resazurin reduction assay (IC50: Cu1: 29,18±2,83µM; Cu2L1: 13,78±0,57µM; Cu2L2: 9,31±0,16µM), showing IC50 values significantly lower than CDDP (65,1±5,6µM). In summary, these copper complexes display a promising anticancer action on 2D and 3D human osteosarcoma models, supporting their potential as alternative therapeutic agents.

132. P8-04. DEVELOPMENT OF A GFP-BASED MINI-REPORTER TO INVESTIGATE THE REGULATORY ROLE OF THE 3'UTR IN WEST NILE VIRUS

Daniela Bailez¹, Valentina Capolicchio², Jimena Rada³, Gastón Pascual⁴, Javier Cotignola⁵, Geraldine Gueron⁶, Juan Manuel Carballeda⁷, Ayelen Toro⁸

1. IQUIBICEN-FCEN-UBA; Laboratorio de Inflamación y Cáncer
 2. IQUIBICEN-FCEN-UBA; Laboratorio de Inflamación y Cáncer
 3. IQUIBICEN-FCEN-UBA; Laboratorio de Inflamación y Cáncer
 4. IQUIBICEN-FCEN-UBA; Laboratorio de Inflamación y Cáncer
 5. IQUIBICEN-FCEN-UBA; Laboratorio de Inflamación y Cáncer
 6. IQUIBICEN-FCEN-UBA; Laboratorio de Inflamación y Cáncer
 7. Universidad de Hurlingham; Laboratorio de Virología Molecular
 8. IQUIBICEN-FCEN-UBA; Laboratorio de Inflamación y Cáncer
- bailezdaniela@gmail.com

West Nile virus (WNV) is a mosquito-borne flavivirus responsible for recurrent outbreaks in humans and equines. In 2024, more than 1,400 human cases were reported across 19 European countries, underscoring its persistent public health impact. WNV is primarily transmitted by *Culex* mosquitoes in an enzootic cycle with birds, while humans and equines act as incidental dead-end hosts. Infections in humans can progress to severe neuroinvasive disease, and no specific antiviral treatment is currently available. The WNV genome consists of a single-stranded, positive-sense RNA of approximately 11 kb, flanked by untranslated regions (UTRs). These highly structured regions are essential for replication, genome circularization, and host adaptation, yet their roles remain less characterized in WNV than in other flaviviruses. In particular, the 3'UTR contains conserved structural elements that may influence viral fitness and host responses. To investigate these functions, we developed a GFP-based mini-reporter system in which the 5' and 3'UTRs flank the GFP coding sequence under the control of a constitutive promoter. This vector will be evaluated in different cell lines, including BHK, A549 and Vero, to assess its regulatory potential and interaction with host factors. We believe this reporter system provides a versatile tool to study WNV 3'UTR-mediated regulation and its interplay with host factors.

133. P8-05. LONG-TERM EFFECTS OF DL-CHOLINE BITARTRATE SUPPLEMENTATION IN RATS: IMPLICATIONS OF STEREOISOMERISM FOR NUTRITIONAL SUPPLEMENTS

Luciana Sielecki¹, Gregorio Fariña², Camila Spagnuolo³, Ri-

cardo Orzuza⁴, Leonardo Cacciagiu⁵, Carola Bozal⁶, Gabriela Berg⁷, Nahuel Fernandez Machulsky⁸, Vanesa Macri⁹, Valeria Zago¹⁰

1. Universidad de Buenos Aires, Departamento de Bioquímica Clínica; Laboratorio de Lípidos y Aterosclerosis
 2. Universidad de Buenos Aires, Departamento de Bioquímica Clínica; Laboratorio de Lípidos y Aterosclerosis
 3. Universidad de Buenos Aires, Departamento de Bioquímica Clínica; Laboratorio de Lípidos y Aterosclerosis
 4. Universidad de Buenos Aires, Facultad de Odontología; Cátedra de Bioquímica General y Bucal
 5. Universidad de Buenos Aires, Facultad de Odontología; Cátedra de Bioquímica General y Bucal
 6. Universidad de Buenos Aires, Facultad de Odontología; Cátedra de Histología y Embriología
 7. Universidad de Buenos Aires, Departamento de Bioquímica Clínica; Laboratorio de Lípidos y Aterosclerosis
 8. Universidad de Buenos Aires, Departamento de Bioquímica Clínica; Laboratorio de Lípidos y Aterosclerosis
 9. Universidad de Buenos Aires, Facultad de Odontología; Cátedra de Bioquímica General y Bucal
 10. Universidad de Buenos Aires, Departamento de Bioquímica Clínica; Laboratorio de Lípidos y Aterosclerosis
- lsielecki@ffyb.uba.ar

Intestinal dysbiosis has been linked to cardiovascular disease, mediated by trimethylamine N-oxide (TMAO), among other factors. To investigate its impact on various metabolic pathways, an animal model supplemented with DL-choline bitartrate (DLCB), the precursor of TMAO, was developed. We aim to report incidental findings observed during the model set-up. Adult male Wistar rats were assigned to groups: control (C), high-fat and sucrose diet (HFSD), and HFSD supplemented with 0.5% (HFSD0.5) and 1.0% DLCB (HFSD1.0). Animals were fed ad libitum for 14 weeks, with body weight, caloric intake, and clinical signs monitored. Euthanasia was performed with sodium pentothal, blood samples for creatinine and lipid profile analysis and tissues for histological analysis were collected. $p < 0.05$ was considered significant. At sacrifice, HFSD1.0 (338±88g) weighed significantly less than HFSD (463±22g; $p = 0.006$), but no difference was observed versus C (426±27g) or HFSD0.5 (407±61g). Notably, bladder stones were found in all DLCB-supplemented rats, and three HFSD1.0 animals required humane euthanasia. Their kidneys exhibited inflammatory cells infiltration and fibrosis in the interstice space; and tubular damage with the presence of calcium deposits in the medullary region. A significant increase in total cholesterol was observed in the HFSD1.0 group compared to C, HFSD and HFSD0.5, as well as non-HDLc ($p < 0.05$). Creatinine levels showed a trend towards increase in the HFSD1.0 group (3.09 ± 2.70 mg/dL) compared with HFSD (0.39 ± 0.08 mg/dL; $p = 0.06$) and HFSD0.5 ($0.38 [0.29 - 1.36]$ mg/dL; $p = 0.06$). These findings indicate that DLCB supplementation, especially at 1.0%, is associated with renal impairment in male Wistar rats.

134. P8-06. MUSCARINIC RECEPTORS AS TARGETS OF METRONOMIC CHEMOTHERAPY IN MDA-MB468 TRIPLE-NEGATIVE BREAST CELLS

Fermín Echalecu¹, Guadalupe Weintraub², Alejandro Español³

1. Escuela ORT; Área de Química y Biotecnología
 2. Escuela ORT; Área de Química y Biotecnología
 3. CEFYBO-CONICET-UBA; Laboratorio de Inmunofarmacología Tumoral
- echalecufer@gmail.com

Breast cancer has the highest incidence and mortality rates among women. The triple negative (TN) subtype is typically treated with high doses of paclitaxel or doxorubicin. However, resistance to chemotherapy is a frequent problem, leading to the use of high doses of chemotherapeutics, which causes adverse effects. Searching for new therapies is key to improving antitumor treatments. Metronomic chemotherapy (MC) involves the continuous administration of low-dose chemotherapeutic agents, reducing adverse effects. Previously we demonstrated the efficacy of a MC with paclitaxel or doxorubicin

combined with the agonist of muscarinic acetylcholine receptor subtype2 (m2AChR) arecaidine in luminal breast cancer cells. By Western blot (Wb) and MTT we determined that TN MDA-MB468 cells express functional m2AChR, since the addition of arecaidine decreased viability in a concentration-dependent manner. By MTT we confirmed that these cells are sensitive to treatment with paclitaxel (EC50: 2.31×10^{-8} M) or doxorubicin (EC50: 2.99×10^{-7} M) and in the presence of the first effective concentration of arecaidine (10-5M) these curves shift to the left (EC50paclitaxel+arecaidine: 2.47×10^{-9} M; EC50doxorubicin+arecaidine: 7.58×10^{-8} M). The effects of metronomic combination of arecaidine (10-5M) with suboptimal concentrations of paclitaxel (10-9M) or doxorubicin (10-8M) reduced VEGF-A expression by Wb (paclitaxel+arecaidine: $22.3 \pm 2.0\%$ and doxorubicin+arecaidine: $22.0 \pm 1.4\%$) and tumor angiogenesis by TIA (vessels/mm²) (cells: 4.7 ± 0.2 ; paclitaxel+arecaidine: 2.9 ± 0.3 ; doxorubicin+arecaidine: 3.0 ± 0.2 , both $p < 0.001$ vs cells). We can conclude that the combinations studied exert their effect by activating m2AChR. This would induce lower expression of VEGF-A, resulting in decreased tumor angiogenesis, which would position these combinations as a valid option for breast cancer therapy.

135. P8-07. TRACKING CARDIOMYOCYTE PROLIFERATION IN A HUMAN INDUCED PLURIPOTENT STEM CELL-DERIVED DOUBLE-FLUORESCENT REPORTER LINE

Joaquín Etchepareborda¹, Joaquín Smucler², Lucía Moro³, Ariel Waisman⁴

1. Instituto de Neurociencias (INEU), CONICET, Buenos Aires, Argentina; Laboratorio de Investigación Aplicada a Neurociencias (LIAN) - FLENI
 2. Instituto de Neurociencias (INEU), CONICET, Buenos Aires, Argentina; Laboratorio de Investigación Aplicada a Neurociencias (LIAN) - FLENI
 3. Instituto de Neurociencias (INEU), CONICET, Buenos Aires, Argentina; Laboratorio de Investigación Aplicada a Neurociencias (LIAN) - FLENI
 4. Instituto de Neurociencias (INEU), CONICET, Buenos Aires, Argentina; Laboratorio de Investigación Aplicada a Neurociencias (LIAN) - FLENI
- joaco.etc@gmail.com

Adult mammalian cardiomyocytes are postmitotic and do not proliferate after cardiac injury, leading to fibrotic scar formation. However, postnatal mammals and certain model organisms like fish and newts retain cardiac regenerative capacity through cardiomyocyte proliferation. We hypothesized that postmitotic cardiomyocytes derived from human induced pluripotent stem cells (hiPSCs) can re-enter the cell cycle upon appropriate stimulation. Here, we engineered a double-fluorescent reporter hiPSC line combining H2B-emiRFP670 for nuclei tracking and FUCCI reporter (mVenus-hGeminin) for S/G2/M cell cycle phases using the PiggyBac transposon system. Stable clonal lines were generated through antibiotic selection. hiPSCs were differentiated into cardiomyocytes using the WNT ON/OFF methodology, confirmed by TNNT2 immunofluorescence and spontaneous beating. Cardiomyocytes were purified via lactate selection and matured until day 50. The double-reporter system successfully tracked cell cycle dynamics in both undifferentiated hiPSCs and in hiPSC-derived cardiomyocytes. Indeed, live imaging revealed proliferating cardiomyocytes at day 23 of differentiation. We next assessed treatment of temporally matured cardiomyocytes with pro-proliferative compounds CHIR99021 (GSK3 β inhibitor activating WNT signaling) and neuregulin, which have been shown to induce proliferation of cardiomyocytes in mice. After 72 hours of treatment, we observed a significant increase in the proportion of mVenus-positive cardiomyocytes in S/G2/M phases, demonstrating successful cell cycle re-entry. We developed a robust hiPSC-based platform enabling quantitative analysis of human cardiomyocyte proliferation. Our findings demonstrate that temporally mature hiPSC-derived cardiomyocytes can re-enter the cell cycle in response to specific stimuli, providing a valuable model for cardiac regenerative medicine research.

136. P8-08. TESTICULAR FEATURES IN DIVERSITY OUT-BRED OLD MICE UNDER LONG-TERM METFORMIN

TREATMENT

Micaela Rozenblum¹, Alina Cavallotti Gomez², Yun Zhu³, Johanna Gabriela Miquet⁴, Ricardo Saúl Calandra⁵, Andrzej Bartke⁶, Rong Yuan⁷, Mónica Beatriz Frungieri⁸

1. *Instituto de Biología y Medicina Experimental (IBYME), Fundación IBYME, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Ciudad de Buenos Aires, Argentina.; Neuro-inmuno-endocrinología testicular*

2. *Instituto de Biología y Medicina Experimental (IBYME), Fundación IBYME, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Ciudad de Buenos Aires, Argentina.; Neuro-inmuno-endocrinología testicular*

3. *Department of Internal Medicine, Southern Illinois University School of Medicine, Springfield, Illinois, USA*

4. *Departamento de Química Biológica, Facultad de Farmacia y Bioquímica e Instituto de Química y Físicoquímica Biológicas (IQUIFIB), UBA-CONICET, Buenos Aires, Argentina.*

5. *Instituto de Biología y Medicina Experimental (IBYME), Fundación IBYME, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Ciudad de Buenos Aires, Argentina.*

6. *Department of Internal Medicine, Southern Illinois University School of Medicine, Springfield, Illinois, USA.*

7. *Department of Internal Medicine, Southern Illinois University School of Medicine, Springfield, Illinois, USA.*

8. *Instituto de Biología y Medicina Experimental (IBYME), Fundación IBYME, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Ciudad de Buenos Aires, Argentina.; Neuro-inmuno-endocrinología testicular*
michaelarosenblum1@gmail.com

Although the antidiabetic drug metformin (Met) has been proposed as an anti-aging agent, its effects on the testis remain controversial. Earlier, we described that testicular aging in the Syrian hamster is associated with altered histology, oxidative stress and fibrosis. Unexpectedly, 2-month Met treatment in aged hamsters further increased these harmful changes. Now, we investigated the impact of long-term metformin supplementation in Diversity Outbred (DO) mice that received standard (std) diet or Met diet (0,1 % w/w) ad libitum from 2-month-old to 19-month-old. In 19-month-old DO mice, long-term metformin treatment did not affect non-fasted blood glucose levels, body and testicular weights, the gonadosomatic index, the number of seminiferous tubules/mm² [mean±S.E.M.,(n); std diet: 30.3±2.59,(10); Met diet: 30.9±3.15,(7), $p>0.05$] or tubular diameter [mean±S.E.M.,n; std diet: 224±7.75,(10); Met diet: 213±8.89,(7); $p>0.05$]. Oxidative stress and fibrosis (which include accumulation of collagen) are hallmarks in aging tissues. No diet-associated changes were seen in testicular lipid peroxidation [TBARS assay; nmol MDA/μg protein; mean±S.E.M.,(n); std diet: 383.6±37.0,(10); Met diet: 384.1±39.4,(8), $p>0.05$]. Instead, in picosirius red-stained sections, metformin significantly increased collagen deposition (% of total area picosirius red-stained; mean±S.E.M.,(n); std diet: 4.95±0.28,(9); Met diet: 5.80±0.35,(7); $p<0.05$) and tubular wall thickening (μm; mean±S.E.M.,(n); std diet: 1.19±0.04,(10); Met diet: 1.40±0.02,(7); $p<0.05$) in 19-month-old DO mice. In brief, our previous studies indicate that acute metformin supplementation exerts harmful effects in the aging testis of healthy (non-obese/non-diabetic) individuals. Instead, long-term treatment seems to have no or mild-moderate impact in testes of non-obese/non-diabetic old rodents, perhaps as result of the triggering of homeostatic mechanisms.

137. P8-09. PARTICIPATION OF CANCER STEM CELLS IN THE EFFECT OF METRONOMIC CHEMOTHERAPY ON MDA-MB231 CELLS

Julia Zuk¹, Camila Herrero², Alejandro Español³

1. *CEFYO-CONICET-UBA; Laboratorio de Inmunofarmacología Tumoral*

2. *CEFYO-CONICET-UBA; Laboratorio de Inmunofarmacología Tumoral*

3. *CEFYO-CONICET-UBA; Laboratorio de Inmunofarmacología Tumoral*

juliazuk9@campus.fmed.uba.ar

Triple-negative (TN) breast cancer is treated with high doses of paclitaxel which can induce treatment resistance. Metronomic chemotherapy based on the administration of low doses of paclitaxel plus carbachol has emerged as an alternative. Nicotinic receptors are present in breast tissue and their activation by nicotine decreases the efficacy of conventional chemotherapy, although its effect on metronomic chemotherapy with paclitaxel and carbachol (MCpc) is unknown. This study aimed to determine the efficacy of MCpc in TN MDA-MB231 cells, the cancer stem cell (CSC) participation and its possible nicotinic modulation. By MTT we determined that MCpc reduced cell viability in the absence or presence of nicotine (35.0±3.8%; 36.7±4.1% respectively vs. baseline, both $p<0.001$). We observed an increase in sensitivity to paclitaxel in residual cells to MCpc in the absence (97.3±3.3%) or presence (84.9±10.8%) of nicotine (both $p<0.001$ vs. baseline), and a decrease in the expression of the ABCG2 pump determined by Wb ($p<0.01$ vs. baseline). Since modifications in sensitivity to paclitaxel and ABCG2 expression may be indicative of variation in the proportion of CSC, by Wb we determined that MCpc decreased the expression of typically stemness markers SOX2, OCT4 and Nanog (all $p<0.01$ vs. baseline). These results were confirmed by flow cytometry indicating a decrease in CSC-proportion due to MCpc ($p<0.01$). We conclude that MCpc was effective against MDA-MB231 cells, increasing their sensitivity to conventional chemotherapy in the absence or presence of nicotine, indicating that could be a useful neoadjuvant strategy for the treatment of TN breast tumors in smoker patients.

138. P8-10. SEX STEROID MODULATION OF GLYPHOSATE EFFECTS ON BONE MATRIX DEPOSITION

Valentina Dobladez¹, María Celia Fernandez², Patricia Penisi³, Ayelen Martin⁴

1. *Centro de Investigaciones Endocrinológicas "Dr. Cesar Bergada", CEDIE, CONICET, FEI, Div. Endocrinología Hospital de Niños "Dr. Ricardo Gutierrez", Ciudad Autónoma de Buenos Aires, Argentina; Laboratorio de factores de crecimiento y biología tumoral*

2. *Centro de Investigaciones Endocrinológicas "Dr. Cesar Bergada", CEDIE, CONICET, FEI, Div. Endocrinología Hospital de Niños "Dr. Ricardo Gutierrez", Ciudad Autónoma de Buenos Aires, Argentina.; Laboratorio de factores de crecimiento y biología tumoral*

3. *Centro de Investigaciones Endocrinológicas "Dr. Cesar Bergada", CEDIE, CONICET, FEI, Div. Endocrinología Hospital de Niños "Dr. Ricardo Gutierrez", Ciudad Autónoma de Buenos Aires, Argentina.; Laboratorio de factores de crecimiento y biología tumoral*

4. *Centro de Investigaciones Endocrinológicas "Dr. Cesar Bergada", CEDIE, CONICET, FEI, Div. Endocrinología Hospital de Niños "Dr. Ricardo Gutierrez", Ciudad Autónoma de Buenos Aires, Argentina.; Laboratorio de factores de crecimiento y biología tumoral*
vdobladez@cedie.org.ar

Sex steroids play crucial roles in the growth and development of long bones. Glyphosate, a widely used herbicide, has controversial endocrine-disrupting effects. We demonstrated that exposure to low doses of glyphosate alters bone mineral density and quality in juvenile male rats, likely through modifications in matrix deposition during bone development. Objective: To analyze the possible role of sex steroids in modifying bone matrix deposition in cells exposed to low doses of glyphosate. Methods: Human osteosarcoma cells (SaOS-2) were cultured under control conditions (C), and under estradiol (E2), testosterone (T), or dihydrotestosterone (DHT) treatment, with or without 100 ng/ml glyphosate (Gly). Cell viability and matrix deposition (Alizarin Red staining) under differentiation media were assessed. Results: Treatment with T increased cell viability, whereas DHT or E2 treatment had no significant effect (T: $p=0.0022$; DHT/E2: $p=ns$ vs.C) on SaOS-2 cells. Glyphosate treatment reduced cell viability (Cvs.Gly: $p=0.023$). This reduction was also observed in co-culture with androgens (Tvs.T+Gly: $p=0.004$; DHTvs.

DHT+Gly;p=0.05), but not with E2 (E2vs.E2+Gly;p=0.456). Under differentiation media, a decrease in mineralized matrix deposition was detected with T or E2 treatment, while DHT had no effect (T;p=0.004; E2;p=0.019; DHT;p=ns vs.C). Glyphosate treatment reduced matrix deposition (Cvs.Gly;p=0.006); this reduction persisted in co-culture with DHT (DHTvs. DHT+Gly;p=0.05), but not with T (Tvs.T+Gly;p=ns). In co-culture with E2, an increase in matrix deposition was detected (E2vs.E2+Gly;p=0.017), abrogating and surpassing the glyphosate effect. Conclusion: T-but not DHT- and E2 have differential effects on bone matrix deposition in the presence of glyphosate. Whether these effects are mediated by estrogenic pathways requires further investigation.

139. P8-11. BEYOND MONOTHERAPY: METFORMIN ENHANCES THE CYTOTOXIC IMPACT OF 5-FU IN SKIN CARCINOMA CELLS

Fiorella Orsini Zanetti¹, Daniela Pérez Visñuk², Lola Martínez Ibarguren³, Liliana María Elena Finocchiaro⁴, Gerardo Claudio Glikin⁵, Marcela Solange Villaverde⁶

1. Instituto de Oncología Ángel H. Roffo, FMED, UBA; Unidad de Transferencia Genética y Laboratorio de Metabolismo Tumoral, Departamento Biología Celular, Área Investigación.

2. Instituto de Oncología Ángel H. Roffo, FMED, UBA; Unidad de Transferencia Genética y Laboratorio de Metabolismo Tumoral, Departamento Biología Celular, Área Investigación.

3. Instituto de Oncología Ángel H. Roffo, FMED, UBA; Unidad de Transferencia Genética y Laboratorio de Metabolismo Tumoral, Departamento Biología Celular, Área Investigación.

4. Instituto de Oncología Ángel H. Roffo, FMED, UBA; Unidad de Transferencia Genética y Laboratorio de Metabolismo Tumoral, Departamento Biología Celular, Área Investigación.

5. Instituto de Oncología Ángel H. Roffo, FMED, UBA; Unidad de Transferencia Genética y Laboratorio de Metabolismo Tumoral, Departamento Biología Celular, Área Investigación.

6. Instituto de Oncología Ángel H. Roffo, FMED, UBA; Unidad de Transferencia Genética y Laboratorio de Metabolismo Tumoral, Departamento Biología Celular, Área Investigación.

orsinifiorella@gmail.com

Cutaneous squamous cell carcinoma (cSCC) remains a significant dermatological challenge. Topical 5-fluorouracil (5-FU) is effective against superficial skin lesions; however, recurrence rates at 12 months and beyond remain high. Metformin (MET), a widely prescribed antidiabetic drug, has demonstrated anticancer potential through several mechanisms. The aim of this study was to evaluate the effect of combining 5-FU with MET on the human cSCC cell line A431. Using crystal violet viability assays over 72 h, we assessed the impact of 5-FU (1–1000 μ M) and/or MET (1–15 mM) on cell viability. As monotherapies, the half-maximal inhibitory concentration (IC₅₀) was 14 μ M for 5-FU and 3.3 mM for MET. Combination assays revealed a synergistic effect between the two drugs ($p < 0.05$, Combeneft analysis). Similar results were obtained by flow cytometry (FC), which showed increased membrane permeability following the MET/5-FU combination (2.5 mM and 10 μ M, respectively; IP incorporation assay). Interestingly, A431 cells also displayed increased complexity after treatment with 5-FU or the MET/5-FU combination (SCS, FC). To explore the involvement of autophagy, we inhibited the process with chloroquine (CQ, 100 μ M). Preliminary results suggest that CQ partially rescued A431 cells from the cytotoxic effects of 5-FU. Finally, MET may prevent the mitochondrial hyperpolarization induced by 5-FU (TMRM, FC). Taken together, our findings indicate that combining 5-FU with MET significantly enhances cytotoxicity in A431 cells, potentially through autophagy induction, supporting the therapeutic potential of this combination in cSCC.

140. P8-12. MICROCT ANALYSIS OF BONE MICROARCHITECTURE IN A GROWTH MODEL FED A YOGURT-BASED

DIET

Hernán Mascias¹, Marina Soledad Bonanno², Magali Zeni Coronel³, Morena Longo⁴, Claudia Vénica⁵, Diego Vazquez⁶, Ailin Gomez⁷, María Luz Pita Martín de Portela⁸, María Cristina Perotti⁹, Susana Zeni¹⁰, Mariana Seijo¹¹

1. INIGEM/CONICET/UBA.; Laboratorio de Osteopatías metabólicas

2. INIGEM/CONICET/UBA.; Laboratorio de Osteopatías metabólicas

3. INIGEM/CONICET/UBA.; Laboratorio de Osteopatías metabólicas

4. INIGEM/CONICET/UBA.; Laboratorio de Osteopatías metabólicas

5. Instituto de Lactología Industrial (INLAIN, UNL/CONICET), Facultad de Ingeniería Química, Santa Fe. Argentina; Instituto de Lactología Industrial

6. Universidad de Buenos Aires, Facultad de Odontología; Cátedra de Diagnóstico por imágenes.

7. Universidad de Buenos Aires, Facultad de Odontología; Cátedra de Diagnóstico por imágenes.

8. INIGEM/CONICET/UBA.; Laboratorio de Osteopatías metabólicas.

9. Instituto de Lactología Industrial (INLAIN, UNL/CONICET), Facultad de Ingeniería Química, Santa Fe. Argentina; Instituto de Lactología Industrial

10. INIGEM/CONICET/UBA.; Laboratorio de Osteopatías metabólicas

11. INIGEM/CONICET/UBA.; Laboratorio de Osteopatías metabólicas

hernomascias@gmail.com

Improved calcium bioavailability during developmental stages may positively influence bone quality. In previous studies we demonstrated that certain prebiotics increase calcium absorption and bioavailability. Objective: Evaluate changes in bone structure using a two yogurt-based food matrix developed by INLAIN (UNL/CONICET, Santa Fe). Methods: At weaning male rats (n=8/group) received for 30 days a control diet prepared according to AIN'93-G (C), a diet based on regular yogurt (YC), or a diet based on lactose-reduced yogurt containing GOS (YE). The following parameters were evaluated in distal femur via high-resolution micro-computed tomography (microCT): Bone mineral density (BMD; g/cm³), Percent bone volume (BV/TV–Tissue Volume;%), Trabecular number (Tb.N;1/mm) and Trabecular separation (Tb.Sp;mm), Trabecular pattern factor (Tb.Pf;1/mm), Structure model index (SMI). Results (media $\pm$ DS in the following order C;YC;YE): although the comparisons were not significant for all parameters, some trends are observed: BMD was slightly higher in YE and YC compared to C (0.886 $\pm$ 0.093; 0.937 $\pm$ 0.044; 0.935 $\pm$ 0.055). BV/TV increased progressively from C, YC to YE (18.9 $\pm$ 2.6; 19.4 $\pm$ 5.2; 20.1 $\pm$ 7.6). Tb.N increased slightly from C to YE (1.70 $\pm$ 0.30; 1.73 $\pm$ 0.38; 1.76 $\pm$ 0.77), while Tb.Sp also increased in YE (0.59 $\pm$ 0.27; 0.58 $\pm$ 0.23; 0.69 $\pm$ 0.40), while Tb.Pf (7.93 $\pm$ 2.36; 7.31 $\pm$ 1.33; 6.46 $\pm$ 3.32) and SMI decreased in YE (1.5 $\pm$ 0.2; 1.4 $\pm$ 0.2; 1.3 $\pm$ 0.5). Conclusion: Slight increases in BMD, BV/TV, and Tb.N suggest greater bone mass and trabecular number in YE, while the decrease in Tb.Pf and SMI indicates a more connected, plate-like trabecular structure. Despite the increase in Tb.Sp, the overall pattern in YE supports a potential positive effect of the dairy matrix on bone quality during growth, likely due to enhanced calcium absorption and improved bone formation.

141. P8-13. DIFFERENTIAL CYTOTOXIC AND CHEMOPREVENTIVE RESPONSES OF ERUCA VESICARIA LEAF EXTRACTS IN 2D AND 3D HEPG2 MODELS

Andreina Quevedo Enríquez¹, Orlando G Elso², Valeria P Sülsen³, Daniel Zappia⁴, Katja Kološa⁵, Alja Štern⁶, Bojana Žegura⁷, Roxana N Peroni⁸

1. Instituto de Investigaciones Farmacológicas (ININFA, UBA-CONICET); Laboratorio de Transporte de drogas

2. Departamento de Química Orgánica y UMYMFOR, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires-CONICET, Ciudad Universitaria. Facultad de Farmacia y Bioquímica, Cátedra de Farmacognosia, Univer-

sidad de Buenos Aires; Laboratorio de Biocatálisis

3. Instituto de Química y Metabolismo del Fármaco (IQUIMEFA), CONICET-Universidad de Buenos Aires; Facultad de Farmacia y Bioquímica, Cátedra de Farmacología, Universidad de Buenos Aires

4. Instituto de Investigaciones Farmacológicas (ININFA, UBA-CONICET); Facultad de Farmacia y Bioquímica, Cátedra de Química Medicinal, Universidad de Buenos Aires

5. National Institute of Biology, Večna pot 121, Ljubljana, 1000 Slovenia; Department of Genetic Toxicology and Cancer Biology

6. National Institute of Biology, Večna pot 121, Ljubljana, 1000 Slovenia; Department of Genetic Toxicology and Cancer Biology

7. National Institute of Biology, Večna pot 121, Ljubljana, 1000 Slovenia; Department of Genetic Toxicology and Cancer Biology

8. Instituto de Investigaciones Farmacológicas (ININFA, UBA-CONICET). Facultad de Farmacia y Bioquímica, Cátedra de Farmacología, Universidad de Buenos Aires; Laboratorios de transporte de Drogas
andreinaquevedo89@gmail.com

The biological activity of *Eruca vesicaria* remains a subject of debate, as it has demonstrated both chemopreventive and cytotoxic properties, with varying results depending on the experimental model and cellular context. To address this duality, a methanol/water leaf extract was fractionated, and two key fractions, dichloromethane (DCM, enriched in isothiocyanates and sulfur compounds) and ethyl acetate (AE, enriched in polyphenols), were evaluated in HepG2 cells grown as two-dimensional (2D) monolayers or three-dimensional (3D) spheroids. Marked differences were observed between models. After 24h exposure to doxorubicin (DOXO), the IC_{50} was 2.5 $\mu\text{g/mL}$ in 2D versus 20.5 $\mu\text{g/mL}$ in 3D, indicating decreased sensitivity in spheroids. Fractions of *Eruca vesicaria* leaves displayed moderate cytotoxicity, and differences were also observed between the models (DCM: IC_{50} 130 $\mu\text{g/mL}$ in 2D vs 300 $\mu\text{g/mL}$ in 3D; AE: IC_{50} 780 $\mu\text{g/mL}$ in 2D vs 940 $\mu\text{g/mL}$ in 3D). Co-exposure of non-toxic DCM extract concentrations potentiated cytotoxicity of DOXO at low concentrations only in spheroids, suggesting synergistic potential. In contrast, non-toxic concentrations of the AE fraction counteracted DOXO-induced cytotoxicity, consistent with a chemopreventive effect. These findings highlight that, compared to monolayers, the HepG2 spheroid model has decreased sensitivity to DOXO and *E. vesicaria* DCM and AE fractions, supporting the use of advanced culture systems for translational evaluation. Ongoing research is focused on evaluating whether the differential effects observed in 3D systems for DCM versus AE fractions are related to distinct modulation of efflux transporters or metabolic enzymes.

142. P8-14. VASOACTIVE INTESTINAL PEPTIDE MODULATES NEURAL PROGENITOR SUSCEPTIBILITY TO ZIKA VIRUS INFECTION DURING THEIR DIFFERENTIATION PROCESS TO NEURON-LIKE CELLS

Valentina Tacchino¹, Mathias Chemen², Soledad Rodríguez Varela³, Daiana Rios⁴, Ignacio Rojas Campion⁵, Claudia Pérez Leirós⁶, Vanesa Hauk⁷, Leonardo Romorini⁸, Cybele García⁹, Daiana Vota¹⁰

1. IQUIBICEN CONICET; Laboratorio de Estrategias Antivirales y Laboratorio de Inmunofarmacología

2. IQUIBICEN CONICET; Laboratorio de Estrategias Antivirales y Laboratorio de Inmunofarmacología

3. LIAN-CONICET; Fundación FLENI

4. IQUIBICEN CONICET; Laboratorio de Inmunofarmacología

5. IQUIBICEN CONICET; Laboratorio de Inmunofarmacología

6. IQUIBICEN CONICET; Laboratorio de Inmunofarmacología

7. IQUIBICEN CONICET; Laboratorio de Inmunofarmacología

8. LIAN-CONICET; Fundación FLENI

9. IQUIBICEN CONICET; Laboratorio de Estrategias Antivirales

10. IQUIBICEN CONICET; Laboratorio de Inmunofarmacología
valentacchino19@gmail.com

Zika virus (ZIKV) infection during early pregnancy is associated with

congenital neurological disorders, although not all neonates from infected women are affected. We previously showed that ZIKV infection of first-trimester cytotrophoblast-derived cells (Tb) alter their soluble factor secretion, indirectly impacting neural progenitors (NPs) survival and metabolism. The vasoactive intestinal peptide (VIP), produced by the placenta, modulates Tb and NP susceptibility to ZIKV. Here, we aimed to investigate how neuronal differentiation influences NP susceptibility to infection and the potential protective effect of VIP. NPs derived from human embryonic stem cells were infected with a local ZIKV isolate for 1 h ($MOI=0.5$) and then cultured for 14 days in medium promoting differentiation into neuron-like cells (NLCs), in the absence or presence of VIP (1-10 nM). Infectious viral particles were quantified by plaque assay. Stemness- and differentiation-related gene expression was analyzed by RT-qPCR. Bright-field microscopy was used to monitor morphology, and TUJ-1 expression was assessed by flow cytometry. ZIKV-infected NPs undergoing differentiation showed increased viral replication, with significantly higher production of infectious particles compared to undifferentiated progenitors ($p<0.05$, d2). VIP significantly reduced viral particle production at multiple stages of differentiation ($p<0.05$, d2-5-14). Moreover, VIP-treated differentiating NPs exhibited enhanced neurite extension compared to untreated cultures. Preliminary transcriptional analyses suggest that VIP counteracts ZIKV-induced alterations in stemness- and differentiation-related genes. Our findings indicate that VIP modulates NP and NLC susceptibility to ZIKV, contributing to the maintenance of progenitor identity and supporting proper neuronal differentiation.

ORALES 7 - SAIC - ONCOLOGÍA 2

CÁNCER DE MAMA

DATE & TIME: 18/11/2025 13:00 - 14:30 H

Chairs: Ignacio León, Federico Monczor

143. O7-01. PI3K/AKT INHIBITION REDUCES PROLIFERATION, MIGRATION, AND TUMOR GROWTH IN LUMINAL BREAST CANCER MODELS WITH FGFR2 ACTIVATION AND RUNX2 OVEREXPRESSION

Karen Sestúa¹, María Sol Rodríguez², Celine Almeida Gouvêa³, Isabel Alicia Lüthy⁴, Virginia Novaro⁵, Cecilia Pérez Piñero⁶

1. Instituto de Biología y Medicina Experimental (IBYME - CONICET); Laboratorio de Hormonas y Cáncer

2. Instituto de Biología y Medicina Experimental (IBYME - CONICET); Laboratorio de Hormonas y Cáncer

3. Instituto de Biología y Medicina Experimental (IBYME - CONICET); Laboratorio de Hormonas y Cáncer

4. Instituto de Biología y Medicina Experimental (IBYME - CONICET); Laboratorio de Hormonas y Cáncer

5. Instituto de Biología y Medicina Experimental (IBYME - CONICET); Laboratorio de Proteínas Quinasas y Oncología Molecular

6. Instituto de Biología y Medicina Experimental (IBYME - CONICET); Laboratorio de Hormonas y Cáncer
karenessetua06@gmail.com

Breast cancer (BrCa) is the leading cause of cancer-related death in women. About 80% of tumors express hormone-receptors and receive endocrine therapy, yet endocrine-resistance frequently emerges. We showed that FGF2/FGFR2 signaling promotes hormone-independent growth and metastasis, and that RUNX2-overexpression enhances invasion and endocrine resistance. AKT2 correlates with elevated RUNX2 and poor prognosis. We hypothesize that AKT2, activated by FGF/FGFR, regulates RUNX2 and drives progression. Aim: To test the AKT inhibitor MK2206 (MK) in T47D-control (C), FGFR2-constitutively active (R2CA), and RUNX2-overexpressing (RUNX2) cells. To evaluate the PI3K inhibitor alpelisib (ALP) in vivo in control-xenografts and MK ex vivo in C- and RUNX2-tumors. Results: FGF2 increased proliferation in all models, strongest in RUNX2 ($*p<0.05$, $137\pm12\%$ vs C: $100\pm8\%$) and R2CA ($***p<0.001$, $164\pm12\%$ vs C: $100\pm7\%$). MK reversed this effect dose-dependently, though RUNX2 and R2CA showed reduced-sensitivity, suggesting compensatory pathways. MK-alone reduced proliferation, more

strongly in RUNX2 and R2CA vs C, indicating AKT-dependence for basal growth. In migration assays, MK-0.1 μ M significantly reduced migration in R2CA (** $p < 0.01$) but not in C. ALP inhibited tumor growth in control-xenografts (** $p < 0.001$), and MK reduced Ki67 in RUNX2-tumors ex vivo (%Ki67: 31 ± 5 vs 26 ± 4 , * $p < 0.05$). Conclusion: AKT inhibition decreases proliferation across models, with context-specific sensitivity. RUNX2 and R2CA show incomplete reversal of FGF2 effects, suggesting compensatory signaling. PI3K inhibition with ALP suppressed tumor growth in controls, while MK reduced proliferation in RUNX2-tumors. These findings highlight PI3K/AKT as a mediator of FGFR2/RUNX2-driven progression and support its targeting, potentially in combination therapies, for luminal BrCa with high-RUNX2 expression.

144. O7-02. DETECTION OF PIK3CA MUTATIONS IN BREAST CANCER FFPE SAMPLES USING TARGETED AMPLICON SEQUENCING

Camila Ximena Peñalva¹, Micaela Vivanco², Paola De Luca³, Romina Albite⁴, Marisol Delea⁵, Julieta Pandolfi⁶, Carlos David Bruque⁷, Virginia Novaro⁸

1. Hospital de Alta Complejidad El Calafate SAMIC, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

2. IBYME-CONICET, Buenos Aires.; Instituto de Biología y Medicina Experimental

3. IBYME-CONICET, Buenos Aires.; Instituto de Biología y Medicina Experimental

4. Hospital Italiano de Buenos Aires.; Servicio de Anatomía Patológica

5. Hospital de Alta Complejidad El Calafate SAMIC, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

6. Hospital Italiano de Buenos Aires; Servicio de Anatomía Patológica

7. Hospital de Alta Complejidad El Calafate SAMIC, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

8. IBYME-CONICET, Buenos Aires.; Instituto de Biología y Medicina Experimental
camilaximenapenalva@gmail.com

The PI3K/AKT pathway is one of the most frequently altered signaling cascades in solid tumors and, in breast cancer, it strongly associates with therapeutic resistance and poor prognosis. Since 2019, the detection of PIK3CA genetic variants has been an essential criterion for prescribing alpelisib, a selective PI3K α inhibitor. To develop a cost-effective tool adapted to local practice, we designed primers targeting exons 8, 10, and 21 of PIK3CA, and generating amplicons of 246–282 bp. These cover the most prevalent somatic variants among breast cancer patients in the Argentine population. PCR conditions were optimized for DNA extracted from formalin-fixed, paraffin-embedded (FFPE) samples. Amplicons were sequenced on the MiSeq platform using the AmpliSeq™ for Illumina® kit, achieving an average sequencing depth of ~1000X. Variants were reported at an allele frequency threshold of $\geq 5\%$. The NGS panel was tested in 12 breast cancer samples previously analyzed with the commercial Cobas® kit, demonstrating high sensitivity and specificity for detecting PIK3CA genetic variants. Results were concordant with targeted PCR assays and offered additional advantages by enabling the detection of low-frequency variants. The observed mutation distribution was consistent with published data, further supporting the clinical relevance of this approach. Additional validation on an expanded set of samples is ongoing. Overall, this study highlights the feasibility of implementing next-generation sequencing methodologies tailored to local laboratory conditions and lays the groundwork for the routine incorporation of this approach to the molecular diagnosis of solid tumors in Argentina, contributing to patient stratification and selection of targeted therapies.

145. O7-03. DIFFERENTIAL RESPONSE OF HUMAN BREAST CANCER CELL LINES TO A CLINICALLY RELEVANT DOSE OF GAMMA RADIATION (2 GY) WHEN COMBINED WITH CATIONIC AMPHIPHILIC AND NON-CATIONIC AM-

PHIPHILIC H1-ANTI-HISTAMINES USED IN ARGENTINA

Joselyn Revelo Argoti¹, Tamara Galarza², Alicia Klecha³, Micaela Cignetti⁴, Stefania Casciaro⁵, Marcela López Nigro⁶, Nora Mohamad⁷, Gabriela Martín⁸

1. Facultad de Farmacia y Bioquímica-UBA; Laboratorio de Radioisótopos

2. Facultad de Farmacia y Bioquímica-UBA; Laboratorio de Radioisótopos

3. Facultad de Farmacia y Bioquímica.UBA-Facultad de Ingeniería y Ciencias Agrarias.UCA; Laboratorio de Radioisótopos

4. Facultad de Farmacia y Bioquímica. UBA.; Citogenética Humana y Genética Toxicológica (CIGETOX)

5. INFIBIOC. Facultad de Farmacia y Bioquímica. UBA; Citogenética Humana y Genética Toxicológica (CIGETOX)

6. INFIBIOC. Facultad de Farmacia y Bioquímica. UBA; Citogenética Humana y Genética Toxicológica (CIGETOX)

7. Facultad de Farmacia y Bioquímica-UBA; Laboratorio de Radioisótopos

8. Facultad de Farmacia y Bioquímica.UBA-CONICET; Laboratorio de Radioisótopos-Laboratorio de Radiobiología y Oncología Molecular
jossyrevelo@gmail.com

Radiotherapy helps prevent breast cancer recurrence, yet radio-resistance remains a major drawback. Clinical observations associated the post-diagnostic use of cationic amphiphilic (CAD) H1-antihistamines (H1-A) with improved survival in breast cancer patients compared with non-CAD H1-A. Pre-clinical studies demonstrated HR1-A antitumor activity, but their efficacy was influenced by physicochemical traits; particularly, only CAD HR1-A killed tumor cells at high concentrations. This study investigated the combination of 2 Gy irradiation and CAD (loratadine, desloratadine) or non-CAD H1-A (cetirizine, fexofenadine) on proliferation, viability, death and DNA damage in breast cancer cells MDA-MB-231 and MCF-7. In both cell lines CAD H1-A reduced reproductive survival (clonogenic assay, IC50c: 3–8 μ M) and viability (MTT assay, IC50v: 30–65 μ M), while non-CAD HR1-A required higher concentrations to affect clonogenicity (IC50c ≥ 75 μ M) and did not alter viability up to 100 μ M. Irradiation halved clonogenicity ($p < 0.01$) but did not affect viability. Combined treatments, 2 Gy+HR1-A at IC50c, further reduced colony formation for all H1-A except fexofenadine ($p < 0.05$). Viability was not modified by 2 Gy+H1-A 0.1 μ M or IC50c. Nonetheless, viability was halved by 2 Gy+CAD H1-A at IC50v ($p < 0.01$). Cell count with an automated analyzer paralleled viability results. Only CAD H1-A at IC50v increased cell death (propidium iodide uptake-flow cytometry, $p < 0.01$) in both cell lines irradiated or not, though irradiation alone had no effect. Additionally, CAD HR1-A at IC50c and IC50v raised the DNA damage index (alkaline comet assay). These findings suggest CAD H1-A enhance radiation-induced cytotoxicity and DNA damage, supporting their potential as radiosensitizers in breast cancer therapy.

146. O7-04. GENOTOXIC STRESS AND APOPTOSIS MEDIATE THE ANTITUMORAL ACTIVITY OF A COLEUS NEOCHILUS EXTRACT IN BREAST CANCER CELLS

Carla Luciana Mayora Justel¹, Verónica González-Pardo², María del Carmen Esandi³, Ariana Bruzzzone⁴

1. Instituto de Investigaciones Bioquímicas de Bahía Blanca INIBIBB-UNS-CONICET, Camino la Carrindanga Km 7, 8000 Bahía Blanca, Argentina Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur, San Juan 670, 8000 Bahía Blanca, Argentina; Laboratorio de ciencias básicas y de la implementación en cáncer

2. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur, San Juan 670, 8000 Bahía Blanca, Argentina Instituto de Ciencias Biológicas y Biomédicas del Sur INBIOSUR-UNS-CONICET, San Juan 670, 8000 Bahía Blanca, Argentina; Laboratorio de química biológica

3. Instituto de Investigaciones Bioquímicas de Bahía Blanca INIBIBB-UNS-CONICET, Camino la Carrindanga Km 7, 8000 Bahía Blanca, Argentina Departamento de Biología,

Bioquímica y Farmacia, Universidad Nacional del Sur, San Juan 670, 8000 Bahía Blanca, Argentina; Laboratorio de neurofisiología y farmacología molecular
 4. Instituto de Investigaciones Bioquímicas de Bahía Blanca INIBBB-UNS-CONICET, Camino la Carrindanga Km 7, 8000 Bahía Blanca, Argentina.; Laboratorio de ciencias básicas y de la implementación en cáncer carlamayorajus@gmail.com

Coleus spp. have diverse ethnobotanical applications, most notably for their medicinal properties. In previous studies, we demonstrated that the ethyl acetate fraction (BRAE) of the ethanolic extract of *Coleus neochilus* reduced proliferation, viability, and clonogenic potential of human breast cancer cell lines. The present study aims to elucidate the mechanisms underlying these antitumoral effects. Apoptosis was evaluated by Annexin V/PI assay, and genotoxicity by comet assay. MCF-7 and MDA-MB-231 breast cancer cells were treated with BRAE (25 µg/mL, 48 h) or vehicle. Hydrogen peroxide (0.5 µM, 30 min) was used as a positive control. The results show that BRAE reduced cell viability and increased the proportion of late apoptotic cells in both cell lines (MCF-7: -14% viable cells $p < 0.001$, +140% late apoptotic cells, $p < 0.001$; MDA-MB-231: -11% viable cells, $p < 0.001$; +115% late apoptotic cells, $p < 0.001$). Notably, a marked rise in necrosis was detected only in MCF-7 (+124%, $p < 0.001$), whereas no significant differences in early apoptosis were observed in either line. Comet assay revealed a pronounced increase in DNA strand breaks following BRAE treatment (MCF-7: +181% tail length, $p < 0.001$; MDA-MB-231: +253%, $p < 0.001$). Overall, these results suggest that BRAE exerts its antitumoral effects through apoptosis and genotoxic stress. Future studies are required to establish the causal relationship between DNA damage and cell death. These insights highlight the potential of BRAE as a source of bioactive compounds with therapeutic relevance in breast cancer.

147. O7-05. GLYPICAN-3 MODULATES SELF-RENEWAL AND PLURIPOTENCY OF BREAST CANCER STEM CELLS

Maia Yazmín Bialí*, Luciana Cañonero*, Lizeth Ariza Bareño, Diego Javier Brites Neira, Andrés Bechis, Laura Todaro, Alejandro Urteger
Instituto de Oncología "Ángel H. Roffo" - UBA; Área Investigación
 maiabialí@hotmail.com
 *equal contribution

Cancer stem cells (CSCs) play key roles in tumor recurrence and metastasis. These cells are capable of self-renewal and generating heterogeneous progeny with varying tumorigenic potential. The epithelial-mesenchymal transition (EMT) can either expand or reduce CSC pools depending on the cellular context. Our previous work showed that Glypican-3 (GPC3) expression reverses EMT in breast cancer cells and modulates several signaling pathways, including Wnt/β-catenin, closely related to CSC biology. Based on this, we investigated whether GPC3 influences breast CSC populations. We evaluated the mammosphere-forming capacity of breast cancer cells with genetically modified GPC3 expression. MDA-MB231-vector control cells (GPC3-negative) produced only small clusters, whereas MDA-MB231-GPC3 cells generated abundant, well-organized mammospheres with diameters about 50% larger than controls. qPCR analysis of RNA from mammospheres revealed a 30- to 60-fold increase in NANOG and OCT4 levels, confirming the enrichment of stem-like populations in these 3D cultures. Interestingly, mammospheres exhibited about 30% lower GPC3 expression than the corresponding MDA-MB231-GPC3 monolayers. Consistently, MDA-MB231-GPC3 adherent monolayers also displayed higher NANOG and OCT4 than controls, suggesting that GPC3 contributes to the expansion of stem-like subpopulations. In addition, in silico analysis of the TCGA dataset revealed that tumors with high GPC3 expression displayed upregulation of stemness-associated genes, including SOX, ALDH1A1, and KLF4 (FDR0.5). Gene set enrichment confirmed positive association with pathways involved in stem cell maintenance and proliferation

(e.g., GOBP_SOMATIC_STEM_CELL_POPULATION_MAINTENANCE, FDR<0.05, NES=1.51; GOBP_REGULATION_OF_STEM_CELL_PROLIFERATION, FDR<0.05, NES=1.39). Taken together, our findings indicate that GPC3 promotes breast CSC populations, opening new perspectives on its role in tumor progression.

148. O7-06. LET-7B-5P EFFECT ON TRIPLE NEGATIVE BREAST CANCER GROWTH, PROGRESSION AND METFORMIN SENSITIVITY

Erick Nicolas Merizalde, Juana Moro, Georgina Daniela Scalise, Agustina Grinpelc, Leandro Vera Sanchez, Micaela Vivanco, Florencia Cascardo, Maira Garay, Azul Muiño, Virginia Novaro, Adriana De Siervi, Paola De Luca
Instituto de Biología y Medicina Experimental (IBYME-CO-NICET); Laboratorio de Proteínas Quinasas y Oncología Molecular
 erickmerizalde13@gmail.com

Triple-negative breast cancer (TNBC) is an aggressive subtype with limited therapeutic options. MiRNAs are key regulators in cancer biology and our previous studies showed that let-7b-5p is reduced in PAM50 basal-like breast cancer tissue. In vitro, overexpression of let-7b-5p decreased cell viability, clonogenicity, and migration, while enhancing adhesion in TNBC cell lines. The present study aimed to investigate the tumor-suppressive role of let-7b-5p in vivo and to evaluate potential therapeutic strategies to modulate its activity. In xenografts derived from MDA-MB-231 cells, let-7b-5p overexpression significantly reduced tumor growth. Similarly, in orthotopic 4T1 tumors, treatment with a single dose of a let-7b-5p mimic decreased tumor size at early time points, although no effects on metastasis were observed in neither model. Bioinformatic analysis identified metformin, a commonly used antidiabetic drug, as a potential modulator of let-7b-5p. Functional studies revealed that metformin did not alter let-7b-5p expression at tested doses. However, combined treatment with metformin and let-7b-5p produced an additive reduction in MDA-MB-231 cell viability, comparable to higher doses of metformin alone, though this effect was absent in 4T1 cells. No additive or synergistic effects were observed on migration or clonogenic capacity; in fact, a negative interaction was detected in clonogenic assays in MDA-MB-231 cells. Overall, let-7b-5p exerts tumor-suppressive activity in vivo and its combination with metformin shows limited but promising additive effects in TNBC. These findings highlight the potential of integrating miRNA-based strategies with drug repositioning to advance personalized therapeutic approaches in TNBC.

149. O7-07. LOCALIZED THERAPY OF BREAST CANCER WITH DOXORUBICIN-LOADED MICROSPHERES: AN ALTERNATIVE TO SYSTEMIC TREATMENT IN LUMINAL METASTATIC AND TRIPLE-NEGATIVE MODELS

Luisa Ambrosio¹, Aitana Álvaro Martín², Galo Sosa Apaza³, Leo Saldain⁴, María Gisela Verón⁵, Paola Rojas⁶
 1. Instituto de Biología y Medicina Experimental (IBYME), CONICET, Buenos Aires, Argentina.; Carcinogenesis Hormonal
 2. Departamento de ciencias experimentales, Universidad Francisco de Vitoria, Madrid, España; Departamento de ciencias experimentales
 3. Universidad Nacional de San Martín, Buenos Aires, Argentina.; Universidad de San Martín
 4. Instituto de Biología y Medicina Experimental (IBYME), CONICET, Buenos Aires, Argentina.; Carcinogenesis Hormonal
 5. Centro Atómico Bariloche, CONICET, Río Negro, Argentina; Materiales
 6. Instituto de Biología y Medicina Experimental (IBYME), CONICET, Buenos Aires, Argentina.; Carcinogenesis Hormonal
 luisa.ambrosio.15@gmail.com

Chemotherapy is widely used in breast cancer treatment, both in neoadjuvant and adjuvant settings. However, its significant adverse effects highlight the need for strategies that reduce systemic toxicity. Drug delivery systems such as nanoparticles and microparticles offer benefits like tumor-specific targeting and controlled drug release,

which can help minimize side effects. Microspheres, in particular, can serve as effective drug carriers or embolizing agents. In this study, we evaluated sulfonated polyvinyl alcohol (SPVA) microspheres loaded with doxorubicin (Doxo-SPVA), developed at the Centro Atómico Bariloche, for localized breast cancer treatment. We aimed to assess their therapeutic effects on both primary tumors and metastases. We used two models: the luminal murine C7-2-HI tumor, which develops spontaneous lung metastases 42 days after subcutaneous implantation in female BALB/c mice, and a triple-negative breast cancer patient-derived xenograft (PDX 815) established in NSG mice. When tumors reached ~30 mm², animals were treated with local injections of Doxo-SPVA (1–2 mg or 2–2 mg), empty SPVA (2 mg), or no treatment (n = 5–6/group), administered weekly for three weeks. Tumor growth was monitored twice weekly, and tumors and lungs were collected one week after the final dose. In the triple-negative PDX model, Doxo-SPVA treatment significantly reduced tumor size compared to controls (p = 0.0075). However, C7-2-HI tumors and lung metastases showed no significant differences. These results suggest that Doxo-SPVA microspheres could be promising candidates for local treatment of triple-negative tumors. Local Doxo-SPVA therapy may offer a valuable alternative when systemic chemotherapy is not feasible.

150. 07-08. PRECLINICAL ASSAY OF ARYL HYDROCARBON RECEPTOR LIGANDS AS ADJUVANTS TO ENDOCRINE THERAPY IN THE TREATMENT OF HORMONE-DEPENDENT BREAST CANCER

Rosalía Seña Acosta¹, Shirley Peñaranda Carlo², Yanina Langle³, María Pelagatti⁴, Paola Cardozo⁵, Marianela Abrigo⁶, Eduardo Sandes⁷, Andrea Loaiza Pérez⁸

1. Instituto de Oncología "Ángel H. Roffo" - Facultad de Medicina - UBA; Área de Investigación - Dpto. Immunobiología
 2. Instituto de Oncología "Ángel H. Roffo" - Facultad de Medicina - UBA; Área de Investigación - Dpto. Immunobiología
 3. Instituto de Oncología "Ángel H. Roffo" - Facultad de Medicina - UBA; Área de Investigación - Dpto. Bioterio y Cáncer Experimental
 4. Instituto de Oncología "Ángel H. Roffo" - Facultad de Medicina - UBA; Área de Investigación - Dpto. Bioterio y Cáncer Experimental
 5. Instituto de Oncología "Ángel H. Roffo" - Facultad de Medicina - UBA; Área de Investigación - Dpto. Bioterio y Cáncer Experimental
 6. Instituto de Oncología "Ángel H. Roffo" - Facultad de Medicina - UBA; Área de Investigación - Dpto. Bioterio y Cáncer Experimental
 7. Instituto de Oncología "Ángel H. Roffo" - Facultad de Medicina - UBA; Área de Investigación - Dpto. Biología Celular
 8. Instituto de Oncología "Ángel H. Roffo" - Facultad de Medicina - UBA; Área de Investigación - Dpto. Immunobiología
- rosalia0719@gmail.com

Introduction: Tamoxifen (TMX) is the standard post-surgical adjuvant treatment for estrogen-dependent breast cancer. Recurrence is associated with an increase in breast cancer stem cells (BCSCs). On the other hand, aryl hydrocarbon receptor ligands (AhR), aminoflavone (AF) and benzothiazole (5F203), reduce the presence of BCSCs in cell lines derived from the M05 breast cancer mouse model and in the MCF-7 human cell line. Our Goal: To study whether in vivo treatment with AhR ligand AF can reduce the presence of BCSCs induced by TMX and to evaluate whether AhR ligands decrease the expression of BCSC markers in MCF-7 cell line. **Methods:** BALB/c mice transplanted with M05 tumors (n=30 per two assays) were treated with: Control, Vehicle, TMX, AF, and TMX+AF. Tumor growth, final weight, and mammosphere-forming capacity were evaluated. In addition, the percentage of BCSCs (CD24/CD44⁺) in MCF-7 spheres treated with: TMX, 5F203, TMX+5F203, AF, and TMX+AF was measured by flow cytometry. **Results:** Control, vehicle, TMX, and AF tumors grew until week 10 (end of assay), the TMX+AF combination resulted in smaller tumor size and weight. AF and TMX+AF produce a significant decrease in mammosphere formation compared to control and TMX, indicating BCSCs inhibition. In addition, a decrease in BCSCs markers was observed in spheres

treated with 5F203 (0.26%) and TMX+5F203 (0.14%), versus control (1.4%) and TMX (2%); AF 0.9%, versus TMX+AF 3.2%. **Conclusions:** AF and 5F203 have an antitumor effect associated with the reduction of BCSCs, enhancing the action of TMX.

151. 07-09. SPARC AND MT1-MMP EXPRESSION CORRELATE IN BREAST TUMORS OBTAINED FROM A COHORT OF PATIENTS FROM THE INSTITUTE A.H. ROFFO

Naiara Rodríguez Padilla¹, Marianela Sciacca², María del Pilar Carballo³, Ezequiel Lacunza⁴, Érica Rojas Bilbao⁵, Ana María Eiján⁶, Pablo Saez⁷, Catalina Lodillinsky⁸

1. Instituto de Oncología Ángel H. Roffo, Universidad de Buenos Aires, Buenos Aires, Argentina; Área de Investigación
 2. Instituto de Oncología Ángel H. Roffo, Universidad de Buenos Aires, Buenos Aires, Argentina; Área de Investigación
 3. Instituto de Oncología Ángel H. Roffo, Universidad de Buenos Aires, Buenos Aires, Argentina.; Departamento de Patología
 4. School of Medical Sciences, National University of La Plata, La Plata, Argentina; CINIBA
 5. Instituto de Oncología Ángel H. Roffo, Universidad de Buenos Aires, Buenos Aires, Argentina.; Departamento de Patología
 6. Instituto de Oncología Ángel H. Roffo, Universidad de Buenos Aires, Buenos Aires, Argentina; Área de Investigación
 7. Department of Biochemistry and Molecular Cell Biology (IBMZ), Center for Experimental Medicine, Hamburg, Germany.; Cell Communication and Migration Laboratory,
 8. Instituto de Oncología Ángel H. Roffo, Universidad de Buenos Aires, Buenos Aires, Argentina.; Área de Investigación
- naiairapadilla@gmail.com

The membrane-associated metalloprotease type I (MT1-MMP) is associated with tumor invasion. In breast cancer (BC), we have reported that it is essential in the transition from in situ to invasive tumors. Based on the differential MT1-MMP expression after MCF10DCIS.com cells intraductal injection in mice, two cell populations were isolated. Transcriptome analysis was performed and compared against a set of human high-grade DCIS. We found SPARC, up-regulated in both, worse prognosis-human DCIS and MT1-MMP-high population, highlighting this gene as a promising target in early BC progression. In a breast tumour cohort from the Institute A.H. Roffo (n=62) SPARC and MT1-MMP expression was analysed by IHQ. Both were upregulated in tumour tissue compared normal epithelium (p<0.001). Besides, the expression of both proteins correlates in this cohort (R²: 0.507; p<0.001). This correlation was also observed at the mRNA level in BC from the TCGA database (p< 2.2e-16). In KO SPARC LM38-LP cell line, both MT1-MMP expression and degradative capacity are reduced (p<0.05). An interaction between SPARC and TGF-β1 was observed (STRING platform). The TGFβRI inhibitors SB431542 and Galunisertib reduced SPARC expression in both murine and human cell lines. Also, exogenous SPARC increased p-SMAD 2/3, while in KO SPARC cells, p-SMAD 2/3 was reduced. In vivo, Galunisertib decreased the proportion and area of invasive tumors compared to the control after intraductal injection of LM38-LP cells (p= 0.04). Finally, we propose that co-expression between SPARC and MT1-MMP is mediated by TGFβR, proposing TGFβRI as a possible molecular target for SPARC-positive tumors.

ORALES 8 - SAIC - BIOINFORMÁTICA

DATE & TIME: 18/11/2025 13:00 - 14:30 H

Chairs: Fiorella Belforte, Priscila Pagnotta

152. 08-01. OPEN-SOURCE AND REPRODUCIBLE PIPELINE FOR PEDIATRIC GLIOMA RNA-SEQ DATA: INTEGRATING PUBLIC DATASETS INTO AN INTERACTIVE PLATFORM FOR BIOMARKER DISCOVERY

Gisela Pattarone¹, Marina Perona², Hebe Durán³, Irene L. Ibañez⁴

1. Comisión Nacional de Energía Atómica - Instituto de Nanociencia y Nanotecnología (INN-CNEA-CONICET); Gerencia de Investigación y Aplicaciones, Subgerencia de

Tecnología y Aplicaciones de Aceleradores, Laboratorio de Desarrollo de Nanosistemas para Aplicaciones Diagnósticas y Terapéuticas

2. *Comisión Nacional de Energía Atómica - Consejo Nacional de Investigaciones Científicas y Técnicas; Departamento de Radiobiología, División Bioquímica Nuclear*

3. *Consejo Nacional de Investigaciones Científicas y Técnicas, Instituto de Nanociencia y Nanotecnología (INN-CNEA-CONICET) - Comisión Nacional de Energía Atómica; Gerencia de Investigación y Aplicaciones, Subgerencia de Tecnología y Aplicaciones de Aceleradores, Laboratorio de Desarrollo de Nanosistemas para Aplicaciones Diagnósticas y Terapéuticas*

4. *Consejo Nacional de Investigaciones Científicas y Técnicas, Instituto de Nanociencia y Nanotecnología (INN-CNEA-CONICET) - Comisión Nacional de Energía Atómica; Gerencia de Investigación y Aplicaciones, Subgerencia de Tecnología y Aplicaciones de Aceleradores, Laboratorio de Desarrollo de Nanosistemas para Aplicaciones Diagnósticas y Terapéuticas*
giselapattarone@gmail.com

Pediatric gliomas are one of the leading causes of cancer-related morbidity and mortality in children, with limited therapeutic options and poor prognosis. The increasing availability of next-generation sequencing data enables integrative analyses to identify molecular biomarkers and potential therapeutic targets. This study aimed to develop a scalable and reproducible pipeline for genomic data analysis in pediatric gliomas. A meta-analysis was performed using public RNA-seq datasets (SRA, GEO), including 6700 samples curated for quality and consistency. From these, 46 well-characterized samples were prioritized to ensure methodological coherence. The pipeline integrates BioPySRA for data retrieval, Nextflow with nf-core/rnaseq for standardized RNA-seq processing, and additional modules for variant calling (VCF). Data structuring and management were implemented in PostgreSQL and MongoDB, supporting large-scale, flexible analyses. The automated workflow enabled end-to-end processing, from raw FASTQ download and preprocessing to transcriptomic profiling and variant identification. The integration of genomic and transcriptomic analyses led to: identification of key therapeutic targets, such as IDH1/IDH2, EGFR, CDKN2A/B, MGMT, and TERT; molecular classification of pediatric gliomas, facilitating personalized treatment approaches; and evaluation of therapeutic strategies, including inhibitors targeting IDH, BRAF, EGFR, and CDK4/6. To enhance accessibility and translational impact, results were deployed through an interactive Shiny web application, providing researchers, clinicians, and decision-makers with user-friendly access to gene expression profiles, mutational landscapes, and biomarker-driven insights. Beyond confirming known alterations, the novelty of this work lies in delivering a robust, standardized and reproducible framework for large-scale genomic data integration in pediatric gliomas, paving the way for precision oncology.

153. O8-02. DEVELOPMENT OF A COMPUTER DASHBOARD FOR REAL-TIME MONITORING OF QUALITY OF CARE PARAMETERS IN AN EMERGENCY DEPARTMENT AND PREVENTION OF ADVERSE EVENTS

Patricia Mariana Delnero¹, Carlos Hurtado², Pablo Roberto Manjarín³, Guillermo Alberto Keller⁴

1. *Hospital General de Agudos Donación Francisco J. Sanjoanni; Comité de Investigación Clínica*

2. *Hospital General de Agudos Donación Francisco J. Sanjoanni; Departamento de Urgencias*

3. *Hospital General de Agudos Donación Francisco J. Sanjoanni; Departamento de Urgencias*

4. *Universidad de Buenos Aires, Facultad de Medicina, Centro de Vigilancia y Seguridad de Medicamentos; Laboratorio de Medicina Personalizada y Data Mining*
patriciamdelnero@gmail.com

Background: Emergency department overcrowding could lead to increased morbidity and mortality. The study of this phenomenon

allows for the identification of early warning parameters for interventions and to improve patient outcomes and safety with a real time monitor panel. Aim: to evaluate correlation between emergency department occupancy rates and the incidence of causes of morbidity and mortality. Methods: A single-center, observational, registry-based cohort study was performed including all consecutive adults admitted to the general emergency department during one year. The bed occupancy rate, length of stay in the emergency department, and occurrence of unexpected cardiac arrests were evaluated for each day. A correlation analysis was performed between the numerical variables, and potential cutoff points for the occupancy rate were defined to assess it as a risk factor for increased mortality and unnecessary prolongation of stay. Results: During the study period, 2,209 adult patients were admitted to our registry. Among these, 108 patients experienced in-hospital (emergency department) cardiac arrest (68 [62%] linked to pre-existing terminal illnesses). A significant association was found between bed occupancy (>50%) and prolonged care times (RR 1.56, [1.21 to 2.02]), hospital deviation (RR 1.12, [1.05 to 1.19], and direct discharge from the emergency room (RR 1.60, [1.26 to 2.10]). This reallition increases exponentially depending on bed occupancy, with prolongations (X2) of care times when occupancy is greater than 80%. Conclusion: Maximum emergency department occupancy was strongly associated with deterioration of quality of care parameters. Adequate monitoring would be important to reduce unexpected outcomes.

154. O8-03. IN SILICO IDENTIFICATION OF PROTEIN-PROTEIN INTERACTION DOMAINS IN THE RNA-BINDING PROTEIN RRM1 OF TRYPANOSOMA BRUCEI

M. Clara Corso¹, Analía Nittolo², Ana L. Benacerraf³, Timothy J. Cardozo⁴, Javier G. De Gaudenzi⁵, Gabriela V. Levy⁶

1. *Instituto de Investigaciones Biotecnológicas, Universidad Nacional de San Martín (UNSAM) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). - Escuela de Bio y Nanotecnologías (EByN), Universidad Nacional de San Martín.; Regulación postranscripcional de genes*

2. *Universidad Nacional de La Matanza, Departamento de Ciencias de la Salud, San Justo, Argentina. - Comisión de Investigaciones Científicas (CIC-PBA); Regulación postranscripcional de genes*

3. *New York University School of Medicine, New York, NY, United States; NYU Langone Health*

4. *New York University School of Medicine, New York, NY, United States; NYU Langone Health*

5. *Instituto de Investigaciones Biotecnológicas, Universidad Nacional de San Martín (UNSAM) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). - Escuela de Bio y Nanotecnologías (EByN), Universidad Nacional de San Martín.; Regulación postranscripcional de genes*

6. *Instituto de Investigaciones Biotecnológicas, Universidad Nacional de San Martín (UNSAM) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). - Escuela de Bio y Nanotecnologías (EByN), Universidad Nacional de San Martín.; Regulación postranscripcional de genes*

m.clara.corso@gmail.com

In trypanosomatids, transcription is polycistronic and gene expression was long thought to be regulated mainly at the post-transcriptional level by RNA-binding proteins (RBPs). These proteins, including the conserved serine/arginine-rich (SR) family, play essential roles in RNA transcription, processing, export, and mRNA stability, while chromatin state and epigenetic marks have also emerged as relevant contributors to gene regulation. *Trypanosoma brucei* RRM1 (TbRRM1) is a nuclear RBP involved in RNA metabolism and chromatin organization, whose depletion alters transcription elongation, promotes chromatin compaction, and induces R-loop accumulation. Recently, our group demonstrated through computational and molecular studies that the RNA-binding domains of the T. cruzi SR protein, an ortholog of TbRRM1, provide a platform for drug interaction, highlighting the potential of SR proteins as novel trypanocidal targets. In a previous study, we identified TbRRM1 partners by liquid chromatography tandem-mass spectrometry (LC-MS/MS), revealing several previously uncharacterized interacting proteins.

The aim of the present work was to apply different molecular docking tools (ICM and AlphaFold) to identify TbRRM1 domains involved in protein-protein interactions and validate candidate partners. By integrating results from different predictors, we confirmed TbZFP3 (Tb927.3.740), the ATP-dependent RNA helicase (Tb927.11.4380), and Elongation Factor 1 alpha (Tb927.10.2090), among others, as interactors of TbRRM1. Furthermore, our findings revealed the homo-dimerization capacity of TbRRM1, providing new insights into its biological role and/or regulation. Together, these results contribute to clarifying the function of TbRRM1, deepening our understanding of Trypanosoma biology, and pointing to potential therapeutic targets.

155. O8-04. INTEGRATION OF TRANSCRIPTOMIC DATA TO IDENTIFY SYSTEMIC BIOMARKERS OF CELIAC DISEASE

Julián Francisco Maggio¹, Gabriel Alejandro De Diego², Gabriel Tolosa³, Mauricio César De Marzi⁴

1. Universidad Nacional de Luján; Grupo de Investigaciones Básicas y Aplicadas en Inmunología y Bioactivos (GIBAIB), Instituto de Ecología y Desarrollo Sustentable (INEDES) (Universidad Nacional de Luján - CONICET), Argentina; Universidad Nacional de Luján, Departamento de Ciencias Básicas, Argentina; FOCIS Center of Excellence - Vaccines and Immuno Therapies against Infections and Cancers (VITIC); Comisión de Investigaciones Científicas (CIC).
2. Universidad Nacional de Luján; Grupo de Investigaciones Básicas y Aplicadas en Inmunología y Bioactivos (GIBAIB), Instituto de Ecología y Desarrollo Sustentable (INEDES) (Universidad Nacional de Luján - CONICET), Argentina; Universidad Nacional de Luján, Departamento de Ciencias Básicas, Argentina; FOCIS Center of Excellence - Vaccines and Immuno Therapies against Infections and Cancers (VITIC).
3. Universidad Nacional de Luján; Universidad Nacional de Luján, Departamento de Ciencias Básicas, Argentina.
4. Universidad Nacional de Luján; Grupo de Investigaciones Básicas y Aplicadas en Inmunología y Bioactivos (GIBAIB), Instituto de Ecología y Desarrollo Sustentable (INEDES) (Universidad Nacional de Luján - CONICET), Argentina; Universidad Nacional de Luján, Departamento de Ciencias Básicas, Argentina; FOCIS Center of Excellence - Vaccines and Immuno Therapies against Infections and Cancers (VITIC).

julianmaggio18@gmail.com

The diagnosis of celiac disease is complex due to its clinical variability and heterogeneous response to a gluten-free diet, highlighting the need for novel immunological biomarkers. Differential expression analysis was performed on three RNA-Seq datasets from duodenal biopsies (GSE131705, GSE146190, GSE159495), identifying differentially expressed genes (DEGs; $|\log_2FC| \geq 0.5$, 1 and 1.5). These were integrated into protein-protein interaction (PPI) networks to extract central nodes (hub DEGs). Subsequently, PBMCs microarray dataset (GSE113469) from patients on a gluten-free diet and controls were analysed, evaluating the presence and expression level of the previously identified hub DEGs. The results showed that several duodenal hub DEGs also exhibit differential expression in PBMCs. Overexpression of DLGAP5, ERBB2, CD24, FCGR3A, GBP1, and PFKFB4 was observed, as well as underexpression of ABCC2, SLC151, and FCGR3B. High expression of GBP1 and FCGR3A indicates persistent immune activation, being markers of response to IFN- γ /type II IFN and IgG-mediated activity. Overexpression of PFKFB4, DLGAP5, and CD24 suggests metabolic reprogramming towards glycolysis, proliferation of immune subpopulations, and changes in the adaptive immune response. Downregulation of FCGR3B indicates a lower activation of neutrophils, and its deletion has been linked with autoimmune diseases. ABCC2 and SLC15A1, which are related to drug metabolism, appear to have no connection with celiac disease despite their low expression in PBMCs. These findings suggest that some of the hub DEGs identified in the intestine could serve as non-invasive biomarkers for systemic monitoring of celiac disease, establishing a strong molecular correlation between local inflammation and systemic response in the blood.

156. O8-05. VALIDATION OF A BIOINFORMATICS PIPELINE FOR GERMLINE CNVS DETECTION AND FUNCTIONAL ANNOTATION FROM SHORT-READ HIGH-THROUGHPUT DNA SEQUENCING TECHNOLOGY

Martín M. Ledesma¹, Carmen L. Massini², Betiana M. Ziegler³, Micaela Carcione⁴, Claudia P. Radic⁵, Florencia Gili-berto⁶, Liliana C. Rossetti⁷, Carlos D. De Brasi⁸, Miguel M. Abelleiro⁹

1. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM).; Bioinformática
2. Instituto de Inmunología, Genética y Metabolismo (INIGEM), CONICET-Universidad de Buenos Aires (UBA). Buenos Aires, Argentina.; Distrofinopatías
3. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM).; Genética Molecular de la Hemofilia
4. Instituto de Inmunología, Genética y Metabolismo (INIGEM), CONICET-Universidad de Buenos Aires (UBA). Buenos Aires, Argentina.; Distrofinopatías
5. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM).; Genética Molecular de la Hemofilia
6. Instituto de Inmunología, Genética y Metabolismo (INIGEM), CONICET-Universidad de Buenos Aires (UBA). Buenos Aires, Argentina.; Distrofinopatías
7. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM).; Genética Molecular de la Hemofilia
8. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM).; Genética Molecular de la Hemofilia
9. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM).; Genética Molecular de la Hemofilia

mmlledesma88@gmail.com

The detection of germline copy number variants (CNVs) is a critical challenge in genomics and clinical genetics. Through a collaborative project between the laboratories of Molecular Genetics of Hemophilia (IMEX, CONICET-ANM), Dystrophinopathies (FyB-UBA/INIGEM, UBA-CONICET) and Bioinformatics Unit (IMEX, CONICET-ANM), we have developed a reliable and reproducible process for CNV detection and annotation, based on the GATK4 Germline CNV calling framework from whole exome (WES) and genome (WGS) sequencing, combining Bash scripting for high-throughput processing and R/Bioconductor for data integration and analysis. Read depth quantification was performed using CollectReadCounts, and cohort-wide Bayesian modeling was executed via GermlineCNVCaller. CNV genotyping was completed using PostprocessGermlineCNVCalls, generating VCF outputs per sample. Although no explicit Bayes Factor is reported, the model provides QA-scores-Phred-scaled supporting the copy number call which, categorized into five confidence levels for filtering. The pipeline was validated on two patients with partial gene deletion (two in F8 and one in DMD gene) all cases were previously confirmed by gap-PCR and MLPA, in addition an artificial (WES) with a deletion in DMD were generated and evaluated, successfully recovering expected events in all cases. CNV calls were combined across samples to determine recurrence and categorized accordingly. Variant tables were annotated using ClinVar, DGV, and gnomAD-SV, allowing functional interpretation and assessment the clinical relevance. The CNV calling-pipeline is currently offered as a high-level technological service (STAN), combining validated tools, advanced statistics, and multi-layered annotation. The workflow is fully reproducible for large cohorts, and adaptable to translational genomics and precision medicine research project.

157. O8-06. CHARACTERIZATION AND DIFFERENTIAL EXPRESSION ANALYSIS OF FMR1 MRNA ISOFORMS IN HUMAN TISSUES WITH LONG READ SEQUENCING

Marina Luz Ingravidì¹, Laura Kamenetzky², Liliana Dain³, Iana Ferder⁴

1. Instituto de Biociencias, Biotecnología y Biología transla-

cional, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Genética y Genómica de enfermedades hereditarias humanas

2. Instituto de Biociencias, Biotecnología y Biología translacional, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Genómica y Bioinformática de Patógenos

3. Instituto de Biociencias, Biotecnología y Biología translacional, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Genética y Genómica de enfermedades hereditarias humanas

4. Instituto de Biociencias, Biotecnología y Biología translacional, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Genética y Genómica de enfermedades hereditarias humanas
maru.luz98@gmail.com

The FMR1 gene (chromosome X), is implicated in four genetic disorders and, through alternative splicing, generates numerous isoforms. We are interested in Fragile X-associated Primary Ovarian Insufficiency (FXPOI) and the expression of isoforms in ovarian tissue. The aim of this work is to characterize and study the expression profile of FMR1 isoforms in granulosa cells (CG) and blood (S1 and S2, before and after ovarian hyperstimulation, respectively) from women enrolled in an ovidonation program without FXPOI. RNA was extracted from 5 patients with technical replicates for two samples. FMR1 was amplified using primers spanning the first and last exons, and amplicon-seq libraries were prepared for Oxford Nanopore sequencing. Data was processed with Dorado, demultiplexed, and mapped to GRCh38 using Minimap2. Isoforms were collapsed using FLAIR, clustered by sequence identity, and analyzed with SUPPA2. Samples yielded, on average, 481,605 reads, of which 91.6% aligned to FMR1. Out of the 82 distinct isoforms identified, 75 were unannotated. The most abundant isoforms, that represent >70% of the total reads from each sample, matched 3 known transcripts, while low-abundance isoforms showed variability between samples. For differential expression analysis, 27 isoforms were selected based on specificity and sensitivity established by ROC curves. S1 and S2 showed similar profiles, while S1/CG and S2/CG, showed 3 and 4 differentially expressed isoforms, respectively. These results pave the way for future disease biomarker research.

158. O8-07. DIGITAL PATHOLOGY AS A TOOL TO IDENTIFY PREDICTIVE MARKERS IN OSTEOSARCOMA

Alejo De Luca¹, Matías Valenzuela Alvarez², Gastón Angelini Marquiani³, Maximiliano Hernán D'adamo⁴, Mónica Loresi⁵, Germán Farfalli⁶, José Ignacio Albergo⁷, Luis Aponte⁸, Pablo Roitman⁹, Malena Mazza¹⁰, Marcela F. Bolontrade¹¹

1. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano Buenos Aires (HIBA)- Universidad del Hospital Italiano (IUHI), Buenos Aires, Argentina.; Laboratorio de Procesos Remodelativos y Nichos Celulares

2. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano Buenos Aires (HIBA)- Universidad del Hospital Italiano (IUHI), Buenos Aires, Argentina.; Laboratorio de Procesos Remodelativos y Nichos Celulares

3. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano Buenos Aires (HIBA)- Universidad del Hospital Italiano (IUHI), Buenos Aires, Argentina.; Laboratorio de Procesos Remodelativos y Nichos Celulares

4. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano Buenos Aires (HIBA)- Universidad del Hospital Italiano (IUHI), Buenos Aires, Argentina.; Laboratorio de Histología y Microscopia

5. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano Buenos Aires (HIBA)- Universidad del Hospital Italiano (IUHI), Buenos Aires, Argentina.; Laboratorio de Histología y Microscopia

6. Ortopedia oncológica, Hospital Italiano Buenos Aires (HIBA);

7. Ortopedia oncológica, Hospital Italiano Buenos Aires (HIBA);

8. Ortopedia oncológica, Hospital Italiano Buenos Aires (HIBA);

9. Anatomía patológica, Hospital Italiano Buenos Aires (HIBA);

10. Anatomía patológica, Hospital Italiano Buenos Aires (HIBA);

11. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano Buenos Aires (HIBA)- Universidad del Hospital Italiano (IUHI), Buenos Aires, Argentina.; Laboratorio de Procesos Remodelativos y Nichos Celulares
alejo.de@comunidad.ub.edu.ar

Osteosarcoma (OS) is the most common primary malignant bone tumor, predominantly affecting children and young adults. Despite aggressive treatment strategies, prognosis remains poor when pulmonary metastases occur, making early identification of predictive histological markers crucial. Conventional prognostic indicators, such as tumor necrosis rate following chemotherapy, remain limited in their ability to reliably predict metastatic outcome. In this study, we applied Masson's Trichrome staining combined with whole slide scanning and digital pathology analysis using QuPath to explore novel histopathological features that could serve as predictive markers of OS progression. Comparative histological evaluation revealed distinct patterns between diagnostic tumor biopsies and primary tumor resections, with collagen content showing a tendency to be higher in tumor resections (36,69±18,43% and 56,66±16,66%), suggesting extracellular matrix remodeling during tumor progression. Moreover, quantitative assessment of necrosis demonstrated a trend in which tumors exhibiting high necrotic areas were more frequently associated with metastatic dissemination compared to tumors with low necrotic percentage (62,94±30,24% and 71,50±32,60%). These findings support the hypothesis that extensive necrosis may foster an aggressive tumor phenotype and facilitate metastatic spread. Our results highlight the potential of integrating histochemical staining with digital pathology tools to improve predictive accuracy in OS. Although preliminary, these results suggest that necrosis quantification and collagen deposition analysis may contribute to refining risk stratification and patient management. Further studies with larger cohorts are required to validate these observations and establish robust digital pathology-based methodologies capable of guiding clinical decision-making in OS.

159. O8-08. EXPLORING THE RUNX-KLF4 AXIS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA: COMPUTATIONAL AND EXPERIMENTAL APPROACHES

Di Gaudio, Anabel¹, Salaberry, Pedro J², Schor, Ignacio E³, Couto, Facundo L⁴, Rubinstein, Natalia⁵, Raimondi, Ana R⁶

1. Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE), UBA-Conicet; Laboratorio de Biología del Cáncer Bucal

2. Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE), UBA-Conicet; Departamento de Fisiología, Biología Molecular y Celular, FCEN, UBA; Regulación de la Expresión Génica desde un Enfoque Integrativo

3. Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE), UBA-Conicet; Departamento de Fisiología, Biología Molecular y Celular, FCEN, UBA; Regulación de la Expresión Génica desde un Enfoque Integrativo

4. Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3), FBMC-FCEN-UBA; Laboratorio de Mecanismos Moleculares de la Metástasis

5. Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3), FBMC-FCEN-UBA; Laboratorio de Mecanismos Moleculares de la Metástasis

6. Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE), UBA-Conicet; Universidad de Buenos Aires, Cátedra de Anatomía Patológica-Facultad de Odontología (FOUBA); Laboratorio de Biología del Cáncer Bucal

anabeldigaudio@gmail.com

Head and neck squamous cell carcinomas (HNSCC) are highly prevalent and associated with high morbidity and limited therapeutic options. TF KLF4 is central to maintain epithelial homeostasis. We showed that its ablation in tongue epithelial compartment which includes stem cells (SC) induced preneoplastic lesions. KLF4 is also critical for SC maintenance and CSC generation in TNBC. RUNX1 has been reported to modulate KLF4 expression in TNBC cell lines (Couto et al, 2023). Here, we investigate RUNX-mediated regulation of KLF4 in HNSCC. We analyzed mRNA expression in TCGA-HN-

SCC versus adjacent tissue using UALCAN and assessed KLF4 and CD44 expression in Cal27 and HaCaT cells upon RUNX inhibition with Al-10-104, inhibitor of RUNX transcriptional activity, (0.25 and 10 μ M, 72 h) by RT-qPCR. Results. RUNX expression is inversely proportional to KLF4 expression in HNSCC TCGA samples (p-value 1.56E-03). RUNX1, RUNX2, and RUNX3 were over-expressed in HNSCC versus adjacent tissue (p-values 1.82E-02, 3.93E-02 and 1.62E-12 respectively). We found that the presence of RUNX consensus sites in the KLF4 promoter suggests potential regulatory interactions. We confirmed RUNX binding to KLF4 promoter by ChIP-seq data from several tissues, using ChIP-Atlas tools. Preliminary in vitro results showed that Al-10-104-mediated RUNX inhibition upregulated KLF4 in keratinocytes, but not in neoplastic Cal27 cells. Expression levels of the stemness marker CD44 appear to be upregulated upon RUNX inhibition in both cell lines. These findings suggest that RUNX negatively regulates KLF4 in keratinocytes, highlighting a potential role for the RUNX-KLF4 axis in HNSCC and warranting further investigation.

160. O8-09. TARGETING DISEASE ASSOCIATED REGIONS OF THE HUMAN GENOME WITH ADAPTIVE SAMPLING BY LONG READ SEQUENCING

Aldana Claps¹, Marina Luz Ingravid², Tania Castro³, Julieta Laiseca⁴, Dante Navares⁵, Natalia Macchiaroli⁶, Emilio Kolumensky⁷, Ines Sananez⁸, Ianina Ferder⁹, Laura Kamenetzky¹⁰, Melisa Taboas¹¹, Lilianna Dain¹²

1. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán". Buenos Aires, Argentina and Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina.; -

2. Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina.; -

3. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán". Buenos Aires, Argentina.; -

4. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán". Buenos Aires, Argentina.; -

5. Laboratorio MANLAB. Buenos Aires, Argentina.; -

6. Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina.; -

7. Hackensack Meridian Health - Center for Discovery and Innovation, United States.; -

8. Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina.; -

9. Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina.; -

10. Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina.; -

11. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán". Buenos Aires, Argentina.; -

12. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán". Buenos Aires, Argentina and Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina.; -
aldanaclaps@gmail.com

Oxford Nanopore Technologies (ONT) sequencing allows real-time basecalling of the region of the genome being sequenced. This characteristic is useful for a particular sequencing strategy called Adaptive Sampling (AS), a method designed to enrich regions of interest by rejecting off-target regions. In this work, we performed targeted long-read sequencing (T-LRS) using AS in

samples from 5 patients with different clinical characteristics: congenital cardiopathy (n=1), congenital adrenal hyperplasia (n=2), fragile-X syndrome (n=1) and Friedreich ataxia (n=1). A total of 769 targets were positively selected to T-LRS based on in silico panel genes or genomic regions associated with the four entities. After sequencing for 32 hours, between 1.7 and 9.2M reads were generated for each sample. More than 93% of the reads were mapped to the human genome (hg38) using minimap2. An in house pipeline was developed to detect different types of genetic and epigenetic variants using modbamtools, modkit, whatshap and claire3. In this early stage, the pipeline was applied to the sample from the Fragile-X Syndrome patient. The results show a mosaic of the CGG expansion in the 5'UTR of FMR1 gene. A 33% (+/- 13.9 SD) of FMR1 promoter was methylated. The triplets count was between 192-618 and shows a complete loss of interruptions. In conclusion, this technique allows the user to detect the exact amount of repetitions, the loss of the interruptions, as well as the presence of expansion mosaics while reducing the number of wet-lab methods needed.

POSTERS 9 - AAFE - FARMACOLOGÍA 2

DATE & TIME: 18/11/2025 13:00 - 14:30 H

Chairs: Guillermina Hernando, María Laura Barreiro Arcos

161. P9-13. ANALYSIS OF FIROCOXIB CONCENTRATIONS IN DOMESTIC CATS: INFLUENCE OF THE SURGICAL PROCEDURE

Sabrina Passini¹, Laura Montoya², Agustina Monfrinotti³, Martin Lupi⁴, Teo Quattrocchi⁵, Claudio Miguez⁶

1. UBA FCV; Cátedra de Farmacología

2. UBA FCV; Cátedra de Farmacología

3. UBA FCV; Cátedra de Farmacología

4. UBA FCV; Cátedra de Farmacología

5. UBA FCV; Cátedra de Farmacología

6. UBA FCV; Cátedra de Cirugía

spassini@fvet.uba.ar

Firocoxib (FCX) is a selective COX-2 inhibitor with analgesic and anti-inflammatory properties, commonly used in veterinary medicine. However, its pharmacokinetics in felines have not yet been fully characterized, particularly in surgical settings. The aim of this study was to compare plasma concentrations of FCX in domestic cats undergoing different routine surgical procedures (sterilization or dental procedures) with those in non-operated patients. Three groups of cats were included: Group A (no surgical intervention), Group B (dental scaling), and Group C (castration). All animals received oral FCX (Previcox®3mg/kg) 2h prior to the surgical intervention (B,C). Blood samples were collected at predetermined time points, and plasma concentrations determined by HPLC/UV were analyzed and compared. No adverse reactions or rescue analgesic requirements were observed in any of the groups. Plasma concentration ranges during surgical procedures were 0.13–0.65 μ g/ml and 0.10–0.80 μ g/ml for B and C, respectively, and 0.06–0.5 μ g/ml for A. No significant differences were found when comparing these ranges. However, at 24h, lower concentrations were observed in A, with significant differences detected only when compared with C. Plasma concentrations monitored during both surgical procedures remained above the reported value required to inhibit COX-280 for 24h in most patients. The higher plasma concentrations of FCX observed in B and C may be attributed to a combination of factors such as drug metabolism, distribution or excretion alterations, and interactions with anesthetics. Oral administration of FCX at 3mg/kg in cats an effective alternative for controlling inflammatory processes and pain during and after surgical procedures.

162. P9-14. LOCAL TOXICITY AND PHARMACOKINETICS OF A TOPICAL LIPOSOMAL FORMULATION FOR THE TREATMENT OF CUTANEOUS LEISHMANIASIS

Francesca Papera¹, Diego N. Ríos², Monica Sanchez³, Jesica Piovano⁴, Eliana Martinez⁵, Dolores C. Carrer⁶

1. Instituto Ferreyra - INIMEC - CONICET - Universidad

Nacional de Córdoba; Biofísica y nanotecnología
 2. Instituto Ferreyra - INIMEC - CONICET - Universidad Nacional de Córdoba; Biofísica y Nanotecnología
 3. Instituto Ferreyra - INIMEC - CONICET - Universidad Nacional de Córdoba; Neurobiología
 4. Instituto Ferreyra - INIMEC - CONICET - Universidad Nacional de Córdoba; Bioterio
 5. Instituto Ferreyra - INIMEC - CONICET - Universidad Nacional de Córdoba; Bioterio
 6. Instituto Ferreyra - INIMEC - CONICET - Universidad Nacional de Córdoba; Biofísica y Nanotecnología
 fpapera@immmf.uncor.edu

Cutaneous leishmaniasis (CL) is a parasitic disease transmitted by the bite of phlebotomine sandflies, which acquire the parasite by feeding on an infected mammal (zoonoses). Current therapies for CL are limited by toxicity and administration challenges. Topical formulations represent a promising strategy. The formulation under evaluation is a hydrogel containing phospholipids (PC) and miltefosine (Milt), which has shown encouraging efficacy in preclinical studies and in a clinical case. Local irritation was assessed in adult male Wistar rats using a modified Draize test (ISO 10993-23:2021; OECD 402). The evaluation was performed in an acute and in a chronic assay at five different drug concentrations and evaluated for up to 72 hours. To validate the irritation model, additional animals were treated with known irritants (0.5M NaOH and 10% SDS), confirming the method's sensitivity. Visual observation results show that none of the PC-Milt concentrations or controls caused irritation; histopathological evaluations are in progress. Finally, serum concentration of miltefosine after either oral or topical administration was measured. Three (oral) or twenty-seven male Wistar rats divided in three groups (topical) received the drug. Each animal received a single dose of the aqueous Milt solution or Milt-PC topical formulation. Plasma levels were quantified by HPLC-MS/MS at multiple time points. Preliminary data indicate that oral administration leads to approximately 4-fold higher systemic exposure than the topical route.

163. P9-15. FLURALANER, A NOVEL ECTOPARASITICIDE FOR USE IN CATTLE: DEVELOPMENT AND VALIDATION OF A UFLC-MS/MS METHOD FOR THE ASSESSMENT OF ITS PLASMA PHARMACOKINETIC BEHAVIOUR

Andrea Mariela Berkovic¹, Lucila Canton², Vanesa Gramuglia³, Carlos Lanusse⁴, Ignacio Alvarez⁵, Laura Moreno⁶

1. Centro de Investigación Veterinaria de Tandil (CIVETAN), Facultad de Ciencias Veterinarias, UNCPBA-CICPBA-CO-NICET; Laboratorio de Farmacología

2. Centro de Investigación Veterinaria de Tandil (CIVETAN), Facultad de Ciencias Veterinarias, UNCPBA-CICPBA-CO-NICET; Laboratorio de Farmacología

3. Centro de Investigación Veterinaria de Tandil (CIVETAN), Facultad de Ciencias Veterinarias, UNCPBA-CICPBA-CO-NICET; Laboratorio de Farmacología

4. Centro de Investigación Veterinaria de Tandil (CIVETAN), Facultad de Ciencias Veterinarias, UNCPBA-CICPBA-CO-NICET; Laboratorio de Farmacología

5. Centro de Investigación Veterinaria de Tandil (CIVETAN), Facultad de Ciencias Veterinarias, UNCPBA-CICPBA-CO-NICET; Laboratorio de Farmacología

6. Centro de Investigación Veterinaria de Tandil (CIVETAN), Facultad de Ciencias Veterinarias, UNCPBA-CICPBA-CO-NICET; Laboratorio de Farmacología

anmaberko@gmail.com

Fluralaner is a novel isoxazoline compound used to control ectoparasites in domestic animals. Since resistance to widely used drug families is increasing, fluralaner is being developed as a pharmacological alternative for ectoparasite control in cattle. However, no validated UFLC-MS/MS method has yet been described for its detection and quantification in bovine plasma, which is essential to characterise its pharmacokinetic behaviour and to optimise pharmaceutical formulations under development. This study aimed to

develop and validate a reliable UFLC-MS/MS method for the quantification of fluralaner in bovine plasma. The method was comprehensively validated in terms of linearity, precision (repeatability and reproducibility), accuracy, specificity, limit of detection (LOD), limit of quantification (LOQ), stability, recovery, and matrix effect (ME), using rigorous experimental procedures and statistical analyses. The LOD was established at 10 ng/mL, highlighting the method's high sensitivity. Absolute recovery ranged from 87% to 133%, and relative standard deviation (RSD%) ranged from 2% to 9% for intra-assay and from 5% to 10% for inter-assay, indicating excellent precision. Furthermore, both recovery (70%–133%) and precision (RSD%≤10%) were within acceptable analytical limits. The method also demonstrated good linearity, accuracy, robustness, and low measurement uncertainty, supporting its suitability for fluralaner determination in bovine plasma. Given its strong performance in the validation process, this method provides a critical tool for future pharmacokinetic and tissue studies of fluralaner in cattle.

164. P9-16. ANTIBIOFILMIC ACTIVITY AND MECHANISM OF ACTION OF THE COPPER(II) TERNARY COMPLEX WITH 5-HYDROXYTRYPTOPHAN AND 1,10-PHENANTHROLINE AGAINST CLINICALLY RELEVANT MICROORGANISMS

Juan J. Martínez Medina¹, Florencia A. Chyht², Lorena E. Guevara³, Libertad L. López Tévez⁴, Evelina G. Ferrer⁵, Patricia A. M. Williams⁶

1. Instituto de Investigaciones en Procesos Tecnológicos Avanzados (INIPTA, CONICET-UNCAUS); Laboratorio de Microbiología

2. Universidad Nacional del Chaco Austral; Laboratorio de Microbiología

3. Universidad Nacional del Chaco Austral; Laboratorio de Microbiología

4. Universidad Nacional del Chaco Austral; Laboratorio de Microbiología

5. Centro de Química Inorgánica (CEQUINOR, CONICET-UNLP); -

6. Centro de Química Inorgánica (CEQUINOR, CONICET-UNLP); -

juanjoc_mm09@yahoo.com.ar

The incidence of infections caused by antibiotic-resistant bacteria is steadily increasing, creating the need for new, effective antimicrobial agents. Biofilm formation represents an important virulence factor that allows microorganisms to better adhere to surfaces, potentially causing serious health complications associated with higher morbidity and mortality. We have previously synthesized and characterized the copper(II) ternary complex with 5-hydroxytryptophan and the auxiliary ligand 1,10-phenanthroline (Cu5-HTPfen). This complex has shown antimicrobial properties against bacterial strains from clinical isolates with a marked bactericidal effect and a synergistic effect when combined with commercial antibiotics. The aims of this study were to determine the antibiofilm activity of the complex and verify DNA cleavage as a mechanism of action against clinical isolate strains. The antibiofilm activity against clinical isolate *Staphylococcus aureus* strains (methicillin-resistant, MRSA) was evaluated using the crystal violet method in pre- and post-adhesion assays. DNA cleavage of DNA isolated from *Staphylococcus aureus* and *Escherichia coli* strains was determined by agarose gel electrophoresis. The results showed that the complex reduced biofilm formation in MRSA strains, even at subinhibitory concentrations with a dose-dependent behavior. The complex reduced biofilm formation by less than 50% in the pre-adhesion assay, while the reduction exceeded 50% in the post-adhesion assay. Additionally, the mode of action of the complex was analyzed through DNA cleavage assays of genomic DNA extracted from *Escherichia coli* and *Staphylococcus aureus* strains. In all the cases, DNA cleavage was evidenced by the disappearance of the corresponding band in the lanes where the DNA was exposed to the complex.

165. P9-17. COMPARATIVE ANALYSIS OF ESTIMATED AND OBSERVED PLASMA CONCENTRATIONS IN A MULTIPLE-DOSE REGIMEN OF FIROCOXIB IN DOGS

Agustina Monfrinotti¹, Luis Ambros², Ezequiel Lopez³, Teo Quattrocchi¹, Barbara Almoño⁵, Laura Montoya⁶

1. Universidad de Buenos Aires. Facultad de Ciencias Veterinarias.; Cátedra de Farmacología

2. Universidad de Buenos Aires. Facultad de Ciencias Veterinarias.; Cátedra de Farmacología

3. Universidad de Buenos Aires. Facultad de Ciencias Veterinarias.; Cátedra de Farmacología

4. Universidad de Buenos Aires. Facultad de Ciencias Veterinarias.; Cátedra de Farmacología

5. Universidad de Buenos Aires. Facultad de Ciencias Veterinarias.; Cátedra de Farmacología

6. Universidad de Buenos Aires. Facultad de Ciencias Veterinarias.; Cátedra de Farmacología

amonfrinotti@fvet.uba.ar

To estimate plasma concentrations (PC) of a drug following a multiple-dose regimen based on single-dose data, linear pharmacokinetic principles can be applied, provided the drug follows first-order kinetics and exhibits linear pharmacokinetics. Having previously confirmed these conditions in an 8-day multiple-dose study with firocoxib (FCX)—a selective COX-2 non-steroidal anti-inflammatory drug (NSAID)—in dogs, the objective of the present work was to validate predicted maximum plasma concentrations (C_{max}) and area under the curve (AUC) values calculated using the accumulation factor (AF), by comparing them to observed data from the multiple-dose regimen. C_{max} and AUC values were estimated for days 2, 3, 5, and 8 using appropriate formulas for steady-state and non-steady-state conditions. These predicted values were then statistically compared with those obtained from the pharmacokinetic analysis of the multiple-dose study. According to the estimation formulas, some mean±DS values obtained for days 3 and 5 were: C_{max} (μg/ml): 0.70±0.25 and 1.03±0.25; AUC (h*ug/ml): 8.67±2.08 and 13.33±4.28, respectively. In comparison, the observed values for the same days were: C_{max} (μg/ml): 1.04±0.30 and 1.16±0.42; AUC (h*ug/ml): 13.83±3.91 and 13.69±4.94. The AF calculated by formula was 1.22±0.09, while the AF obtained from the AUC ratio (day 8/day 1) was 1.22±0.59. No statistically significant differences were found between observed and estimated values for C_{max}, AUC (steady and non-steady-state), and AF. The results of this study demonstrate that estimation methodologies based on accumulation factors are a valid tool for predicting drug exposure under multiple-dose regimens.

166. P9-18. EXPLORING PLANT-DERIVED ALKALOIDS AS MOLECULAR MODULATORS OF ANGIOGENESIS

Priscila A. Lanza¹, Pablo D. Cassani², Ana V. Basso³, María C. Carpinella⁴, Mariano D. Vera⁵, Mariana B. Joray⁶

1. Instituto de Investigaciones en Biodiversidad y Biotecnología (INBIOTEC) - CONICET - UNMdP; QUIAMM (Grupo de Química Analítica y Modelado Molecular) - Dpto Química y Bioquímica - FCEyN

2. Instituto de Investigaciones en Biodiversidad y Biotecnología (INBIOTEC) - CONICET - UNMdP; QUIAMM (Grupo de Química Analítica y Modelado Molecular) - Dpto Química y Bioquímica - FCEyN

3. Centro de Investigación y Desarrollo en Inmunología y Enfermedades Infecciosas (CIDIE) - CONICET - UCC; Laboratorio de Química Fina y Productos Naturales

4. Centro de Investigación y Desarrollo en Inmunología y Enfermedades Infecciosas (CIDIE) - CONICET - UCC; Laboratorio de Química Fina y Productos Naturales

5. Instituto de Investigaciones en Biodiversidad y Biotecnología (INBIOTEC) - CONICET - UNMdP; QUIAMM (Grupo de Química Analítica y Modelado Molecular) - Dpto Química y Bioquímica - FCEyN

6. Centro de Investigación y Desarrollo en Inmunología y Enfermedades Infecciosas (CIDIE) - CONICET - UCC; Laboratorio de Química Fina y Productos Naturales
planza@mdp.edu.ar

The search for new strategies to modulate angiogenesis has gained increasing attention. Chronic deregulation of this process contrib-

utes to tumor growth as well as to several inflammatory and ocular diseases, making the identification of new antiangiogenic molecules a priority in drug development. The flora of Argentina represents a valuable source of bioactive compounds. In our previous work, the ethanol extract of *Zanthoxylum coco* showed remarkable antiangiogenic activity, leading to the isolation of β-fagarine as one of its active constituents. In a subsequent stage of the same study, further investigation of this extract enabled the isolation of a second alkaloid, γ-fagarine, which also displayed antiangiogenic activity. The biological effects of the compounds were evaluated through in vitro assays. Tube formation experiments using bovine aortic endothelial cells demonstrated inhibition of capillary-like network formation. In addition, the effects of the alkaloids on VEGF-induced cell migration, invasion, and proliferation were investigated. Molecular modeling studies were also conducted. Protein models built from the crystallographic structures of VEGFR-2 (PDB ID: 4ASD, 2P2I, 4AGC) and PKC-α / PKC-β2 (PDB ID: 3IW4 and 2I0E, respectively) were employed. Docking studies were followed by molecular dynamics simulations and binding free energy analyses. The obtained results suggested that the interaction of β-fagarine and γ-fagarine with PKC isoforms may contribute to understanding the antiangiogenic effect observed in vitro. Overall, our findings highlight *Z. coco* as a promising source of antiangiogenic molecules and point to β-fagarine and γ-fagarine as valuable leads for the rational design of improved analogs.

167. P9-19. DESIGN AND CHARACTERIZATION OF BOVINE SERUM ALBUMIN HYDROGELS: A PROMISING PLATFORM FOR CONTROLLED DRUG DELIVERY

Eva María del Mar Velez¹, Carolina Maldonado-Galdeano², Rosana chehin³, Silvina Chaves⁴

1. Instituto de Investigaciones en Medicina Molecular y Celular Aplicada; Biotecnología

2. Centro de Referencias para Lactobacilos; Inmunología

3. Instituto de Investigaciones en Medicina Molecular y Celular Aplicada; Neurología

4. Instituto de Investigaciones en Medicina Molecular y Celular Aplicada; Biotecnología

emvelez.ev@gmail.com

Improving drug transport and controlled release at target sites requires innovative strategies. In this regard, hydrogels, three-dimensional networks capable of holding substantial water and solutes, play an important role. Here, we explore the development of bovine serum albumin (BSA) hydrogels as effective carriers for drug delivery applications. To achieve this, BSA aggregation was studied under specific conditions involving pH (7 and 5), buffer (PBS, TRIS-HCl), mild denaturation temperature (65°C), and incubation time. The process was monitored using fluorescence spectroscopy and aggregation rate analysis. The resulting hydrogels were dehydrated and evaluated for absorption capacity and molecule release profile, simulating physiological fluids. Promising hydrogels were evaluated in vivo using BALB/c mice, examining inflammatory responses following oral or systemic administrations. Selected hydrogels exhibited minimal immune response and efficient distribution. In addition, it can be biodegraded enzymatically and naturally in PBS without promoting aggregation with native albumin under physiological conditions. Hydrogels formed at pH 7.4 with high BSA concentrations (≥ 80%) displayed robust aggregation. Upon dehydrating and rehydrating in water or DMEM culture media, hydrogels obtained with 15 mg/mL BSA exhibited enhanced absorption capacity and variable drug release profiles, depending on properties of the compound. The proteinaceous nature of these hydrogels provides opportunities for functionalization with specific antibodies, potentially enabling targeted drug delivery within the body. This study highlights the potential of BSA-based hydrogels as safe and efficient drug carriers, suggesting their potential for advancing therapeutic interventions. However, further research is required to fully explore their capabilities and optimize their application in biomedical settings

168. P9-20. NTINOCICEPTIVE EFFICACY OF A SELF-NA-NOEMULSIFYING MARINE OMEGA-3 FORMULATION IN CHRONIC NEUROPATHIC PAIN INDUCED BY SCIATIC

NERVE CONSTRICTION IN RATS

Karem Alejandra Arrigoni-Rodríguez¹, Florencia Elorriaga², Carlos Laino³, María Eugenia Olivera⁴

1. *Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba y CONICET-UNC; Unidad de Investigación y Desarrollo en Tecnología Farmacéutica*

2. *Instituto de Biotecnología, Centro de Investigación e Innovación Tecnológica Universidad Nacional (CENIT), Universidad Nacional de La Rioja, La Rioja, Argentina.; Instituto de Biotecnología*

3. *Instituto de Biotecnología, Centro de Investigación e Innovación Tecnológica Universidad Nacional (CENIT), Universidad Nacional de La Rioja, La Rioja, Argentina.; Instituto de Biotecnología*

4. *Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba y CONICET-UNC; Unidad de Investigación y Desarrollo en Tecnología Farmacéutica (UNITEFA)*

karem.arrigoni@unc.edu.ar

Chronic neuropathic pain is difficult to manage, and therapies with consistent efficacy are limited. Omega-3 fatty acids (O3) exhibit anti-inflammatory and nociceptive modulatory effects, but low oral bioavailability can restrict sustained analgesic action. Pre-emulsification of marine oils has been shown to enhance intestinal absorption, and self-nanoemulsifying drug delivery systems (SNEDDS) represent a technological strategy to optimize oral delivery of bioactive lipids such as O3. This study evaluated the antinociceptive efficacy of a SNEDDS formulated with marine O3-enriched oil (OM), comparing its effects to conventional OM and saline control, in a chronic neuropathic pain model induced by sciatic nerve constriction (CCI) in male Wistar rats. Treatments were administered intragastrically at 720 mg/kg O3 once daily for 7 days. Behavioral assessments included Hot Plate Test (thermal nociception), Von Frey Filaments Test (mechanical allodynia), Rotarod Test (motor coordination), and Walking Track Test (motor function). Evaluations were conducted at baseline (Day -3) and Days 7 and 14 post-CCI, recording paw withdrawal latency, minimal force eliciting response, latency to fall, and gait parameters, as appropriate. Both OM and SNEDDS significantly improved pain-related behaviors compared to saline ($p < 0.05$), with SNEDDS showing a trend toward greater and more consistent antinociceptive effects. Increasing the sample size in the SNEDDS group is expected to confirm this trend, reinforcing the functional advantage of the formulation over conventional oil. These findings suggest that SNEDDS enhances the functional efficacy of marine O3 in chronic neuropathic pain, optimizing oral delivery and the consistency of analgesic effects beyond conventional oil administration

169. P9-21. PHARMACOKINETICS OF MELOXICAM AFTER INTRAMUSCULAR ADMINISTRATION IN LLAMAS (LAMA GLAMA)

Verónica E. Kreil¹, Ezequiel López², Bárbara Almoño³, Ernestina Anan Fain Binda⁴, M. Florencia Gallelli⁵, Laura Montoya⁶

1. *Universidad de Buenos Aires, Facultad de Ciencias Veterinarias; Cátedra de Farmacología*

2. *Universidad de Buenos Aires, Facultad de Ciencias Veterinarias; Cátedra de Farmacología*

3. *Universidad de Buenos Aires, Facultad de Ciencias Veterinarias; Cátedra de Farmacología*

4. *Universidad de Buenos Aires, Facultad de Ciencias Veterinarias; Cátedra de Farmacología*

5. *Universidad de Buenos Aires, Facultad de Ciencias Veterinarias; Instituto de Investigación y Tecnología en Reproducción Animal (INITRA)*

6. *Universidad de Buenos Aires, Facultad de Ciencias Veterinarias; Cátedra de Farmacología*
kreil@fvet.uba.ar

Meloxicam (MLX) is a non-steroidal anti-inflammatory drug widely

used in veterinary medicine for inflammation and pain. Its use in llamas requires caution due to limited available information and potential physiological differences compared with other domestic species. The aim of this study was to determine the pharmacokinetic profile of MLX in llamas following intramuscular (IM) administration. Six female llamas, 6 ± 2 years old and weighing 150 ± 23 kg, were included. A single IM dose of MLX (0.5 mg/kg) was administered in the triceps muscle. Blood samples were collected from both jugular veins at 10, 20, 30, 45, and 60 minutes, and at 2, 3, 4, 6, 8, 10, 12, 15, 24, 30, 48, 72, and 96 hours. Plasma MLX concentrations were determined by high-performance liquid chromatography (HPLC) with UV detection, using methods previously validated in our laboratory. Chromatographic integration and analysis were performed with Chromeleon 6.8®. Non-compartmental pharmacokinetic analysis was carried out using Phoenix WinNonlin version 8.0 (Certara). No pain at the IM injection site or other adverse reactions were observed. Pharmacokinetic parameters obtained were: C_{max} 2.09 ± 0.19 $\mu\text{g/ml}$, T_{max} 6 ± 1.26 h, AUC_{inf} 38.27 ± 9.18 $\mu\text{g} \cdot \text{h/ml}$, $t_{1/2\lambda}$ 20.39 ± 4.26 h, and MRT_{inf} 22.28 ± 4.04 h. Results show that MLX has a rapid onset and a prolonged half-life, similar to other species. At the administered dose, MLX may allow for extended dosing intervals, as plasma concentrations remained above the theoretical therapeutic threshold (minimum effective concentration 0.2 $\mu\text{g/ml}$).

170. P9-22. COMPLEX GENERIC DRUGS PRODUCTS (CGDP): A CHALLENGE TO DRUG INTERCHANGEABILITY

Mariano Hector Nuñez¹, Néstor Pinca², Guido Pesce³

1. *Institute of Pharmacology, School of Medicine, University of Buenos Aires, Argentina; Farmacovigilancia*

2. *Third Chair of Pharmacology, School of Medicine, University of Buenos Aires, Argentina.; Farmacovigilancia*

3. *Institute of Pharmacology, School of Medicine, University of Buenos Aires, Argentina; Farmacovigilancia*

mariano.nunez@gmail.com

Introduction: Complex Generic Drug Products (CGDPs) represent a growing challenge in clinical pharmacology, mainly due to the difficulty in establishing pharmaceutical equivalence and bioequivalence, which are essential to ensure interchangeability. Objective: Characterize selected CGDPs of high therapeutic value, identify the sources of their complexity, and classify them according to the Hussaerts framework. Materials and Methods: The Food and Drug Administration (FDA) list of CGDPs was reviewed. From this list, a subgroup of products were selected and their sources of complexity were analyzed. Results: Eight CGDPs were selected: betamethasone acetate + sodium phosphate, intravitreal dexamethasone, fluticasone/umeclidinium/vilanterol,latanoprost, paliperidone palmitate, vaginal progesterone, injectable semaglutide, and tirzepatide. Each product exhibits one or more features of CGDPs, which include complex formulations/dosage forms, complex active pharmaceutical ingredients, complex routes of administration, or the combination of APIs with medical devices. Conclusion: The interchangeability of CGDPs cannot be evaluated using the same regulatory criteria as small-molecule drugs. Beyond physicochemical characterization, immunogenicity studies, pharmacokinetics, pharmacodynamics, and even clinical trials may be required to ensure therapeutic equivalence. These products represent both scientific and regulatory challenges and highlight the need to reassess conventional approaches to therapeutic equivalence / interchangeability.

POSTERS 10 - AAFE - FARMACOLOGÍA 3

DATE & TIME: 18/11/2025 13:00 - 14:30 H

Chairs: Natalia Alza, Daniela Quinteros

171. P10-17. β -LAPACHONE-BODIPY AS A PROMISING SELECTIVE CYTOTOXIC AGENT FOR NSCLC: IN VITRO MECHANISTIC EVIDENCE OF OXIDATIVE STRESS AND MITOCHONDRIAL DYSFUNCTION

Mariana D. Kovalovsky-Barreiro¹, Eufirio N. da Silva Júnior², Claudia Anesini³, María L. Barreiro Arcos⁴, Horacio E. Romeo⁵

1. Institute of Biomedical Research (BIOMED-CONICET), Faculty of Engineering and Agricultural Sciences, Pontifical Catholic University of Argentina (UCA), Av. Alicia Moreau de Justo 1600 (C1107AFB), Buenos Aires, Argentina.; Laboratory of Physiology and Experimental Microsurgery
2. Institute of Exact Sciences, Federal University of Minas Gerais (UFMG), Belo Horizonte, Brazil.; Department of Chemistry
3. Institute of Chemistry and Drug Metabolism (IQUIMEFA), Faculty of Pharmacy and Biochemistry, University of Buenos Aires (UBA), Buenos Aires, Argentina.; Department of Pharmacognosy
4. Institute of Biomedical Research (BIOMED-CONICET), Faculty of Engineering and Agricultural Sciences, Pontifical Catholic University of Argentina (UCA), Av. Alicia Moreau de Justo 1600 (C1107AFB), Buenos Aires, Argentina.; Laboratory of Physiology and Experimental Microsurgery
5. Institute of Biomedical Research (BIOMED-CONICET), Faculty of Engineering and Agricultural Sciences, Pontifical Catholic University of Argentina (UCA), Av. Alicia Moreau de Justo 1600 (C1107AFB), Buenos Aires, Argentina.; Laboratory of Physiology and Experimental Microsurgery
mlbarreiro@yahoo.com.ar

Background: Non-small cell lung cancer (NSCLC) remains a major clinical challenge due to its high mortality and resistance to conventional therapies. Therefore, the search for selective agents that minimize cytotoxicity in normal cells is essential. β -lapachone-BODIPY (β -lap-Qd), a chemically synthesized derivative of β -lapachone, has emerged as a promising candidate. **Aim:** This study aimed to evaluate the cytotoxic effects of β -lap-Qd on LP07 lung adenocarcinoma cells, focusing on mitochondrial function and reactive oxygen species (ROS) involvement. **Methods and Results:** In vitro assays demonstrated a concentration-dependent cytotoxic effect of β -lap-Qd on LP07 cells, with a CC50 of 18.4 μ M, while no significant toxicity was observed in MCR-5 normal lung fibroblasts (MTT-test; p less than 0.05; $n=3$ independent experiments). Apoptotic morphological changes, including chromatin condensation and nuclear fragmentation, were detected using DAPI staining and fluorescence microscopy. Apoptosis was further confirmed by caspase-3 activation (p less than 0.01) and DNA ladder fragmentation. Alterations in mitochondrial membrane potential were observed using JC-1 staining and flow cytometry, showing initial hyperpolarization followed by depolarization, temporally associated with apoptosis. Moreover, β -lap-Qd significantly increased $O_2^{\cdot -}$ generation (p less than 0.01), suggesting apoptosis via oxidative stress and mitochondrial dysfunction. Notably, no mitochondrial colocalization of β -lap-Qd was observed, indicating an indirect effect on these organelles. **Conclusion:** β -lap-Qd exhibits potent and selective pro-apoptotic activity in LP07 lung cancer cells, mediated by ROS production and mitochondrial dysfunction. These findings highlight its potential as a novel selective cytotoxic agent for NSCLC and support its evaluation in vivo studies. **Keywords:** lung adenocarcinoma; β -lapachone-BODIPY; apoptosis; ROS

172. P10-18. MODULATORY EFFECTS OF MINTHSTACHYS VERTICILLATA AQUEOUS EXTRACT ON TRPV1: IN SILICO, IN VITRO AND IN VIVO EVIDENCE

- Rodríguez Basso Angeles Gloria¹, María Andrea Carranza², Pedro Martín³, Hernán Bach⁴, Héctor Juan Prado⁵, Susana Beatriz Gorzalczy⁶
1. a Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Cátedra de Farmacología
 2. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica-CONICET; Cátedra de Farmacología
 3. Universidad Nacional de La Plata, Facultad de Ciencias Exactas-CONICET; Centro Científico Tecnológico CONICET -La Plata
 4. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Cátedra de Farmacobotánica y Museo de Farmacobotánica
 5. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica-CONICET; Departamento de Tecnología Farma-

céutica, Cátedra de Tecnología Farmacéutica II
6. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Cátedra de Farmacología
angelesbasso@gmail.com

Chronic abdominal pain is a frequent and debilitating symptom in gastrointestinal disorders such as irritable bowel syndrome and inflammatory bowel diseases, in which the TRPV1 channel plays a key role as a modulator of nociception and neuroinflammation. In this context, the effects of the aqueous extract of *Mintostachys verticillata* (peperina), traditionally used in Argentine folk medicine for digestive disorders, were evaluated on TRPV1 through a three-level approach: molecular docking, in vitro studies, and an in vivo model of visceral pain. Docking studies showed that five compounds from the extract were able to establish interactions with the key residues Tyr511 and Ser512 of TRPV1, with caffeoyl-rosmarinic acid displaying the most stable binding to both amino acids. In HEK293 cells transfected with TRPV1, the extract acted as a partial agonist, increasing current amplitude 2.61 ± 0.32 -fold compared to control and blocking $61.0 \pm 0.7\%$ of capsaicin (250 nM)-evoked current. In a murine model of intracolonic capsaicin-induced visceral pain, oral administration of the extract (62.5–500 mg/kg) dose-dependently reduced pain-related behaviors and referred mechanical hyperalgesia. These findings demonstrate, for the first time, the ability of *M. verticillata* to interact with and modulate TRPV1, providing preliminary evidence of its potential antinociceptive effect in visceral pain associated with gastrointestinal disorders.

173. P10-19. ORAL PETECHIAE ASSOCIATED WITH ADALIMUMAB TREATMENT IN A PEDIATRIC PATIENT WITH UL-CERATIVE COLITIS: CASE REPORT

- Lucía Tovar Grimoldi¹, María Clara Peralta², Agustina Sanchez Cavalieri³, Roberto Alejandro Diez⁴, Florencia Amato⁵
1. Área de Farmacovigilancia; BIOSIDUS S.A.U.
 2. Área de Farmacovigilancia; BIOSIDUS S.A.U.
 3. Área de Farmacovigilancia; BIOSIDUS S.A.U.
 4. Cátedra II de Farmacología; Facultad de Medicina de la Universidad de Buenos Aires
 5. Área de Farmacovigilancia; BIOSIDUS S.A.U.
l.tovar@biosidus.com.ar

Pediatric ulcerative colitis (UC) tends to be more severe than in adults, with a risk of malnutrition and growth retardation. Anti-TNF α biological therapies, such as adalimumab, have transformed management by achieving clinical remission, mucosal healing, and improved development. A 13-year-old male patient with UC limited to the sigmoid colon, confirmed by colonoscopy and biopsy. With a history of moderate asthma and autoimmune hypothyroidism, he started adalimumab (Hyrimoz 40 mg SC every 2 weeks) in November 2024, with a favorable clinical response. In January 2025, he presented with petechiae on the oral mucosa, particularly on the palate, with mild gingival bleeding, without skin or systemic involvement. Laboratory tests were normal except for mild eosinophilia (7.4%). Hematological and immunological causes were ruled out, and an idiosyncratic adverse effect of adalimumab was considered. Given the therapeutic benefit and the risk of UC reactivation, it was decided to continue therapy under supervision. Currently, the patient has intermittent oral lesions. Oral manifestations associated with adalimumab are rare and poorly documented. This case highlights the importance of balancing risks and benefits, prioritizing sustained remission and patient growth. According to the pharmacovigilance assessment, this reaction is considered to be of probable causality, as it is temporally related to the administration of the drug, is not explained by other causes such as the underlying condition or the use of other drugs or substances, and is intermittent, with a tendency to improve when concentrations decrease, although it reappears with new administrations, in accordance with the WHO definition.

174. P10-20. USE OF VITAMIN D AND CALCIUM IN OUTPATIENTS AFFILIATED WITH A SOCIAL HEALTH INSURANCE SYSTEM IN CORRIENTES AND RESISTENCIA, 2024–2025

Sergio Daniel Morales¹, María Teresa Rocha², María Eugenia Horna³, Lorena dos Santos Antola⁴, Isabel Hartman⁵

1. Facultad de Medicina. Universidad Nacional del Nordeste; Cátedra de Farmacología.

2. Facultad de Medicina. Universidad Nacional del Nordeste; Cátedra de Farmacología.

3. Facultad de Medicina. Universidad Nacional del Nordeste; Cátedra de Farmacología.

4. Facultad de Medicina. Universidad Nacional del Nordeste; Cátedra de Farmacología.

5. Facultad de Medicina. Universidad Nacional del Nordeste; Cátedra de Farmacología.

morales.sergiodaniel500@gmail.com

Calcium and vitamin D are widely used for the prevention and treatment of bone diseases, although prolonged use beyond the recommended duration may represent inappropriate use. The aim was to evaluate the impact of an educational intervention on prescriptions of vitamin D and calcium in outpatients affiliated to a social health insurance system in Corrientes and Resistencia, during 2024–2025 period. A drug utilization study was conducted using a prescription-indication design, with a before-and-after analysis of an educational intervention targeted at consumers. The intervention consisted of group meetings and personalized counseling, complemented with the distribution of informational materials. Treatment plan forms for prolonged therapy (1 year) including prescriptions of vitamin D, calcium, or their combination were analyzed. The Variables included were sex, age, diagnoses, and prescribed medications. Of 1,250 forms, 80 (7%) corresponded to prescriptions of vitamin D, calcium, or both, for the diagnoses of osteopenia (n=35), osteoporosis (n=25), vitamin D deficiency (n=15), and without diagnosis (n=5). Mean age was 55 years; 60 (75%) were female. Before the educational intervention, the most prescribed drugs were calcium + vitamin D (n=40), calcium (n=20), and vitamin D (n=20). After the intervention, deprescription was achieved in 22 patients: calcium + vitamin D in 15 patients and vitamin D in 7 patients, due to lack of coverage or lack of justification for their indication. The educational intervention successfully reduced the prescription of calcium and vitamin D, promoting the rational use of medications and avoiding unjustified expenses for both patients and the social health system

175. P10-21. ANTIBIOTIC PRESCRIPTION FOR HOSPITALIZED PATIENTS IN THE MEDICAL CLINIC ROOM AT A REFERRAL HOSPITAL. CORRIENTES, 2025

María Eugenia Horna¹, Ludmila Belén Cancian Caamaño², Isabel Hartman³, Lorena dos Santos Antola⁴, María Teresa Rocha⁵

1. Facultad de Medicina-Universidad Nacional del Nordeste; Farmacología

2. Facultad de Medicina-Universidad Nacional del Nordeste; Farmacología

3. Facultad de Medicina-Universidad Nacional del Nordeste; Farmacología

4. Facultad de Medicina-Universidad Nacional del Nordeste; Farmacología

5. Facultad de Medicina-Universidad Nacional del Nordeste; Farmacología

eugeniahorna@med.unne.edu.ar

The World Health Organization (WHO), through the AWARe classification (Access–Warning–Reserve), provides evidence-based guidelines for the selection of antibiotics in the most frequent infections. Aim: To characterize the empirical prescription of systemic antibiotics (ATB) in hospitalized patients in the medical clinic room at a healthcare referral center in Corrientes, and to assess their rationality. A cross-sectional, observational, descriptive research classified as Drug Utilization Study (prescription-indication type) was conducted. Medical records and nursing charts of hospitalized patients between February and July 2025 were analyzed. Variables included age, sex, diagnosis, prescribed antibiotic, presence of comorbidities, and adaptation to WHO AWARe guidelines and other current clinical practice guidelines. From 95 medical records and nursing charts of patients hospitalized in a medical clinic room, 58%

corresponded to male patients, with a mean age of 52 (± 19) years. The most frequent diagnoses were community-acquired pneumonia (27%), diabetic foot infection (23%), hospital-acquired pneumonia (12%), and cellulitis (7%). Monotherapy was prescribed in 26% of cases (mainly ciprofloxacin and clindamycin), while 20% received fixed-dose combinations, predominantly piperacillin/tazobactam. Comorbidities were present in 76% of patients, mainly diabetes mellitus (10%) and hypertension (7%). In most cases, prescriptions were consistent with guidelines; however, empirical use of vancomycin in diabetic foot infections and colistin in pneumonia and pyelonephritis was identified as initial empirical treatment. Strengthening rational antibiotic use, in line with clinical practice guidelines, is an essential strategy to preserve their efficacy and safety.

176. P10-22. GREEN SYNTHESIS OF COPPER AND ZINC NANOMATERIALS BY A PEUMUS BOLDUS AQUEOUS EXTRACT

Gualdieri, Francisco L.¹, Rocha, Gabriela F.², DeMarzi, Mauricio C.³, Guerra, Liliana N.⁴

1. Universidad Nacional de Luján, Departamento de Ciencias básicas, Luján, Buenos Aires, Argentina; Laboratorio de Inmunología

2. Universidad Nacional de Luján, Departamento de Ciencias básicas, Luján, Buenos Aires, Argentina. INEDES-CO-NICET (Instituto Nacional de Ecología y Desarrollo Sustentable) - Universidad Nacional de Luján. Luján, Buenos Aires, Argentina.; Laboratorio de Inmunología

3. Universidad Nacional de Luján, Departamento de Ciencias básicas, Luján, Buenos Aires, Argentina. INEDES-CO-NICET (Instituto Nacional de Ecología y Desarrollo Sustentable) - Universidad Nacional de Luján. Luján, Buenos Aires, Argentina. FOCIS Center of Excellence - Vaccines and Immunotherapies against Infections and Cancers (VITIC).; Laboratorio de Inmunología

4. Universidad Nacional de Luján, Departamento de Ciencias básicas, Luján, Buenos Aires, Argentina. INEDES-CO-NICET (Instituto Nacional de Ecología y Desarrollo Sustentable) - Universidad Nacional de Luján. Luján, Buenos Aires, Argentina. FOCIS Center of Excellence - Vaccines and Immunotherapies against Infections and Cancers (VITIC).; Laboratorio de Inmunología
fran.l.gualdieri@gmail.com

Nanoparticles are potential tools for delivering antioxidant molecules. Green synthesis is a promising technique to develop eco-friendly and less toxic nanomaterials by using biological compounds such as vegetable extracts. We decided to test the capacity of Peumus Boldus extracts (PBE) to synthesize Copper (CuNM) and Zinc (ZnNM) nanomaterials. PBE was obtained from samples of 12 (PBE1) or 30 (PBE2) mg dried leaves/mL heated at 70°C for 14 min. We used CuSO₄ and ZnSO₄ at 0,1M concentration. Resulting particles were characterized by Scanning Electron Microscopy, polyphenol concentration (Folin method using gallic acid as standard [Pph, µg/mL]), antioxidant capacity (inhibition of DPPH radical assay [AC, %]), cytotoxicity using THP-1 cells (MTT assay, % of viable cells) and NO₂ concentration (Griess technique, µM) as cell activation parameter. ANOVA was used as statistical analysis. ZnNM showed flower-like shape with size range of 500-1000 nm, AC: 6,91 $\pm$ 1,85 (PBE1), 15,61 $\pm$ 4,05 (PBE2), Pph: 4,98 $\pm$ 0 (PBE1), 11,17 $\pm$ 0,36 (PBE2). CuNM showed mesoporous-like shape with size range of 300-1000 nm; AC: 15,38 $\pm$ 5,41 (PBE1), 45,89 $\pm$ 2,02 (PBE2); Pph: 19,81 $\pm$ 0,36 (PBE1), 59,98 $\pm$ 0,36 (PBE2). We used 6mg/mL of nanomaterial for cytotoxicity test and NO₂ production. ZnNM showed no significant cytotoxicity (85 $\pm$ 3 (PBE1), 95 $\pm$ 7 (PBE2) vs 100 $\pm$ 5 Control); NO₂: 0,44 $\pm$ 0,68 (PBE1), 0,17 $\pm$ 0,30 (PBE2). CuNM showed significant cytotoxicity (6,7 $\pm$ 0,8 (PBE1) and 13 $\pm$ 1 (PBE2) vs 100 $\pm$ 5 Control; p<0,05); NO₂: 11,50 $\pm$ 8,71 (PBE1), 13,86 $\pm$ 8,23 (PBE2). We demonstrated a direct correlation between dried leaves mass used in nanomaterial synthesis with AC, Pph and lower cytotoxicity. Copper induced higher levels of NO₂ than Zinc, suggesting a relationship with cytotoxicity.

177. P10-23. PHAGE DISPLAY SELECTION OF SINGLE-DO-MAIN ANTIBODIES TARGETING AGGREGATED ALPHA-SYNUCLEIN IN PARKINSON'S DISEASE

Agustín Stagnetto¹, Mora Emilia², Renato Zampini³, Marina Bok⁴, Viviana Parreño⁵, María Laura Guayán⁶, Diego Ploper⁷, Rosana Chehín⁸, Silvana Apichela⁹, Lorena Itatí Ibañez¹⁰, Esteban Vera Pingitore¹¹

1. Instituto de Investigación en Medicina Molecular y Celular Aplicada (IMMCA, CONICET-UNT-SiProSa); -

2. Instituto de Química, Física de los Materiales, Medio Ambiente, y Energía (INQUIMAE, UBA-CONICET); Laboratorio de Ingeniería de Anticuerpos

3. Facultad de Agronomía, Zootecnia y Veterinaria (FAZV, UNT); Centro Experimental de Estudios en Camélidos Sud-americanos

4. Instituto de Virología e Innovaciones Tecnológicas (IVIT, INTA-CONICET); -

5. Instituto de Virología e Innovaciones Tecnológicas (IVIT, INTA-CONICET); -

6. Instituto de Investigación en Medicina Molecular y Celular Aplicada (IMMCA, CONICET-UNT-SiProSa); -

7. Instituto de Investigación en Medicina Molecular y Celular Aplicada (IMMCA, CONICET-UNT-SiProSa); -

8. Instituto de Investigación en Medicina Molecular y Celular Aplicada (IMMCA, CONICET-UNT-SiProSa); -

9. Facultad de Agronomía, Zootecnia y Veterinaria (FAZV, UNT); Centro Experimental de Estudios en Camélidos Sud-americanos

10. Instituto de Química, Física de los Materiales, Medio Ambiente, y Energía (INQUIMAE, UBA-CONICET); Laboratorio de Ingeniería de Anticuerpos

11. Instituto de Investigación en Medicina Molecular y Celular Aplicada (IMMCA, CONICET-UNT-SiProSa); -

astagnetto@hotmail.com.ar

Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder worldwide. Its clinical diagnosis typically occurs when dopaminergic neuronal loss exceeds 60%. The early accumulation of misfolded alpha-synuclein (α Syn), particularly in its aggregated forms, positions it as a key biomarker for early-stage detection. Single-domain antibodies (SdAb), derived from camelid heavy-chain-only immunoglobulins, represent promising molecular tools for recognizing these pathological species. In this work, two Lama glama specimens from distinct breeding centers (Llama 1: FAZV-UNT; Llama 2: IVIT-INTA-CONICET) were immunized with in vitro-assembled α Syn pre-formed fibrils (α Syn PFF), produced and validated in-house following established protocols. Each animal received a differential immunization scheme, evaluating humoral responses via ELISA assays. Upon confirmation of robust seroconversion (anti- α SynPFF IgG titers: Llama 1 $\approx$ 21,900; Llama 2 $\approx$ 10,800), immune SdAb libraries were constructed from peripheral blood lymphocytes. Library sizes (2.58×10^8 and 8.19×10^7 colonies, respectively) enabled Phage Display selection of clones against immobilized α Syn PFFs. Screening of 288 individual clones yielded four high-affinity clones (#1, #2, #3, #4). Sequencing revealed phylogenetic clustering, with clones #1 and #3 sharing higher sequence homology, #4 moderately related, while #2 exhibited notable divergence. Selected clones were expressed recombinantly in *E. coli* and purified via immobilized metal affinity chromatography, with yields ranging from 5 to 17 mg/L. Binding specificity was confirmed by ELISA, and their capacity to recognize α Syn aggregates was validated through immunofluorescence in cellular models. These SdAbs constitute valuable candidates for the development of α Syn-targeted diagnostic tools and hold potential for future applications in mechanistic studies and therapeutic strategies in PD.

178. P10-24. STEVIA GLYCOSIDES MITIGATE SEIZURES AND OXIDATIVE STRESS: PRECLINICAL EVIDENCE FOR EPILEPSY THERAPY

Valentina Pastore¹, Natalia Coletti², Marina Rademacher³, Malena Mihura⁴, Victoria Suarez Jaramillo⁵, Luciana Naso⁶, Mariel Marder⁷

1. Instituto de Química y Físicoquímica Biológica "Dr. Alejandro Paladini" (IQUIFIB) -UBA- CONICET; Laboratorio de Neurofitofarmacología Medicinal

2. Instituto de Química y Físicoquímica Biológica "Dr. Alejandro Paladini" (IQUIFIB) -UBA- CONICET; Laboratorio de Neurofitofarmacología Medicinal

3. Instituto de Química y Físicoquímica Biológica "Dr. Alejandro Paladini" (IQUIFIB) -UBA- CONICET; Laboratorio de Neurofitofarmacología Medicinal

4. Instituto de Química y Físicoquímica Biológica "Dr. Alejandro Paladini" (IQUIFIB) -UBA- CONICET; Laboratorio de Neurofitofarmacología Medicinal

5. Instituto de Química y Físicoquímica Biológica "Dr. Alejandro Paladini" (IQUIFIB) -UBA- CONICET; Laboratorio de Neurofitofarmacología Medicinal

6. Centro de Química Inorgánica Dr. Pedro J. Aymonino (CEQUINOR) UNLP- CONICET

7. Instituto de Química y Físicoquímica Biológica "Dr. Alejandro Paladini" (IQUIFIB) -UBA- CONICET; Laboratorio de Neurofitofarmacología Medicinal
valenpastore20@gmail.com

Stevia rebaudiana Bertoni, widely recognized for its natural sweetening properties, contains bioactive compounds such as stevioside (STV) and rebaudioside A (RebA), which have been associated with multiple health benefits. Nevertheless, their potential neuroprotective and anticonvulsant properties remain poorly understood. The present study aimed to evaluate the anticonvulsant effects of STV and RebA and to elucidate their underlying mechanisms, with particular focus on antioxidant and neuroprotective actions. Anticonvulsant activity was investigated through in vitro and in vivo epilepsy models. In SH-SY5Y neuronal cultures, both compounds (10–100 μ M) mitigated pentylentetrazol (PTZ)-induced neuronal damage, preserved cell viability, and significantly reduced reactive oxygen species production. Electrophysiological recordings performed in HEK293 cells expressing human voltage-gated sodium channels (hNav1.1 and hNav1.2) demonstrated that at 100 μ M, STV and RebA reversibly blocked sodium currents and stabilized the channels in their inactivated state, thus resembling the pharmacological mechanism of classical antiepileptic drugs. In in vivo assays, intraperitoneal administration of STV (100 mg/kg, mice) displayed robust anticonvulsant activity in the subcutaneous PTZ test, significantly reducing clonic seizure incidence, completely suppressing tonic-clonic seizures, and prolonging latency to myoclonic events up to 4 h post-treatment. Moreover, STV attenuated oxidative stress by reducing malondialdehyde levels by 30% and enhancing reduced glutathione concentrations in brain tissue. Taken together, these findings indicate that STV exerts potent anticonvulsant and antioxidant effects through multifaceted mechanisms, supporting its potential as a promising neuroprotective candidate for epilepsy management and other neurological disorders associated with oxidative stress.

179. P10-25. INVOLVEMENT OF CB1 RECEPTORS IN OPIOID ADDICTION: BEHAVIOURAL AND NEUROCHEMICAL STUDIES

Villalobos Vasquez Jesus¹, Opezzo Javier², Höcht Christian³, Balerio Graciela Noemí⁴

1. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Investigaciones Farmacológicas (ININF), CONICET; Laboratorio de Neurobiología de las adicciones

2. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Farmacología; Departamento de Farmacología

3. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Farmacología; Departamento de Farmacología

4. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Investigaciones Farmacológicas (ININF), CONICET, Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Farmacología; Laboratorio de Neurobiología de las adicciones

jvillalobosvasquez1984@gmail.com

Previous studies of our laboratory revealed sex differences in behavioural, molecular, and biochemical responses to morphine (MOR) withdrawal. Stress is a major factor contributing to relapse in drug abuse. The aims of this study were: 1) evaluate behavioural patterns (conditioning, extinction, and stress-induced reinstatement) of MOR rewarding effects, and 2) correlate these patterns with neurochemical changes in reward-related brain nuclei in wild-type (WT) CD1 mice and CB1 receptor knockout (KO CB1) mice of both sexes. MOR (10 mg/kg, sc) rewarding effect was confirmed using the conditioned place preference paradigm, followed by extinction with saline sessions and stress-induced relapse caused by immobilization. Dopamine (DA) and its metabolite DOPAC were quantified in brain homogenates using HPLC with electrochemical detection. Results showed MOR rewarding effects in both sexes of WT and KO CB1 mice ($p < 0.05$), with higher intensity in KO CB1 mice ($p < 0.05$). Extinction occurred across sexes and genotypes, but WT females exhibited greater extinction than males ($p < 0.05$). Stress-induced relapse was only observed in WT females that had extinguished rewarding effects ($p < 0.05$), while KO CB1 mice did not relapse. Although MOR rewarding effects showed no significant sex differences, KO CB1 mice displayed more robust responses compared to WT mice. In addition, elevated DA and DOPAC levels were detected in the nucleus accumbens and caudate putamen during conditioning and reinstatement ($p < 0.05$), in both sexes and genotypes, indicating dopaminergic activation of reward circuits. In conclusion, these findings suggest that CB1 receptors modulate MOR rewarding effects and stress-induced relapse in a sex-dependent manner, highlighting the CB1

180. P10-26. DETECTION OF AGGREGATED A-SYNUCLEIN USING TETRACYCLINE-BASED IMMUNOASSAY AND ELECTROCHEMICAL BIOSENSOR APPROACHES

Silvana Estefanía Soliz Santander¹, María Belén Machín², Agustín Pernicone³, Verónica E. Manzano⁴, Cesar Luis Ávila⁵, Oscar Varela⁶, Santiago De Chazal⁷, Griselda Judith Alvarado⁸, David Ricardo Sharruf Alarcon⁹, Rosana Nieves Chehín¹⁰, Esteban Vera Pingitore¹¹

1. IMMCA (CONICET-UNT-SIPROSA). Pje Dorrego 1080.

Tucumán; Neurociencia

2. IMMCA (CONICET-UNT-SIPROSA). Pje Dorrego 1080.

Tucumán; Neurociencia

3. CIHIDECAR (CONICET-UBA); Glicomiméticos y materiales poliméricos basados en hidratos de carbono y otros componentes de la biomasa

4. CIHIDECAR (CONICET-UBA); Glicomiméticos y materiales poliméricos basados en hidratos de carbono y otros componentes de la biomasa

5. IMMCA (CONICET-UNT-SIPROSA). Pje Dorrego 1080.

Tucumán; Neurociencia

6. CIHIDECAR (CONICET-UBA). Ciudad Universitaria, Pabellón 2, Buenos Aires; Glicomiméticos y materiales poliméricos basados en hidratos de carbono y otros componentes de la biomasa

7. Hospital Ángel C. Padilla, Tucumán; Servicio de Neurología

8. Hospital Ángel C. Padilla, Tucumán; Servicio de Neurología

9. Hospital Ángel C. Padilla, Tucumán; Servicio de Neurología

10. IMMCA (CONICET-UNT-SIPROSA). Pje Dorrego 1080.

Tucumán; Neurociencia

11. IMMCA (CONICET-UNT-SIPROSA). Pje Dorrego 1080.

Tucumán; Neurociencia

tefi.9625@gmail.com

Aggregated α -synuclein (aSyn) species arise early in Parkinson's disease (PD), representing promising biomarkers for early diagnosis. However, their sensitive and selective detection remains challenging due to its low abundance, polymorphic structure, and poor antibody recognition. Our previous research demonstrated that tetracycline derivatives selectively bind to polymeric aSyn structures without interacting with its monomeric forms. Leveraging this knowledge, we evaluated two tetracycline-derived using an immunoassay and an electrochemical biosensor. We developed an immunoassay

based on sandwich ELISA assays (Enzyme-Linked Immunosorbent Assay), that distinguished between aggregated and monomeric aSyn in PBS (phosphate-buffered saline). The platform was further assessed in a chemically defined medium resembling human cerebrospinal fluid (CSF) spiked with aSyn aggregates, to identify potential interferents substances and design strategies to mitigate their effects. We identified NaHCO_3 as the main interferent compound and tested strategies such as dialysis and pH adjustment, which recovered the attenuated signal in CSF samples containing aggregated aSyn. In the biosensor approach, a thiolated doxycycline derivative was used to form a monolayer on the gold electrode and characterized by cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS). This technique exhibited a concentration-dependent shift in the oxidation peak with aggregated aSyn between 0,1-10 ng/ml. Our findings advance early PD diagnosis by enabling sensitive detection of aSyn aggregates, supporting timely intervention and improved disease management. Furthermore, immunoassays and electrochemical biosensors present affordable alternatives that could facilitate large-scale clinical adoption, including point-of-care applications.

181. P10-27. ERYTHRINA CRISTA-GALLI: AN ARGENTINE NATIVE SPECIES WITH MULTI-FUNCTIONAL POTENTIAL FOR NEURODEGENERATIVE DISEASES TREATMENT

Marina Rademacher¹, Natalia Coletti², Victoria Suarez³, Leonardo Martín Anconatani⁴, Malena Mihura⁵, Ignacio Agudelo⁶, Damijan Knez⁷, Rafael Alejandro Ricco⁸, Valentina Pastore⁹, Muriel Marder¹⁰

1. Instituto de Química y Fisicoquímica Biológicas Prof. Dr. Alejandro C. Paladini (IQUIFIB). UBA-CONICET. Facultad de Farmacia y Bioquímica. Buenos Aires, Argentina; Laboratorio de Neuro-Fito-Farmacología Medicinal

2. Instituto de Química y Fisicoquímica Biológicas Prof. Dr. Alejandro C. Paladini (IQUIFIB). UBA-CONICET. Facultad de Farmacia y Bioquímica. Buenos Aires, Argentina.; Laboratorio de Neuro-Fito-Farmacología Medicinal

3. Instituto de Química y Fisicoquímica Biológicas Prof. Dr. Alejandro C. Paladini (IQUIFIB). UBA-CONICET. Facultad de Farmacia y Bioquímica. Buenos Aires, Argentina.; Laboratorio de Neuro-Fito-Farmacología Medicinal

4. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Farmacología. Cátedra de Farmacobotánica. Buenos Aires, Argentina.; Laboratorio de Farmacobotánica

5. Instituto de Química y Fisicoquímica Biológicas Prof. Dr. Alejandro C. Paladini (IQUIFIB). UBA-CONICET. Facultad de Farmacia y Bioquímica. Buenos Aires, Argentina.; Laboratorio de Neuro-Fito-Farmacología Medicinal

6. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Farmacología. Cátedra de Farmacobotánica. Buenos Aires, Argentina.; Laboratorio de Farmacobotánica

7. Universidad de Liubliana. Facultad de Farmacia. Departamento de Química Medicinal. Liubliana, Eslovenia.; Laboratorio de Química Medicinal

8. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Farmacología. Cátedra de Farmacobotánica. Buenos Aires, Argentina.; Laboratorio de Farmacobotánica

9. Instituto de Química y Fisicoquímica Biológicas Prof. Dr. Alejandro C. Paladini (IQUIFIB). UBA-CONICET. Facultad de Farmacia y Bioquímica. Buenos Aires, Argentina; Laboratorio de Neuro-Fito-Farmacología Medicinal

10. Instituto de Química y Fisicoquímica Biológicas Prof. Dr. Alejandro C. Paladini (IQUIFIB). UBA-CONICET. Facultad de Farmacia y Bioquímica. Buenos Aires, Argentina; Laboratorio de Neuro-Fito-Farmacología Medicinal
marina.radem@gmail.com

Erythrina crista-galli (ceibo, ECG) is a native species from Argentina, commonly cultivated as an ornamental tree but also used in folk medicine. In this study, we evaluated the multifunctional potential of ceibo leaf extracts for the treatment of neurodegenera-

tive disorders (NDD). Two preparations were obtained: an infusion (ECGi, 5% w/w) and a tincture (ECGt, 10% w/w). Phytochemical analysis revealed phenolics, flavonoids, and hydroxycinnamic acids. Chromatographic analysis (TLC, HPLC) suggested apigenin as one of the potential bioactive compounds in ECGt. Both extracts exhibited radical scavenging activity in DPPH and ABTS assays, as well as iron-chelating capacity in the ferrozine assay. In vitro, ECG extracts inhibited murine acetylcholinesterase (mAChE) and butyrylcholinesterase (mBChE), as well as recombinant human cholinesterase (hAChE) and butyrylcholinesterase (hBChE). They also inhibited murine monoamine oxidases A and B (mMAO-A, mMAO-B) and recombinant human monoamine oxidases A and B (hMAO-A, hMAO-B). The tincture was more active than the infusion (1 mg/mL). The tincture also displaced [³H]-flunitrazepam binding at the benzodiazepine site of the GABAA receptor. In vivo, mice treated with tincture (300 mg/kg, i.p.) showed no significant behavioral changes in standard tests for anxiety, depression, sedation, or locomotion. However, ex vivo tissue analysis revealed cholinesterase inhibition and a trend toward reduced mMAO-B activity. Moreover, a tendency to decrease lipid peroxidation (TBARS) and increase glutathione (GSH) levels was observed. Overall, these findings support the multifunctional neuroprotective potential of *E. crista-galli* through antioxidant, enzyme inhibitory, and GABAergic mechanisms, highlighting its promise for NDD treatment.

182. P10-28. MULTI-TARGET INHIBITION OF A-SYNUCLEIN PATHOLOGY BY DCT IN PARKINSON'S DISEASE MODELS

María Laura Guayán¹, Rita Raisman-Vozari², Laurent Ferrié³, Bruno Figadère⁴, Rosana Chehin⁵, Diego Ploper⁶

1. Instituto de Investigación en Medicina Molecular y Celular Aplicada (CONICET - UNT - SIPROSA); IMMCA

2. Paris Brain Institute-ICM, Inserm, Sorbonne Université, CNRS, Hôpital Pitié Salpêtrière, 75013 Paris, France;

3. BioCIS, CNRS, Université Paris Saclay, 92290 Châtenay-Malabry, France; □

4. BioCIS, CNRS, Université Paris Saclay, 92290 Châtenay-Malabry, France; □

5. Instituto de Investigación en Medicina Molecular y Celular Aplicada (CONICET - UNT - SIPROSA); IMMCA

6. Instituto de Investigación en Medicina Molecular y Celular Aplicada (CONICET - UNT - SIPROSA); IMMCA

mlauraguayan@gmail.com

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the accumulation of misfolded α-synuclein (αS) into amyloid aggregates, a process thought to underlie both neuronal dysfunction and disease propagation. Although several tetracyclines (TCs) display neuroprotective properties in experimental models, their antibiotic activity severely restricts long-term therapeutic application. To address this limitation, we synthesized and screened ten novel non-antibiotic TC derivatives for safety and activity against αS pathology. From this screening, DCT was identified as the most promising candidate. DCT was non-cytotoxic in SH-SY5Y cells and demonstrated a robust capacity to modulate αS aggregation. Kinetic assays revealed a marked prolongation of the lag phase and a reduction in fibril growth rate. In addition, DCT caused a near-complete suppression of seeding activity in both in vitro fibrillization assays and transgenic SH-SY5Y-αS-RFP cells. These results highlight its potential to interfere with the prion-like propagation of αS pathology. Morphological analysis revealed that fibrils formed in the presence of DCT were structurally distinct from control aggregates. In cellular models, DCT significantly reduced oxidative stress and diminished intracellular αS puncta triggered by αS preformed fibrils. Furthermore, pharmacological studies demonstrated that DCT is capable of crossing the blood-brain barrier, reinforcing its translational potential. Taken together, these results establish DCT as a novel non-antibiotic tetracycline derivative that targets multiple pathological mechanisms of αS in PD, justifying its further preclinical development as a disease-modifying candidate.

183. P10-29. EARLY LIFE STRESS, ANXIETY, AND ADDICTIVE

BEHAVIORS: THE MODULATORY ROLE OF OXYTOCIN

Thomas Balmaceda¹, Sebastián Rosenblunn², Gabriela Acosta³

1. Instituto de Neurociencia Cognitiva y Traslacional (INCYT)-CONICET-Universidad Favaloro, Fundación INECO; LABORATORIO DE NEUROBIOLOGÍA DEL ESTRÉS TEMPRANO

2. Instituto de Neurociencia Cognitiva y Traslacional (INCYT)-CONICET-Universidad Favaloro, Fundación INECO; LABORATORIO DE NEUROBIOLOGÍA DEL ESTRÉS TEMPRANO

3. Instituto de Neurociencia Cognitiva y Traslacional (INCYT)-CONICET-Universidad Favaloro, Fundación INECO; LABORATORIO DE NEUROBIOLOGÍA DEL ESTRÉS TEMPRANO thomasbalmaceda5@gmail.com

Anxiety disorders are among the most prevalent mental health conditions, while behavioral addictions, also referred to as non-substance addictions, are defined by compulsive and repetitive behaviors that cause significant functional impairment without the involvement of psychoactive substances. Early life stress (ELS), particularly during perinatal and childhood stages, has been consistently associated with disrupted brain maturation and greater vulnerability to psychiatric disorders such as anxiety, depression, and psychosis. In this neurodevelopmental context, oxytocin has attracted increasing interest because of its role in regulating stress responses, modulating anxiety, and facilitating social bonding, positioning it as a potential biomarker and mediator of ELS effects. The present study aimed to explore (a) the relationship between anxiety levels and addictive behaviors, and (b) the associations between anxiety, adverse childhood experiences, and the putative modulatory role of oxytocin. We conducted an observational, non-randomized, consecutive, analytical, and open study. Fifty-one young adults (22 men, 29 women) completed the Hamilton Anxiety Scale, an adverse childhood experiences questionnaire, and a behavioral addictions self-report scale. Results indicated that participants who reported adverse childhood experiences showed higher anxiety levels compared to controls (Wilcoxon, $p = 0.11$). No significant association was found between anxiety and behavioral addictions. Although oxytocin concentrations were not directly measured, findings suggest that reduced availability or dysregulation of the oxytocinergic system may underlie the observed vulnerability to anxiety. These results reinforce the notion that ELS shapes emotional processing across development and support the hypothesis that oxytocin acts as a protective factor.

184. P10-30. ANTITUMOR IMMUNOTHERAPY WITH SALMONELLA TYPHI CVD915: NEW COMBINED STRATEGIES

Alejandrina Vendrell¹, María José Gravisaco², Claudia Mongini³, Agustina Tesone⁴, Alfonsina Diebel⁵, Florencia Menay⁶, Juan Carlos Goin⁷, Claudia Inés Waldner⁸

1. Centro de Estudios Farmacológicos y Botánicos (CE-FyBO). CONICET-UBA. Loci Labs (actual); Laboratorio de Inmunología Celular y Molecular (LICYM)

2. Instituto de Agrobiotecnología y Biología Molecular (IABI-MO). Instituto Nacional de Tecnología Agropecuaria (INTA); Laboratorio de Inmunología y Vacunas aviares

3. Instituto de Virología y Innovaciones Tecnológicas (IVI-T)-Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET)-Instituto Nacional de Tecnología Agropecuaria (INTA); Laboratorio de Microvesículas, Exosomas y mRNA

4. Centro de Estudios Farmacológicos y Botánicos (CE-FyBO). CONICET-UBA; Laboratorio de Inmunología Celular y Molecular (LICYM)

5. Centro de Estudios Farmacológicos y Botánicos (CE-FyBO). CONICET-UBA; Laboratorio de Inmunología Celular y Molecular (LICYM)

6. Instituto de Investigaciones Biomédicas (BIOMED) UCA-CONICET; Laboratorio de Neuroinmunomodulación y Oncología Molecular

7. Centro de Estudios Farmacológicos y Botánicos (CE-FyBO). CONICET-UBA; Laboratorio de Farmacología Molecular (LAFAM)

8. Centro de Estudios Farmacológicos y Botánicos (CE-FyBO). CONICET-UBA; Laboratorio de Inmunología Celular y Molecular (LICYM)

alejandrinavendrell@gmail.com

Non-antigen-specific immunotherapy aims to promote an antitumor immune response in the host without the need to identify tumor antigens. We previously demonstrated the efficacy of the attenuated *Salmonella* Typhi vaccine strain CVD915 as an immunotherapeutic agent, administered intratumorally (IT), in murine models of mammary adenocarcinoma (LM3) and T-cell lymphoma (EL4). In this study, we evaluated whether treatment with live CVD915, combining IT + IN (intranasal), in LM3 tumor-bearing mice improves the therapeutic response promoted by IT inoculation alone. We showed that IT + IN treatment reduced tumor growth ($p \leq 0.05$, at 20 days post-treatment start (dpt)) and prolonged survival ($p \leq 0.05$), compared with IT or IN. These results indicate that the combined IT and IN regimen was more effective against mammary adenocarcinoma than either of the individual treatments. We previously demonstrated that live CVD915, but not dead CVD915 (dCVD915), exerts cytotoxic activity against EL4 cells in vitro. Here, we investigated whether IT dCVD915 can exert an antitumor effect in vivo in the EL4 tumor model. We determined that dCVD915 reduced EL4 tumor growth at 7 and 12 dpt, compared with control ($p \leq 0.05$). This therapeutic effect was significantly lower than that exerted by live CVD915 ($p \leq 0.05$). These results suggest that dCVD915, although not directly cytotoxic to EL4 cells, can promote a significant antitumor therapeutic response in the host. This *Salmonella*-based immunotherapeutic strategy could be a powerful tool for cancer treatment, applied alone or in combination with other therapies

185. P10-31. SALMONELLA TYPHI ADMINISTERED INTRA-TUMORALLY IS ONCOLYTIC AND INDUCES AN ANTI-TUMOR IMMUNE RESPONSE IN A MOUSE MODEL OF T-CELL LYMPHOMA

Alfonsina Diebel¹, Agustina Tesone², Alejandrina Vendrell³, Claudia Mongini⁴, Florencia Menay⁵, María José Gravisaco⁶, Juan Carlos Goin⁷, Claudia Inés Waldner⁸

1. Centro de Estudios Farmacológicos y Botánicos (CEFy-BO). CONICET-UBA; Laboratorio de Inmunología Celular y Molecular
 2. Centro de Estudios Farmacológicos y Botánicos (CEFy-BO). CONICET-UBA; Laboratorio de Inmunología Celular y Molecular
 3. Loci Labs
 4. Instituto de Virología y Innovaciones Tecnológicas (IVIT)-Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET)-Instituto Nacional de Tecnología Agropecuaria (INTA); Laboratorio de Microvesículas, Exosomas y mRNA
 5. Instituto de Investigaciones Biomédicas (BIOMED) UCA-CONICET; Laboratorio de Neuroinmunomodulación y Oncología Molecular
 6. Instituto de Agrobiotecnología y Biología Molecular. Instituto Nacional de Tecnología Agropecuaria (INTA); Laboratorio de Inmunología y Vacunas aviares
 7. Centro de Estudios Farmacológicos y Botánicos (CEFy-BO). CONICET-UBA; Laboratorio de Farmacología Molecular (LAFAM)
 8. Centro de Estudios Farmacológicos y Botánicos (CEFy-BO). CONICET-UBA; Laboratorio de Inmunología Celular y Molecular
- alfonsinadiebel@gmail.com

Immunotherapy is currently a key strategy in the fight against cancer. Previously, we demonstrated that the immunotherapy based on an attenuated *Salmonella* Typhi vaccine strain (S.Ty21a, licensed for human use) reduces tumor growth, incidence of colonized lymph nodes, and increases survival in mice bearing EL4 T cell-lymphoma. In this work, the early antitumor effects of S. Ty21a on the EL4 mouse model and immunological mechanisms involved were evaluated. It was demonstrated that S. Ty21a exerted an oncolytic effect per se and also induced an early activation of the immune system in secondary lymphoid organs. The cytotoxic effect on the tumor was evidenced by extensive areas of necrosis (25-60%) and the presence of an inflammatory infiltrate (mostly neutrophils) 1

day post-treatment (1dpt). Immunotherapy promoted, at 4 dpt, an expansion of lymphocytes (similar to twofold compared to control) and a decrease in regulatory T cells in both tumor-draining lymph nodes (TDLNs) and the spleen of treated animals ($p \leq 0.05$ in all cases). Furthermore, *Salmonella* induced an extrafollicular immune response in TDLNs and an early activation of B cells with plasma cell formation. Moreover, immunization promoted a cytotoxic effector response characterized by IFN- γ production by CD8⁺ and B220⁺ lymphocytes in TDLNs ($p \leq 0.05$, at 4 dpt). These findings demonstrate that S. Ty21a not only exerts a direct oncolytic effect, but also remodels the tumor microenvironment, promoting an effective anti-tumor immune response

POSTERS 11 - SAIC - GENÉTICA 2

DATE & TIME: 18/11/2025 15:00 - 16:30 H

**Chairs: Cecilia Soledad Fernandez,
Ana María Buzaleh**

186. P11-13. DOUBLE IGHV REARRANGEMENTS IN A LATIN AMERICAN COHORT OF CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS

Carmen Stanganelli¹, Juana Cabrera², Andrea Bender³, Evangelina Agriello⁴, Davi Coe Torres⁵, Gerson Moura Ferreira⁶, Maria Paula Albert Einstein⁷, San Pablo, Brazil, Eliana Saul Furquim Werneck Abdelhay⁸, Irma Slavutsky⁹

1. IHEMA, Academia Nacional de Medicina; División Patología Molecular
 2. IHEMA, Academia Nacional de Medicina; División Patología Molecular
 3. Laboratorio de Especialidades Bioquímicas
 4. Laboratorio de Especialidades Bioquímicas
 5. Hospital Israelita Albert Einstein, San Pablo, Brazil,
 6. National Cancer Institute (INCA), Rio de Janeiro, Brazil; Specialized Laboratory Division
 7. National Cancer Institute (INCA), Rio de Janeiro, Brazil; Specialized Laboratory Division
 8. National Cancer Institute (INCA), Rio de Janeiro, Brazil; Specialized Laboratory Division
 9. IMEX, CONICET-ANM; Laboratorio de Genética de Neoplasias Linfoides
- carmen.stanganelli13@gmail.com

The IGHV (immunoglobulin heavy variable) mutational status (MS), allows to stratify patients with chronic lymphocytic leukemia (CLL) into mutated (M) (<98% identity to the germline) or unmutated (U) ($\geq 98\%$), with different outcome. A small subgroup carries double productive IGHV rearrangements (DPR). We evaluate the frequency and characteristics of DPR in 1409 CLL patients: 1231 Argentinean and 179 Brazilian. RT-PCR and bidirectional sequencing were performed. The study was approved by the Institutional Ethics Committees. All individuals provided their informed consent. We found 1444 productive rearrangements (PR): 1208 single and 23 DPR (1.9%) in Argentinean series, 15 with concordant mutational status (MS) and 8 discordant, while Brazilian series showed 167 single, 10 DPR and 1 triple PR, 10 with concordant MS and 1 discordant. As a whole we found 2.41% DPR/triple cases. An increased percentage of U-CLL was observed in Brazilian series ($p < 0.0001$). The most frequent family combinations in DPR group were VH3+VH4 and VH2+VH3 in Argentinean and Brazilian series, respectively. In the whole cohort DPR group showed over-representation of the VH2 family compared to cases with one PR ($p = 0.0122$) and IGHV2-5 gene was over-represented in both, the whole cohort and Brazilian patients ($p < 0.04$). Stereotyped receptors were absent in the DPR Brazilian patients. Molecular clonal evolution was observed in two cases studied twice. A similar frequency of IGHV DPR (2.41%) to those described in the literature (~2%) was found. Differences observed between series reinforce the role of genetic background and environmental factors in CLL pathogenesis

187. P11-14. EXPANDING THE GENETIC SPECTRUM OF ALPORT SYNDROME: DIAGNOSTIC YIELD AND NOVEL VARIANTS IN AN ARGENTINE COHORT

Mariela Pace¹, Paula Inés Buonfiglio², Sofía Grinberg³, Car-

los David Bruque⁴, Marisol Delea⁵, Vanesa Lotersztajn⁶, Mariel Ormazabal⁷, Mercedes Villanueva⁸, Ana Belén Elgoyhen⁹, Viviana Dalamón¹⁰

1. Instituto de Investigaciones en Ingeniería Genética y Biología Molecular "Dr. Héctor N. Torres" - INGEBI/CONICET, Buenos Aires, Argentina.; Laboratorio de Fisiología y Genética de la Audición
 2. Instituto de Investigaciones en Ingeniería Genética y Biología Molecular "Dr. Héctor N. Torres" - INGEBI/CONICET, Buenos Aires, Argentina.; Laboratorio de Fisiología y Genética de la Audición
 3. Instituto de Investigaciones en Ingeniería Genética y Biología Molecular "Dr. Héctor N. Torres" - INGEBI/CONICET, Buenos Aires, Argentina.; Laboratorio de Fisiología y Genética de la Audición
 4. Unidad de Conocimiento Traslacional Hospitalaria Patagónica (UCT-HP)-CONICET. "Hospital de Alta Complejidad SAMIC", El Calafate, Santa Cruz, Argentina.; -
 5. Unidad de Conocimiento Traslacional Hospitalaria Patagónica (UCT-HP)-CONICET. "Hospital de Alta Complejidad SAMIC", El Calafate, Santa Cruz, Argentina.; -
 6. Servicio de Genética del Hospital Militar Central "Cirujano Mayor Dr. Cosme Argerich", Buenos Aires, Argentina.; -
 7. Servicio de Genética del Hospital General de Niños "Dr Pedro Elizalde", Buenos Aires, Argentina.; -
 8. Servicio de Genética del Hospital General de Niños "Dr Pedro Elizalde", Buenos Aires, Argentina.; -
 9. Instituto de Investigaciones en Ingeniería Genética y Biología Molecular "Dr. Héctor N. Torres" - INGEBI/CONICET, Buenos Aires, Argentina.; Laboratorio de Fisiología y Genética de la Audición
 10. Instituto de Investigaciones en Ingeniería Genética y Biología Molecular "Dr. Héctor N. Torres" - INGEBI/CONICET, Buenos Aires, Argentina.; Laboratorio de Fisiología y Genética de la Audición
- marielavpace@gmail.com

Alport syndrome (AS) is a genetically heterogeneous disorder with an estimated prevalence of 1 in 5,000 individuals caused by pathogenic variants in COL4A3, COL4A4, and COL4A5 genes, resulting in progressive renal failure due to glomerulonephropathy, variable sensorineural hearing loss, and ocular abnormalities. Genetic testing is essential for confirming the clinical diagnosis and enabling early intervention. We analyzed 13 unrelated patients with clinical suspicion of AS using a combined diagnostic approach involving whole exome sequencing (WES) and multiplex ligation-dependent probe amplification (MLPA) techniques. Variant classification followed ACMG/AMP guidelines, and specific Hearing Loss Variant Curation Expert Panel (HL-VCEP) recommendations. Pathogenic, likely pathogenic, and VUS variants were identified in 9 of the 13 patients (69%). Detected variants included single nucleotide variants (SNVs) and small insertions/deletions. Two novel COL4A5 variants—c.3302delG p.(Gly1101Glu*51) and c.947G>C p.(Gly316Ser)—were identified and classified as Likely Pathogenic according to ACMG criteria. In another patient, a likely pathogenic variant in the NLRP3 gene suggested a possible alternative diagnosis of Muckle Wells Syndrome. This study highlights the diagnostic yield and the advantages of WES for detecting pathogenic SNVs and small indels associated with AS. Although MLPA was used to assess copy number variants, no CNVs were identified in this cohort. The detection of novel variants expands the mutational landscape of AS in an underrepresented population in local databases. Integrating genetic findings with clinical evaluation enhances diagnostic precision and supports early management and genetic counseling of patients.

188. P11-15. IDENTIFICATION OF GENE VARIANTS RELATED TO SENSORINEURAL HEARING LOSS IN ARGENTINA AS A FIRST STEP INTO PERSONALIZED MEDICINE

Maria T. Bernardi¹, Memoona Ramzan², Laura Calderon³, Paula Scaglia⁴, Romina Armando⁵, Victoria L. Khatchikian⁶, Marina Conrad⁷, Natalia Vazquez⁸, Maria Esnaola Azcoiti⁹, Marcelo A. Marti¹⁰, Betina Beider¹¹, Maria G. Ropelato¹², Silvina Olha¹³, Mustafa Tekin¹⁴, Katherina Walz¹⁵

1. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales; (IQUIBICEN) CONICET Buenos Aires 1428 Argentina
 2. University of Miami Miller School of Medicine Miami FL 33136 USA.; John P. Hussman Institute for Human Genomics
 3. Hospital de Niños Dr. R. Gutierrez Buenos Aires 1330 Argentina; Servicio de Otorrinolaringología
 4. Hospital de Niños Dr. R. Gutierrez, Buenos Aires, Argentina; División de Endocrinología
 5. Hospital de Niños Dr. R. Gutierrez, Buenos Aires, Argentina; Sección Genética Médica
 6. Facultad de Ciencias Exactas y Naturales (IQUIBICEN) CONICET Buenos Aires 1428 Argentina.; Instituto de Química Biológica
 7. Universidad Austral, Pilar, Buenos Aires, Argentina; Departamento de Ingeniería Biomédica
 8. Hospital de Niños Dr. R. Gutierrez, Buenos Aires, Argentina; Sección Genética Médica
 9. Hospital de Niños Dr. R. Gutierrez, Buenos Aires, Argentina; División de Endocrinología
 10. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (FCEyN-UBA); IQUIBICEN
 11. Hospital Municipal de Trauma y Emergencias Dr. Federico Abete, Malvinas Argentinas, Buenos Aires, Argentina; Servicio de Otorrinolaringología
 12. Hospital de Niños Dr. R. Gutierrez, Buenos Aires, Argentina; División de Endocrinología
 13. Hospital de Niños Dr. R. Gutierrez Buenos Aires 1330 Argentina.; Servicio de Otorrinolaringología
 14. University of Miami Miller School of Medicine, Miami, FL, USA; Dr. John T. Macdonald Foundation Department of Human Genetics
 15. Facultad de Ciencias Exactas y Naturales, CONICET Buenos Aires 1428 Argentina.; IQUIBICEN
- mariat.bernardi@gmail.com

Congenital hearing loss affects 2-3 in every 1000 births, being ~50-60% of those related to genetic causes that are mostly associated with sensorineural hearing loss (HL). It can be classified into syndromic (~25%) or non-syndromic (NS, ~75%) forms based on the presence or absence of other symptoms. There are ~150 genes associated with NSHL. Despite these advances, the Argentinian population remains understudied. To contribute to the discovery of the genetic landscape of hearing loss in the Argentinian population patients with cochlear implants were identified, and after signing the informed consent and answering a specific questionnaire, they were sequentially admitted to the research protocol. The first group (n=22) received a clinical diagnosis at an average age of 4+/-1 years, the average age for the first cochlear implant was 8+/-1 years and for all of them this was the first genetic test. At recruitment the average age was 11+/-2 years. Specific examination of the DNF1 locus (GJB2 pathogenic variants and/or deletions in GJB6) followed by exome sequencing (at 100X paired end on BGI-SEQ500 platform) was performed. The percentage of alleles in this cohort that presented variations in the DNF1 locus was ~40% explaining ~30% of the cases, confirming incidences and mutations previously described. In addition, new variants in the ACTG1, MYO7a and OTOF genes were identified. Our results add into the still scarce landscape of hearing loss related variants in the Argentinian genetic pool and open the possibility to personalized treatment when gene therapy is an option.

189. P11-16. INVERTED HETEROARM DUPLICATION OF 18P WITH 18Q DELETION: REPORT OF A RARE DE NOVO CHROMOSOMAL ANOMALY AND ITS CYTOGENETIC-MOLECULAR CHARACTERIZATION

Cynthia Gabriela Bravo¹, Candela Ruiz², Ana Goussies³, Aldana Claps⁴, Alejandra Chaves⁵, Cecilia Montes⁶, Evelyn Torchinsky⁷, Julieta Laisecca⁸, Fabiana Guerrisi⁹, Lilian Franzini¹⁰, Mariana Asinari¹¹, Melisa Taboas¹², Tania Castro¹³, Rosana Perotti¹⁴, Wanda Montes¹⁵, Roxana Cerretini¹⁶

1. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr

Carlos G. Malbrán"; Laboratorio de Diagnóstico Genético
 2. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr Carlos G. Malbrán"; Laboratorio de Diagnóstico Genético
 3. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr Carlos G. Malbrán"; Laboratorio de Diagnóstico Genético
 4. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr Carlos G. Malbrán"; Laboratorio de Diagnóstico Genético
 5. Hospital de Niños de la Santísima Trinidad - Córdoba; División Genética Médica
 6. Hospital de Niños de la Santísima Trinidad - Córdoba; División Genética Médica
 7. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr Carlos G. Malbrán"; Laboratorio de Diagnóstico Genético
 8. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr Carlos G. Malbrán"; Laboratorio de Diagnóstico Genético
 9. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr Carlos G. Malbrán"; Laboratorio de Diagnóstico Genético
 10. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr Carlos G. Malbrán"; Laboratorio de Diagnóstico Genético
 11. Hospital de Niños de la Santísima Trinidad - Córdoba; División Genética Médica
 12. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr Carlos G. Malbrán"; Laboratorio de Diagnóstico Genético
 13. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr Carlos G. Malbrán"; Laboratorio de Diagnóstico Genético
 14. Hospital de Niños de la Santísima Trinidad - Córdoba; División Genética Médica
 15. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr Carlos G. Malbrán"; Laboratorio de Diagnóstico Genético
 16. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr Carlos G. Malbrán"; Laboratorio de Diagnóstico Genético
 cyngabr@gmail.com

The inverted heteroarm duplication of 18p with 18q deletion constitutes an extremely rare chromosomal anomaly associated with severe intellectual disability and characteristic dysmorphisms. We present the case of a 22-month-old male patient referred to Medical Genetics due to neonatal hypotonia, sucking difficulties, and facial dysmorphisms. Born from a controlled term pregnancy with neonatal cyanotic episodes, son of healthy non-consanguineous parents with an asymptomatic sibling. The clinical picture was characterized by severe neurodevelopmental delay, recurrent hospitalizations due to respiratory infections, growth retardation, and multiple dysmorphisms including microbrachycephaly, ocular hypertelorism, upslanting palpebral fissures, arched eyebrows, small low-set nose and ears, proximally placed thumbs, scoliosis, retractile testes, and severe psychomotor delay. The cytogenetic study through GTG (analysis by vali.ai) banding and FISH with subtelomeric probes revealed karyotype 46,XY,der(18)(pter@q21::p11.2@p11.3) dn[20].ish der(18)(subtel18p+,subtel18p+)[15], confirming the presence of two 18p subtelomeric signals on the derivative chromosome. The CGH-array analysis identified partial trisomy 18p11.32p11.22 of 10.85 Mb and partial monosomy 18q21.32q23 of 21.38 Mb, both classified as pathogenic. Parental studies confirmed normal karyotype, establishing the de novo origin of the rearrangement, probably originated by aberrant replicative mechanisms such as FOSTES/MMBIR or abnormal DNA repair during gametogenesis or early embryogenesis. The observed phenotype mainly correlates with the 18q deletion, being consistent with previously reported cases. This case contributes to the phenotypic and cytogenetic-molecular characterization of this rare chromosomal anomaly, emphasizing the importance of comprehensive family genetic counseling.

190. P11-17. DISCOVERY OF GENETIC VARIANTS IN IMMUNE RELATED GENES IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS THROUGH TRANSCRIPTOMIC SEQUENCING

Ignacio Gomez Mercado¹, María Cecilia Riccheri², Geraldine Gueron³, Javier Cotignola⁴, María Sol Ruiz²

1. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer

2. Hospital Nacional Posadas, El Palomar, Buenos Aires, Argentina.; Servicio de Pediatría

3. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer

4. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer

5. CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina; Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer
 nachogomez0899@gmail.com

Introduction: Acute lymphoblastic leukemia (ALL) is the leading cause of cancer-related mortality in children. Current treatments are associated with acute and long-term toxicity. The immune component of the tumor microenvironment is an under-explored factor that could play a role in disease prognosis. Materials and methods: We performed RNA-seq (Illumina) of bone marrow samples from 32 pediatric ALL patients from Argentina. We performed whole-transcriptome for identification of single nucleotide variant (SNV) using CTAT-Mutations. We evaluated 843 genes that could alter the interaction with immune cells in the tumor microenvironment (Reactome). Variants were filtered and annotated using public germline and somatic variant databases. Results: To select for high-confidence variants (95% specificity) we developed a threshold value based on the QUAL parameter from the variant calling step, by comparing variants shared between technical replicates and performing ROC curves. After filtering and annotation, we found 11 variants in 9 patients, being 8/11 classified by Franklin as TIER3 in CEP290, UBE3B, CPNE3, DUSP4, DAPP1, RNF135, TBC1D10C and TLR1; 2/11 as TIER1 in TP53, KRAS; and 1/11 as TIER4 in BTN3A3. Patients harboring these variants presented a significantly lower enrichment score in the "MHC_Class_II_Antigen_Presentation" pathway (q-val<0.01). The variant found in UBE3B is located in the active site, and associated with a lower enrichment score in the "Antigen presentation through MHC-class-II" pathway. Conclusions: Further analysis of the variants found in this study has the potential to identify novel mechanisms modulating the interaction between the immune system and leukemic cells in ALL.

191. P11-18. SHORT STATURE ASSOCIATED WITH NOVEL HETEROZYGOUS ACAN VARIANTS

Paula Scaglia¹, Ana Keselman², Debora Braslavsky³, Nora Sanguineti⁴, María Esnaola Azcoiti⁵, Agustín Izquierdo⁶, Ana Sol Riesco⁷, Florencia Villegas⁸, Hamilton Cassinelli⁹, Romina Armando¹⁰, Ignacio Bergada¹¹, Gabriela Ropelato¹²

1. Centro de Investigaciones Endocrinológicas "Dr. César Bergada" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina. Unidad de Medicina Traslacional, Hospital de

Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Laboratorio de genómica

2. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; División de Endocrinología

3. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; División de Endocrinología

4. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; División de Endocrinología

5. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Laboratorio de genómica

6. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Laboratorio de genómica

7. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Laboratorio de genómica

8. Sección Genética Médica, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Sección Genética Médica

9. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; División de Endocrinología

10. Sección Genética Médica, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Sección Genética Médica

11. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; División de Endocrinología

12. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Laboratorio de genómica

pscaglia@cedie.org.ar

Heterozygous loss-of-function ACAN variants were initially described in individuals with short stature (SS) and advanced bone age (BA), but the phenotypic spectrum has since broadened to include skeletal abnormalities, facial dysmorphisms, and early-onset osteoarthritis. We report clinical and molecular findings in four unrelated families with ACAN defects. We studied 5 prepubertal patients and 3 affected fathers. Clinical evaluation included detailed anthropometry and phenotyping, BA assessment, radiological and laboratory screening. Next-generation sequencing of SS candidate genes was performed, and prioritized variants were confirmed by Sanger sequencing. Variant interpretation followed ACMG/AMP and ClinGen guidelines. We identified a novel likely pathogenic ACAN splicing variant, paternally inherited, in 3 patients from 2 families: NM_001369268.1:c.7302+1G>A. Patient 1, born small for gestational age (SGA), presented with SS and relative macrocephaly, later developing body disproportion, brachydactyly, and joint hypermobility with adequate BA. Her paternal relatives had SS (130-140cm) and adult-onset joint pain. In contrast, two sisters from an unrelated family with the same splicing variant (patients 2 and 3) were born adequate for gestational age and showed advanced BA.

Patient 4, born SGA, presented severe SS (-4.9 SDS) but no disproportion. He carried a novel likely pathogenic nonsense variant, NM_001369268.1:c.4339G>T; NP_001356197.1:p.(E1447*), inherited from his affected father. Finally, a de novo nonsense pathogenic previously reported variant, NM_001369268.1:c.871C>T, NP_001356197.1:p.(Q291*), was identified in one isolated case. This study highlights the wide phenotypic variability of ACAN-related SS, even among individuals harboring the same variant. Genetic testing plays a crucial role in establishing the diagnosis in children with SS of unknown origin.

192. P11-19. ANALYSIS OF COMPLEX CHROMOSOMAL REARRANGEMENTS BY ARRAY-CGH

Aldana Claps¹, Tania Castro², Julieta Laiseca³, Ana Gousies⁴, Evelyn Torchinsky⁵, Wanda Montes⁶, Candela Ruiz⁷, Andrea Rodriguez⁸, Cynthia Bravo⁹, Lilian Franzi¹⁰, Fabiana Guerisio¹¹, Carolina Dellamea¹², María Victoria Freire¹³, Pablo Almazán¹⁴, Julia Mugnani¹⁵, Ruyh Schumiachkin¹⁶, Cecilia Montes¹⁷, Rosana Perotti¹⁸, Alejandra Chaves¹⁹, Mariana Asinari²⁰, Soledad Davila²¹, Marilena Antinori²², Bárbara Casali²³, Sandra Rozental²⁴, Roxana Cerretino²⁵, Liliana Dain²⁶, Melisa Taboas²⁷

1. Centro Nacional de Genética Médica; Diagnostico Molecular

2. Centro Nacional de Genética Médica; Diagnostico Molecular

3. Centro Nacional de Genética Médica; Diagnostico Molecular

4. Centro Nacional de Genética Médica; Citogenética

5. Centro Nacional de Genética Médica; Diagnóstico Prenatal

6. Centro Nacional de Genética Médica; Citogenética

7. Centro Nacional de Genética Médica; Citogenética

8. Centro Nacional de Genética Médica; Citogenética

9. Centro Nacional de Genética Médica; Citogenética

10. Centro Nacional de Genética Médica; Citogenética

11. Centro Nacional de Genética Médica; Citogenética

12. Hospital Castelan, Chaco; -

13. Hospital Provincial Neuquén, Neuquén; -

14. Hospital Provincial Neuquén, Neuquén; -

15. Subsecretaría de Discapacidad, Rehabilitación e Inclusión, Ministerio de Salud de la Provincia de Córdoba, Córdoba; Área de Genética Médica

16. Subsecretaría de Discapacidad, Rehabilitación e Inclusión, Ministerio de Salud de la Provincia de Córdoba, Córdoba; Área de Genética Médica

17. Hospital de Niños de la Santísima Trinidad, Córdoba; División genética médica

18. Hospital de Niños de la Santísima Trinidad, Córdoba; División genética médica

19. Hospital de Niños de la Santísima Trinidad, Córdoba; División genética médica

20. Hospital de Niños de la Santísima Trinidad, Córdoba; División genética médica

21. Hospital de Alta Complejidad Pte Juan D Perón, Formosa; Servicio de Biología Molecular

22. Hospital de la madre y el niño, Formosa; -

23. Hospital de Niños Ricardo Gutiérrez, Buenos Aires; Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología

24. Hospital de Niños Ricardo Gutiérrez; Centro Nacional de Genética Médica, Buenos Aires; Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología; Citogenética

25. Centro Nacional de Genética Médica; Citogenética

26. Centro Nacional de Genética Médica; Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Diagnóstico molecular; Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3),

27. Centro Nacional de Genética Médica; Diagnostico Molecular

aldanaclaps@gmail.com

The study of chromosomal abnormalities has been fundamental to understanding multiple genetic diseases. Traditionally, conventional cytogenetic analysis has allowed the identification of large chromosomal aberrations, but it has limited resolution for detect-

ing alterations of smaller size or structural complexity. In this context, array-based comparative genomic hybridization (array-CGH) technology has emerged as a powerful tool for the detection of copy number variants (CNVs) at the submicroscopic level, offering significantly higher resolution than conventional methods, as well as its ability to identify cryptic chromosomal rearrangements. We present 7 cases referred to our institution in which chromosomal rearrangements were detected by array-CGH. Among them, 3 presented a normal karyotype and 1 with Beckwith-Wiedemann suspicion. The SurePrint G3 unrestricted CGH platform (8x60K, Agilent) was used. The Aberration Detection Method 2 (ADM-2) algorithm was used for bioinformatics analysis, and the minimum number of consecutive oligos considered a copy number alteration was 3. The rearrangements were later confirmed by FISH. We detected 4 derived chromosomes: der(Y)t(X;Y), der(X)t(11;X), der(18)t(18;18), der(19)t(16;19), the latter involving chromothripsis. The remaining 3 had: inv dup del(8p), inv dup del(10q) and dup trip(Xq). The detection of these types of alterations is important not only for the accurate diagnosis, but also for understanding the molecular mechanisms beyond these rearrangements and the genetic counseling for patients and families.

193. P11-20. CONTEXT-DEPENDENT PROMOTER METHYLATION OF BMP3, NDRG4, AND SEPTIN9 ACROSS SPORADIC CRC, LYNCH, AND FAP: PAIRED MUCOSA-TUMOR ANALYSIS AND MMR-STRATIFIED PERFORMANCE

Chiara María Mastromarino¹, Satu Mäki-Nevala², Alisa Olkinuora³, Julieta Natalia Soarez⁴, Tamara Alejandra Piñero⁵, Florencia Lohmann⁶, Hernán García-Rivello⁷, Carlos Alberto Vaccaro⁸, Toni T Seppälä⁹, Jukka-Pekka Mecklin¹⁰, Päivi Peltonmäki¹¹, Walter Hernan Pavicic¹²

1. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) (HIBA-IUHI-CONICET), CABA, Argentina. Programa de Cáncer Hereditario (ProCanHe) y Registro Epidemiológico (REM), HIBA, CABA, Argentina; ProCanHe

2. Biomedicum Helsinki, University of Helsinki, Helsinki, Finland; Medical Genetics

3. University hospital Basel, Basel, Switzerland; Medical Genetics

4. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) (HIBA-IUHI-CONICET), CABA, Argentina; ProCanHe

5. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) (HIBA-IUHI-CONICET), CABA, Argentina. Programa de Cáncer Hereditario (ProCanHe) y Registro Epidemiológico (REM), HIBA, CABA, Argentina; ProCanHe

6. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) (HIBA-IUHI-CONICET), CABA, Argentina. Programa de Cáncer Hereditario (ProCanHe) y Registro Epidemiológico (REM), HIBA, CABA, Argentina; ProCanHe

7. Servicio de Patología del Hospital Italiano de Buenos Aires (HIBA), CABA, Argentina.; Servicio Patología

8. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) (HIBA-IUHI-CONICET), CABA, Argentina. Programa de Cáncer Hereditario (ProCanHe) y Registro Epidemiológico (REM), HIBA, CABA, Argentina; ProCanHe

9. Helsinki University Hospital, Helsinki, Finland; Department of Surgery

10. Well Being Services County of Central Finland, Jyväskylä, Finland; Department of Science

11. Biomedicum Helsinki, University of Helsinki, Helsinki, Finland; Medical Genetics

12. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) (HIBA-IUHI-CONICET), CABA, Argentina. Programa de Cáncer Hereditario (ProCanHe) y Registro Epidemiológico (REM), HIBA, CABA, Argentina; ProCanHe
chiarabkp@gmail.com

Promoter CpG-island (CpGi) methylation of BMP3, NDRG4, and SEPTIN9 underpins FDA-cleared CRC screening tests, yet performance in paired mucosa-tumor (M-T) samples and in Lynch/FAP is less defined. Quantify T-M methylation change ($\Delta\beta$) and the discrimination (AUC) of a three-gene panel, including MMR (dMMR/pMMR) stratification. We analyzed paired M-T samples from sporadic,

Lynch, and FAP series using EPIC methylation arrays. For each gene we averaged probes within the promoter CpGi, compared TvsM within patient (patient block; visit adjustment), and estimated ROC/AUC with 95% CIs (AUC 0.5 = chance; 1.0 = perfect). Absolute β was higher in tumor than mucosa for all genes (e.g., BMP3 0.152 vs 0.089; NDRG4 0.163 vs 0.123; SEPTIN9 0.234 vs 0.178). Paired $\Delta\beta$ was significant in Lynch (SEPTIN9 +0.093, $p=1.6\times 10^{-5}$; BMP3 +0.030, $p=0.012$; NDRG4 +0.016, $p=0.022$), modest in FAP (SEPTIN9 +0.037, $p=0.050$), and non-significant in sporadic. Three-gene AUC: overall 0.621; Lynch 0.923 (0.861–0.984), FAP 0.707 (0.570–0.844), sporadic 0.608 (0.509–0.707). Single-gene AUC: SEPTIN9 0.726 > NDRG4 0.647 > BMP3 0.641. In sporadic, dMMR showed larger $\Delta\beta$ (BMP3 +0.158; NDRG4 +0.130; SEPTIN9 +0.062) than pMMR (BMP3 +0.010; NDRG4 –0.006; SEPTIN9 –0.076), with NDRG4 significant (Wilcoxon $p=0.0169$); AUCs were 0.667 and 0.651, respectively. In Lynch, dMMR had SEPTIN9 +0.114 ($p=0.00025$) and AUC 0.986 (0.964–1.000). Mucosal β varied by location (Kruskal–Wallis $p\leq 2.2\times 10^{-12}$) and rose slightly with age; sex effects were absent. Promoter methylation is context-dependent; SEPTIN9 is the strongest single marker, and discrimination is highest in Lynch—especially dMMR. Findings support series/MMR-specific thresholds and external validation.

194. P11-21. GENETIC LANDSCAPE OF HEREDITARY BREAST AND OVARIAN CANCER

Camila Ximena Peñalva¹, Belén Fiamma Figueredo², Ana Letícia Fernandes Gomes³, Héctor Martín Cifuentes⁴, Sofía de La Fuente⁵, Agustín Izquierdo⁶, Mónica Paola Bellazzi⁷, Gimena Alejandra Machado⁸, Sabrina Soledad Fernandez⁹, Emilio Batagelj¹⁰, Janeth Lara Alcántara¹¹, Julián Sánchez Loria¹², Tomás J. Poklepovich Caride¹³, Gonzalo Raúl Acevedo¹⁴, Guillermo Corró¹⁵, Marisol Delea¹⁶, Carlos David Brunque¹⁷

1. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

2. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

3. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

4. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

5. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

6. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

7. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

8. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

9. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

10. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

11. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

12. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

13. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

14. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

15. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

16. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

17. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

18. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

19. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

20. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

21. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

22. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

23. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

24. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

Centro Nacional de Genómica y Bioinformática
 14. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 15. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 16. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 17. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 camilaximenapenalva@gmail.com

Hereditary breast and ovarian cancer (HBOC) is the most frequent hereditary cancer syndrome, primarily caused by pathogenic variants in BRCA1/BRCA2. Identifying these variants is essential for diagnosis, prevention, and family counseling. We analyzed cancer type distribution, the spectrum of BRCA1/BRCA2 and other cancer-related genes in patients referred for genetic testing. We conducted a retrospective review of oncology patients referred to our genetics laboratory from 2022 to the present. Genetic testing for hereditary cancer predisposition included detection of single nucleotide variants (SNVs) and copy number variants (CNVs). Detected variants were characterized by type, genomic location, and classified following ACMG and expert-specific guidelines. Sixty-six patients were enrolled, of whom 56 (85%) presented HBOC. Among these 56 patients, 23 (41%) carried variants in cancer susceptibility genes. Pathogenic, likely pathogenic and uncertain significance variants in BRCA1/2 contributed to 53% (13/23) of these cases. Small variants accounted for 69.2 % (9/13) of the variants detected in BRCA1/2, in which 61.5% (8/13) were indels and 7.7 % (1/13) were SNVs. The remaining 30.8 % (4/13) consisted of copy number variants (CNVs). We confirmed HBOC as the leading indication for genetic testing among hereditary cancer patients. BRCA1/BRCA2 remained the most frequently affected genes, accounting for 48% of Pathogenic variants in HBOC patients. Pathogenic variants were mostly indels, highlighting the importance of their detection alongside SNVs and CNVs. These findings stress the value of comprehensive multigene panel testing for patient diagnosis and management.

195. P11-22. GENOTYPE-PHENOTYPE CHARACTERIZATION IN TWINS WITH A NOVEL NONSENSE WT1 VARIANT

Lourdes Correa Brito¹, Jimena Lopez Dacal², Paula Scaglia³, María Esnaola Azcoiti⁴, Evangelina Zubimendi⁵, Agustín Izquierdo⁶, Miguel Liern⁷, Miguel Podestá Jr⁸, Andrea Arcari⁹, Romina P. Grinspon¹⁰, María Gabriela Ropelato¹¹, Rodolfo A. Rey¹²

1. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina; Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina

2. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina; .

3. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina; Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina

4. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina; Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina

5. Centro de Investigaciones Endocrinológicas "Dr. César

Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina; .

6. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina; Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina

7. Unidad de Nefrología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina; .

8. Unidad de Urología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina; .

9. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina; .

10. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina; .

11. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina; Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina

12. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET - FEI - División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina; Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, C1425EFD Buenos Aires, Argentina

lcorrea@cedie.org.ar

WT1 is essential for renal and gonadal development. Genotype–phenotype correlation exists for missense variants in exons 8 and 9 (Denys-Drash syndrome) and splice-site variants in intron 9 affecting the +KTS isoforms of WT1 (Fraser syndrome). However, loss-of-function (LOF) variants have not been well characterized. Aim: to predict the clinical impact by applying the lumping and splitting criteria in two twin patients carrying a LOF variant in WT1 that do not fit the typical Denys-Drash or Fraser phenotypes. A novel heterozygous pathogenic variant, NM_024426.6:c.658C>T, NP_077744.4:p.(Gln220Ter), was identified in WT1 in two twins with Wilms tumor and 46,XY gonadal dysgenesis. The evidence supported a split of its phenotypic spectrum into three distinct groups. Denys-Drash syndrome, associated with missense variants exhibiting dominant-negative effects, presents with early-onset glomerulopathy, predisposition to Wilms tumor, and gonadal dysgenesis. Fraser syndrome, linked to intron 9 mutations affecting +KTS isoforms, manifests as late-onset glomerulopathy, gonadal dysgenesis, and high risk of gonadoblastoma. Finally, a yet undefined entity is associated with truncating variants, leading to haploinsufficiency. Our patients, with a novel truncating variant, present early-onset Wilms tumour and partial gonadal dysgenesis. There is no evidence of glomerulopathy or gonadoblastoma until the age of 11 years. The cases reported here do not fit in the known Denys-Drash or Fraser syndromes, as could be anticipated by the genetic finding in the WT1 gene. The risks of late-onset renal failure and gonadal tumour cannot be excluded, which warrants a close follow-up for renal function and gonadal tumour development in these cases.

ORALES 9 - SAIC - GENÉTICA

DATE & TIME: 18/11/2025 17:00 - 18:30 H

Chairs: Irma Slavutsky, Carina Marcela Rivolta

196. O9-01. FROM PHENOTYPE TO GENOTYPE: UNCOVERING MOLECULAR DIVERSITY IN ARGENTINE LIMB-GIRDLE MUSCULAR DYSTROPHIES (LGMD) PATIENTS

Carmen Llamas Massini¹, Micaela Carcione², Micaela Ciepelinski³, Agustina Bernardi⁴, Florencia Giliberto⁵

1. Laboratorio de Distrofinopatías, Cátedra de Genética,

Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Buenos Aires, Argentina; Instituto de Inmunología, Genética y Metabolismo INIGEM, (UBA-CONICET), Buenos Aires, Argentina.; Laboratorio de Distrofinopatías, FFyB (UBA); INIGEM (UBA-CONICET)

2. Laboratorio de Distrofinopatías, Cátedra de Genética, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Buenos Aires, Argentina; Instituto de Inmunología, Genética y Metabolismo INIGEM, (UBA-CONICET), Buenos Aires, Argentina.; Laboratorio de Distrofinopatías, FFyB (UBA); INIGEM (UBA-CONICET)

3. Laboratorio de Distrofinopatías, Cátedra de Genética, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Buenos Aires, Argentina; Instituto de Inmunología, Genética y Metabolismo INIGEM, (UBA-CONICET), Buenos Aires, Argentina.; Laboratorio de Distrofinopatías, FFyB (UBA); INIGEM (UBA-CONICET)

4. Laboratorio de Distrofinopatías, Cátedra de Genética, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Buenos Aires, Argentina; Instituto de Inmunología, Genética y Metabolismo INIGEM, (UBA-CONICET), Buenos Aires, Argentina.; Laboratorio de Distrofinopatías, FFyB (UBA); INIGEM (UBA-CONICET)

5. Laboratorio de Distrofinopatías, Cátedra de Genética, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Buenos Aires, Argentina; Instituto de Inmunología, Genética y Metabolismo INIGEM, (UBA-CONICET), Buenos Aires, Argentina.; Laboratorio de Distrofinopatías, FFyB (UBA); INIGEM (UBA-CONICET)
carllames@gmail.com

Background: Limb-girdle muscular dystrophies (LGMD) are a group of rare myopathies caused by pathogenic variants in more than 30 different genes. Their diagnosis is challenging due to overlapping phenotypes and broad genetic heterogeneity. **Objectives:** To describe the spectrum of molecular alterations in an Argentine cohort with clinical suspicion of LGMD, analyzed by NGS as part of a diagnostic initiative with nationwide reach (ADM, 2024–2025), and to support genetic diagnosis in complex neuromuscular presentations. **Methodology:** Whole-exome sequencing (WES) by NGS (Macrogen) was performed in 30 patients with clinically suspected LGMD. Segregation by Sanger sequencing, CNV analysis (WES-based, IMEX facility), and ACMG-based variant classification were applied when indicated. **Results:** Pathogenic or likely pathogenic variants were identified in 19 patients (63.3%). Three patients (10%) carried variants of uncertain significance (VUS) in genes potentially related to their clinical picture. In 8 cases (26.7%), no variants were found or the evidence was insufficient to establish a molecular diagnosis. LGMD-compatible diagnoses were confirmed in 16 patients. The most frequently affected genes were COL6A1, COL6A2, and COL6A3, followed by CAPN3, SGCA, FKTN, ANOS, DES, CAV3, and POMT1. Variants in genes associated with other neuromuscular conditions were found in 5 patients. Two undiagnosed cases had SMCHD1 variants and are under evaluation for facioscapulohumeral dystrophy. Segregation studies were performed in 2 families, and one exome-based CNV involving DMD was detected. **Conclusions:** These findings highlight the diagnostic utility of genomic testing in neuromuscular disorders and its relevance for accurate variant interpretation, especially in clinically heterogeneous or genetically complex cases.

197. O9-02. DUAL GENETIC DIAGNOSIS IN A PEDIATRIC PATIENT: THE ROLE OF RNA ANALYSIS IN DETECTING A DMD DEEP INTRONIC VARIANT AND AN EFTUD2 MULTI-EXON DELETION

María Eugenia Focuberta¹, Soledad Monges², Verónica Gorris³, Fabiana Lubieniecki⁴, Sofía Corbaz⁵, Luis Pablo Graviña⁶, María Gabriela Obregon⁷

1. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Laboratorio de Biología Molecular-Servicio de Genética

2. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garra-

han"; Servicio de Neurología

3. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Laboratorio de Inmunología Molecular

4. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Servicio de Patología

5. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Servicio de Neurología

6. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Laboratorio de Biología Molecular-Genética

7. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan"; Servicio de Genética

eugetoncu@gmail.com

Patients with multiple genetic diseases (MGD) present a particular diagnostic challenge. Whole exome sequencing (WES) studies estimate that 0.4%–4% of patients are affected by MGD. We report a patient initially suspected of having Mandibulofacial dysostosis, Guion-Almeida type (MFDGA), who, at 14 months of age, presented with weakness and markedly elevated serum creatine kinase levels (12,000 U/L). Muscle biopsy confirmed complete dystrophin deficiency, consistent with Duchenne muscular dystrophy. The patient underwent extensive genetic testing, including MLPA of the DMD gene, next-generation sequencing (NGS) panels for neuromuscular and skeletal disorders, and WES, all of which were negative. Karyotype and chromosomal microarray analysis also revealed no abnormalities. In the absence of a molecular diagnosis, muscle-derived mRNA analysis was performed, revealing a pseudo-exon inclusion from intron 22 in the DMD transcript (r.2949_2950 ins2949+889_2949+1147) and identifying the causative variant c.2949+964G>A. Given that the EFTUD2 gene is expressed in skeletal muscle, its transcript was also sequenced from the biopsy, revealing a heterozygous deletion of exons 7-9. The DMD variant has been previously reported in only three cases in the Leiden Open Variation Database. Notably, deep intronic variants account for ~1% of dystrophinopathy cases and are not detectable by routine diagnostic methods. EFTUD2 deletions are reported in approximately 7% of MFDGA cases; however, the deletion identified in our patient was not detected by chromosomal microarray, skeletal disorders panel, or WES. This case highlights the value of RNA analysis of candidate genes in patients with negative results from standard genetic testing.

198. O9-03. ASSOCIATION OF F8-MUTATION PROFILE AND SINGLE NUCLEOTIDE VARIANTS (SNVS) IN IMMUNOREGULATORY GENES WITH IMMUNE TOLERANCE INDUCTION OUTCOME IN SEVERE HEMOPHILIA A PATIENTS WITH FVIII INHIBITORS

Hector Martin Cifuentes¹, Betiana Ziegler², Pamela Radic³, Martin Abelleyro⁴, Andrea Cocca⁵, Belén Fiamma Figueredo⁶, Camila Ximena Peñalva⁷, Sofía de La Fuente⁸, Guillermo Corró⁹, Carlos David Bruque¹⁰, María Emilia Villegas¹¹, Julián Sánchez Loria¹², Tomás J. Poklepovich Caride¹³, Carlos de Brasi¹⁴, Daniela Neme¹⁵, Marisol Delea¹⁶, Liliana Rossetti¹⁷

1. Unidad de Conocimiento Traslacional Hospitalaria Patagónica, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina; Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM). Ciudad de Buenos Aires, Argentina; Unidad de Conocimiento Traslacional Hospitalaria Patagónica; Laboratorio de Genética Molecular de la Hemofilia (GMH)

2. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM). Ciudad de Buenos Aires, Argentina; Laboratorio de Genética Molecular de la Hemofilia (GMH)

3. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM). Ciudad de Buenos Aires, Argentina; Laboratorio de Genética Molecular de la Hemofilia (GMH)

4. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM). Ciudad de Buenos Aires, Argentina; Laboratorio de Genética Molecular de la Hemofilia (GMH)

5. Fundación de la Hemofilia. Ciudad de Buenos Aires, Ar-

gentina Fundación de la Hemofilia. Ciudad de Buenos Aires, Argentina; Fundación de la Hemofilia

6. Unidad de Conocimiento Traslacional Hospitalaria Patagónica, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina; Unidad de Conocimiento Traslacional Hospitalaria Patagónica

7. Unidad de Conocimiento Traslacional Hospitalaria Patagónica, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica

8. Unidad de Conocimiento Traslacional Hospitalaria Patagónica, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina; Unidad de Conocimiento Traslacional Hospitalaria Patagónica

9. Unidad de Conocimiento Traslacional Hospitalaria Patagónica, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina; Unidad de Conocimiento Traslacional Hospitalaria Patagónica

10. Unidad de Conocimiento Traslacional Hospitalaria Patagónica, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina; Unidad de Conocimiento Traslacional Hospitalaria Patagónica

11. Unidad Operativa Centro Nacional de Genómica y Bioinformática - ANLIS "Dr. Carlos G. Malbrán"; Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM). Ciudad de Buenos Aires, Argentina; Unidad Operativa Centro Nacional de Genómica y Bioinformática; Laboratorio de Genética Molecular de la Hemofilia (GMH)

12. Unidad Operativa Centro Nacional de Genómica y Bioinformática - ANLIS "Dr. Carlos G. Malbrán"; Unidad Operativa Centro Nacional de Genómica y Bioinformática

13. Unidad Operativa Centro Nacional de Genómica y Bioinformática - ANLIS "Dr. Carlos G. Malbrán"; Unidad Operativa Centro Nacional de Genómica y Bioinformática

14. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM). Ciudad de Buenos Aires, Argentina; Laboratorio de Genética Molecular de la Hemofilia (GMH)

15. Fundación de la Hemofilia. Ciudad de Buenos Aires, Argentina.; Fundación de la Hemofilia

16. Unidad de Conocimiento Traslacional Hospitalaria Patagónica, Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica

17. Instituto de Medicina Experimental (IMEX), CONICET-Academia Nacional de Medicina (ANM). Ciudad de Buenos Aires, Argentina; Laboratorio de Genética Molecular de la Hemofilia (GMH)

bioq.mcifuentes@gmail.com

Introduction: Hemophilia A (HA) is an X-linked recessive bleeding disorder caused by deficiency of factor VIII activity (FVIII:C). Large intron 22 inversions in F8 gene (Inv22) account for ~45% of severe HA cases, while deletions, duplications, or small variants (SNVs, indels) explain the remainder. The most serious complication of HA-therapy is the development of neutralizing antibodies (inhibitors) against FVIII, occurring in 20–30% of severe patients. The strategy for inhibitor eradication is immune tolerance induction (ITI). Approximately 60–80% of patients achieve tolerance after ITI, although outcomes remain variable. **Aim:** This study aimed to analyze the F8-mutation profile and selected SNVs in immunoregulatory genes, and to evaluate their influence on ITI outcome in a cohort of Argentinean patients with severe HA. **Materials and Methods:** We analyzed F8 mutations in 64 severe HA patients with inhibitors undergoing ITI: 39 carried Inv22 and 25 had non-Inv22 mutations. Four SNVs were investigated: IL10-rs1800896 (allele-specific-PCR), TNFA-rs1800629, CTLA4-rs5742909, and CTLA4-rs231775 (PCR-RFLP). ITI success was defined as complete inhibitor eradication, whereas ITI failure corresponded to persistent inhibitors after 33 months of uninterrupted therapy. **Results:** The presence of the rs1800896 A/G genotype in IL10, was significantly associated with ITI success, achieving FVIII inhibitor eradication (OR=11.0; 95% CI: 1.22–99.31; P=0.019) in Inv22+ cases. This

polymorphic-variant may serve as a predictive biomarker of ITI outcome. **Conclusion:** Identifying genetic factors associated with treatment response in HA is crucial to guide personalized therapy, refine clinical decision-making, and promote a more efficient use of healthcare resources.

199. O9-04. BIOTINIDASE DEFICIENCY: DIVERSITY OF GENETIC VARIANTS AND THEIR CLINICAL IMPACT IN A LOCAL COHORT

Silene Silvera-Ruiz¹, Celia Angaroni², Carola Grosso³, Lourdes Peralta⁴, Adriana Becerra⁵, Guillermo Guelbert⁶, Gonzalo Castro⁷, Gabriela Barbás⁸, Laura Laróvere⁹

1. Hospital de Niños de la Santísima Trinidad. Ministerio de Salud de Córdoba; Centro de Estudio de las Metabolopatías Congénitas.

2. Hospital de Niños de la Santísima Trinidad. Ministerio de Salud de Córdoba; Centro de Estudio de las Metabolopatías Congénitas.

3. Hospital de Niños de la Santísima Trinidad. Ministerio de Salud de Córdoba; Centro de Estudio de las Metabolopatías Congénitas. Cátedra de Clínica Pediátrica, Facultad de Ciencias Médicas, UNC

4. Hospital de Niños de la Santísima Trinidad. Ministerio de Salud de Córdoba; Centro de Estudio de las Metabolopatías Congénitas

5. Hospital de Niños de la Santísima Trinidad. Ministerio de Salud de Córdoba.; Sección Enfermedades Metabólicas

6. Hospital de Niños de la Santísima Trinidad; Sección Enfermedades Metabólicas

7. Ministerio de Salud de Córdoba; Departamento Laboratorio Central

8. Ministerio de Salud de Córdoba; Departamento Laboratorio Central

9. Hospital de Niños de la Santísima Trinidad. Ministerio de Salud de Córdoba; Centro de Estudio de las Metabolopatías Congénitas. Cátedra de Clínica Pediátrica, Facultad de Ciencias Médicas, UNC

silenesilvera@gmail.com

Introduction: Biotinidase deficiency (BD) is an autosomal recessive inborn error of biotin metabolism. Measurement of enzyme activity and molecular analysis of the BTD gene are complementary tools to confirm the diagnosis, determine severity, guide treatment, and provide family genetic counseling. **Objective:** To characterize BTD gene variants in patients with BD and analyze genotype–phenotype correlations regarding enzyme activity and clinical presentation. **Material/Methods:** A total of 23 patients diagnosed between 2007–2025 were studied. Biotinidase enzyme activity was measured in dried blood spots and plasma. Molecular analysis of the BTD gene was performed in 20 patients using PCR and Sanger sequencing. **Results:** Of the 23 patients, 17 were detected through newborn screening and 6 were diagnosed later (>2 months). Twelve pathogenic BTD variants were identified, including missense, nonsense, frameshift, and intronic changes. The most frequent variants were c.38_44delinsTCC (p.Cys13fs) and c.1270G>C (p.Asp424His), present in 12 and 10 patients, respectively. Less common variants included c.873delT (p.Ser391ArgfsTer23), c.1098G>A (p.Trp366Ter), c.1535C>T (p.Thr512Met), and the intronic c.250-15delT. Genotype–enzyme activity correlation allowed the identification of borderline cases between partial and profound BD. Patients homozygous for p.Asp424His showed residual activity compatible with partial BD, whereas carriers of frameshift or nonsense variants presented with profound deficiency. **Conclusion:** Molecular analysis of the BTD gene provides critical information for BD diagnosis, complementing enzyme activity measurement and enabling better classification of patients for appropriate treatment. The identification of recurrent variants contributes to characterizing the local population and facilitates interpretation of results in both neonatal and clinical diagnostic contexts.

200. O9-05. GENETICS IN HYPERTROPHIC CARDIOMYOPATHY: EVIDENCE FROM A PATIENT COHORT

Belén Fiamma Figueredo¹, Camila Ximena Peñalva², Luis

Enrique Gomez³, Ana Letícia Fernandes Gomes⁴, Héctor Martín Cifuentes⁵, Sofía de La Fuente⁶, Agustín Izquierdo⁷, Mercedes Sáenz Tejeira⁸, Gisela Marina Streitenberger⁹, Monica Paola Bellazzi¹⁰, Gimena Alejandra Machado¹¹, Sabrina Soledad Fernandez¹², Maria Laura Ruggero¹³, Julián Sánchez Loria¹⁴, Tomás J. Poklepovich Caride¹⁵, Gonzalo Raul Acevedo¹⁶, Guillermo Corró¹⁷, Marisol Delea¹⁸, Carlos David Bruque¹⁹

1. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 2. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 3. División de Cardiología - Hospital General de Agudos Dr. Juan A. Fernández. Buenos Aires, Argentina.; -
 4. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 5. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 6. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 7. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 8. División de Cardiología. Hospital General de Agudos Dr. Juan A. Fernández. Buenos Aires, Argentina.; -
 9. Servicio de Cardiología, Hospital De Alta Complejidad El Cruce SAMIC.; -
 10. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 11. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 12. Unidad de Enfermedades Poco Frecuentes-Hospital de Alta Complejidad El Calafate-SAMIC, El Calafate, Santa Cruz, Argentina.; -
 13. Tribunal Superior de Justicia de Santa Cruz, Santa Cruz, Argentina.; -
 14. Unidad Operativa Centro Nacional de Genómica y Bioinformática - ANLIS "Dr Carlos G. Malbrán"; -
 15. Unidad Operativa Centro Nacional de Genómica y Bioinformática - ANLIS "Dr Carlos G. Malbrán"; -
 16. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 17. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 18. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
 19. Hospital de Alta Complejidad El Calafate - SAMIC, El Calafate, Santa Cruz, Argentina.; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET
- figueredobelenfiamma@gmail.com

Introduction: Hypertrophic cardiomyopathy (HCM) is the most common hereditary heart disease, characterized by left ventricular hypertrophy, myocyte disarray and myocardial fibrosis. Variants in genes encoding sarcomeric proteins account for approximately 60% of HCM cases. The disease can manifest in different morphological patterns and the variable penetrance of sarcomeric gene variants explains the clinical heterogeneity, ranging from asymptomatic individuals to patients with advanced heart failure or malignant arrhythmias. This study analyzes hypertrophic cardiomyopathy patients from a larger cohort with identified genetic variants, focusing on those carrying curated sarcomeric gene variants. **Materials and Methods:** The cohort included 57 patients and relatives (44

probands), with a mean age of 37 years, presenting HCM. Genetic testing was performed at SAMIC Hospital, El Calafate, between 2023 and 2025. Variant classification was performed in our genetics laboratory, following American College of Medical Genetics and gene-specific expert guidelines. Results: In this cohort of 44 probands, 16 (36.4%) did not carry sarcomeric variants, while 28 (63.6%) carried variants in sarcomeric genes. Of these 28 probands, 23 carried single variants in MYH7 (57%), MYBPC3 (39%) or TNNI3 (4%) and the remaining 5 probands carried double variants. Conclusion: This cohort demonstrated the predominance of MYH7 and MYBPC3 variants, while double variants in some probands highlight the potentially complex phenotypic impact of compound genetic changes. These findings underscore the value of genetic testing for accurate diagnosis and risk stratification, facilitating the correlation of variants with clinical outcomes, supporting precision management and family screening.

201. O9-06. GERMLINE APC TESTING IN ARGENTINE FAMILIAL ADENOMATOUS POLYPOSIS: RARE FRAME-SHIFT AND RECURRENT LARGE REARRANGEMENTS ACROSS HOSPITAL SERIES

Julieta Natalia Soares¹, Alisa Olkinuora², Karina Yonamine³, Juan Garona⁴, Mariana Coraglio⁵, Karina Collia Ávila⁶, Carlos Alberto Vaccaro⁷, Taina Nieminen⁸, Päivi Peltomäki⁹, Walter Hernán Pavicic¹⁰

1. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) (HIBA-IUHI-CONICET), CABA, Argentina. Programa de Cáncer Hereditario (ProCanHe) y Registro Epidemiológico (REM), HIBA, CABA, Argentina.; ProCanHe
2. Biomedicum Helsinki, University of Helsinki, Helsinki, Finland. University hospital Basel, Basel, Switzerland.; Medical Genetics
3. Hospital El Cruce; Servicio de Gastroenterología
4. Unidad de Investigaciones Biomédicas en Cáncer (IBio-CAN), Centro de Medicina Traslacional, Hospital El Cruce, Argentina.; Centro de Oncología Molecular y Traslacional, Universidad Nacional de Quilmes, Argentina
5. Hospital de Gastroenterología "Dr. Carlos Bonorino Udaondo", Ciudad Autónoma de Buenos Aires, Argentina; Unidad de Proctología
6. Hospital de Gastroenterología "Dr. Carlos Bonorino Udaondo", Ciudad Autónoma de Buenos Aires, Argentina.; Unidad de Proctología
7. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) (HIBA-IUHI-CONICET), CABA, Argentina.; Programa de Cáncer Hereditario (ProCanHe) y Registro Epidemiológico (REM), HIBA, CABA, Argentina.
8. Biomedicum Helsinki, University of Helsinki, Helsinki, Finland.; Medical Genetics
9. Biomedicum Helsinki, University of Helsinki, Helsinki, Finland; Medical Genetics
10. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) (HIBA-IUHI-CONICET), CABA, Argentina.; Programa de Cáncer Hereditario (ProCanHe) y Registro Epidemiológico (REM), HIBA, CABA, Argentina. julioesores@gmail.com

Familial adenomatous polyposis (FAP) arises from germline APC variants. Besides truncating changes, large rearrangements and promoter 1B deletions are recognized and may be missed without copy-number assays. We sought to define the variant spectrum and diagnostic yield in an Argentine series using Sanger sequencing plus MLPA, and to refine deletion breakpoints. We analyzed 15 unrelated probands with clinical FAP from Hospital El Cruce (HEC); a Hospital Udaondo series (70 probands) was used to assess recurrence across centers. Testing comprised bidirectional Sanger of all APC exons and MLPA (P043-E1). Long-range PCR with Sanger primer walking delineated breakpoints. Segregation was assessed in two families (two relatives each). We found a rare frameshift, NM_000038.6:c.4183dup (p.Ser1395LysfsTer3), in three probands (including one from Udaondo), classifiable as Likely Pathogenic (ACMG PVS1, PM2). MLPA detected a recurrent multiexon deletion spanning exons 12–17 with partial loss of exon 18 in three unrelated

proband (one from Udaondo); long-range PCR mapped the breakpoints to chr5:112,817,707–112,838,822 (hg38) (~21.1 kb). Two additional probands showed copy-number loss at APC promoter 1B (two P043 probes), with breakpoint resolution pending. Overall, 6/15 HEC probands carried pathogenic/likely pathogenic APC alterations; cross-series comparison showed recurrent c.4183dup and large deletions. Combined Sanger+MLPA yielded substantial diagnoses and revealed a rare truncating frameshift with supportive co-segregation, plus recurrent large rearrangements including promoter 1B losses—findings relevant for management and cascade testing. A literature/database review (to August 2025) found no ClinVar/LOVD entries for c.4183dup and no Argentine cohort reporting APC promoter 1B deletions, underscoring the local relevance.

202. 09-07. LNCRNAs AS EMERGING BIOMARKERS IN INFLAMMATORY BOWEL DISEASE: A MULTICENTER STUDY IN THE ARGENTINE POPULATION

Valeria Cristina Soler Rivero¹, Sofía Quesada², Ayelén D. Rosso³, Ma. Jimena Cerezo⁴, Renata A. Spiazzi⁵, Ana Omon-
te⁶, Laura Parks⁷, Debora Pellegrini⁸, Ignacio Zubiaurre⁹,
Glenda Ernst¹⁰, Karina Mariño¹¹, David Abramson¹², Claudia
Fuxman¹³, Juan Manuel Rey¹⁴, Roberto Huertas¹⁵, Fabio Na-
chman¹⁶, Alberto Penas-Steinhardt¹⁷, Fiorella S. Belforte¹⁸

1. Universidad Nacional de Luján; GEC

2. Universidad Nacional de Luján; GEC

3. Universidad Nacional de Luján; GEC

4. Hospital Nacional A. Posadas; Servicio de Gastroenterología

5. Hospital Nacional A. Posadas; Servicio de Gastroenterología

6. Hospital Nacional A. Posadas; Servicio de Gastroenterología

7. Hospital Británico de Buenos Aires; Servicio de Gastroen-
terología

8. Hospital Británico de Buenos Aires; Servicio de Gastroen-
terología

9. Hospital Británico de Buenos Aires; Servicio de Gastroen-
terología

10. Hospital Británico de Buenos Aires; Servicio de Gastroen-
terología

11. Instituto de Biología y Medicina Experimental; Lab. de
Glicómica Funcional y Molecular

12. Hospital Universitario Fundación Favaloro; Servicio de
Gastroenterología

13. Hospital Universitario Fundación Favaloro; Servicio de
Gastroenterología

14. Hospital Universitario Fundación Favaloro; Servicio de
Gastroenterología

15. Hospital Universitario Fundación Favaloro; Servicio de
Gastroenterología

16. Hospital Universitario Fundación Favaloro; Servicio de
Gastroenterología

17. Universidad Nacional de Luján; GEC

18. Universidad Nacional de Luján; GEC

valeriasoler614@gmail.com

Inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn's disease (CD) are chronic multifactorial pathologies with increasing prevalence related to environmental and urbanization factors. In the search for biomarkers, long non-coding RNAs (lncRNAs) have gained relevance due to their role in gene regulation and their ability to reflect pathogenic mechanisms. In particular, LINC01272 is associated with a proinflammatory profile, promoting NF-κB activation, cytokine production, and epithelial-mesenchymal transition, contributing to the loss of epithelial integrity. In contrast, ANRIL exhibits opposite behavior, with protective functions linked to the modulation of CDKN2A/B locus genes and the preservation of the intestinal barrier through the negative regulation of inflammatory pathways. This functional antagonism positions them as candidates of interest in the context of IBD. In this multicenter study, which included referral hospitals in Argentina, peripheral blood cell fractions (PBCF) and fecal cellular fraction (FCF) from patients with UC, CD, and healthy controls were analyzed. Extractions, reverse transcription, and relative quantification of lncRNAs were performed using qPCR normalized with GAPDH. The results showed systemic overexpression of LINC01272 in UC and a decrease in CD, while

locally, overexpression was observed in both pathologies. On the other hand, ANRIL showed systemic reduction in UC and CD, with a tendency to increase in local matrices. These findings highlight the viability of using non-invasive matrices such as PBCF and FCF in the identification of molecular biomarkers and reinforce the translational potential of lncRNAs in IBD.

203. 09-08. TEN YEARS OF EXPERIENCE IN THE MOLECULAR DIAGNOSIS OF MELAS IN ARGENTINE PEDIATRIC PATIENTS

Cynthia Noeli Ferrari¹, Mariana Amina Loos², Giovanna Aschettino³, Silvina Gómez Montoya⁴, Mara Cecilia Bonetto⁵,
María Paula Rodríguez⁶, Noelia Piergrossi⁷, Cristina Noemi
Alonso⁸, María Mercedes Pérez⁹, Hilda Verónica Aráoz¹⁰

1. Hospital de Pediatría Garrahan; Unidad de Genómica

2. Hospital de Pediatría Garrahan; Servicio de Neurología

3. Hospital de Pediatría Garrahan; Unidad de Genómica

4. Hospital de Pediatría Garrahan; Servicio de Neurología

5. Hospital de Pediatría Garrahan; Laboratorio de Biología

Molecular-Genética y Unidad de Genómica

6. Hospital de Pediatría Garrahan; Unidad de Genómica

7. Hospital de Pediatría Garrahan; Unidad de Genómica

8. Hospital de Pediatría Garrahan; Unidad de Genómica

9. Hospital de Pediatría Garrahan; Unidad de Genómica

10. Hospital de Pediatría Garrahan; Laboratorio de Biología
Molecular-Genética y Unidad de Genómica

cynthiaferrari10@gmail.com

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) is a multisystem disorder caused by mitochondrial DNA (mtDNA) variants. Accurate molecular diagnosis remains challenging but essential for clinical management and genetic counseling. AIM: To characterize the molecular findings in a cohort of pediatric patients with clinical suspicion of MELAS over a 10-year period. To assess heteroplasmy dynamics across different tissues and to evaluate the impact of next-generation sequencing (NGS) on diagnostic yield. PATIENTS AND METHODS: A retrospective study between 2015-2025 at Hospital Garrahan. Twenty-eight patients who met the clinical criteria for MELAS were included. Blood or urine-DNA samples from the cases and 18 mothers were analyzed. Molecular diagnosis was performed using Sanger sequencing, MLPA or NGS. Heteroplasmy levels were quantified by MLPA/NGS. Fisher's exact and Wilcoxon signed-rank tests were used. RESULTS: Molecular diagnosis was established in 23 patients. Seven pathogenic variants were identified in six genes. The most frequent variant was MT-TL1:m.3243A>G (67%) followed by MT-ND5:m.13513G>A (10%). Traditional methods diagnosed 16 patients; NGS identified seven additional cases (p= 0.04) and identified two novel variants. Maternal inheritance was confirmed in 16/18. Heteroplasmy levels were systematically higher in urine than in blood in cases analyzed (p = 0.03). CONCLUSIONS: This 10-year experience highlights the importance of integrating NGS into the diagnostic workflow for MELAS. This approach significantly increased diagnostic yield and also enabled the detection of novel variants. Urine was more sensitive than blood for detecting mtDNA variants. This study underscores that comprehensive, multi-tissue molecular analyses are essential for accurate diagnosis.

204. 09-09. CYTOGENETIC EVALUATION IN PRENATAL DIAGNOSIS: IDENTIFICATION AND CHARACTERIZATION OF NUMERICAL AND STRUCTURAL CHROMOSOMAL ABNORMALITIES

Evelyn, Torchinsky¹, Patricia, Pastore², Wanda, Montes³, Miguel, Contreras⁴, Miguel, Aguirre⁵, Roxana, Cerretini⁶, María Ester, Mollica⁷

1. Centro Nacional de Genética Médica, Administración
Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr.
Carlos G Malbrán", Buenos Aires, Argentina; Departamento
de Diagnóstico Genético

2. Centro Nacional de Genética Médica, Administración
Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr.
Carlos G Malbrán", Buenos Aires, Argentina; Departamento

de Diagnostico Genético

3. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina; Departamento de Diagnostico Genético

4. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina; Departamento de Genética Médica

5. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina; Departamento de Genética Médica

6. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina; Departamento de Diagnostico Genético

7. Centro Nacional de Genética Médica, Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) "Dr. Carlos G Malbrán", Buenos Aires, Argentina; Departamento de Diagnostico Genético
evetorchinsky@gmail.com

Prenatal cytogenetic diagnosis is an essential tool in the evaluation of pregnancies at risk for chromosomal abnormalities. A retrospective descriptive study was conducted on prenatal cytogenetic diagnosis during the period 2015–2025, comprising 1306 processed samples. Among them, 961 corresponded to amniotic fluid (AF), 246 to chorionic villi (CV), and 14 to other fluids such as cystic hygroma. Of the total, 370 samples were referred from other institutions, mainly from Buenos Aires City and its metropolitan area. A total of 382 chromosomal abnormalities were identified, including 333 numerical anomalies (257 in AF and 76 in CV) and 45 structural anomalies (36 in AF and 9 in CV), distributed between balanced and unbalanced rearrangements. Among numerical abnormalities, trisomy 21 was the most frequent (48%), followed by trisomy 18 (27%), monosomy X (13%), and trisomy 13 (8%). Structural abnormalities mainly included robertsonian and reciprocal translocations, as well as derivatives associated with parental rearrangements. The indications for invasive diagnosis have progressively changed over the decade. While in the early years, reproductive history or advanced maternal age predominated, in recent years, the growing impact of first-trimester combined screening and confirmation of ultrasound findings such as omphalocele, cystic hygroma, hydrocephalus, congenital heart disease, holoprosencephaly, among others, has become more prominent. In line with international literature, prenatal cytogenetic diagnosis using conventional techniques remains the gold standard for detecting chromosomal abnormalities, providing essential information for genetic counseling and reproductive decision-making.

POSTERS 12 - SAIC - METABOLISMO Y NUTRICIÓN 1
DATE & TIME: 18/11/2025 17:00 - 18:30 H
Chairs: **Esteban Martín Repetto, Silvia Bianchi, Veronica Mikszowicz**

205. P12-01. COMPARISON BETWEEN A BALANCED DIET AND DIETS ENRICHED WITH LARD AND BEEF FAT ON THE METABOLISM OF MALE C57BL/6J MICE APPLIED FOR A SHORT PERIOD

Rocio Aguero¹, María Inés Conte², María Ángeles Monclus³, Miguel Walter Fornes⁴

1. IHEM; LIAM

2. IHEM; LIAM

3. IHEM; LIAM

4. IHEM; LIAM

rocio.aguero.mol@gmail.com

C57BL6J mice are a widely used model for the evaluation of fat-enriched diets. The objective of this work was to evaluate whether two saturated fats had different effects on the metabolism of 12-week-old male C57BL6J mice. The mice were randomly divided into 3 groups and fed for 16 weeks with: balanced feed (C; n=4), feed

enriched with 24% wt/wt beef fat (B; n=4), or 24% wt/wt lard (P; n=4). The composition of the prepared feeds, food intake, nutritional status, body weight, organ weight indices relative to body weight, and plasma biochemical parameters were evaluated. Food intake and fat intake were higher for the fat-enriched groups than for the balanced feed. Group P had a higher energy intake and body weight than the other groups, but also had a lower testicle and epididymis weight indices relative to body weight than the other groups. Group B had a higher cholesterol, LDL, and atherogenic index than the other groups, but also had a lower GPT value than the other groups. The glucose was lower for the fat-enriched groups than for the balanced feed. There were no statistically significant differences in feed efficiency, liver and fat weight indices relative to body weight, HDL, triglycerides, and GOT. The data were analyzed with an ANOVA test and post hoc Tukey HSD test or Kruskal test and post hoc Dunn test as appropriate. Although mice in groups B and P ingested the same amount of total fat, they had different effects on organ indices and biochemical parameters.

206. P12-02. METFORMIN AMELIORATED MORPHOLOGICAL ALTERATIONS IN THE KIDNEYS CAUSED BY A HIGH-FAT DIET IN RATS

Silvana María Cantú¹, Hyun Jin Lee², Adriana Donoso³, Ana María Puyó⁴, Marcelo Roberto Choi⁵

1. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Ciencias Biológicas. Cátedra de Anatomía e Histología. Buenos Aires, Argentina; Univer-

sidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC). Laboratorio de estudios del síndrome metabólico experi-

mental. Buenos Aires, Argentina.; Cardiorrenometabolismo

2. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Ciencias Biológicas. Cátedra de Anatomía e Histología. Buenos Aires, Argentina; Univer-

sidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC). Laboratorio de estudios del síndrome metabólico experi-

mental. Buenos Aires, Argentina.; Cardiorrenometabolismo

3. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Ciencias Biológicas. Cátedra de Anatomía e Histología. Buenos Aires, Argentina; Univer-

sidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC). Laboratorio de estudios del síndrome metabólico experi-

mental. Buenos Aires, Argentina.; Cardiorrenometabolismo

4. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Ciencias Biológicas. Cátedra de Anatomía e Histología. Buenos Aires, Argentina; Univer-

sidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC). Laboratorio de estudios del síndrome metabólico experi-

mental. Buenos Aires, Argentina.; Cardiorrenometabolismo

5. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Ciencias Biológicas. Cátedra de Anatomía e Histología. Buenos Aires, Argentina; Univer-

sidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC). Laboratorio de estudios del síndrome metabólico experi-

mental. Buenos Aires, Argentina.; Cardiorrenometabolismo

standard diet (SD) and tap water; HFD: 50% w/w bovine fat added to the SD and tap water; CM: C+500mg/kg/day of M in the water; HFDM: CM+HFD. Body (BW) and kidneys weight (LKW, RKW) were measured. Kidneys were processed for conventional histology (H&E) and Sirius Red stains, and for transmission electron microscopy (TEM). Statistical analysis: ANOVA with Tukey post-

smcantu77@gmail.com

The global consumption of high-fat diets (HFD) is widespread and impacts severely on morphology and function of different organs, such as the kidneys. This study evaluated if metformin (M) could ameliorate kidney's morphological alterations caused by HFD. Male Sprague-Dawley rats were studied for 4, 8 and 12 weeks, randomly divided into four groups for each time (n=4-6): C (Control): standard diet (SD) and tap water; HFD: 50% w/w bovine fat added to the SD and tap water; CM: C+500mg/kg/day of M in the water; HFDM: CM+HFD. Body (BW) and kidneys weight (LKW, RKW) were measured. Kidneys were processed for conventional histology (H&E) and Sirius Red stains, and for transmission electron microscopy (TEM). Statistical analysis: ANOVA with Tukey post-

hoc tests. M prevented renal mass reduction from week 8 (renal mass index (%) = $\{[(\text{LKW}+\text{RKW})/\text{BW}]\times 100\}$; HFDM8 and HFDM12 vs HFD8 and HFD12, $p<0.05$ respectively). From week 8, M diminished intracytoplasmic vacuoles observed in the tubular cortex cells of the HFD groups, and by week 12, the vacuoles disappeared (HFDM8 and HFDM12 vs. HFD8 and HFD12, respectively). From week 4, M prevented renal corpuscle area reduction caused by HFD (HFDM4, HFDM8 and HFDM12 vs. HFD4, HFD8 and HFD12, $p<0.01$, respectively). Fibrosis percentage increase was prevented by M from week 4 comparing HFDM vs. HFD ($p<0.01$ for each time). Finally, from week 8, M markedly ameliorated podocyte foot process alterations for all the HDFM vs. HFD groups. To conclude, M was effective in improving structural and ultrastructural alterations in the kidneys caused by HFD.

207. P12-03. COENZYME Q10 (COQ10) SUPPLEMENTATION ON HIGH-FAT (HF) FED RATS: IMPACT ON MARKERS OF MITOCHONDRIAL BIOGENESIS AND OXIDATIVE STRESS

Elizabeth Robello¹, Mario Contin², Hyun Jin Lee³, Silvana M. Cantú⁴, Natalia L. Rukavina Mikusic⁵, Carlos A. Fontecilla Chavarro^{1*}, Agustín Lucini Mas⁷, Marcelo R. Choi⁸, César G. Fraga⁹, Valeria Tripodi¹⁰, Laura B. Valdez¹¹, Monica Gallea-no¹²

1. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. CONICET- Universidad de Buenos Aires (IBI-MOL), Buenos Aires, Argentina.; Departamento de Ciencias Químicas, Cátedra de Fisicoquímica

2. CONICET, Argentina. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. INTECFyB -Universidad de Buenos Aires, Buenos Aires, Argentina.; Departamento de Ciencias Químicas, Cátedra de Química Analítica

3. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. INFIBIOC, Universidad de Buenos Aires, Buenos Aires, Argentina.; Departamento de Ciencias Biológicas, Cátedra de Anatomía e Histología

4. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. INFIBIOC, Universidad de Buenos Aires, Buenos Aires, Argentina.; Departamento de Ciencias Biológicas, Cátedra de Anatomía e Histología

5. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. INFIBIOC, Universidad de Buenos Aires, Buenos Aires, Argentina.; CONICET-Universidad de Buenos Aires (IATIMET), Buenos Aires, Argentina.; Departamento de Ciencias Biológicas, Cátedra de Anatomía e Histología

6. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. CONICET- Universidad de Buenos Aires (IBI-MOL), Buenos Aires, Argentina.; Departamento de Ciencias Químicas, Cátedra de Fisicoquímica

7. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. CONICET- Universidad de Buenos Aires (IBI-MOL), Buenos Aires, Argentina.; Departamento de Ciencias Químicas, Cátedra de Fisicoquímica,

8. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. CONICET-Universidad de Buenos Aires (IATIMET), Buenos Aires, Argentina.; Departamento de Ciencias Biológicas, Cátedra de Anatomía e Histología

9. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. CONICET- Universidad de Buenos Aires (IBI-MOL), Buenos Aires, Argentina.; Departamento de Ciencias Químicas, Cátedra de Fisicoquímica

10. CONICET, Argentina. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. INTECFyB -Universidad de Buenos Aires, Buenos Aires, Argentina.; Departamento de Ciencias Químicas, Cátedra de Química Analítica

11. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. CONICET- Universidad de Buenos Aires (IBI-MOL), Buenos Aires, Argentina.; Departamento de Ciencias Químicas, Cátedra de Fisicoquímica

12. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. CONICET- Universidad de Buenos Aires (IBI-MOL), Buenos Aires, Argentina.; Departamento de Ciencias Químicas, Cátedra de Fisicoquímica

erobello@ffyb.uba.ar

Previously, we showed that CoQ10 supplementation increased cardiac [CoQ9] and [CoQ10] and mitigated alterations in mitochondrial complex activities in HF-fed animals. Here, we investigated changes in peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1α) in heart and their relationship with mitochondrial biogenesis and oxidative stress. Male rats were divided into four groups for 12 weeks: control diet (10% calories from fat, C), control diet + CoQ10 (50 mg/kg/day, CQ), HF diet (60% calories from fat, HF), and HF diet + CoQ10 (HFCQ). PGC-1α expression levels were C: 1.00 ± 0.08 , CQ: 0.7 ± 0.1 , HF: $1.5\pm 0.3^*$, and HFCQ: 1.5 ± 0.4 ($*p<0.05$ vs. C). Mitochondrial transcription factor A (Tfam), marker of mitochondrial biogenesis, showed a similar profile [C: 0.98 ± 0.08 , CQ: 0.9 ± 0.2 , HF: $1.6\pm 0.04^*$, HFCQ: 1.4 ± 0.2 ($*p<0.05$ vs. C)]. Oxidative stress-related parameters showed distinct responses. CoQ10 supplementation: i) did not affect the HF-induced increase in NADPH-oxidase 4 expression; ii) reduced thiobarbituric acid reactive substances (TBARS) in both diets (-39% in CQ vs. C and -36% in HFCQ vs. HF, $p<0.05$); iii) lowered protein-bound nitrotyrosine only in HF-fed animals (-37% in HFCQ vs. HF, $p<0.05$). Overall, these results suggest that CoQ10 supplementation does not modulate the increase in mitochondrial biogenesis induced by HF diet, which may represent an adaptive response to diet-induced metabolic stress. Instead, CoQ10 supplementation appears to influence oxidative stress pathways at specific points. Further studies are warranted to clarify the redox mechanisms involved in potential CoQ10-mediated cardioprotection.

208. P12-04. DIETARY CHIA SEED REDUCES GLUCOSE-6-PHOSPHATASE/GLUCOKINASE RATIO AND FOXO1 MRNA EXPRESSION IN AN EXPERIMENTAL MODEL OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD)

Michelle Berenice Vega Joubert¹, María Eugenia Oliva², Paola Inés Ingaramo³, María Eugenia D'Alessandro⁴

1. Facultad de Bioquímica y Ciencias Biológicas. Universidad Nacional del Litoral. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina.; Laboratorio de Estudio de Enfermedades Metabólicas Relacionadas con la Nutrición

2. Facultad de Bioquímica y Ciencias Biológicas. Universidad Nacional del Litoral. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina.; Laboratorio de Estudio de Enfermedades Metabólicas Relacionadas con la Nutrición.

3. Facultad de Bioquímica y Cs. Biológicas, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina.; Instituto de Salud y Ambiente del Litoral (ISAL)

4. Facultad de Bioquímica y Ciencias Biológicas. Universidad Nacional del Litoral. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina.; Laboratorio de Estudio de Enfermedades Metabólicas Relacionadas con la Nutrición.

mvegajoubert@fbcb.unl.edu.ar

Metabolic dysfunction-associated steatotic liver disease (MASLD) is recognized as the hepatic manifestation of Metabolic Syndrome (MS). Previously, we demonstrated that supplementation with chia seed in an experimental model of MS induced by a sucrose-rich diet (SRD) improves glucose tolerance, reduces gluconeogenic enzyme activities (phosphoenolpyruvate carboxykinase and fructose-1,6-bisphosphatase), and modulates AMPK, pAMPK, pAKT protein levels. The aim of this study was to expand upon these findings by evaluating the effects of chia seed on the activity of other key enzymes and transcription factors involved in glucose metabolism in SRD fed rats. In addition, Insulin Receptor Substrate-1 (IRS-1) was evaluated. Male Wistar rats were fed a reference diet (RD) or a SRD for 6 months. A third group received the SRD in which chia seed was incorporated as a source of dietary fat during the last 3 months (SRD+CHIA). We analyzed in liver: Glucose-6-Phosphatase (G-6-Pase), Glucokinase (GK), and Hexokinase (HK) enzyme activities;

IRS-1 and peroxisome proliferator-activated receptor gamma coactivator 1- α (PGC-1 α) protein expression; and forkhead box O1 (FOXO1) mRNA levels. The results showed that chia seed reduced G-6-Pase activity, increased GK activity and decreased G-6-Pase/GK ratio in SRD-fed rats. No differences were observed in HK activity among the groups. Additionally, chia seed decreased FOXO-1 mRNA expression in SRD-fed rats. Similar levels of IRS-1 and PGC-1 α protein expression were observed among the three experimental groups. In conclusion, chia seed could be considered a potential nutritional strategy for mitigating impaired glucose metabolism in a MASLD model.

209. P12-05. EFFECTS OF SALVIA HISPANICA L. (CHIA SEED) ADMINISTERED PREVENTIVELY ON OXIDATIVE STRESS, FIBROSIS AND INFLAMMATION IN RATS FED A LONG-TERM HIGH-SUCROSE DIET

Paola Guadalupe Illesca¹, Noelia Villafañe², Adriana Benmelej³, María Eugenia Oliva⁴, María Eugenia D'Alessandro⁵

1. Facultad de Bioquímica y Ciencias Biológicas. Universidad Nacional del Litoral. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Laboratorio de Estudio de Enfermedades Metabólicas Relacionadas con la Nutrición (LEEMREN)

2. Facultad de Bioquímica y Ciencias Biológicas. Universidad Nacional del Litoral; Cátedra de Morfología Normal

3. Facultad de Bioquímica y Ciencias Biológicas. Universidad Nacional del Litoral; Cátedra de Morfología Normal

4. Facultad de Bioquímica y Ciencias Biológicas. Universidad Nacional del Litoral. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Laboratorio de Estudio de Enfermedades Metabólicas Relacionadas con la Nutrición (LEEMREN)

5. Facultad de Bioquímica y Ciencias Biológicas. Universidad Nacional del Litoral. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Laboratorio de Estudio de Enfermedades Metabólicas Relacionadas con la Nutrición (LEEMREN)

pillesca@fbc.unl.edu.ar

Chronic consumption of diets high in fat and/or sugar cause ectopic lipid deposition in skeletal muscle (SkM). Lipotoxicity has been associated with deleterious metabolic impact in this tissue. We previously showed that chronic high-sucrose diet (HSD) feeding increases reactive oxygen species (ROS), reduces antioxidant defenses and promotes fibrosis in rat SkM. The administration of chia seeds prevented some of these alterations. In this study, we aimed to deepen our understanding of the structural and redox status impairment in SkM from long-term HSD-fed rats, as well as to investigate the potential preventive effects of dietary chia. Male Wistar rats were divided into two groups and received HSD or HSD where chia seed was incorporated as source of dietary fat for 15 weeks (HSD+Chia). A reference group consumed a control diet all the time. In SkM were analyzed: i) triglycerides content, ii) sarcopenia index, iii) collagen deposition, iv) Nuclear Factor kappa B (NF- κ B) protein levels, vi) Nuclear factor erythroid 2-related factor 2 (Nrf2) and Transforming Growth Factor beta (TGF- β) gene expression. Statistical analysis was performed using one-way ANOVA and Newman-Keuls test, $p < 0.05$ was considered significant. Chia seed prevented lipotoxicity, sarcopenia and fibrosis observed in the SkM of long-term SRD-fed rats. Furthermore, chia decreased NF- κ B levels and TGF- β gene expression, although no significant effect was observed on Nrf2 mRNA levels. The present results demonstrate the protective effects of chia seed on SkM impairment caused by HSD consumption. Also provides novel insights into the molecular mechanisms involved, with potential therapeutic application.

210. P12-06. EFFECTS OF SHORT AND LONG-TERM HIGH-SUCROSE DIET CONSUMPTION ON CEREBRAL CORTEX ENERGY METABOLISM AND ACETYLCHOLINESTERASE ACTIVITY IN MALE RATS

Camila Bonilla¹, Matias Rodrigo Vargas², Magali Estefanía Petean³, María Eugenia D'Alessandro⁴, María Del Rosario Ferreira⁵

1. Facultad de Bioquímica y Cs. Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición.

2. Facultad de Bioquímica y Cs. Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición.

3. Facultad de Bioquímica y Cs. Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición.

4. 1-Facultad de Bioquímica y Cs. Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición

5. 1-Facultad de Bioquímica y Cs. Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición.

camio1bonilla@gmail.com

Metabolic Syndrome (MetS) is linked to a higher risk of neurodegenerative diseases. However, the mechanism involved are not fully elucidated. We previously showed that high-sucrose diet (HSD) administration to male rats for 3 weeks (wk) induce several peripheral metabolic abnormalities, that intensify and are accompanied by other disorders, after long-term (15 wk) dietary administration. In this experimental model of MetS, we also demonstrated that 3 wk and 15 wk HSD-fed rats develop cognitive decline in a similar magnitude, although there are differences in their cortical redox status. In order to expand our previous research, we aimed to investigate the effect of 3-wk and 15-wk HSD exposure on energy metabolism-related molecules and acetylcholinesterase (AChE) activity in the cerebral cortex of male rats. Male Wistar rats (8-wk-old) received a HSD or a control diet (CD) during 3 wk or 15 wk. In the cerebral cortex of these animals, we analyzed: a- GLUT-3, hexokinase (HK), total AMPK (tAMPK) and pThr172AMPK protein levels by Western Blot, b-Acetylcholinesterase activity. GLUT-3, HK, tAMPK and pThr172AMPK were significantly increased ($P < 0.05$) in 3 wk HSD-fed rats when compared with 3 wk CD-fed rats. However, a significative reduction ($P < 0.05$) in GLUT-3, tAMPK and pThr172AMPK was observed in 15 wk HSD-fed rats when compared with the age-matched controls. HK protein levels were similar at this time point. AChE activity was higher ($P < 0.05$) in 15 wk HSD-fed rats than in 15 wk CD-fed rats. Our findings provide further evidence linking peripheral metabolic disorders to brain and cognitive dysfunction.

211. P12-07. EFFECT OF LIGARIA CUNEIFOLIA INFUSION ("ARGENTINE MISTLETOE") ON PLASMATIC CHOLESTEROL, BODY MASS INDEX AND BLOOD VISCOSITY IN DYSLIPIDEMIC PATIENTS

Francisco Pons¹, Martín Pérez², Mariana Ferrero³, Leda Urli⁴, Juan Francisco Alonso⁵, Diego Crosetti⁶, José González⁷, Bruno Wienzicki⁸, Cecilia Dobrecky⁹, Daniel De Vuono¹⁰, Marcelo Wagner¹¹, Rodolfo Daniel Leiva¹², Cristina Carnovale¹³, Alejandra Luquita¹⁴

1. Facultad de Ciencias Médicas UNR; Cátedra de Biofísica - Laboratorio de Biología Sanguínea

2. Facultad de Ciencias Médicas UNR; Cátedra de Biofísica - Laboratorio de Biología Sanguínea

3. Facultad de Ciencias Médicas UNR; Cátedra de Biofísica - Laboratorio de Biología Sanguínea

4. Facultad de Ciencias Médicas UNR; Cátedra de Biofísica - Laboratorio de Biología Sanguínea

5. Facultad de Ciencias Médicas UNR; Cátedra de Biofísica - Laboratorio de Biología Sanguínea

6. Facultad de Ciencias Médicas UNR; Cátedra de Biofísica - Laboratorio de Biología Sanguínea

7. Facultad de Ciencias Médicas UNR; Cátedra de Biofísica - Laboratorio de Biología Sanguínea

8. Facultad de Ciencias Medicas UNR; Catedra de Biofisica - Laboratorio de Biologia Sanguinea
 9. Facultad de Farmacia y Bioquimica UBA; Catedra de Farmacobotanica
 10. Hospital Provincial del Centenario; Laboratorio Central
 11. Facultad de Farmacia y Bioquimica UBA; Catedra de Farmacobotanica
 12. Hospital Provincial del Centenario; Servicio de Cardiologia
 13. Facultad de Ciencias Bioquimicas y Farmaceuticas UNR - CONICET; IFISE
 14. Facultad de Ciencias Medicas UNR - Consejo Superior de Investigaciones (CIUNR); Catedra de Biofisica - Laboratorio de Biologia Sanguinea
- franciscopons2001@gmail.com

Ligaria cuneifolia (Lc) is traditionally used in folk medicine to reduce plasma cholesterol and improve blood flow. Objective: To evaluate the effect of Lc infusions on plasma cholesterol, body weight (W), body mass index (BMI) and blood viscosity (Vs) in dyslipidemic patients. Methods: Ten patients (50 ± 15 years) from the Cardiology Service, Hospital Provincial Centenario, received lyophilized Lc extract to be prepared and consumed as an infusion three times per week for 31 days. Baseline (B) and after treatment (TLc) blood samples were collected. Measurements included: total cholesterol (TCho), HDL cholesterol (HDLcho), LDL cholesterol (LDLcho) colorimetrically and Vs assessed with a rotational viscometer. Height and weight were measured following current standardized anthropometric techniques. Relative viscosity (VSr) and BMI were calculated. Statistical analysis was performed using the Wilcoxon test for paired data. Results: Median (95% CI) values were: TCho, B: 242 (205–250) vs TLc: 232 (180–261), ns; HDLcho, B: 67 (51–86) vs TLc: 75 (53–83), ns; LDLcho, B: 185 (140–203) vs TLc: 168 (101–181)*; VSr, B: 3.09 (2.19–3.72) vs TLc: 2.97 (1.64–3.79), ns; W, B 64.85 (60.2–70.5) vs TLc: 64.75 (59–69.6)*; BMI, B: 22.5 (19.7–25.7) vs TLc: 22.2 (19.2–25.6)*, (* $p < 0.05$ vs. B; ns: non significant vs B). Conclusion: Lc significantly reduced LDLcho and BMI, without altering TCho, HDLcho or VSr. Since elevated LDLcho and obesity are modifiable cardiovascular risk factors, these findings suggest that Lc may represent a complementary strategy for cardiovascular disease prevention.

212. P12-08. SUSTAINABLE RECOVERY OF POLYPHENOLS FROM AGROINDUSTRIAL DISCARDED SWEET CHERRIES (*PRUNUS AVIUM* L.) PRESERVES TIGHT JUNCTION INTEGRITY AND PREVENTS TNF α -INDUCED INTESTINAL PERMEABILITY IN CACO-2 CELLS

Agostina Aramburu¹, Gisela Mazaira², María Florencia Barranta³, Ana María Rojas⁴, Alejandra Erlejman⁵

1. ITAPROQ- CONICET, Depto. de Industrias FCEN, UBA, Argentina.; Laboratorio de optimización de la calidad de alimentos preservados
 2. IQUIBICEN CONICET, Depto. de Química Biológica FCEN, UBA, Argentina.; Laboratorio de Biología Celular y Molecular
 3. ITAPROQ- CONICET, Depto. de Industrias FCEN, UBA, Argentina.; Laboratorio de optimización de la calidad de alimentos preservados
 4. ITAPROQ- CONICET, Depto. de Industrias FCEN, UBA, Argentina.; Laboratorio de optimización de la calidad de alimentos preservados
 5. IQUIBICEN CONICET, Depto. de Química Biológica FCEN, UBA, Argentina.; Laboratorio de Biología Celular y Molecular
- aramburuagostina@gmail.com

Sweet cherries (*Prunus avium* L.) are a rich source of bioactive compounds, particularly polyphenols. This study evaluated the effects of polyphenols extracted from sweet cherries discarded by the agroindustry, on TNF α -induced intestinal permeability. Polyphenol content was analyzed by HPLC. The non-digested extract (ND Ext) was enriched in anthocyanins (714.9 ± 21.2 mg/100 g powder), along with minor amounts of flavonoids and hydroxycinnamates. A digested extract (Dig Ext) was generated using an in vitro Dynamic Human

Digestion system, yielding 517.5 ± 86.3 mg/100 g powder of total anthocyanins ($n = 3$). Differentiated Caco-2 cells were used as an intestinal barrier model. Cells were pre-incubated with polyphenol extracts (0.25–1 μ M) or Cy (1 μ M) for 30 min, followed by TNF α (10 ng/mL, 6h). Extract concentrations were expressed as cyanidin-3-O-glucoside (Cy) equivalents. Barrier integrity was assessed by Western blot analysis of tight junction proteins ZO-1 and Occludin. TNF α reduced ZO-1 to 59.3% ($\pm 7.8\%$) and Occludin to 70.8% ($\pm 6.9\%$) relative to control (100%). Cy fully prevented this reduction ($n = 6$, $p < 0.01$), and ND Ext at 0.25 μ g/mL also provided complete protection ($n = 8$, $p < 0.01$), whereas Dig Ext needed 0.5 μ g/mL to reach ZO-1 85% and Occludin 100% ($p < 0.004$ and 0.03 vs significantly different TNF α). In conclusion, polyphenols from agroindustrial discarded sweet cherries prevent TNF α -induced intestinal permeability, with protective effects preserved after digestion. These results highlight discarded cherries as a sustainable source of anti-inflammatory polyphenols, supporting their potential in developing novel bioactive compounds aligned with circular economy strategies.

213. P12-09. SYSTEMIC INFLAMMATION AND PULMONARY NEUTROPHILIC INFLAMMATION IN A MOUSE MODEL OF DIET-INDUCED OBESITY

Florencia S. Barrera¹, Carla Florencia Guzman², Inalén Del V. Chacon³, Jonathan Mayron Ramirez⁴, Rivero, L.⁵, Morales, I.⁶, Barberis, S.⁷, Mattar Dominguez, Ma⁸, Lopez, Cm⁹, Dario C. Ramirez¹⁰, Sandra E. Gomez Mejiba¹¹

1. IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.
 2. IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.
 3. IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.
 4. IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.
 5. IMIBIO-CCT-SL-CONICET; Laboratory of Bromatology, CONICET-San Luis & National University of San Luis, San Luis, Argentina
 6. IMIBIO-CCT-SL-CONICET; Laboratory of Bromatology, CONICET-San Luis & National University of San Luis, San Luis, Argentina
 7. IMIBIO-CCT-SL-CONICET; Laboratory of Bromatology, CONICET-San Luis & National University of San Luis, San Luis, Argentina
 8. UNSL; Laboratorio de Microbiología e Inmunología, Universidad Nacional de San Luis, San Luis, San Luis, Argentina
 9. IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.
 10. IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.
 11. IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.
- fsoledadbarrera@gmail.com

In obesity, a chronic positive energy balance leads to adipose tissue (AT) inflammation. This leads to a state of metaflammation in the systemic compartment. Inflammation mediators produced locally

at inflamed AT can affect several organs, including the lung. TNF α , a proinflammatory cytokine produced by inflamed AT, can affect gene expression in the pulmonary microvasculature, leading to increased retention and activation of neutrophils, a process known as pulmonary neutrophilic inflammation (PNI). This study aimed to characterize pulmonary and systemic neutrophilic inflammation in a mouse model of diet-induced obesity. To accomplish this aim, we used male C57BL/6J mice, which were divided into two groups: one group received an obesogenic diet (ObD) composed of 22% cow fat and 10% fructose in the drinking water, whereas the control group (CoD) received standard food and drinking water. Weights were monitored weekly, fasting blood glucose levels were measured every 6 weeks, and blood pressure was measured every 2 months. At the end of the study, an oral glucose tolerance test was performed to measure whole body insulin resistance. To assess inflammation and oxidative stress, TNF α , IL-6, iNOS, MPO (protein and activity), protein-carbonyls, protein-chlorotyrosine and protein-nitrotyrosine in lung homogenates and serum were measured by ELISA. Compared with CoD-fed mice, ObD-fed mice presented increased blood pressure, reduced insulin sensitivity, and increased markers of systemic inflammation and PNI. These observations open new avenues for investigating how the PNI in obese individuals can increase obesity-associated metabolic risk.

214. P12-10. TISSUE-SPECIFIC REDOX ADAPTIVE RESPONSES TO CHRONIC HIGH INTENSITY INTERVAL TRAINING IN RAT

Christian Saporito-Magriñá¹, Lila Lopez Montañana², Agustín Bautista Silva³, Juan Ignacio Bellida⁴, Guadalupe Pagano⁵, Federico Marino⁶, Ludmila Moyano Libertini⁷, Leonella Ariana Danzi⁸, Gabriela Noceti⁹, Juan Manuel Gaetani¹⁰, Andrea Fellet¹¹, Marisa Gabriela Repetto¹²

1. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Químicas, Química General e Inorgánica, Buenos Aires, Argentina. Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL, UBA-CONICET), Buenos Aires, Argentina.; Estrés oxidativo y agregados proteicos

2. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Químicas, Química General e Inorgánica, Buenos Aires, Argentina. Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL, UBA-CONICET), Buenos Aires, Argentina.; Estrés oxidativo y agregados proteicos

3. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Químicas, Química General e Inorgánica, Buenos Aires, Argentina.; Estrés oxidativo y agregados proteicos

4. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Químicas, Química General e Inorgánica, Buenos Aires, Argentina.; Estrés oxidativo y agregados proteicos

5. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Químicas, Química General e Inorgánica, Buenos Aires, Argentina.; Estrés oxidativo y agregados proteicos

6. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Químicas, Química General e Inorgánica, Buenos Aires, Argentina.; Estrés oxidativo y agregados proteicos

7. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Químicas, Química General e Inorgánica, Buenos Aires, Argentina.; Estrés oxidativo y agregados proteicos

8. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Químicas, Química General e Inorgánica, Buenos Aires, Argentina.; Estrés oxidativo y agregados proteicos

9. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Fisiología, Buenos Aires, Argentina.; IQUIMEFA-CONICET

10. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Fisiología, Buenos Aires, Argentina.;

IQUIMEFA-CONICET

11. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Fisiología, Buenos Aires, Argentina.; IQUIMEFA-CONICET

12. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Químicas, Química General e Inorgánica, Buenos Aires, Argentina. Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL, UBA-CONICET), Buenos Aires, Argentina.; Estrés oxidativo y agregados proteicos
saporito.cm@gmail.com

High intensity interval training (HIIT) consists of explosive bursts of exercise interspersed with brief periods of rest and is known to induce oxidative stress, although the sources and timing of oxidant generation remain unclear. This work aims to evaluate whether 8 weeks of forced swimming in a HIIT modality promotes muscle adaptation as well as oxidative stress and damage in epitrochlear muscle, heart, and blood. Animals displayed uneven adaptation to the protocol, with some completing long training sessions and others refusing to swim. Therefore, only those performing at least 200 bouts were considered for analysis. These trained rats exhibited significantly greater swimming resistance in the final test compared with sedentary controls, indicating improved endurance. No structural cardiac alterations were detected, yet lipid peroxidation measured as TBARS increased markedly in the heart of HIIT rats, showing a 400% rise in comparison to sedentary animals ($p < 0.01$). In contrast, lipid peroxidation in epitrochlear muscle did not differ significantly between groups. Red blood cell glutathione levels also remained unchanged, suggesting no systemic depletion of this major antioxidant. Interestingly, a significant increase in protein thiols was detected in trained animals ($p < 0.05$), pointing toward a compensatory redox adaptation. Together, these results indicate that HIIT swimming elicits tissue-specific responses, with the heart being more susceptible to oxidative lipid damage, while skeletal muscle and blood exhibit limited oxidative alterations. The observed increase in protein thiols may represent an adaptive mechanism counteracting oxidative stress rather than direct damage. Overall, findings highlight heterogeneous redox outcomes across tissues under HIIT.

215. P12-11. EFFECTS OF PARENTERAL SUPPLEMENTATION OF ANTIOXIDANT MINERALS AND VITAMINS IN INFLAMMATORY STATUS AND HEPATIC GLUTATHIONE COWS DURING THE PERIPARTUM PERIOD

Emmanuel Angeli¹, Gino Storani², Silvina Addona³, Hugo H Ortega⁴, Gustavo J Hein⁵

1. ICIvet-Litoral (UNL-CONICET), Esperanza, Santa Fe, Argentina; Laboratorio de Biología Celular y Molecular Aplicada (LBCMA)

2. ICIvet-Litoral (UNL-CONICET), Esperanza, Santa Fe, Argentina; Laboratorio de Biología Celular y Molecular Aplicada (LBCMA)

3. ICIvet-Litoral (UNL-CONICET), Esperanza, Santa Fe, Argentina; Laboratorio de Biología Celular y Molecular Aplicada (LBCMA)

4. ICIvet-Litoral (UNL-CONICET), Esperanza, Santa Fe, Argentina; Laboratorio de Biología Celular y Molecular Aplicada (LBCMA)

5. ICIvet-Litoral (UNL-CONICET), Esperanza, Santa Fe, Argentina; Laboratorio de Biología Celular y Molecular Aplicada (LBCMA)

eangeli@fcv.unl.edu.ar

The peripartum period in dairy cows is characterized by a proinflammatory state and insulin resistance, during which hepatic gluconeogenesis (HG) plays a critical role in supporting milk production. This study evaluated the effects of parenteral vitamin and mineral supplementation on systemic and hepatic inflammatory responses, as well as on HG, in peripartum cows. The supplemented group (SG; $n = 11$) received subcutaneous injections of 5 mL ADAPTADOR Vit® and 5 mL ADAPTADOR Min® (Biogénesis Bagó, Buenos Aires; containing vitamin A palmitate 3.5%, vitamin E acetate 5%, copper edetate 1%, zinc edetate 4%, manganese edetate 1%, and

sodium selenite 0.5%) at -60, -30, and +7 days relative to calving. The control group (CG; n = 11) received two injections of 5 mL 0.9% sodium chloride solution. Serum IL-1 and IL-6 concentrations were measured using commercial ELISA kits (Thermo Fisher Scientific, USA). Hepatic protein abundance of IL-1, TNF- α , and the key HG enzymes phosphoenolpyruvate carboxykinase (PEPCK) and propionyl-CoA carboxylase (PCCA) was determined by Western blot. Supplemented cows showed lower serum IL-1 and IL-6 levels (P < 0.05). Hepatic IL-6 abundance was also reduced in SG on day 4 postpartum (P 0.05). Similarly, no treatment effects were observed for PEPCK or PCCA (P > 0.05). These results suggest that vitamin and mineral supplementation attenuates systemic and hepatic inflammation without altering hepatic gluconeogenesis during the peripartum period.

**ORALES 10 - SAIC - ONCOLOGÍA 3
NUEVAS TERAPIAS ONCOLÓGICAS
DATE & TIME: 19/11/2025 9:00 - 10:30 H
Chairs: Yanina Langle, Melina Dattilo**

216. O10-01. NEUTRALIZING SOLUBLE TNF IMPROVES TRASTUZUMAB DERUXTECAN EFFECTIVENESS IN HER2+ BREAST CANCER PRECLINICAL MODELS

María Eliana Ladera Gómez¹, Camila Jencquel², Sofía Bruni³, María Florencia Mercogliano⁴, Roxana Schillaci⁵

1. Instituto de Biología y Medicina Experimental (IBY-ME-CONICET), Buenos Aires, Argentina; Laboratorio de Inmunología Tumoral

2. Instituto de Biología y Medicina Experimental (IBY-ME-CONICET), Buenos Aires, Argentina.; Laboratorio de Inmunología Tumoral

3. Instituto de Biología y Medicina Experimental (IBY-ME-CONICET), Buenos Aires, Argentina.; Laboratorio de Inmunología Tumoral.

4. Instituto de Biología y Medicina Experimental (IBY-ME-CONICET), Buenos Aires, Argentina; Laboratorio de Inmunología Tumoral

5. Instituto de Biología y Medicina Experimental (IBY-ME-CONICET), Buenos Aires, Argentina.; Laboratorio de Inmunología Tumoral
m.ladera@ibyme.org.ar

Trastuzumab deruxtecan (T-DXd) is a primary treatment for HER2+ breast cancer, but resistance and toxicity limit its effectiveness. Soluble tumor necrosis factor alpha (sTNF) induces trastuzumab resistance via mucin 4 (MUC4) upregulation, and its neutralization with the dominant-negative protein INB03 (DN) restores sensitivity. We evaluated whether sTNF blockade enhances T-DXd efficacy and modulates immune response in HER2+ preclinical models. Female nude mice bearing JIMT-1 tumors received T-DXd (5, 2.5, or 1.25 mg/kg), DN, or the combinations, while FVB mice with syngeneic Fo5 tumors received T-DXd (1.25 mg/kg), DN, or both. In JIMT-1 tumors, T-DXd at 5 mg/kg inhibited growth by 83% (p<0.0001), 2.5 mg/kg by 61% (p<0.001), and 1.25 mg/kg by 37% (p<0.05), whereas combination with DN increased inhibition to 98% (p<0.0001), 81% (p<0.0001), and 73% (p<0.0001), respectively. Similarly, in Fo5 tumors, the T-DXd + DN increase growth inhibition to 66% (p<0.0001). DN addition to T-DXd enhanced significantly macrophage tumor infiltration and M1-like polarization in both models. In Fo5 tumors, DN further increased CD8⁺ T cell infiltration. Because DXd was hypothesized to activate type I interferon (IFN-I) signaling, we examined cGAS and ISG15 expression. In JIMT-1, T-DXd increased cGAS and ISG15 expression, with DN potentiating these effects, particularly at lower T-DXd doses. In Fo5, DN and T-DXd independently increased cGAS/ISG15, with additive effect when combined. Thus, sTNF blockade augments T-DXd antitumor activity, enabling lower effective doses, reshaping the immune microenvironment, and engaging IFN-I pathways. These findings support DN as a potential adjuvant to improve T-DXd efficacy in HER2+ breast cancer.

217. O10-02. CORRELATION BETWEEN THE IMMUNE CHECKPOINT HLA-G AND E-CADHERIN EXPRESSION IN PATIENTS WITH BLADDER CANCER

Damian Ezequiel Moavro¹, Berta Sáez Gutiérrez², Edgardo Daniel Carosella³, Marcela Nilda García⁴, María Belén Palma⁵

1. Cátedra de Citología, Histología y Embriología, FCM, UNLP, Argentina.; 2) Hospital Interzonal General de Agudos "Gral. San Martín", La Plata, Argentina.

2. Hospital San Juan de Dios, Zaragoza, España.; Grupo INDIVO. Universidad San Jorge, Zaragoza, España.

3. Université Paris Diderot, Paris, Francia; CEA, SRHI, IUH, Hôpital Saint-Louis

4. FCM, UNLP, Argentina; Cátedra de Citología, Histología y Embriología

5. Cátedra de Citología, Histología y Embriología, FCM, UNLP, Argentina.; LIAN, Instituto de Neurociencias (INEU-CONICET), FLENI, Belén de Escobar, Argentina.
dmoavro@med.unlp.edu.ar

Bladder cancer is one of the most common urological neoplasms. In Argentina, it accounts 3% of all neoplasms, with a predominance in males. Approximately 95% of these tumors are of epithelial origin, with transitional cell carcinoma (TCC) being the most frequent (80% of cases). According to morphological analyses, TCC is classified into low- and high-histological grade. The most aggressive tumors are typically high-grade or display any of the following findings: loss of cell adhesion molecules such as E-cadherin, epithelial-mesenchymal transition, detrusor muscle invasion, or immune checkpoints (IC) expression. An important IC is HLA-G, which acts as a local immunosuppressor. Currently, treatment involves tumor resection or radical cystoprostatectomy, combined with chemotherapy or immunotherapy. Considering the relevance of immunomodulatory therapies, we propose to evaluate the correlation between HLA-G and E-cadherin expression in TCC biopsies. For this purpose, we used TCC samples obtained from patients at a public hospital in La Plata. Samples were immunostained using anti-HLA-G and anti-E-cadherin antibodies. Finally, Pearson's correlation coefficient was calculated. We found that HLA-G expression was predominantly observed in high-grade lesions, while low-grade tumors showed absent or mild expression. E-cadherin, normally expressed in urothelium, was diminished in selected regions of high-grade tumors. The combined analysis of both markers demonstrated an inverse correlation. Given the morbidity and mortality associated with conventional treatments for aggressive tumors, we suggest staining E-cadherin, a marker commonly available in daily practice. Low expression in TCC would indicate high HLA-G. Therefore, HLA-G immunostaining is recommended to advise the use of immunotherapy as an effective alternative.

218. O10-03. HISTONE DEACETYLASE INHIBITION AS A THERAPEUTIC STRATEGY IN MYCN-AMPLIFIED RETINOBLASTOMA

Milagros Dinardi¹, María Belén Cancela², Santiago Zugbi³, Andrea Llera⁴, Eduardo Cafferata⁵, Paula Schaiquevich⁶

1. Hospital de Pediatría Garrahan; Unidad de Tratamientos Innovadores

2. Hospital de Pediatría Garrahan; Unidad de Tratamientos Innovadores

3. Hospital de Pediatría Garrahan; Unidad de Tratamientos Innovadores

4. Fundación Instituto Leloir; Laboratorio de Terapia Celular y Molecular

5. Fundación Instituto Leloir; Laboratorio de Terapia Celular y Molecular

6. Hospital de Pediatría Garrahan; Unidad de Tratamientos Innovadores

milidinardi55@gmail.com

Retinoblastoma (RB) is the most common intraocular tumor in children. A subset of patients with MYCN-amplified (MYCNa) RB exhibits a more aggressive disease and is resistant to standard-of-care (SOC) treatments. Among targeted therapeutic agents, histone deacetylase inhibitors (HDACi) have shown preclinical efficacy in other MYCNa pediatric tumors, such as neuroblastoma. Given the role of HDACs in MYCN-driven transcriptional activation and tumor

progression, this study aims to evaluate the therapeutic potential of HDACi in MYCNa RB cell models. Dose-response curves were generated for SOC drugs (melphalan, topotecan, carboplatin) and HDACi (panobinostat, vorinostat) using the commercial RB cell line Y79 and three patient-derived MYCNa RB1/+ primary cultures (RBT-7, RB3823, RBG-1). The concentration reducing cell proliferation by 50% (IC50) and the synergy activity between compounds were calculated using the combined index (CI, Compusyn). Across the evaluated RB cells, IC50 values ranged from 11.8 to 41.2 nM for panobinostat and from 1.2 to 1.5 μ M for vorinostat. Preliminary data suggest that panobinostat requires lower concentrations than vorinostat to achieve comparable effects, indicating that it is a more potent HDACi. In Y79 cells, the combination SOC + IC25 panobinostat significantly reduced the SOC IC50s ($p < 0.05$, $CI < 1$): melphalan (10 to 3.7 μ M), topotecan (30 to 8.1 nM), and carboplatin (70 to 25.7 μ M). In the metastatic model RBG-1, carboplatin IC50 decreased from 115 to 60 μ M in combination with panobinostat. These findings support HDACi, particularly panobinostat, as promising therapeutic agents for MYCNa retinoblastoma. The observed synergy with SOC therapies highlights the translational potential of these combinations and reinforces the need for further in vivo preclinical validation.

219. O10-04. ANTITUMOR ACTIVITY OF CANNABIS SATIVA PHYTOCANNABINOIDS IN A MURINE BREAST CANCER MODEL

Gabriela Pataccini¹, Sebastián Giulianelli², Mariana Lozada³, Gregorio Bigatti⁴

1. Instituto de Biología y Medicina Experimental (IByME-CO-NICET), CABA, Argentina; Laboratorio de carcinogenesis hormonal

2. Instituto de Biología de Organismos Marinos, IBIO-MAR-CCT CENPAT-CONICET, Puerto Madryn, Argentina.; Laboratorio de reproducción y biología integrativa de invertebrados marinos

3. Instituto de Biología de Organismos Marinos, IBIO-MAR-CCT CENPAT-CONICET, Puerto Madryn, Argentina.; Proyecto Interdisciplinario de Cannabis

4. Instituto de Biología de Organismos Marinos, IBIO-MAR-CCT CENPAT-CONICET, Puerto Madryn, Argentina.; Proyecto Interdisciplinario de Cannabis
gaby.pataccini@gmail.com

Breast cancer (BC) is the most commonly diagnosed cancer type and the second leading cause of cancer-related death in women worldwide. Preclinical studies have shown that cannabinoids exhibit antitumor properties, mainly through CB1 and CB2 receptors. Here, we evaluated the effect of full-spectrum phytopreparations from Cannabis sativa flowers on in vivo tumor growth using a luminal subtype murine BC model, the most prevalent form of the disease. Murine carcinoma 59-2-HI was transplanted subcutaneously into the inguinal flank of female BALB/c mice. Once tumors reached ~35 mm², animals were randomly assigned into treatment or control groups. Phytopreparations were obtained by alcoholic extraction, resin evaporation, and resuspension in sesame oil (vehicle). Four INASE-registered variants (CONICET) were tested: CONICET (CONI, tipo I, THC); Mariquita Sánchez (MS, tipo II, ratio 3:1 CBD/THC); Pachamama (PACHA, tipo III, ratio 16:1 CBD/THC) and CBG. Cannabinoids were administered orally at 45 mg/kg three times per week or 22.5 mg/kg six times per week. Tumor size was monitored with a caliper, and after ~15 days, mice were sacrificed for tumor collection, weighing, and fixation in 4% formalin. All four variants reduced tumor growth compared with controls. Significant differences in final tumor weight were observed only with MS, while CONI, PACHA, and CBG showed a trend toward reduction. These findings suggest that oral administration of cannabinoid phytopreparations may have therapeutic potential against luminal BC. Ongoing histopathological analyses aim to determine their impact on cell cycle proteins and hormone receptor expression.

220. O10-05. BORONTYROSINE FOR BORON NEUTRON CAPTURE THERAPY: PRELIMINARY STUDIES IN AN EXPERIMENTAL ORAL CANCER MODEL

Mónica A. Palmieri¹, María Silvina Olivera², Agustina M. Por-

tu³, Michael Torgov⁴, Tioga Martin⁵, Paula Curotto⁶, Paula Ramos⁷, Silvia Thorp⁸, Debora N. Frydryk Benitez⁹, Ignacio Czornenki¹⁰, Marcela A. Garabalino¹¹, Emiliano C.C. Pozzi¹², Karen Morrison¹³, Kendall Morrison¹⁴, Andrea Monti Hughes¹⁵, Verónica A. Trivillin¹⁶

1. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (UBA), CABA, Argentina; Departamento de Biodiversidad y Biología Experimental (DBBE)

2. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Química y Biodistribución

3. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; Departamento de Radiobiología

4. TAE Life Sciences, USA; Química

5. TAE Life Sciences, USA; Química

6. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Reactor RA-3

7. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Reactor RA-3

8. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Dosimetría

9. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina / Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (UBA), CABA, Argentina; Departamento de Radiobiología

10. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Departamento de Radiobiología

11. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Departamento de Radiobiología

12. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Reactor RA-3

13. TAE Life Sciences, USA; Histología

14. TAE Life Sciences, USA; Investigación

15. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; Departamento de Radiobiología

16. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; Departamento de Radiobiología
monicaalepalmieri@gmail.com

Boron Neutron Capture Therapy (BNCT) combines preferential tumor uptake of ¹⁰B compounds and neutron irradiation. BNCT mediated by BPA (boronophenylalanine) was proved useful in multiple clinical trials and we demonstrated its therapeutic effect in the hamster cheek pouch oral cancer model. However, BPA has limitations. BTS is a borylated L-tyrosine analogue with interesting characteristics related to solubility, boron delivery and tumor-to-blood ratios. In this study we evaluated BTS for the treatment of oral tumors with BNCT in an experimental cancer model. Tumor bearing hamsters were injected intravenously with a BTS solution (250 mg/ml) at different doses: 39 mg B/kg (4 animals), 50 mg B/kg (5 animals) and 60 mg B/kg (3 animals). Blood, tumor, precancerous tissue, normal pouch tissue, liver were analyzed by ICP-OES and neutron autoradiography. BNCT mediated by BTS (39 mg B/kg), 2.6 Gy to precancerous tissue, has been selected to evaluate tumor control and toxicity during one month. Biodistribution studies showed that BTS (39 mg B/kg) compared to BPA (40 mg B/kg (previous studies), exhibited significantly therapeutic boron concentration values in the tumor (102 vs 54 ppm, $p = 0.007$) and significantly higher tumor/blood and tumor/precancerous tissue ratios compared to BPA. Higher BTS doses (50 and 60 mg B/kg) do not improve these ratios and were found to increase boron concentration in the dose limiting tissue, the precancerous tissue. Microdistribution studies have shown an heterogeneous distribution of BTS similar to BPA. BNCT studies are undergoing. BTS is a promising boron compound for the treatment of oral tumors with BNCT.

221. O10-06. ENHANCING TRASTUZUMAB-DERUXTECAN ANTITUMOR ACTIVITY BY BLOCKING SOLUBLE TNF IN

HER2+ AND HER2-LOW BREAST CANCER

Camila Jencquel¹, Marla Ladera², Sofía Bruni³, Roxana Schillaci⁴, María Florencia Mercogliano⁵

1. *Instituto de Biología y Medicina Experimental (IBY-ME-CONICET); Inmunología Tumoral*

2. *Instituto de Biología y Medicina Experimental (IBY-ME-CONICET); Inmunología Tumoral*

3. *Instituto de Biología y Medicina Experimental (IBY-ME-CONICET); Inmunología Tumoral*

4. *Instituto de Biología y Medicina Experimental (IBY-ME-CONICET); Inmunología Tumoral*

5. *Instituto de Biología y Medicina Experimental (IBY-ME-CONICET); Inmunología Tumoral*

jencquel.camila2@gmail.com

Breast cancer is the leading cause of death in women. Approved for HER2-positive and HER2-low metastatic breast cancer, trastuzumab-deruxtecan (T-DXd) is an antibody-drug conjugate. Deruxtecan payload, a potential activator of the type I interferon pathway, inhibits topoisomerase I. We previously showed that soluble TNF (sTNF) induces mucin 4 (MUC4) expression, masking the trastuzumab-binding site on HER2. Blocking sTNF with a dominant-negative protein (DN), sensitizes cells to trastuzumab. We evaluated whether sTNF blockade enhances T-DXd efficacy in HER2+ and HER2-low in vitro models. HER2+MUC4+ JIMT-1 and HER2-low MUC4+ MDA-MB-231 cell lines were used to assess proliferation and internalization by Incucyte, and binding by flow cytometry. DN (10 µg/ml) increased T-DXd binding (78% in MDA-MB-231 and 23% in JIMT-1; $P < 0.01$ and < 0.05) and internalization (49% and 70%; $P < 0.01$) by immunofluorescence. T-DXd reduced cell proliferation by 33% at 5 µg/ml ($P < 0.001$) in JIMT-1 compared with control. DN enhanced the antiproliferative effect at lower T-DXd doses (40% at 2.5 µg/ml in JIMT-1; 22% and 30% at 5 and 10 µg/ml in MDA-MB-231 vs. IgG; $P < 0.0001$, 0.001, 0.001). T-DXd alone or with DN in both cell lines and DN alone in MDA-MB-231, increased ISG15 expression by western blot, suggesting activation of interferon-related pathways. Our findings suggest that combining DN with T-DXd could maintain or enhance antitumor activity while potentially allowing for dose reduction, minimizing toxicity. Moreover, T-DXd induced activation of interferon-stimulated proteins, which may trigger an antitumor immune response.

222. O10-07. COMBINED RETINOID THERAPY WITH HDAC INHIBITION ENHANCES DIFFERENTIATION AND REDUCES TUMORIGENICITY IN NEUROBLASTOMA CELLS

Federico Julián Garde¹, Camila Rodríguez², Abel Luis Cargno³

1. *CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Departamento de Química Biológica.; Laboratorio de Diferenciación Celular y Cáncer*

2. *CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Departamento de Química Biológica.; Laboratorio de Diferenciación Celular y Cáncer*

3. *CONICET - Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Departamento de Química Biológica.; Laboratorio de Diferenciación Celular y Cáncer*
fedegarde97@gmail.com

As a persistent oncological challenge, high-risk neuroblastoma (NB) continues to carry a poor prognosis despite therapeutic advances. Since NB arises from impaired differentiation of sympathoadrenal progenitors, strategies promoting maturation have therapeutic interest. Retinoic acid (RA) is clinically used as a differentiating agent, but resistance limits its efficacy. Valproic acid (VPA), a histone deacetylase inhibitor, exhibits antiproliferative and pro-differentiation effects in several cancers. Based on reports of synergy between retinoids and HDAC inhibitors, we investigated the combined effect of all-trans retinoic acid (ATRA) and VPA in NB. The human SK-N-SH NB cell line was treated for 5 days with DMSO, ATRA (10 µM), VPA (2 mM), or ATRA+VPA. While the

Trypan Blue exclusion assay showed no significant differences in viability, the combination treatment produced the most pronounced antiproliferative effect, assessed via confluency, MTT, and clonogenic assays, compared to each monotherapy. Morphology analysis by TUJ1 immunofluorescence confirmed neuronal differentiation in all treatments, with the combination yielding the greatest effect, reflected in a higher percentage of neurite-bearing cells and longer neurites. In 3D spheroid models the combination treatment resulted in the smallest spheroid size. Spheroid migration assay showed that ATRA+VPA most potently inhibited migratory capacity, with significantly reduced migration distance compared to all other groups. Overall, ATRA+VPA promoted differentiation and impaired tumor-associated features more effectively than either agent alone. This combinatorial approach may help overcome the impaired differentiation characteristic of high-risk neuroblastoma and represents a promising therapeutic strategy.

223. O10-08. FUELING DISRUPTION IN PROSTATE CANCER BY CO-RELEASING MOLECULES AS GLYCOLYTIC PATHWAY INHIBITORS

Gastón Pascual¹, Nicolás Coto², Rocío Seniuk³, Agustina Sabater⁴, Pablo Sanchis⁵, Danushki Herath⁶, Javier Cotignola⁷, Elba Vazquez⁸, Roberta Foresti⁹, Roberto Motterlini¹⁰, Ayelen Toro¹¹, Geraldine Gueron¹²

1. *IQUIBICEN-CONICET; Laboratorio de Inflamación y Cáncer*

2. *IQUIBICEN-CONICET; Laboratorio de Inflamación y Cáncer*

3. *IQUIBICEN-CONICET; Laboratorio de Inflamación y Cáncer*

4. *IQUIBICEN-CONICET; UADE; MDACC; Laboratorio de Inflamación y Cáncer*

5. *IQUIBICEN-CONICET; UADE; MDACC; Laboratorio de Inflamación y Cáncer*

6. *UPEC-INSERM-IMRB; Biología del sistema neuromuscular*

7. *IQUIBICEN-CONICET; Laboratorio de Inflamación y Cáncer*

8. *IQUIBICEN-CONICET; Laboratorio de Inflamación y Cáncer*

9. *UPEC-INSERM-IMRB; Biología del sistema neuromuscular*

10. *UPEC-INSERM-IMRB; Biología del sistema neuromuscular*

11. *IQUIBICEN-CONICET; Laboratorio de Inflamación y Cáncer*

12. *IQUIBICEN-CONICET; Laboratorio de Inflamación y Cáncer*
gastonpascual@gmail.com

Carbon monoxide (CO) modulates cellular metabolism by targeting hemoproteins and other redox-sensitive enzymes, thereby influencing bioenergetic and signaling pathways. CO-releasing molecules (CO-RMs), designed for controlled CO delivery, are emerging as potential therapeutic agents in cancer. This study assessed the metabolic impact of CORM-401 in prostate cancer (PCa) cells. Initially, intracellular CO accumulation was validated using the hemoCD1 probe ($p < 0.001$), without affecting cell viability after CO-RMs treatment. Subsequently, CORM-401 treatment significantly reduced ATP levels ($p < 0.0001$), LDH activity ($p < 0.01$), and intracellular lactate ($p < 0.01$), indicating impaired glycolysis. In line with these findings, functional metabolic profiling revealed a decreased extracellular acidification rate ($p < 0.0001$) measured by Seahorse XF Analyzer, confirming glycolytic inhibition; no effects were observed with the CO-RM backbone (MnS), attributing the activity to CO. At the mitochondrial level, this effect was further supported by reduced mitochondrial integrity ($p < 0.05$) and mitochondrial DNA copy number, as shown by decreased expression of ND1, COX2, and CYTB ($p < 0.0001$). Furthermore, stem-like features were suppressed, with CO-RMs reducing spheroid size in hanging drop assays ($p < 0.0001$) and colony formation in clonogenic assays ($p < 0.01$). Altogether, these findings demonstrate that CORM-401 disrupts glycolysis and mitochondrial function in PCa cells, thereby impairing metabolic homeostasis and reducing tumorigenic potential.

224. O10-09. EVALUATION OF ANTITUMORAL EFFECT OF POROUS MICROSPHERES FOR CHEMOEMBOLIZATION IN RATS EXCLUDING EMBOLIC COMPONENT

Clara Sanchez Terrero¹, Luciana Cañonero², Lizeth Ariza Barreño³, Alejandro Urtreger⁴, Silvia Vornetti⁵, Noemí Jordanovskí⁶, Luciano Parodi⁷, Andrés Vidal⁸, Irina Viatela⁹, Miguel O. Prado¹⁰, Gisela Rutty Solá¹¹, Ana Cristina Zarlenga¹², Jorge

Cardoso Cúneo¹³

1. Comisión Nacional de Energía Atómica; Centro Oncológico de Medicina Nuclear del Instituto Roffo (UBA-CNEA), Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina.
 2. Instituto de Oncología Ángel H. Roffo, Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina; Área investigación
 3. Instituto de Oncología Ángel H. Roffo, Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina; Área investigación
 4. Instituto de Oncología Ángel H. Roffo, Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina; Área investigación
 5. Policlínico del docente, Lavalle 1974, C1051 Ciudad Autónoma de Buenos Aires; Servicio de Anatomía Patológica
 6. Policlínico del docente, Lavalle 1974, C1051 Ciudad Autónoma de Buenos Aires; Servicio de Anatomía Patológica
 7. Comisión Nacional de Energía Atómica, Centro Atómico Ezeiza, Cam. Real Presbítero González y Aragón 15, B1802 Ezeiza, Provincia de Buenos Aires, Argentina; División Bioterio
 8. Comisión Nacional de Energía Atómica, Centro Atómico Ezeiza, Cam. Real Presbítero González y Aragón 15, B1802 Ezeiza, Provincia de Buenos Aires, Argentina; División Bioterio
 9. Comisión Nacional de Energía Atómica; Departamento Materiales Nucleares, Centro Atómico Bariloche (CNEA, CONICET), Av. Bustillo 9500, R8402AGP, S.C. de Bariloche, Argentina.
 10. Comisión Nacional de Energía Atómica; Departamento Materiales Nucleares, Centro Atómico Bariloche (CNEA, CONICET), Av. Bustillo 9500, R8402AGP, S.C. de Bariloche, Argentina.
 11. Comisión Nacional de Energía Atómica; Centro Oncológico de Medicina Nuclear del Instituto Roffo (UBA-CNEA), Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina.
 12. Comisión Nacional de Energía Atómica; Centro Oncológico de Medicina Nuclear del Instituto Roffo (UBA-CNEA), Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina.
 13. Servicio de Cirugía Gastroenterológica. Instituto Oncológico Ángel H. Roffo. (UBA) Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina; Fundación José A. Balseiro, Centro Atómico Ezeiza, Cam. Real Presbítero González y Aragón 15, B1802 Ezeiza, Argentina.
- clarasanchez@gmail.com

Microspheres (MS) for chemoembolization (CE) of liver tumors are delivered into tumoral arterioles producing an antitumoral effect by combining two mechanisms: ischemia, caused by embolization, and localized drug release. The aim of this work is to study the in vivo effect of doxorubicin (dox) released from loaded porous MS (PMS) for CE in a subcutaneous rat tumor model, excluding the embolization component. Materials and methods. PMS (25-45 μ m produced at CNEA), BDIX rats (CNEA), and the DHDK12/TRb rat colon adenocarcinoma cell line (ECACC, UK) were used. In vitro: cells were exposed to empty PMS, dox-loaded PMS, or free dox, to evaluate cell viability. In vivo: Rats were injected subcutaneously in right flank with 1.5×10^6 cells. When tumors reached 5-7 mm, they were injected with either empty PMS (group I, N= 15) or dox-loaded PMS (group II, N= 15). After 10 days, rats were euthanized and tumors were resected to calculate tumor volume (TV), means were compared using t-test. Samples were fixed in formalin 10% for histological analysis. Results. In vitro: empty PMS had no effect in cell viability, while dox-loaded PMS and, in a greater extent, free dox significantly reduced cell viability compared with control. In vivo: all rats developed tumors. Mean TV was 129.1 ± 52 mm³ in group I vs. 77.7 ± 28 mm³ in group II ($P < 0.05$). Histological analysis revealed unique focal and multiple isolated necrotic areas, without significant differences between groups. Conclusion. In this subcutaneous rat model, PMS significantly reduced tumor growth exclusively by local drug release, independently of embolization

225. O11-01. IMPACT OF NUTRITIONAL HYPERCHOLESTEROLEMIA ON GINGIVAL COMPLEX AND TOOTH-SUPPORTING STRUCTURES IN EXPERIMENTAL PERIODONTITIS

Melina Sosa De Lucca¹, María Eugenia Antona², Ricardo Orzuza³, Andrea Ferreira Monteiro⁴, Cecilia Ramos⁵, Valeria Zago⁶, Silvia María Friedman⁷, Tammy Steimetz⁸, Elisa Vanesa Macri⁹

1. Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM).
 2. Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM).
 3. Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM).
 4. Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM).
 5. Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM).
 6. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC), Departamento de Bioquímica Clínica.; Laboratorio de Lípidos y Aterosclerosis, Buenos Aires.
 7. Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM).
 8. Universidad de Buenos Aires, Facultad de Odontología, Cátedra de Anatomía Patológica; Laboratorio de Patología Bucal.
 9. Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM).
- melina.sosa@odontologia.uba.ar

Periodontitis (P) is a chronic inflammatory disease characterized by progressive destruction of the gingival complex and tooth-supporting structures. Hypercholesterolemia may exacerbate periodontal breakdown through alterations in inflammation and bone metabolism. This study aimed to evaluate the impact of diet-induced hypercholesterolemia on insertion and protective periodontal structures during experimental P. Adult Wistar rats were fed a standard diet (Control group, C) or a cholesterol-enriched diet (DHC group) for 21 days. Experimental periodontitis was then induced in all animals by placing a ligature around the lower first molars. Three days after induction, the rats were euthanized for sample collection. Serum lipid profiles were determined. Periodontal parameters were assessed by mandibular radiovisiography, histomorphometry of alveolar bone (osteoblastic and erosive surfaces, periodontal ligament height (PL.h)), and evaluation of gingival collagen fibers and oxidative stress (DCFH-DA oxidation, catalase activity). T-test (SPSS), $p < 0.05$. DHC rats showed hypercholesterolemia (T-cholesterol: 187.86 ± 65.07 mg/dL vs C: 58.57 ± 3.41 mg/dL, $p < 0.0001$), increased alveolar bone resorption ($81.59 \pm 3.09\%$ vs C: $70.81 \pm 1.67\%$, $p < 0.01$), reduced osteoblastic surfaces ($4.51 \pm 0.45\%$ vs C: $17.32 \pm 1.57\%$, $p < 0.0001$), decreased bone support ($43.26 \pm 4.89\%$ vs C: $48.53 \pm 2.59\%$, $p < 0.05$), and increased PL.h ($486.71 \pm 40.59 \mu$ m vs C: $399.09 \pm 25.28 \mu$ m, $p < 0.01$). Gingival oxidative stress and collagen fibers were also altered (DCFH-DA: 23.15 ± 0.25 vs C: 9.98 ± 0.48 , $p < 0.0001$; collagen fibers: $41.44 \pm 6.75\%$ vs C: $70.03 \pm 7.82\%$, $p < 0.001$). Diet-induced hypercholesterolemia affects periodontal tissues, worsening periodontitis through increased oxidative stress and attachment loss. This underscores the vulnerability of hypercholesterolemic individuals and the need for an interdisciplinary approach to manage cholesterol levels and mitigate periodontal progression.

ORALES 11 - SAIC - METABOLISMO Y NUTRICIÓN 2
 DATE & TIME: 19/11/2025 9:00 - 10:30 H
 Chairs: Gustavo Hein, María del Rosario Ferreira Cordoneda

226. O11-02. CADMIUM-INDUCED PLACENTAL ALTERATIONS IN PREGNANT RATS: OXIDATIVE STRESS, INFLAMMATION, AND MODULATORY ROLE OF SOY PROTEIN

Veronica Biaggio¹, Laura Virginia Gatica², Maria Veronica

Perez Chaca³, Silvana Piguillem⁴, Maria Eugenia Ciminari⁵, Silvana Alvarez⁶

1. IMIBIO-CONICET

2. IMIBIO-CONICET

3. UNSL; Laboratorio de Morfofisiologia-UNSL

4. UNSL; Laboratorio de Morfofisiologia-UNSL

5. UNSL; Laboratorio de Morfofisiologia-UNSL

6. IMIBIO-CONICET

vbiaggio@gmail.com

Cadmium (Cd) is a heavy metal with known reproductive toxicity. During pregnancy, placental exposure to Cd may disrupt cellular homeostasis via oxidative stress and inflammation, affecting fetal development. This study evaluated Cd-induced placental alterations in rats and the potential modulatory effect of soy protein. Four groups of female Wistar rats were used: casein control (Cas-Co), casein with Cd (Cas-Cd), soy control (Soy-Co), and soy with Cd (Soy-Cd). Cd was administered at 15 ppm in drinking water. All analyses were performed on placental tissue collected at 20G. TBARS, CAT and GPx activity, and nitrite levels were measured. Gene expressions of MT I, MT II, Nrf-2, NOX-2, SOD-2, CAT, GPx, VEGF, IL-6, and eNOS were assessed by conventional RT-PCR. In Soy-Cd group Nrf-2, SOD and MT I expression increased ($p<0.05$, $p<0.01$, $p<0.001$). While mRNA NOX-2 and MT II expression decreased ($p<0.01$; $p<0.01$; $p<0.00$, respectively). eNOS expression was significantly increased ($p<0.01$) in Soy-Cd group, in line with VEGF activation, suggesting an adaptive angiogenic response to oxidative damage. Histological sections revealed trophoblastic disorganization, vascular congestion, and edema in Cd groups. Soy-treated placentas showed partial preservation of architecture, with clearer labyrinthine zones and reduced tissue damage. Gestational Cd exposure induces molecular and structural placental changes. Soy protein demonstrated a modulatory effect, partially mitigating damage and promoting adaptive responses, including activation of angiogenic pathways mediated by VEGF and eNOS.

227. O11-03. DIETARY ANTHOCYANINS AS PROTECTIVE AGENTS AGAINST URBAN AIR POLLUTION-INDUCED INFLAMMATORY AND METABOLIC ALTERATIONS: SEX-SPECIFIC RESPONSES IN A MURINE MODEL

Agustin Lucini Mas¹, Natalia Magnani², Silvia Alvarez³, Pablo Evelson⁴, César G. Fraga⁵, Mónica Galleano⁶

1. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina. CONICET- Universidad de Buenos Aires. Instituto de Bioquímica y Medicina Molecular "Profesor Alberto Boveris" (IBIMOL). Buenos Aires, Argentina.; Departamento de Ciencias Químicas. Cátedra de Fisiología.

2. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina. CONICET- Universidad de Buenos Aires. Instituto de Bioquímica y Medicina Molecular "Profesor Alberto Boveris" (IBIMOL). Buenos Aires, Argentina.; Departamento de Ciencias Químicas. Cátedra de Química General e Inorgánica.

3. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina. CONICET- Universidad de Buenos Aires. Instituto de Bioquímica y Medicina Molecular "Profesor Alberto Boveris" (IBIMOL). Buenos Aires, Argentina.; Departamento de Ciencias Químicas. Cátedra de Fisiología.

4. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina. CONICET- Universidad de Buenos Aires. Instituto de Bioquímica y Medicina Molecular "Profesor Alberto Boveris" (IBIMOL). Buenos Aires, Argentina.; Departamento de Ciencias Químicas. Cátedra de Química General e Inorgánica.

5. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina. CONICET- Universidad de Buenos Aires. Instituto de Bioquímica y Medicina Molecular "Profesor Alberto Boveris" (IBIMOL). Buenos Aires, Argentina.; Departamento de Ciencias Químicas. Cátedra de Fisiología.

6. Universidad de Buenos Aires. Facultad de Farmacia y

Bioquímica, Buenos Aires, Argentina. CONICET- Universidad de Buenos Aires. Instituto de Bioquímica y Medicina Molecular "Profesor Alberto Boveris" (IBIMOL). Buenos Aires, Argentina.; Departamento de Ciencias Químicas. Cátedra de Fisiología. alucini@docente.ffyb.uba.ar

Chronic exposure to pollutants presents in urban air (UA) induces a persistent low-grade inflammatory state, initially in the lungs and subsequently systemically, which may contribute to metabolic dysregulation. The aim of this study was to evaluate the capacity of dietary anthocyanins—bioactive compounds with antioxidant and anti-inflammatory properties—to prevent low-grade inflammation and related metabolic disturbances caused by chronic exposure to UA. BALB/c mice ($n=12$, 6 males, 6 females) were randomized and exposed to filtered air (FA) or UA in whole-body exposure chambers for 12 weeks. Within each exposure condition, animals received either a control diet (C) or a diet supplemented with maqui berry extract as a source of anthocyanins. In males: i) the proinflammatory cytokine IL-6 in bronchoalveolar lavage (BAL) was not altered by UA exposure, but was reduced by the supplemented diet, and ii) no significant differences were detected in body weight, fasting glucose, triglycerides, and cholesterol, but oral glucose tolerance test (OGTT) revealed a higher peak glucose concentration (Cmax) in C-UA compared to C-FA, which was partially prevented by dietary supplementation. In contrast to males, in females: i) UA exposure increased IL-6 in BAL, and diet supplementation did not modify this response, and ii) no significant differences were detected in body weight, fasting glucose, triglycerides, cholesterol, and OGTT response. In conclusion, anthocyanin supplementation in the diet attenuated inflammatory response in lungs and partially prevented metabolic disturbances induced by UA exposure in males but not in females.

228. O11-04. EFFECT OF DIET COMPOSITION ON PGC-1A AND GLUCONEOGENIC ENZYMES EXPRESSION IN A GENETIC MICE MODEL OF ACUTE INTERMITTENT PORPHYRIA

María del Carmen Martínez¹, Johanna Romina Zuccoli², Ana María Buzaleh³, Esther Noemí Gerez⁴

1. 1-Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín, Argentina.; -Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires.; Porfirias Experimentales

2. 1-Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín, Argentina.; Porfirias Experimentales

3. 1-Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín, Argentina.; -Universidad Favaloro, Buenos Aires, Argentina.; Porfirias Experimentales

4. 1-Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín, Argentina.; -Universidad Católica Argentina, Buenos Aires, Argentina.; Porfirias Experimentales mcmartin@qb.fcen.uba.ar

Acute Intermittent Porphyria is due to porphobilinogen deaminase (PBG-D) deficiency. Porphyric neuropathy is associated with high levels of 5-aminolevulinic acid and porphobilinogen due to 5-aminolevulinic acid synthetase (ALA-S) induction, first and regulatory heme enzyme. Fasting is one of the triggering factors of acute attacks. Changes in diet composition altered heme pathway inducing ALA-S1 activity/expression in females PBG-D deficient mice (AIP, PBGD^{-/-}). Fasting also decreased blood glucose levels. PGC-1 α regulates hepatic ALAS-1 expression and gluconeogenesis through glucose-6-phosphatase (G6Pase) and phosphoenolpyruvate carboxykinase (PEPCK). The aim was to further investigate the effect of diet composition measuring mRNA expression of PGC-1 α , G6Pase and PEPCK, in AIP mice. Results were compared with C57BL/6 (WT). WT and AIP of both sexes were divided in three groups: groups 1 and 2 received standard diet (Purina 3: 5% lip-

ids, 40% carbohydrates, 23% proteins; 12 weeks); group 3 received standard diet +15% commercial olive oil (20% lipids, 34% carbohydrates, 19.5% proteins; 12 weeks); groups 2 and 3 were fasted 16 hours prior euthanasia. In WT females, mRNA induction was observed; PGC-1 α : 2.3-fold (fasting), 1.0-fold (oil+fasting); PEPCK: 5-fold (fasting), 6.8-fold (oil+fasting); G6Pase: 2.3-fold (fasting), 4.0-fold (oil+fasting). In AIP the induction was lower than in WT due to fasting: PGC-1 α (1.3-fold, males), PEPCK (1.7-fold, males; 1.0-fold, females) and G6Pase (0.5-fold, males; 0.7-fold, females); without significant modification by oil addition. In conclusion, PGC-1 α and gluconeogenic enzymes mRNA induction due to fasting was different among WT, AIP, and sex, with WT females being the most affected. No relationship was observed with the diet composition.

229. O11-05. EFFECTS OF KRILL OMEGA-3 SUPPLEMENTATION ON THYMUS AND SERUM FATTY ACID PROFILES IN GROWING RATS FED A SATURATED FAT DIET

María Fernanda Godoy¹, Anabel Impa Condori², María Silvia Giacomino³, María Susana Feliu⁴

1. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. Buenos Aires, Argentina.; Cátedra de Nutrición.
2. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. Buenos Aires, Argentina.; Cátedra de Nutrición.
3. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. Buenos Aires, Argentina.; Cátedra de Bromatología.
4. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. Buenos Aires, Argentina.; Cátedra de Nutrición. godoymfernanda@gmail.com

Omega-3 fatty acids play a crucial role in thymus maturation and development. Objective: to analyze the effect of diet containing butter, as fat source, with and without the supplementation with krill oil as source of omega-3, on thymus and serum fatty acid profiles of growing rats. Weanling Wistar rats received for 10 days normocaloric diet and fat was provided by butter (B group). The other group received the same diet supplemented with 24mg omega-3/day of krill oil (BK). Control group (C) received diet AIN⁹³. Thymus and serum fatty acids profiles were determined by gas chromatography. Statistical analysis: ANOVA and post hoc tests. Results (%Area, as Mean $\pm$ SD): THYMUS PALMITIC: C:22.72 $\pm$ 1.73a; B:26.49 $\pm$ 1.85b; BK:24.42 $\pm$ 3.43b OLEIC: C:16.35 $\pm$ 3.80a; B:22.43 $\pm$ 5.63b; BK:23.01 $\pm$ 5.83b. LINOLEIC: C:9.72 $\pm$ 1.48b; B:3.40 $\pm$ 0.64a; BK:4.05 $\pm$ 0.43a. LINOLENIC: C:0.52 $\pm$ 0.11b; B:0.28 $\pm$ 0.01a; BK:0.30 $\pm$ 0.10a. ARACHIDONIC: C:14.12 $\pm$ 2.12b; B:7.66 $\pm$ 2.36a; BK:7.96 $\pm$ 3.56a. EPA: C:0.45 $\pm$ 0.07a; B:0.69 $\pm$ 0.21a; BK:1.49 $\pm$ 0.52b. DHA: C:0.61 $\pm$ 0.13a; B:0.51 $\pm$ 0.10a; BK:1.19 $\pm$ 0.49b. SERUM PALMITIC: C:17.79 $\pm$ 1.37a; B:23.90 $\pm$ 1.20b; BK:24.73 $\pm$ 1.61b OLEIC: C:11.39 $\pm$ 2.19a; B:24.55 $\pm$ 1.79c; BK:21.10 $\pm$ 2.57b. LINOLEIC: C:22.88 $\pm$ 2.34b; B:7.19 $\pm$ 0.47a; BK:7.83 $\pm$ 1.23a. LINOLENIC: C:1.07 $\pm$ 0.29b; B:0.26 $\pm$ 0.04a; BK:0.39 $\pm$ 0.10a. ARACHIDONIC: C:17.15 $\pm$ 0.86c; B:9.42 $\pm$ 1.89b; BK:7.17 $\pm$ 0.47a. EPA: C:1.07 $\pm$ 0.13a; B:0.74 $\pm$ 0.18a; BK:4.75 $\pm$ 1.21b. DHA: C:3.11 $\pm$ 0.55b; B:1.43 $\pm$ 0.23a; BK:3.95 $\pm$ 0.91b. Means with no letter (a,b,c) in common, were different ($p < 0.05$). In thymus and serum, all experimental groups showed higher levels of palmitic and oleic acids and lower levels of linoleic, arachidonic and alpha-linolenic acids than C. In serum, EPA and DHA were lower in B than in C. Conclusion: Short-term krill oil supplementation successfully enhanced thymic and serum EPA and DHA levels, counteracting the potential negative effects of dietary saturated fatty acids on omega-3 fatty acid status in growing rats.

230. O11-06. EFFECTS OF ZINC SUPPLEMENTATION ON ADIPOSE TISSUE IN RATS FED A HIGH-FAT AND FRUCTOSE DIET DURING GROWTH

Agustina Medina¹, Josefina Marinchevich², Ezequiel Hid³, Juan Manuel Gaetani⁴, Gabriela Noceti⁵, Mónica Galleano⁶, Carolina Canifí⁷, Rosana Elesgaray⁸, Cristina Arranz⁹

1. Cátedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Instituto de la Química y Metabolismo del Fármaco (IQUIMEFA), CONICET, Universidad de Buenos Aires, Ciudad de Buenos Aires, Argentina; Laboratorio de Investigaciones Cardiovascular, Renal e Hipertensión Arterial

2. Cátedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Instituto de la Química y Metabolismo del Fármaco (IQUIMEFA), CONICET, Universidad de Buenos Aires, Ciudad de Buenos Aires, Argentina; Laboratorio de Investigaciones Cardiovascular, Renal e Hipertensión Arterial

3. Cátedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Instituto de la Química y Medicina Molecular; Prof. Alberto Boveris; (IBI-MOL-UBA-CONICET), Ciudad de Buenos Aires, Argentina.

4. Cátedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Instituto de la Química y Metabolismo del Fármaco (IQUIMEFA), CONICET, Universidad de Buenos Aires, Ciudad de Buenos Aires, Argentina; Laboratorio de Investigaciones Cardiovascular, Renal e Hipertensión Arterial

5. Cátedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Instituto de la Química y Metabolismo del Fármaco (IQUIMEFA), CONICET, Universidad de Buenos Aires, Ciudad de Buenos Aires, Argentina; Laboratorio de Investigaciones Cardiovascular, Renal e Hipertensión Arterial

6. Cátedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Instituto de la Química y Medicina Molecular; Prof. Alberto Boveris; (IBI-MOL-UBA-CONICET), Ciudad de Buenos Aires, Argentina.

7. Cátedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Instituto de la Química y Metabolismo del Fármaco (IQUIMEFA), CONICET, Universidad de Buenos Aires, Ciudad de Buenos Aires, Argentina; Laboratorio de Investigaciones Cardiovascular, Renal e Hipertensión Arterial

8. Cátedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Instituto de la Química y Metabolismo del Fármaco (IQUIMEFA), CONICET, Universidad de Buenos Aires, Ciudad de Buenos Aires, Argentina; Laboratorio de Investigaciones Cardiovascular, Renal e Hipertensión Arterial

9. Cátedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires. Instituto de la Química y Metabolismo del Fármaco (IQUIMEFA), CONICET, Universidad de Buenos Aires, Ciudad de Buenos Aires, Argentina; Laboratorio de Investigaciones Cardiovascular, Renal e Hipertensión Arterial
agusmedina@gmail.com

Introduction: Zinc supplementation may reduce metabolic and cardiovascular damage associated with metabolic syndrome, given zinc's antioxidant and anti-inflammatory properties. Objective: To evaluate the effects of zinc supplementation on retroperitoneal adipose tissue (RPAT) in male Wistar rats fed a high-fat and fructose diet (HFFD) during post-weaning growth. Methods: Male Wistar rats were fed from 21 to 81 days of life: control diet (CC, Zinc 30 ppm), zinc supplemented diet (CZ: Zinc 190 ppm), high-fat diet (CFF; 60% pork fat calories, 30 ppm Zinc) and 10% fructose in drinking water, high-fat diet supplemented with zinc (ZFF; 60% fat calories, 190 ppm Zinc) and 10% fructose in drinking water. Adipokine ARNm expression, morphological changes, and oxidative state in RPAT were evaluated at 81 days. Statistics: 2-way ANOVA, post-hoc test: Bonferroni: * $p < 0.05$ vs CC; + $p < 0.05$ vs CFF; & $p < 0.05$ vs CZ; n=9 per group. Results: ZFF rats showed reduced adipocyte hypertrophy (CC:5258 $\pm$ 312; CZ: 3070 $\pm$ 208*; CFF:7203 $\pm$ 454*; ZFF: 5368 $\pm$ 549+, & μ m²) and media layer area/light area of vessels (CC:2.2 $\pm$ 0.4; CZ:3.1 $\pm$ 0.5; CFF:4.8 $\pm$ 0.4**; ZFF:2.7 $\pm$ 0.3+), lower thiobarbituric acid reactive species concentration (CC:0.21 $\pm$ 0.01; CZ:0.09 $\pm$ 0.02*; CFF:0.38 $\pm$ 0.03*; ZFF:0.23 $\pm$ 0.04+, & nmol/mg protein), higher antioxidant superoxide dismutase activity (CC:5.8 $\pm$ 0.3; CZ:12 $\pm$ 2*; CFF:6.4 $\pm$ 0.7; ZFF:11 $\pm$ 2+ uSOD/mg protein) and NRF2 mRNA expression (CC:2.3 $\pm$ 0.4; CZ:8.9 $\pm$ 1.1*; CFF:1.3 $\pm$ 0.2; ZFF:4.6 $\pm$ 0.7+, &). Moreover, RPAT of ZFF showed higher expression levels of adiponectin (CC:0.85 $\pm$ 0.07; CZ:3.0 $\pm$ 0.5*; CFF:0.24 $\pm$ 0.07*; ZFF:2.1 $\pm$ 0.3+) and leptin (CC:0.32 $\pm$ 0.07; CZ:0.53 $\pm$ 0.07; CFF:1.6 $\pm$ 0.2*; ZFF:3.0 $\pm$ 0.5) Con-

clusion: Zinc supplementation during growth reduces cardiovascular and metabolic damage induced by HFFD. In CZ rats, zinc also improves the oxidative stress state and adiponectin expression in RPAT.

231. O11-07. HIGH SALT CONSUMPTION IMPAIRS MITOCHONDRIAL BEHAVIOUR AND PROMOTES OXIDATIVE STRESS IN VISCERAL ADIPOSE TISSUE

Vanessa Touceda¹, Morena Wiszniewski², Paola Finocchietto³, Leonardo Cacciagiú⁴, Silvia Friedman⁵, Germán E. González⁶, Verónica Mikszowicz⁷

1- Instituto de Investigaciones Biomédicas (UCA-CONICET); - Universidad de Buenos Aires, Facultad de Odontología.; 1- Laboratorio de Patología Cardiovascular Experimental e Hipertensión Arterial; - Cátedra de Bioquímica General y Bucal. Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM)

2- Universidad de Buenos Aires, Facultad de Odontología; - CONICET - Universidad de Buenos Aires.; 2- Cátedra de Bioquímica General y Bucal. Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM); - Centro de Estudios Farmacológicos y Botánicos (CEFyBO).

3- 2- Universidad de Buenos Aires, Facultad de Odontología.; 2- Cátedra de Bioquímica General y Bucal. Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM).

4- 2- Universidad de Buenos Aires, Facultad de Odontología; - Hospital General de Agudos Teodoro Álvarez.; 2- Cátedra de Bioquímica General y Bucal. Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM); - Laboratorio Central. Sección Bioquímica.

5- 2- Universidad de Buenos Aires, Facultad de Odontología.; 2- Cátedra de Bioquímica General y Bucal. Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM).

6- 1- Instituto de Investigaciones Biomédicas (UCA-CONICET).; 1- Laboratorio de Patología Cardiovascular Experimental e Hipertensión Arterial.

7- 2- Universidad de Buenos Aires, Facultad de Odontología.; - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); 2- Cátedra de Bioquímica General y Bucal. Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM).

toucedavanessa@gmail.com

Previously, we demonstrated that high salt intake alters visceral adipose tissue (VAT) homeostasis by reducing adipocyte volume and vascularization and promoting fibrosis. Aim: to evaluate the impact of a high-salt diet (HSD) intake on mitochondrial dynamics and oxidative stress in VAT from an animal model. Methods: Male C57BL/6 mice (8 weeks old) were divided into Control (C, n=15) fed a standard diet and HSD diet group (n=15) fed an 8% NaCl diet for 20 weeks. Body weight, food and water intake were recorded weekly, and arterial pressure (AP) was measured by plethysmography. Epididymal AT (EAT) was removed and weighed. In EAT, mitochondrial morphology (TEM), oxidative stress markers (colorimetric assays), and the expression of HIF-1 α and UCP-1 (RT-qPCR) were evaluated. Results: HSD group showed increased water intake ($p<0.001$) without differences in caloric intake compared to C. Body weight gain and VAT mass were lower in HSD ($p<0.001$). In C, mitochondria were predominantly tubular-shaped ($84\pm3\%$), while in the HSD group mitochondria were mostly spherical ($67\pm5\%$), indicating a prevalence of fragmented mitochondria ($p<0.001$). Lipid peroxidation and catalase (CAT) and superoxide dismutase (SOD) activity were elevated in HSD ($p<0.01$ and $p<0.05$, respectively). HIF-1 α and UCP-1 levels were significantly reduced in HSD compared to C ($p<0.001$). Conclusion: A high-salt diet promotes mitochondrial fragmentation, oxidative stress, and reduced HIF-1 α and UCP-1 expression in VAT, suggesting impaired mitochondrial function and adaptive capacity. These alterations may contribute to adipose tissue dysfunction associated with excessive salt intake.

232. O11-08. SERUM AND BREATH CARBON ISOTOPE RA-

TIOS AS POTENTIAL BIOMARKERS OF ADDED SUGAR INTAKE

Noelia Dressl¹, Paula Mantero², Sol Chiozza³, Germán Flekenstein⁴, Gustavo Cernadas⁵, Marcela Zubillaga⁶, Mariana Janjetic⁷, Cinthia Goldman⁸

1. Universidad de Buenos Aires, Facultad de Medicina, Buenos Aires, Argentina; Escuela de Nutrición

2. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Cátedra de Física

3. Universidad de Buenos Aires, Facultad de Medicina, Buenos Aires, Argentina; Escuela de Nutrición

4. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Cátedra de Física

5. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Cátedra de Anatomía

6. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina; Cátedra de Física

7. Universidad de Buenos Aires, Facultad de Medicina, Buenos Aires, Argentina; Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina; Cátedra de Física

8. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Buenos Aires, Argentina; Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina; Cátedra de Física

noelia.dressl@gmail.com

Introduction: Consumption of added sugar has increased, becoming a worldwide concern. An objective biomarker of its intake is needed for nutritional epidemiology. Objective: To investigate the use of total serum 13C/12C carbon isotope ratio (serum-CIR) and breath-CIR as biomarkers of added sugar intake in an adult population. Patients and Methods: Volunteer faculty and administrative staff (18-65y) of the School of Pharmacy and Biochemistry and the School of Nutrition of the UBA were included. The protocol was approved by the Ethics Committee in Clinical Research, FFyB, UBA. The study was conducted within a month, with four appointments for 24h dietary recalls, administration of questionnaires, measurement of weight, height and waist circumference. Breath samples were collected weekly for breath-CIR determination in an Isotope Ratio Mass Spectrometer (Delta Q IRMS, Thermo Scientific, Germany) and a blood sample was obtained for biochemical assessment and serum-CIR measurement. SPSS software was used for statistical analysis. Results: We included 80 volunteers ($40.4\pm10.5y$), 76.3% female. Anthropometric evaluation showed that 2.5% were underweight, 46.3% had normal weight and 51.2% were overweight/obese. Mean total sugar and added sugar intakes were 74.9 g/d and 40.9 g/d; 37.5% exceeded the recommendations of the WHO regarding added sugar intake of total energy intake. Breath-CIR positively correlated with added sugar ($r=0.5215$; $p<0.0001$) and total sugar intake ($r=0.3158$; $p=0.0046$); while serum-CIR correlated with added sugar ($r=0.2861$; $p=0.0106$) but not with total sugar intake ($r=0.1378$; $p=0.2257$). Conclusion: Our results support the use of breath-CIR and serum-CIR as biomarkers of added sugar intake in adults from Argentina.

233. O11-09. FRIED SUNFLOWER OIL CONSUMPTION DURING GROWTH AGGRAVATES LIVER DAMAGE

Melina Sosa De Lucca¹, Morena Wiszniewski², Paola Finocchietto³, Vanesa Macri⁴, María Florencia Quintanilla⁵, Leonardo Cacciagiú⁶, Silvia Friedman⁷, Verónica Mikszowicz⁸

1 Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; 1Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM)

2 Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal; 2CONICET - Universidad de Buenos Aires.; 1Unidad de Investigación en

Bioquímica Traslacional y Metabolismo (UBiTyM); 2Centro de Estudios Farmacológicos y Botánicos (CEFYBO). Buenos Aires, Argentina

3. *1Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; 1Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM)*

4. *1Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; 1Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM)*

5. *1Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; 1Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM)*

6. *1Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; 3Hospital General de Agudos Teodoro Álvarez.; 1Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM); 3Laboratorio Central. Sección Bioquímica. Buenos Aires*

7. *1Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; 1Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM)*

8. *1Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal.; 4Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina.; 1Unidad de Investigación en Bioquímica Traslacional y Metabolismo (UBiTyM)*
melisosa28@gmail.com

Introduction: Consumption of fried vegetable oils has been associated with chronic metabolic disorders. Previously we demonstrated that a diet rich in fried sunflower oil promotes hepatic steatosis and increases oxidative stress. **Objectives:** to evaluate the hepatic effects of fried sunflower oil intake during growth on steatosis development, mitochondrial and lipid droplet alterations and the expression of genes involved in hypoxia, thermogenesis and mitochondrial biogenesis. **Methods:** Male weaning Wistar rats (n=26) were fed three diets for 8 weeks: standard chow diet (C) or supplemented with sunflower oil (SFO) or SFO repeatedly heated for 40 hours (SFOx). Body weight and food consumption were recorded weekly. At wk=8, animals were euthanized, livers were harvested and weighed for hepato-somatic index (HSI%). Steatosis grade, mitochondria morphology and lipid droplets (LD) characteristics were assessed by transmission electron microscopy. Hypoxia (HIF-1 α), thermogenesis (UCP-1) and biogenesis (PGC-1 α) markers were evaluated by RT-qPCR. **Results:** SFOx exhibited higher HSI than SFO and C (p<0.02). Histological analysis revealed mild to moderate steatosis in SFO and SFOx. Both oil groups presented an increased LD density (p<0.05 and p<0.01 vs. C). SFOx presented higher LD density (p<0.05) with smaller size (p<0.001) than SFO. The proportion of tubular mitochondria decreased in SFOx vs SFO (p<0.01) and both vs C (p<0.013 and p<0.001). PGC-1 α , HIF-1 α and UCP-1 levels were increased in SFO (p<0.01 vs C), without changes in SFOx. **Conclusions:** Consumption of SFOx during growth promote differential LD distribution and disruptions in mitochondrial morphology, and fails to activate protective mechanisms, potentially exacerbating liver damage.

ORALES 12 - SAIC - REPRODUCCIÓN

DATE & TIME: 19/11/2025 9:00 - 10:30 H

Chairs: **Mónica Frungieri, Rosanna Ramhorst**

234. O12-01. MATERNAL DIETS ENRICHED IN EXTRA VIRGIN OLIVE OIL AMELIORATES MARKERS OF A PROINFLAMMATORY AND PROFIBROTIC STATE IN THE POSTPARTUM DAM'S HEART

Virginia Taylor¹, Florencia Schibert², Irune Pirrone³, Romina Higa⁴, Alicia Jawerbaum.⁵

1. *CEFYBO-CONICET, FACULTAD DE MEDICINA, UBA; Laboratorio de Reproducción y Metabolismo*

2. *CEFYBO-CONICET, FACULTAD DE MEDICINA, UBA; Laboratorio de Reproducción y Metabolismo*

3. *CEFYBO-CONICET, FACULTAD DE MEDICINA, UBA; Laboratorio de Reproducción y Metabolismo*

4. *CEFYBO-CONICET, FACULTAD DE MEDICINA, UBA;*

Laboratorio de Reproducción y Metabolismo

5. *CEFYBO-CONICET, FACULTAD DE MEDICINA, UBA;*

Laboratorio de Reproducción y Metabolismo

virginiasoledadtaylor@gmail.com

Maternal diabetes causes short- and long-term complications in mothers and offspring. Previously, we found that a maternal diet enriched in extra virgin olive oil (EVOO) prevented impairments in the offspring's heart of diabetic dams. Whether this diet also benefits the heart of the dams is unknown. **Aim:** To evaluate the effect of an EVOO-enriched diet on proinflammatory and profibrotic markers in the heart of diabetic dams at postpartum. **Methods:** A mild pregestational diabetic rat model was induced by neonatal administration of streptozotocin (90 mg/kg sc). Control and diabetic females were mated with healthy males and fed a standard diet supplemented or not with 6% EVOO from one-week preconception to parturition (n=6-8 per group). After one-month postpartum, maternal hearts were collected. Expression of genes and microRNAs modulating the profibrotic and proinflammatory state were measured (qPCR and stem-loop qPCR). **Results:** The heart of diabetic dams showed increased FGF21, TGF β 1, CTGF, TNF α and MMP9 mRNA levels (p<0.05 vs. controls). The increased TNF α and TGF β 1 expression was prevented by the EVOO-enriched maternal diet (p<0.05 vs. diabetic group). Mir-21 and miR-155 levels were reduced in the heart of diabetic dams (0.16- and 0.55-fold, p<0.05 vs. controls), alterations that remained when the dams were fed the EVOO-enriched diet. **Conclusions:** At postpartum, although increased markers of proinflammatory and profibrotic damage were observed in the heart of diabetic dams, increased FGF21 and reduced Mir21 and miR155 are likely compensatory factors. Moreover, the EVOO-enriched maternal diet contributes to ameliorate the proinflammatory/profibrotic state in the heart of diabetic dams.

235. O12-02. EFFECT OF A PRECONCEPTIONAL EXTRA VIRGIN OLIVE OIL-ENRICHED DIET IN DIABETIC MALE RATS ON FETAL METABOLISM AND LIVER HEALTH

Irune Pirrone¹, Alejandro Ranieri², Alicia Jawerbaum³, Evangelina Capobianco⁴

1. *CEFYBO-UBA-CONICET; Laboratorio de reproducción y metabolismo*

2. *CEFYBO-UBA-CONICET; Laboratorio de reproducción y metabolismo*

3. *CEFYBO-UBA-CONICET; Laboratorio de reproducción y metabolismo*

4. *CEFYBO-UBA-CONICET; Laboratorio de reproducción y metabolismo*

iru.pirrone@gmail.com

Background: Paternal diabetes influences fetal development and long-term metabolic health of the offspring. The fetal liver is a key organ for studying metabolic alterations. Extra virgin olive oil (EVOO)-enriched diet has been found to prevent metabolic alterations in experimental models of maternal diabetes. **Aim:** To assess the effect of a paternal EVOO-enriched diet on the metabolism and hepatic oxidative stress in fetuses fathered by male diabetic rats. **Methods:** Control (C) and type 2 diabetic (D, induced by intrauterine programming) male rats were mated with healthy females. A group of D males received a 6% EVOO-enriched diet one month before mating (DO) (n=8). On gestational day 21, fetal male and female plasma and liver were obtained for determination of glycemia, triglyceridemia, cholesterolemia, and transaminases (by commercial kits) and lipid peroxidation (TBARS quantification). **Results:** Fetuses from D fathers showed increased body weight (females: 5.2%; males: 8.3%; p<0.05) and increased liver weight (females: 7.7%; males: 10.7%, p<0.05 vs. controls). No changes were found in glycemia. Cholesterolemia (females: 14%; males: 27.8%, p<0.05) and triglyceridemia (females: 14.3%; males: 9.4%, p<0.05) were increased in fetuses from D fathers vs controls. These alterations were prevented in all the fetuses sired by DO males. In D and DO groups, hepatic TBARS levels were increased (males: 39.9% and 55.9%; females: 47.9.47% and 49.47%, respectively, p<0.05 vs controls). Transaminase levels were similar among groups. **Conclu-**

sions: Paternal diabetes alters fetal growth, metabolism, and hepatic oxidative stress. An EVOO-supplemented diet prior to conception partially prevented the programming of fetal metabolic disorders.

236. O12-03. IDENTIFICATION OF SOCS3 AS A KEY PCOS BIOMARKER IN BLOOD LEUKOCYTES THROUGH SUPERVISED MACHINE LEARNING

María Virginia Acosta¹, María Alejandra Cardozo², Georgina Stegmayer³, María Florencia Andreoli⁴, Verónica Lis Bosquiazzo⁵

1. Instituto de Salud y Ambiente del Litoral (ISAL, UNL-CO-NICET), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina; -
2. Instituto de Salud y Ambiente del Litoral (ISAL, UNL-CO-NICET), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina; -
3. Instituto de Investigación en Señales, Sistemas e Inteligencia Computacional (sinc(i), UNL-CO-NICET), Facultad de Ingeniería y Ciencias Hídricas, Universidad Nacional del Litoral, Santa Fe, Argentina; -
4. Instituto de desarrollo e Investigaciones Pediátricas (IDIP) Prof. Dr. Fernando E. Viteri. HIAEP "Sor María Ludovica" de la Plata-CIC-PBA. La Plata, Buenos Aires, Argentina; Department of Surgical Sciences, Functional Pharmacology and Neuroscience, Uppsala University, Uppsala, Sweden; -
5. Instituto de Salud y Ambiente del Litoral (ISAL, UNL-CO-NICET), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina; - mvacostaperesin@gmail.com

Polycystic ovary syndrome (PCOS) is a prevalent endocrine and reproductive disorder affecting women of reproductive age. This study recruited women with PCOS and healthy controls from the province of Santa Fe (Argentina) to characterise their biochemical profiles and assess the expression of key components of the insulin and leptin signalling pathways: long form of the leptin receptor, suppressor of cytokine signalling 3 (SOCS3), insulin receptor, and insulin receptor substrates, in peripheral blood leukocytes using RT-qPCR techniques. We also developed supervised machine learning (ML) models to explore their potential as molecular biomarkers of metabolic alterations in women with PCOS. The results indicated that the prevalence of PCOS among the surveyed female population of Santa Fe was 8.7%. Although the biochemical values remained within the established reference range, women diagnosed with PCOS exhibited significantly elevated levels of alkaline phosphatase, white blood cells, haemoglobin, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, and insulin, along with a reduced proportion of intermediate cells compared to control women. Gene expression analysis showed a significant increase in SOCS3 mRNA levels in PCOS patients. Furthermore, data analysis employing ML and logistic regression models, suggests that SOCS3 mRNA expression in peripheral blood leukocytes could be used as a potential molecular biomarker for the detection of metabolic alterations in women with PCOS.

237. O12-04. INTERACTION BETWEEN PROGRAMMED METABOLIC ALTERATIONS AND EXPOSURE TO A TOXICANT WITH OBESOGEN ACTIVITY

Marina Labiano¹, Victoria dechanps², Jeremias Pablo Flores Quiroga³, María Florencia Heinecke⁴, Analía Elizabeth Cortez⁵, Rocio Galarza⁶, Alicia Graciela Faletti⁷, Veronica White⁸

1. CEFYBO -UBA - CONICET; Laboratorio de programacion de anomalías metabólicas
2. CEFYBO - UBA - CONICET; Laboratorio de programacion de anomalías metabólicas
3. CEFYBO-UBA-CONICET; Laboratorio de programacion de anomalías metabólicas
4. CEFYBO-UBA-CONICET; Laboratorio de programacion de anomalías metabólicas
5. Facultad de Medicina UBA; Primera Cátedra de Toxicología, Facultad de Medicina UBA
6. CONICET; CeReGeo - FCyt- UAdER
7. CEFYBO-UBA-CONICET; Laboratorio de reproduccion y

metabolismo

8. CEFYBO-UBA-CONICET; Laboratorio de programacion de anomalías metabólicas
marinalabiano@gmail.com

Maternal obesity is associated with increased susceptibility to environmental toxicants, including 3-methylcholanthrene (3MC), a polycyclic aromatic hydrocarbon that activates the aryl hydrocarbon receptor (AHR) and promotes tissue damage. This study aimed to evaluate the effects of maternal obesity on hepatic oxidative stress, protein damage, AHR expression, inflammation, and bone marrow genotoxicity in adult female rat offspring. Female Wistar rats were fed either a standard diet (CT) or a high-fat diet (FD) before mating and throughout lactation. Offspring were weaned onto chow. At postnatal day 60, females received 3MC (0.5 mg/kg, oral gavage, three times/week) or vehicle for seven weeks. Livers and serum were analyzed for TBARS, protein carbonylation, AHR expression (Western blot), IL-1 β (EIA), and DNA damage in bone marrow cells (comet assay). FDV offspring showed an increase in lipoperoxidation and carbonylated proteins compared to controls ($p < 0.05$). Also, exposure to 3MC induced an increase in protein carbonylation only in the controls ($p < 0.05$) and in both controls and FD3MC ($p < 0.05$). IL-1 β levels were increased in CT3MC vs CTV ($p < 0.001$), FDV vs CTV ($p < 0.05$), and FD3MC vs FDV ($p < 0.001$). AHR expression was higher in FDV vs CTV ($p < 0.001$) and FD3MC vs CT3MC ($p < 0.01$). In addition, bone marrow comet assay revealed significant DNA damage in CT3MC vs CTV ($p < 0.001$) and FD3MC vs FDV ($p < 0.01$). These findings demonstrate that maternal obesity enhances vulnerability to 3MC, aggravating hepatic and systemic damage through oxidative stress, protein oxidation, inflammation and bone marrow genotoxicity.

238. O12-05. SEARCH FOR SPERM BINDING SITES FOR S100A9 AND EVALUATION OF ITS CHEMOTACTIC EFFECT

Estefanía Massa¹, Macarena Mendiondo², Marianela Moriconi³, Héctor Guidobaldi⁴, Sergio Ghersevich⁵

1. Universidad Nacional de Rosario; Facultad de Ciencias Médicas
2. Universidad Nacional de Rosario; Bioquímica Clínica-Facultad de Ciencias Bioquímicas y Farmacéuticas
3. UNR; Bioquímica Clínica. Facultad de Ciencias Bioquímicas y Farmacéuticas
4. Universidad Nacional de Córdoba; CEBICEM (UNC), IIBYT (UNC, CONICET)
5. Universidad Nacional de Rosario; Bioquímica Clínica. Facultad de Ciencias Bioquímicas y Farmacéuticas
massaestefania@yahoo.com.ar

Previously, we detected the S100A9 protein in the tubal epithelium and oviductal secretions and found that it modulates in vitro sperm capacitation parameters, such as tyrosine phosphorylation. This study investigated potential sperm receptors for S100A9 and evaluated the protein's effect on sperm chemotaxis. Motile sperm from normozoospermic donors were recovered using the Swim-up technique. The binding of recombinant human S100A9 (hrS100A9) to sperm was assessed via indirect immunofluorescence, revealing three fluorescence patterns: binding to the tail and midpiece; to the head, midpiece, and tail; or no binding. To detect sperm receptors, hrS100A9 was crosslinked with sulfo-SBED reagent and incubated with sperm, followed by UV exposure and biotin transfer to the receptors. Protein bands were analyzed by SDS-PAGE and chemiluminescence, revealing two potential receptors (~76 and ~60 kDa). Chemotaxis assays (custom chambers provided by H. Guidobaldi) using protein gradients showed no significant difference between hrS100A9-treated groups (10^{-9} M: $7.82 \pm 1.37\%$ and 10^{-10} M: $4.83 \pm 3.50\%$) and the progesterone-positive control ($7.91 \pm 3.15\%$, $n=4$, $p > 0.05$). HrS100A9 10^{-9} M showed chemotactic activity similar to that of progesterone. Previous studies have shown that S100A9 interacts with Toll-like receptor 4 (TLR-4) and the receptor for advanced glycation end-products (RAGE) in various cell types. The observed S100A9 binding sites partially coincide with the reported localiza-

tions of TLR-4 and RAGE in spermatozoa. Two potential receptors that may mediate the effects of S100A9 on sperm function were detected but remain to be identified. HrS100A9 exhibits potential chemotactic activity on spermatozoa in vitro.

239. O12-06. SMART NANOGELS IN REPRODUCTIVE MEDICINE: A NEW PLATFORM TO TREAT CHRONIC TESTICULAR INFLAMMATION

Patricia Verónica Jacobo¹, Denisse Ferrer Viñals², Daniela Celaya³, Thaisy Munduruca Pires⁴, Marcelo Rodríguez Peña⁵, Romina Glisoni⁶, María Susana Theas⁷

1. Instituto de Investigaciones Biomédicas (INBIOMED, UBA-CONICET), Facultad de Medicina. UBA, Buenos Aires, Argentina; *Dinámica de la espermatogénesis en el testículo normal y patológico*

2. Instituto de Investigaciones Biomédicas (INBIOMED, UBA-CONICET), Facultad de Medicina. UBA, Buenos Aires, Argentina; *Dinámica de la espermatogénesis en el testículo normal y patológico*

3. Instituto de Investigaciones Biomédicas (INBIOMED, UBA-CONICET), Facultad de Medicina. UBA, Buenos Aires, Argentina; *Dinámica de la espermatogénesis en el testículo normal y patológico*

4. Instituto de Investigaciones Biomédicas (INBIOMED, UBA-CONICET), Facultad de Medicina. UBA, Buenos Aires, Argentina; *Dinámica de la espermatogénesis en el testículo normal y patológico*

5. Universidad de Buenos Aires, Facultad de Medicina, Buenos Aires, Argentina; *Dinámica de la espermatogénesis en el testículo normal y patológico*

6. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Nanobiotecnología (NANOBIOTEC UBA-CONICET), Buenos Aires, Argentina; *Nanobiomateriales*

7. Instituto de Investigaciones Biomédicas (INBIOMED, UBA-CONICET), Facultad de Medicina. UBA, Buenos Aires, Argentina; *Dinámica de la espermatogénesis en el testículo normal y patológico*
 pjacobov@fmed.uba.ar

Chronic inflammation of the testis and epididymis is a growing cause of male infertility, affecting an increasing number of couples and contributing to rising healthcare costs. Experimental autoimmune epididymo-orchitis (EAEO) is a validated rodent model that closely mimics human testicular pathology and impaired spermatogenesis. However, current therapies lack tissue specificity and long-term efficacy, as systemic drug delivery is restricted by the blood-testis barrier and efflux pumps. We developed a minimally invasive, long-acting therapeutic strategy based on thermosensitive nanoplateform Pluronic® F127 micelles for targeted drug delivery to inflamed reproductive tissues and their draining lymph nodes (LN). Normal and EAEO rats received a single intratesticular injection (100 µL) of indocyanine green (ICG)-loaded Pluronic® F127 micelles (ICG-F127, 37.5 µg/mL ICG, 25% w/v F127) or free ICG (37.5 µg/mL). In-vivo fluorescence imaging was performed at different point times during 13 days post-injection. Ex-vivo fluorescence signal was assessed in testis, epididymis, vas deferens, seminal vesicles, and regional LN. ICG-F127 remained in the normal testis for over 13 days, with uptake in the epididymis on day 13 and stable fluorescence and selective accumulation in the draining LN from day 5 onward. In EAEO-rats, fluorescence became detectable in the ipsilateral epididymis as early as day 10, suggesting a differential permeability associated with inflammation. In contrast, free ICG showed rapid clearance and no targeted distribution. This thermosensitive nanoplateform enables sustained, site-specific drug delivery from the testis to epididymis and regional LN, representing a novel strategy to modulate chronic inflammation of reproductive tissues and preserve male fertility.

240. O12-07. ALTERED OVARIAN AND DECIDUAL PPAR PATHWAYS IN DIABETIC PREGNANT DAMS: RELATIONSHIP WITH OVARIAN MICRORNAS AND REGULATION BY MATERNAL DIETS ENRICHED IN EXTRA VIRGIN OLIVE OIL

Florencia Schibert¹, Cintia Romina Gatti², Virginia Taylor³, Evangelina Capobianco⁴, Alicia Jawerbaum⁵

1. Centro de Estudios Farmacológicos y Botánicos-UBA, CONICET; *Reproducción y Metabolismo*

2. Centro de Estudios Farmacológicos y Botánicos-UBA, CONICET; *Reproducción y Metabolismo*

3. Centro de Estudios Farmacológicos y Botánicos-UBA, CONICET; *Reproducción y Metabolismo*

4. Centro de Estudios Farmacológicos y Botánicos-UBA, CONICET; *Reproducción y Metabolismo*

5. Centro de Estudios Farmacológicos y Botánicos-UBA, CONICET; *Reproducción y Metabolismo*
 florenciaschibert1992@gmail.com

Introduction: Previously, we identified a proinflammatory state in the decidua of diabetic rats. PPARs are nuclear receptors that regulate the proinflammatory milieu. PPARs are activated by oleic acid, the major component of extra virgin olive oil (EVOO), and regulated by microRNAs, possibly originated in the ovary. **Aim:** To evaluate proinflammatory state markers, decidua and ovarian PPARs expression, and ovarian microRNAs targeting PPARs in pregnant diabetic rats fed or not with an EVOO-enriched diet. **Methods:** A mild pregestational diabetic rat model was induced by neonatal administration of streptozotocin (90 mg/kg sc). Control and diabetic females bred to healthy males, were fed a diet supplemented or not with 6% EVOO on pre-conception and pregnancy. On day 13.5 of pregnancy samples were collected for stem-loop-RTqPCR, RT-qPCR and WB assays. **Results:** The decidua of diabetic rats showed increased Il-6 expression and FABP4 levels (+323% and +144%, respectively, p<0.05 vs. controls). Reduced PPARgamma expression was observed in decidua and ovary of diabetic dams (-66% and -44% respectively, p<0.05 vs. controls). Reduced PPARalpha expression was observed in decidua and ovary of diabetic dams (-66% and -53% respectively, p<0.05 vs. controls). Increased levels of miR-27 (targeting PPARgamma) and miR-21 (targeting PPARalpha) were observed in the ovary of diabetic dams (+176% and +258% respectively, p<0.05 vs. controls). Most of these alterations were not observed in the diabetic dams fed the EVOO-enriched diet. **Conclusions:** In diabetic rats, the decidual proinflammatory state is possibly related to dysregulation in microRNAs targeting PPAR pathways, alterations mostly prevented by an EVOO-enriched maternal diet.

241. O12-08. COMBINED EFFECTS OF DIET-INDUCED OVERWEIGHT AND 3-METHYLCHOLANTHRENE EXPOSURE ON TESTICULAR HOMEOSTASIS IN RATS

Jeremias Pablo Flores Quiroga¹, Victoria Dechamps², Marina Labiano³, Florencia Heinecke⁴, Rocio Galarza⁵, Analía Elizabeth Cortez⁶, Juan José Casal⁷, Nora Alicia Martínez⁸, Verónica White⁹, Alicia G. Faletti¹⁰

1. CEFYBO-UBA-CONICET; *Laboratorio de Endocrinología Reproductiva y Laboratorio de Programación de Anomalías Metabólicas*

2. CEFYBO-CONICET-UBA; *Laboratorio de Programación de Anomalías Metabólicas*

3. CEFYBO-CONICET-UBA; *Laboratorio de Programación de Anomalías Metabólicas*

4. CEFYBO-CONICET-UBA; *Laboratorio de Programación de Anomalías Metabólicas*

5. CONICET; *CeReGeo-FCyT-UAdER*

6. Primera Cátedra de Toxicología-Facultad de Medicina-UBA

7. IFIBIO-UBA-CONICET/UBA; IFIBIO-UBA-CONICET/UBA

8. IFIBIO-UBA-CONICET

9. CEFYBO-UBA-CONICET; *Laboratorio de Programación de Anomalías Metabólicas*

10. CEFYBO-UBA-CONICET; *Laboratorio de Endocrinología Reproductiva*
 jeropablo@gmail.com

We previously reported that both diet-induced overweight and exposure to 3-methylcholanthrene (3MC), an environmental

polycyclic aromatic hydrocarbon, independently impair testicular structure and sperm quality. Here, we aimed to investigate the individual and combined effects of diet-induced overweight and 3MC exposure on testicular homeostasis, with a focus on functional and structural integrity, and molecular alterations in rats. Prepubertal Sprague Dawley males were fed either a standard (SD) or/and cafeteria diet (CD) and administered vehicle (V) or 3MC (0.1 mg/kg i.p.) three times weekly for 40 days, generating four experimental groups (SDV, CDV, SD3MC, CD3MC). Testicular cell populations and spermatogenic dynamics were analyzed histologically, protein expression of key steroidogenic enzymes (STAR, CYP11A1, 17 β -HSD) by Western blotting, while transcriptomic changes were evaluated by RNA-seq (padj1). 3MC disrupted the spermatogenic cycle by reducing the number of tubules in early stages (I–VI) and accumulating stages VII–VIII ($p < 0.01$ vs SDV), whereas overweight impaired late stages (XII–XIV, $p < 0.05$ vs SDV). Both conditions decreased spermatogonia and Sertoli cells, while only 3MC increased Leydig cells ($p < 0.001$). 3MC reduced STAR and CYP11A1 protein levels ($p < 0.05$ vs SDV), whereas 17 β -HSD was upregulated in CD3MC ($p < 0.05$). Transcriptomic analysis showed overweight upregulated *Ndufa3* and *Scd*, implicating mitochondrial dysfunction and altered lipid metabolism. Conversely, 3MC induced *Cyp2a3* and *Myod1* (xenobiotic response, impaired differentiation) and downregulated *Myb* (proliferation regulator). Combined exposure enhanced inflammatory responses, evidenced by increased *Ifit1b1*, decreased *Lilrb2* and *Pirb*, and upregulation of adhesion-related genes (*Tlr2*, *Micb*, *Tmem176a/b*). These results show that overweight and 3MC act synergistically to disrupt testicular homeostasis, highlighting the male reproductive system as a particularly vulnerable target of obesogens.

242. O12-09. GENERATION OF A REPORTER CELL TO DETERMINE THE BIOLOGICAL ACTIVITY OF GLYCOPROTEIN HORMONES

Tulio Battaglia¹, Agustina Gugliotta², Carlos Javier Villaraza³, Hugo H. Ortega⁴, Belkis Marelli⁵, Florencia Rey⁶, Claudio C. Prieto⁷

1. ICIVET Litoral (UNL-CONICET); Centro de Medicina Comparada
 2. Centro Biotecnológico del Litoral (CBL) - Facultad de Bioquímica y Ciencias Biológicas (FBCB) - Universidad Nacional del Litoral (UNL); Laboratorio de Desarrollo Biotecnológico (LDB)
 3. Centro Biotecnológico del Litoral (CBL) - Facultad de Bioquímica y Ciencias Biológicas (FBCB) - Universidad Nacional del Litoral (UNL); Laboratorio de Desarrollo Biotecnológico (LDB)
 4. ICIVET Litoral (UNL-CONICET); Centro de Medicina Comparada
 5. ICIVET Litoral (UNL-CONICET); Centro de Medicina Comparada
 6. ICIVET Litoral (UNL-CONICET); Centro de Medicina Comparada
 7. Centro Biotecnológico del Litoral (CBL) - Facultad de Bioquímica y Ciencias Biológicas (FBCB) - Universidad Nacional del Litoral (UNL); Laboratorio de Desarrollo Biotecnológico (LDB)
- tuliobattaglia@gmail.com

Equine chorionic gonadotrophin (eCG) is a glycoprotein hormone widely used in veterinary treatments whose efficacy strongly depends on its biological activity. The aim of this study was to develop a reporter cell line to assess biological activity of glycoprotein hormones. CHO-K1 cells were genetically modified to express the bovine follicle-stimulating hormone receptor (FSHR) through three rounds of lentiviral transduction, followed by progressive selection with puromycin. Clones were obtained by the limiting dilution method. The expression of the receptor was assessed by confocal microscopy and flow cytometry. The clone showing the highest receptor expression was subjected to three additional rounds of lentiviral transduction with the reporter vector pLminP_Luc2P_RE16 to establish the luciferase reporter system. Reporter clones were again isolated by limiting dilution, and those with >95% positive cells and

high mean fluorescence intensity were selected. Reporter gene assays were performed using recombinant bovine FSH at 63 and 630 International Units per milliliter, with 4 and 24-h incubation. Clones that showed significant increases ($P < 0.05$) in Relative Light Units (RLU) compared with unstimulated controls were further tested with different glycoprotein hormones (pregnant mare serum gonadotrophin, recombinant eCG, human chorionic gonadotrophin, and recombinant human FSH). Significant increases in RLU ($P < 0.05$) were observed for specific hormones with receptor affinity. These results indicate the successful generation of a reporter cell line expressing FSHR and a luciferase-based reporter system, providing a useful tool for assessing the biological activity of glycoprotein hormones.

POSTERS 13 - SAIC - NEUROCIENCIAS

DATE & TIME: 19/11/2025 9:00 - 10:30 H

Chairs: Juan Beauquis, Karina Formoso

243. P13-01. EFFECT OF AUTOPHAGY INHIBITION AS A NEUROPROTECTIVE MECHANISM IN A MODEL OF PARKINSONISM INDUCED BY 6-HYDROXYDOPAMINE

Daniel Merino¹, María Luz Kerchner², Emilia Nanfra³, Agustina Lagos⁴, Destiny Berón⁵, Ricardo Cabrera⁶, Natalia González⁷

1. Facultad de Ingeniería. Universidad de Mendoza; LINCE-INBIOMED-IMBECU-CONICET
 2. Facultad de Ingeniería. Universidad de Mendoza; LINCE-INBIOMED-IMBECU-CONICET
 3. Facultad de Ciencias Médicas. Universidad de Mendoza; LINCE-INBIOMED-IMBECU-CONICET
 4. Facultad de Ciencias Médicas; LINCE-INBIOMED-IMBECU-CONICET
 5. Facultad de Ingeniería. Universidad de Mendoza; LINCE-INBIOMED-IMBECU-CONICET
 6. Facultad de Ciencias Médicas. Universidad de Mendoza; LINCE-INBIOMED-IMBECU-CONICET
 7. Facultad de Ciencias Médicas@um.edu.ar; LINCE-INBIOMED-IMBECU-CONICET
- fd.merino@alumno.um.edu.ar

This study describes a potential neuroprotective strategies for Parkinson's disease, using a rodent model of hemiparkinsonism induced by an injection of 6-hydroxydopamine (6-OHDA). The mechanisms of neurodegeneration in this disease are linked to oxidative stress, mitochondrial dysfunction, and cellular energy imbalances. The study proposes that autophagy may act as a neuroprotective mechanism. The research evaluated the effects of chloroquine (CQ), which affects autophagy, alone or combined with the neuroactive steroids estradiol (E2) and progesterone (P4). To understand the role of estrogen receptors, they used tamoxifen (T), a receptor blocker. Neuroprotective effects were assessed by measuring muscle electrical activity in male rats, analyzing the mean amplitude (MA), average contraction duration (ACD), and activity time (AT). Data were expressed as mean+SEM and analyzed using two-way ANOVA with Bonferroni post hoc test. The results showed that CQ alone significantly increased MA in rats with hemiparkinsonism. The combination of E2 and P4 further enhanced this effect. Interestingly, blocking estrogen receptors with tamoxifen decreased MA in control groups but increased it in the hemiparkinsonism group treated with the drug combination. Regarding ACD, CQ increased it in the hemiparkinsonism group, and T intensified this effect. The AT was also significantly increased by CQ, with the addition of E2 and P4 causing a further increase. In conclusion, chloroquine, E2, and P4 exert a neuroprotective effect against 6-OHDA-induced dopaminergic damage. This protection seems to involve a synergistic genomic action dependent on E2 signaling and a non-genomic action mediated by P4.

244. P13-02. IMPACT OF PERINATAL PROTEIN MALNUTRITION ON NEURONAL PLASTICITY AND BEHAVIOR: ROLE OF ENVIRONMENTAL ENRICHMENT

Erika I. Georgieff¹, Lucía Janicki², Mariela Chertoff³, Eduardo T. Cánepa⁴

1. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), CONICET- Universidad de Buenos Aires. Buenos Aires, Argentina.; Laboratorio de Neuroepigenética y Adversidades Tempranas, Departamento de Química Biológica Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina.
 2. Facultad de Ciencias Exactas y Naturales - Universidad de Buenos Aires. Buenos Aires, Argentina; Laboratorio de Neuroepigenética y Adversidades Tempranas, Departamento de Química Biológica Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina.
 3. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), CONICET- Universidad de Buenos Aires. Buenos Aires, Argentina.; Laboratorio de Neuroepigenética y Adversidades Tempranas, Departamento de Química Biológica Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina.
 4. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), CONICET- Universidad de Buenos Aires. Buenos Aires, Argentina.; Laboratorio de Neuroepigenética y Adversidades Tempranas, Departamento de Química Biológica Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina.
 georgiefferikaines@gmail.com

Perinatal protein malnutrition is a critical factor that impairs neuronal development and plasticity, leading to persistent alterations in brain structure and function that manifest as behavioral deficits and increased vulnerability to anxiety and depression. Exposure to an enriched environment (EE) significantly enhances learning, memory, and emotional responses. These effects are supported by changes in genes regulating neuronal structure, synaptic plasticity, neurotrophin signaling, and stress response. In this study, we examined the molecular and behavioral consequences of perinatal protein malnutrition in mice and the potential of EE to counteract these alterations. After weaning, animals were housed in either a standard environment (EN) or an EE for five weeks. Behavioral parameters, plasma corticosterone levels, and the expression of genes related to stress response, synaptic plasticity, and glutamatergic neurotransmission in the ventral hippocampus (vHP) were evaluated. Considering the crucial role of dendritic spines in neuronal networks, memory, and cognitive functions, along with the generally accepted view that their structure and function are essential for learning, dendritic morphology in the hippocampus was analyzed using Golgi-Cox staining, and arborization was assessed through Sholl analysis. This study provides new insights into the mechanisms by which perinatal protein malnutrition alters neuronal plasticity and highlights the potential of environmental enrichment to mitigate these effects.

245. P13-03. LONGITUDINAL ANALYSIS OF COGNITIVE DECLINE AND AMYLOID-B LOAD IN A TRANSGENIC RAT MODEL OF ALZHEIMER'S-LIKE BRAIN AMYLOIDOSIS: DISENTANGLING SEXUAL DIMORPHISM AND AGING TO IMPROVE PRECLINICAL MODELING

Martin Habif¹, Mauro Exequiel Alfaro², María Belén González³, Ricardo Francisco Allegri⁴, Diana Alicia Jerusalinsky⁵

1. Instituto de Biología Celular y Neurociencia (IBCN) "Prof. EDUARDO DE ROBERTIS". Facultad de Medicina - Universidad de Buenos Aires & CONICET; Laboratorio de Neuroplasticidad y Neurotoxinas (LaNyN)
2. Instituto de Biología Celular y Neurociencia (IBCN) "Prof. EDUARDO DE ROBERTIS". Facultad de Medicina - Universidad de Buenos Aires & CONICET; Laboratorio de Neuroplasticidad y Neurotoxinas (LaNyN)
3. Instituto de Biología Celular y Neurociencia (IBCN) "Prof. EDUARDO DE ROBERTIS". Facultad de Medicina - Universidad de Buenos Aires & CONICET; Laboratorio de Neuroplasticidad y Neurotoxinas (LaNyN)
4. FLENI (Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia); Neurología Cognitiva, Neuropsicología y Neuropsiquiatría
5. Instituto de Biología Celular y Neurociencia (IBCN) "Prof.

EDUARDO DE ROBERTIS". Facultad de Medicina - Universidad de Buenos Aires & CONICET; Laboratorio de Neuroplasticidad y Neurotoxinas (LaNyN)
 mhabif@fmed.uba.ar

Sex differences in biology were historically overlooked, largely because females were excluded from experimental research, leaving critical gaps in women's health knowledge. Only recently have sex-dependent variations been recognized in disease prevalence, risk, and treatment outcomes. The McGill-R-Thy1-hAPP (Tg) transgenic rat, which harbors two familial Alzheimer's disease (AD) mutations (Swedish/Indiana), provides a robust model to examine such differences. We assessed wild-type (wt) and hemizygous (Tg+/-) rats of both sexes at 4 and 12 months (mo). All groups displayed habituation in the open field (OF) task. In inhibitory avoidance (IA), both wt and Tg+/- females acquired long-term memory (LTM), though retention was maintained only in wt females; Tg+/- males failed to form memory. In novel object recognition (NOR), LTM consolidation occurred exclusively in wt rats. In novel object location (NOL), discrimination was observed in wt and Tg+/- females at 4 mo, but at 12 mo only wt females succeeded. Cognitive impairments were more severe in Tg+/- males and progressed with age. Quantification of brain amyloid- β revealed higher load in males at 4 mo and increased sex-related variability at 12 mo. These findings highlight marked sexual dimorphism in learning and associative memory, particularly in hippocampus-dependent tasks. In the Tg model, such differences are most evident in aversive and spatial memory domains. Considering sex as a biological variable is therefore crucial to refine preclinical AD models and to advance toward precision medicine, enabling more personalized and sustainable strategies for patient care.

246. P13-04. THE EFFECTS OF FLUOXETINE ON FEMALE SOCIAL BEHAVIOR DEPEND ON THE TIMING OF EARLY-LIFE EXPOSURE

Martin G Codagnone¹, Jeremías M Cuello², Giuliana Colonna Soldavini³, María Belén Gomez⁴, Paula D Prince⁵, Analía Reinés⁶

1. Universidad Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Farmacología. CONICET-Universidad de Buenos Aires, Instituto de Biología Celular y Neurociencia "Prof. de Robertis" (IBCN); Laboratorio de neurofarmacología molecular
2. Universidad Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Farmacología. CONICET-Universidad de Buenos Aires, Instituto de Biología Celular y Neurociencia "Prof. de Robertis" (IBCN); laboratorio de neurofarmacología molecular
3. Universidad Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Farmacología. CONICET-Universidad de Buenos Aires, Instituto de Biología Celular y Neurociencia "Prof. de Robertis" (IBCN); laboratorio de neurofarmacología molecular
4. CONICET-Universidad de Buenos Aires, Instituto de Biología Celular y Neurociencia "Prof. de Robertis" (IBCN); Laboratorio de neurofarmacología molecular
5. CONICET-Universidad de Buenos Aires, Instituto de Biología Celular y Neurociencia "Prof. de Robertis" (IBCN); Laboratorio de neurofarmacología molecular
6. Universidad Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Farmacología. CONICET-Universidad de Buenos Aires, Instituto de Biología Celular y Neurociencia "Prof. de Robertis" (IBCN); Laboratorio de neurofarmacología molecular
 martincodagnone@gmail.com

Social interaction is a salient feature of the human brain. Although some neurodevelopmental disorders exhibit social deficits, little is known about their neurobiology. We previously showed that for male rats, the effects of the antidepressant fluoxetine on juvenile social behavior depend on the time-window of exposure. However, it had not been determined whether this time-dependent vulnerability is shared among females. To address this gap, we administered flu-

oxetine (sc.; 10 mg/kg) or saline to female Wistar rats during one of two putative critical windows: the pre-weaning (PreWean; P12-19) or weaning (Wean; P20-27) periods. Behaviour was evaluated between P30-40 in an unfamiliar group-matched pair social paradigm. We studied social play, non-play and recognition behaviors and behaviors directed to the environment and self. Regarding play behaviors, Wean females did fewer pinning bouts and PreWean females had a longer latency to the first pinning. Both groups showed preserved pinning duration. The latency to the first pouncing event was greater for both PreWean and Wean females, but the number and duration of this behavior were similar to controls. None of the treatments impacted female social non-play behaviors or social recognition. PreWean exposure to fluoxetine increased the latency to the first rearing event, while Wean exposure increased rearing duration. Additionally, PreWean exposure decreased the duration of self-grooming events, and Wean exposure decreased the latency to the first of these events. Our results indicate that the timing of early-life fluoxetine exposure is critical in determining its lasting and distinct effects on female juvenile social behaviour.

247. P13-05. BIOMARCADOREZ: TOWARD PRODRONTAL IDENTIFICATION AND STRATIFICATION OF ADOLESCENTS AT HIGH RISK OF DEVELOPING SCHIZOPHRENIA

Martina Belmonte¹, Sofia Lopez Cardoso², Diego Gelman³

1. IBYME; Desarrollo del Sistema Nervioso

2. IBYME; Desarrollo del Sistema Nervioso

3. IBYME; Desarrollo del Sistema Nervioso

m.belmonte@ibyme.org.ar

Schizophrenia is a devastating disorder whose etiology remains unknown. Its diagnosis relies exclusively on observable signs and symptoms that typically emerge in late adolescence or early adulthood. Patients with schizophrenia exhibit cognitive deficits, depression, social withdrawal, as well as metabolic and immunological abnormalities. Nevertheless, the most prominent manifestations are the positive symptoms, such as hallucinations and delusions. These are managed through antipsychotic treatment, although such interventions fail to alleviate cognitive, negative, immunological, or metabolic symptoms. By employing a murine model of schizophrenia, we aim to identify differential biomarkers to develop an objective early diagnosis, as well as pharmacological strategies targeting unattended symptoms. Adult mutant animals display molecular, cellular, physiological, and behavioral phenotypes closely resembling those described in patients. Moreover, they exhibit glucose intolerance, dysregulated fatty acid levels, microglial reactivity, and a distinctive blood profile. A longitudinal assessment of blood parameters, glucose tolerance, and fatty acids across the transition from adolescence to adulthood reveals a differential pattern in the mouse model relative to controls. In parallel, behavioral analyses demonstrate phenotypes associated with negative symptoms in the mutant group, which emerge prior to adulthood. Our findings suggest that combined blood and behavioral analyses may hold translational value for stratifying adolescents at high risk of developing schizophrenia. We propose to assess the clinical potential of our results through the BIOMarcadorEZ project, a retrospective study using complete blood count data from diagnosed patients.

248. P13-06. EFFECT OF HISTONE DEACETYLASE INHIBITOR ON A β CLEARANCE IN AN EXPERIMENTAL MODEL OF ALZHEIMER'S DISEASE

Ibanez J¹, Alba R², MAYRA CORTEZ³, Coria Lucero C⁴, Ledezma C⁵, Torales P⁶, Delgado S¹⁷, DARO C. RAMIREZ⁸, SANDRA E. GOMEZ MEJIBA⁹, ANA C. ANZULOVICH¹⁰, Navigatore Fonzo L¹¹

1. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-

IMIBIO-SL-CONICET-UNSL, Argentina,

2. University of Villa Mercedes, Argentina

3. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-

IMIBIO-SL-CONICET-UNSL, Argentina

4. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-

IMIBIO-SL-CONICET-UNSL, Argentina,

5. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-

IMIBIO-SL-CONICET-UNSL, Argentina,

6. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-

IMIBIO-SL-CONICET-UNSL, Argentina

7. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-

IMIBIO-SL-CONICET-UNSL, Argentina

8. IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and

Translational Medicine, CONICET-San Luis & National Univer-

sity of San Luis, 5700 San Luis, Argentina. Laboratory of Nu-

trition and Experimental Therapeutics CCT-San Luis, National

University of San Luis, San Luis, 5700-San Luis, Argentina.

9. IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and

Experimental Therapeutics CCT-San Luis, National University

of San Luis, San Luis, 5700-San Luis, Argentina.

10. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-

IMIBIO-SL-CONICET-UNSL, Argentina

11. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-

IMIBIO-SL-CONICET-UNSL, Argentina

ibanezjohanna233@gmail.com

Alzheimer's disease (AD) is a leading cause of dementia in elderly individuals. The characteristics of AD include abnormal deposition of amyloid- β (A β) plaques, synaptic degeneration, and neuronal loss. A β is considered a key contributor to the pathophysiology of AD. Acid valproic acid (AV), a histone deacetylase inhibitor, plays important roles in promoting the release of neurotrophic factors and inducing neurogenesis. Previously, we reported that AV improved cognitive performance in the same experimental model. Considering these observations, the objective of this study was to evaluate the effects of AV on the expression of A β , BDNF/TrkB and apolipoprotein E (APOE) in the hippocampus (Hp) of A β -injected rats. Four-month-old male Holtzman rats were divided into three groups: (1) control (saline solution), (2) A β -injected (A β aggregates-10 μ g), and (3) same as (2) and AV (200 mg/kg, in the drinking water for 15 days). The rats were injected into the lateral ventricle (coordinates: AP: -1 mm, L: 1.5 mm, and DV: -3.5 mm). The rats were maintained under 12 h light:12 h dark and received water and food ad libitum. BDNF/TrkB transcript levels were determined by RT-PCR, and A β and Apo E levels were analyzed by immunoblotting in Hp samples. We found that the A β -injected group presented a decrease in the ApoE and BDNF/TrkB levels accompanied by an increase in the A β level. Concomitantly, AV increased the levels of ApoE and BDNF/TrkB in the Hp of A β -injected rats. Our encouraging results provide a new basis for the use of VA in the treatment of AD.

249. P13-07. APPLICATION OF THE PANSS SCALE IN THE CHARACTERIZATION OF PSYCHOTIC SYMPTOMS IN A GROUP OF PATIENTS WITH DRUG RESISTANT EPILEPSY

Antonietta Rubina¹, Luciana D'Alessio²

1. IBCN - UBA CONICET; Laboratorio de Epilepsia, Conducta y Neuropatología

2. IBCN - UBA CONICET; Laboratorio de Epilepsia, Conducta y Neuropatología

antorubina@hotmail.com

The assessment of psychotic disorders in epilepsy it's a situation that generates many difficulties at the moment to differentiate their origins (ictal, psychiatric or both); however, a few tools exist to identify, categorize, and quantify these symptoms. Objectives: examine the presence of positive and negative psychotic symptoms in a population of patients with drug-resistant epilepsy (DRE), and establish the prevalence of psychotic disorders (DSM-IV/Ictal Classification of Psychoses). Methodology: patients consecutively admitted to the VEEG Unit of Ramos Mejia Hospital were evaluated between August 2024 and June 2025. The following were performed: complete neurological, neuropsychological, and psychiatric evaluations (SCID-I, SCID-II, and PANSS), and complementary neuroimaging studies. Results: forty three patients were included (n=19 [44.19%] men, n=23 [55.81%] women; mean age 35 years [SD=12.27892]). The estimated prevalence of psychotic disorder in the assessed population was 16.27%. It is observed that within the positive symptoms, a predominance of the item "behavioral disorganization" and within the negative ones "affective dullness", "poor contact" and "difficulty in abstract thinking". Con-

clusion: based on the results obtained from the patient's contextual analysis, the PANSS scale demonstrates its usefulness in the clinical assessment of psychotic symptoms in patients with DRE.

250. P13-08. EFFECT OF I.C.V. AGGREGATED A β -AMYLOID (1-42) ON DAY-NIGHT PATTERNS OF BEHAVIORAL AND ANXIETY-RELATED PARAMETERS IN THE RAT

Mayra Cortez¹, Coria Lucero C², Alba R³, López M⁴, Toledo F⁵, Delgado S⁶, Dario C Ramirez⁷, Sandra E. Gomez Mejiba⁸, Anzulovich A⁹, Navigatore Fonzo L¹⁰

1. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology, IMIBIO-SL-CONICET-UNSL, San Luis, 5700-San Luis, Argentina.

2. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-IMIBIO-SL-CONICET-UNSL, Argentina

3. University of Villa Mercedes, Argentina

4. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-IMIBIO-SL-CONICET-UNSL, Argentina

5. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-IMIBIO-SL-CONICET-UNSL, Argentina,

6. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-IMIBIO-SL-CONICET-UNSL, Argentina

7. IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.

8. IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.

9. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-IMIBIO-SL-CONICET-UNSL, Argentina

10. IMIBIO-CCT-SL-CONICET; Laboratory of Chronobiology-IMIBIO-SL-CONICET-UNSL, Argentina, maybcortez@gmail.com

Alzheimer's disease (AD) pathology is commonly associated with cognitive decline but is also associated with anxiety and depression. Recently, interest has increased in the behavioral and psychological signs and symptoms of dementia. One especially notable circadian disturbance is the so-called "sundowning syndrome," which is characterized by exacerbated anxiety, agitation, locomotor activity, and delirium occurring in the hours before bedtime. Little is known about temporal patterns in anxiety and agitation, and the neurobiological basis of these rhythms remains unspecified. The objective of this study was to investigate the effects of an intracerebroventricular (i.c.v.) injection of amyloid beta peptide (1-42) on day-night variation in behavioral and anxiety-related parameters in rats. The groups were defined as follows: control (CO) and A β -injected (A β). The rats were maintained under 12 h light: 12 h dark conditions and received food and water ad libitum throughout the entire experiment. The results of the open field test were determined for both experimental groups at ZT2 and ZT14. Compared with the control animals, the A β group presented a reduction in the number of lines crossed in the open field test. The frequency of rearing was also significantly decreased in the A β -injected group. On the other hand, compared with the control animals, the A β group presented significantly increased freezing time and number of bowel movements. The results of the present study show that the administration of A β -amyloid in rats generates behavioral alterations detectable in the open field test, showing both an exploratory deficit and an increase in anxiety-like behaviors.

POSTERS 14 - AAFE - FARMACOLOGÍA 4

DATE & TIME: 19/11/2025 9:00 - 10:30 H

Chairs: Ventura Simonovich, María Laura Barreiro Arcos

251. P14-01. ISOLATION AND CHARACTERIZATION OF BDIP-SP1, A THROMBIN-LIKE SERINE PROTEASE FROM BOTHROPS DIPORUS VENOM

Gisela L. Lopez¹, Caroline R. C. Costa², Emidio B. Neto³, Laura Leiva⁴, Daniel C. Pimenta⁵, Marcos Hikari Toyama⁶, Luciano S. Fusco⁷

1. Instituto de Química Básica y Aplicada del Nordeste Argentino (Consejo Nacional de Investigaciones Científicas y Técnicas - Universidad Nacional del Nordeste); Grupo de Investigación en Proteínas (GrInPro)

2. Instituto de Biociências - Câmpus do Litoral Paulista - São Vicente. UNIVERSIDADE ESTADUAL PAULISTA "JULIO DE MESQUITA FILHO"; BIOMOLPEP

3. Instituto Butantan, São Paulo, SP, Brasil; Laboratorio de Bioquímica y Biofísica

4. Instituto de Química Básica y Aplicada del Nordeste Argentino (Consejo Nacional de Investigaciones Científicas y Técnicas - Universidad Nacional del Nordeste); Grupo de Investigación en Proteínas (GrInPro)

5. Instituto Butantan, São Paulo, SP, Brasil; Laboratorio de Ecología y Evolución

6. Instituto de Biociências - Câmpus do Litoral Paulista - São Vicente. UNIVERSIDADE ESTADUAL PAULISTA "JULIO DE MESQUITA FILHO"; BIOMOLPEP

7. Instituto de Química Básica y Aplicada del Nordeste Argentino (Consejo Nacional de Investigaciones Científicas y Técnicas - Universidad Nacional del Nordeste); Grupo de Investigación en Proteínas (GrInPro)

giselopeczyaccuzzi@gmail.com

Snake venom serine proteases (SVSPs), depending on their effects on the hemostatic system, can be classified as thrombin-like enzymes (TLE-SVSPs), capable of cleaving fibrinogen and promoting fibrin formation through the release of fibrinopeptides A α and/or B β . In this study, we report for the first time the isolation and the biochemical and functional characterization of BdipSP1, a thrombin-like protease from Bothrops diporus venom, a medically relevant species in northeastern Argentina. The enzyme was purified by two chromatographic steps, size-exclusion and reverse-phase chromatography. SDS-PAGE revealed a ~21–22 kDa protein under non-reducing conditions and two smaller subunits under reducing conditions, confirming its heterodimeric nature and fraction homogeneity. The fraction also displayed activity on specific substrates (BAPNA and a thrombin-specific chromogenic substrate). Proteomic analysis of tryptic digests and database comparison confirmed its identity as an SVSP and similarity to other serine proteases. Functionally, BdipSP1 exhibited fibrinogenolytic activity, preferentially degrading the B β chain and, to a lesser extent, the A α chain. Notably, it also hydrolyzed the γ chain, which would imply an inability to form stable fibrin. The minimum coagulant dose was estimated at 3.41 μ g. Neutralization assays demonstrated that F(ab')₂ fragments of the INPB antivenom completely inhibited the coagulant activity of both BdipSP1 and the whole venom. This first characterization of a heterodimeric fibrinogenolytic TLE-SVSP from B. diporus expands our understanding of its pathophysiology. Furthermore, the growing interest in TLE-SVSPs as defibrinogenating agents highlights the value of BdipSP1 as a model for future pharmacological and medical applications.

252. P14-02. VALIDATION OF A DPCR-BASED ASSAY FOR QUANTIFICATION OF DONOR-DERIVED CELL-FREE DNA IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS

Agostina Arrigone¹, Guido Trezeguet Renatti², Matias Moragas³, Daniela Fernandez Souto⁴, Cecilia Gamba⁵, Marcelo Dip⁶, Oscar Imventarza⁷, Esteban Halac⁸, Paula Schaiquevich⁹

1. Hospital de Pediatría JP Garrahan; Unidad de Tratamientos Innovadores

2. Hospital de Pediatría JP Garrahan. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Unidad de Tratamientos Innovadores

3. Hospital de Pediatría JP Garrahan. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Unidad de Virología y Epidemiología Molecular

4. Hospital de Pediatría JP Garrahan; Laboratorio de Histo-compatibilidad, Centro Regional de Hemoterapia

5. Hospital de Pediatría JP Garrahan; Laboratorio de Histo-compatibilidad, Centro Regional de Hemoterapia

6. Hospital de Pediatría JP Garrahan; Servicio de Trasplante

Hepatico

7. Hospital de Pediatría JP Garrahan; Servicio de Trasplante Hepático

8. Hospital de Pediatría JP Garrahan; Servicio de Trasplante Hepático

9. Hospital de Pediatría JP Garrahan. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Unidad de Tratamientos Innovadores

agostinarrigone@gmail.com

Donor-derived cell-free DNA (dd-cfDNA) is a promising non-invasive biomarker for allograft monitoring and transplant surveillance. Current quantification methods, such as next-generation sequencing (NGS), are often expensive and time-consuming, whereas droplet digital PCR (ddPCR) offers a cost-effective and rapid alternative. This study aimed to develop and validate a ddPCR-based method for quantifying dd-cfDNA in pediatric liver transplant recipients (PLTR) and to compare it with NGS. Donor and recipient genomic DNA were genotyped using biallelic deletion/insertion polymorphisms (DIPs). Genomic DNA from healthy volunteers was sonicated and mixed in different proportions to simulate donor- and recipient-derived cfDNA. DNA input, primer concentration, and annealing temperature were optimized. Analytical performance was evaluated in terms of sensitivity, precision, and linearity, with a coefficient of variation (CV) 0.99. In PLTR samples, ddPCR and NGS results were highly correlated ($p = 0.88$, $p < 0.0001$, $n = 19$). Mean bias was +0.33%, with limits of agreement from -2.03 to +2.69, and no systematic trend across concentrations. This validated ddPCR assay represents a reliable and affordable alternative to NGS for dd-cfDNA monitoring, with potential clinical applicability for early detection of graft injury and timely intervention in PLTR.

253. P14-03. MILTEFOSINE-LOADED PLURONIC F127 POLYMERIC MICELLES FOR TARGETING HELA AND H358 CANCER CELLS: DEVELOPMENT, CHARACTERIZATION AND IN VITRO EVALUATION

Johanna Karina Valenzuela Oses¹, Sandro Gomes-Filho², Felipe Lourenco³, Daniela Bassères⁴, Mónica Cristina García⁵

1. Universidad Nacional de Córdoba; Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, UNITEFA

2. Universidad de Sao Paulo; Departamento de Bioquímica, Instituto de Química

3. Universidad de Sao Paulo; Departamento de Farmacia, Facultad de Ciencias Farmacéuticas.

4. Universidad de Sao Paulo; Departamento de Bioquímica, Instituto de Química

5. Universidad Nacional de Córdoba; Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, UNITEFA
jvalenzuela@unc.edu.ar

Miltefosine (MT), an alkylphosphocholine with antineoplastic activity, is limited by its high hemolytic potential. In this work, MT was encapsulated into Pluronic F127 polymeric micelles (MT-F127 PM). A Quality by Design (QbD) strategy with a central composite design was applied to optimize formulation parameters, assessing the effects of hydration temperature, stirring speed, and stirring time on micellar hydrodynamic diameter (dH) and polydispersity index (PI). Second-order models adequately described the influence of these variables, with temperature showing a significant effect ($p < 0.05$) on PI. Optimal conditions (23 °C, 480 rpm, and 20 min) yielded micelles with dH=29.09 nm and PI=0.105, which were experimentally confirmed. Differential scanning calorimetry and thermogravimetric analysis indicated molecular dispersion of MT within the micelles. After 30 days of storage at 4 °C, dH and PI remained stable. Importantly, MT-F127 PM containing 80 µM of MT reduced hemolysis by 80% ($p < 0.05$) compared with free MT at the same concentration. In vitro assays against HeLa cells demonstrated that encapsulated MT preserved its antiproliferative activity. These findings demonstrate that MT-F127 PM reduces hemolytic toxicity while maintaining anticancer efficacy, highlighting their potential as a promising platform to expand the clinical use of MT and other alkylphosphocholines in cancer therapy.

254. P14-04. A QUALITY-BY-DESIGN APPROACH TO DEVELOP AND OPTIMIZE CURCUMIN-LOADED LIPOSOMES AS A NOVEL CARRIER FOR CANCER TREATMENT

Johanna Karina Valenzuela Oses¹, Jazmin Torres², Yamila Contessi³, Francisco Prieto Dapena⁴, Antonio Maria Rabasco⁵, Maria Luisa González Rodríguez⁶, Monica Cristina García⁷

1. Universidad Nacional de Córdoba; Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, UNITEFA, Córdoba, Argentina

2. Universidad Nacional de Córdoba; Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, UNITEFA, Córdoba, Argentina

3. Universidad Nacional de Córdoba; Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, UNITEFA, Córdoba, Argentina

4. Universidad de Sevilla; Facultad de Química, Departamento de Química-Física

5. Universidad de Sevilla; Facultad de Farmacia, Departamento de Farmacia y Tecnología Farmacéutica

6. Universidad de Sevilla; Facultad de Farmacia, Departamento de Farmacia y Tecnología Farmacéutica

7. Universidad Nacional de Córdoba; Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, UNITEFA, Córdoba, Argentina

jvalenzuela@unc.edu.ar

Nanomedicine has enabled the development of advanced platforms for delivering drugs with unfavorable physicochemical properties. Liposomes (L) are particularly attractive due to their ability to enhance solubility and improve cellular uptake. In this study, curcumin (Cur) was encapsulated into L composed of 2-dipalmitoyl-sn-glycero-3-phosphocholine, cholesterol, and the cationic lipid didodecyltrimethylammonium bromide. A quality-by-design (QbD) strategy was implemented using a Taguchi L9 matrix to optimize formulation parameters. Independent variables included rehydration medium (water (W), phosphate buffer solution, or ammonium sulfate), medium concentration (125, 250, or 375 mM), rehydration temperature (37, 42, or 47 °C), number of vortex cycles (3, 5, or 7), and number of extrusion cycles (3, 5, or 7). Responses evaluated were hydrodynamic diameter (dH), polydispersity index (PDI), and electrokinetic potential (ζ). Encapsulation efficiency (η) was quantified by high-performance liquid chromatography after vesicle lysis with 0.5% v/v lauryl sulfate. The optimized Cur-L formulation was subsequently functionalized with gold nanoparticles (AuNPs) for potential use in hyperthermia, and colloidal stability was monitored for 30 days at 4 °C. The optimized Cur-L exhibited nanoscale size (dH=173 nm), narrow distribution (PDI=0.112), high positive ζ (21 mV), and 48% EE under optimal conditions (W as rehydration medium, 42 °C, 5 vortex cycles, and 7 extrusion cycles). Colloidal stability studies revealed only minor variations in size over time. Overall, the QbD approach enabled the rational development of Cur-loaded L with favorable physicochemical properties and stability, highlighting their potential as multifunctional carriers for cancer nanomedicine.

255. P14-05. INNOVATIONS IN ONCOLOGICAL NANOMEDICINE BASED ON FUNCTIONAL NANOPARTICLES

Romina J. Glisoni¹

1. Universidad de Buenos Aires (UBA), Facultad de Farmacia y Bioquímica, Departamento de Microbiología, Inmunología, Biotecnología y Genética, Cátedra de Biotecnología, Junín 956, C1113AAD Buenos Aires, Argentina. ² CONICET - Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Nanobiotecnología (NANOBIOTEC), Buenos Aires, Argentina.; E-mail: rglisoni@ffyb.uba.ar, romy.glisoni@gmail.com

romy.glisoni@gmail.com

This work summarizes recent advances from our group on the design and development of functional nanoparticle platforms for cancer therapy and diagnosis. We focus on innovative nanomedicine strategies that enhance therapeutic efficacy, improve diag-

nostic imaging, and increase safety in oncological applications. Our research includes the green synthesis of polymer-stabilized gold nanoparticles loaded with radiosensitizing agents to improve treatment outcomes in melanoma, employing environmentally friendly methods that align with sustainable chemistry principles. Additionally, we have developed glycosylated polymeric micelles as imaging agents for sentinel lymph node mapping in breast cancer, facilitating more accurate and less invasive diagnostics. Furthermore, polymeric micelles encapsulating antitumoral compounds have demonstrated potent efficacy in aggressive breast cancer models, highlighting the potential for targeted drug delivery to overcome resistance and reduce side effects. These studies showcase the versatility of nanoparticle engineering to overcome biological barriers, achieve targeted delivery, and integrate therapeutic and diagnostic functionalities (theranostics). Our multidisciplinary approach combines physicochemical characterization, in vitro biological evaluation, and translational considerations, aiming to accelerate clinical application. Overall, our work contributes to advancing multifunctional nanoplateforms that address key challenges in precision oncology, including enhanced targeting, controlled drug release, and combined therapeutic-imaging capabilities. Future perspectives will focus on scaling up production, regulatory pathways, and fostering collaborations to facilitate the translation of these technologies into clinical practice.

256. P14-06. ANTIBIOFILM ACTIVITY OF A WOUND HEALING BIOPOLYMERIC MEMBRANE AGAINST PSEUDOMONAS AERUGINOSA AND STAPHYLOCOCCUS AUREUS

Fiamma Barbieri¹, Román Martino², María Cecilia Becers³, Andrea Smania⁴, María Eugenia Olivera⁵

1. UNITEFA-CONICET/Dpto. de Cs. Farmacéuticas FCQ-UNC - Córdoba - Argentina.; GIT-Farma

2. CIQUIBIC-CONICET/Dpto. de Química Biológica Ranwel Caputto FCQ-UNC - Córdoba - Argentina.; Laboratorio Dra. Smania

3. UNITEFA-CONICET/Dpto. de Cs. Farmacéuticas FCQ-UNC - Córdoba - Argentina.; Laboratorio 113

4. CIQUIBIC-CONICET/Dpto. de Química Biológica Ranwel Caputto FCQ-UNC - Córdoba - Argentina.; Laboratorio Dra. Smania

5. UNITEFA-CONICET/Dpto. de Cs. Farmacéuticas FCQ-UNC - Córdoba - Argentina.; GIT-Farma
fiammabarbieri@unc.edu.ar

This study evaluated the antibiofilm activity of a biopolymeric membrane (BAAM) and its individual components: two biopolymers (BP1 and BP2), an antibiotic (Ab), an anesthetic (An), and a plasticizer (PI) against *Staphylococcus aureus* MR 9455 and *Pseudomonas aeruginosa* 191150. Biofilm formation and disruption were assessed by crystal violet staining, viable cell counts, and SEM. The in vitro release kinetics of Ab and An were determined using Franz type diffusion cells and HPLC-PDA for quantification. Results were evaluated by ANOVA ($\alpha = 0.05$; $n = 3$). Formulations containing Ab significantly inhibited biofilm formation in both species ($p < 0.05$). Interestingly, BP1 exhibited inhibitory activity comparable to Ab, and An selectively impaired *P. aeruginosa* biofilms. These inhibitory effects of BP1 and An suggest that BAAM could achieve preventive antibiofilm activity even in the absence of the Ab component. Regarding disruption, Ab and BAAM reduced bacterial viability against biofilms of both strains, with no significant differences between them. BP1 and An also decreased the number of viable cells in *P. aeruginosa* biofilms. These effects were corroborated by the reduced biofilm coverage observed in SEM images of treated samples. The lack of additive inhibitory and disruptive effects of the components within BAAM can be attributed to its slow and sustained release, as demonstrated by studies showing that 31.95% of Ab and 67.07% of An were liberated after 24 h. These findings highlight the dual benefit of BAAM as both a wound-healing and antibiofilm membrane, offering a promising topical approach that combines antimicrobial efficacy with pain relief.

257. P14-07. NIFURTIMOX NANOSUSPENSION: TOWARD IMPROVED PHARMACEUTICAL PERFORMANCE FOR

CHAGAS DISEASE THERAPY

María Sol Magi¹, Lucía López Vidal², Santiago Daniel Palma³, Mónica Cristina García⁴

1. Universidad Nacional de Córdoba, Facultad de Ciencias Químicas, Departamento de Ciencias Farmacéuticas, Ciudad Universitaria, Haya de la Torre and Medina Allende, Science Building 2, Córdoba, X5000HUA, Argentina. Consejo Nacional de Investigaciones Científicas y Técnicas, CONICET, Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, UNITEFA, Córdoba Argentina.; 208

2. UNC, FCQ - CONICET, UNITEFA; 114

3. UNC, FCQ - CONICET, UNITEFA; 114

4. UNC, FCQ - CONICET, UNITEFA; 210

maria.sol.magi@unc.edu.ar

Nifurtimox (NFX) is one of the two approved drugs for treating Chagas disease, a neglected parasitic infection caused by *Trypanosoma cruzi*. Due to its low aqueous solubility, classified within the Biopharmaceutics Classification System (BCS) classes II/IV, NFX exhibits dissolution rate limitations and erratic bioavailability. This study aimed to develop and characterize a NFX nanosuspension (NFX-NS), composed of drug nanocrystals (NFX-NCs), as a strategy to improve its biopharmaceutical performance and enable future pediatric applications. NFX-NS was prepared by wet milling (a top-down, organic solvent-free approach), followed by lyophilization to obtain the solid-state formulation. Physicochemical characterization, solubility, dissolution, and in vitro biological assays were performed. The NFX-NS exhibited a mean particle size of ~200 nm with a polydispersity index < 0.2 , and remained stable for at least 120 days. NFX preserved its crystalline structure after processing, with no relevant alterations in physicochemical properties, indicating minimal interaction with the stabilizer. Compared with raw NFX, NFX-NCs showed a 10-fold increase in aqueous solubility and a marked improvement in dissolution rate. Furthermore, in vitro studies demonstrated significantly enhanced anti-*T. cruzi* activity, along with improved biocompatibility in human endothelial cells. These findings highlight NFX-NS as the first NC-based formulation of NFX, offering a promising therapeutic alternative for pediatric use and a potential strategy to overcome solubility-related limitations of this drug.

258. P14-08. DEVELOPMENT OF A HYALURONIC ACID-TOBRAMYCIN DRY POWDER INHALATION FORMULATION FOR MANAGING PULMONARY INFECTIONS IN CYSTIC FIBROSIS PATIENTS

Yanina de Lafuente¹, María Sol Magi², Joaquín Pagani³, Ana Lidia Apas⁴, Paulina Paez⁵, Álvaro Jiménez-Kairuz⁶

1. Unidad de Investigación y Desarrollo en Tecnología Farmacéutica (UNITEFA), CONICET - UNC, 2Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba.; 210

2. Unidad de Investigación y Desarrollo en Tecnología Farmacéutica (UNITEFA), CONICET - UNC, y Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba.; 210

3. Unidad de Investigación y Desarrollo en Tecnología Farmacéutica (UNITEFA), CONICET - UNC, y Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba.; 116

4. Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba.; 210

5. Unidad de Investigación y Desarrollo en Tecnología Farmacéutica (UNITEFA), CONICET - UNC, y Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba.; 116

6. Unidad de Investigación y Desarrollo en Tecnología Farmacéutica (UNITEFA), CONICET - UNC, y Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba.; 210
yanina.de.lafuente@unc.edu.ar

Tobramycin (TOB) is a standard treatment for lung-infections caused by *Pseudomonas aeruginosa*, a common pathogen infecting cystic fibrosis lungs patients. It is usually administered

intravenously, leading to a high incidence of adverse effects, which could be mitigated through intrapulmonary administration. Currently, TOBI® is the only formulation for inhalation, with a monthly cost of 10,000 U\$S. The work aimed to develop a cost-effective inhalable powder for pulmonary administration that reduces systemic adverse effects and overall treatment costs. The formulation consisted on an ionic complex of hyaluronic acid (HA), a bioadhesive, biocompatible, and biodegradable polymer with recognized safety, and TOB. Complexes were easily prepared by dispersing the raw materials in water, followed by spray-drying technique to obtain the powder. Antimicrobial susceptibility and biofilm inhibition/eradication was studied against *Pseudomonas aeruginosa*. The Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) was determined, with values of 1 and 2 µg/mL, respectively, for TOB, and 0.5 and 1 µg/mL, respectively, for HA-TOB, showing antimicrobial activity. The complexation of TOB did not affect its activity quite the opposite, required less drug to achieve similar results than the TOB. Regarding the biofilm inhibitory activity, the complex exhibited a higher effect than the TOB, from high concentrations to dilute ones (1-0.5-fold-times the MBC). Similarly, the complex showed higher efficacy in the eradication of the biofilm. It is important to remark that the complex improved the bacteria susceptibility and helped to prevent the biofilm formation and the disruption of the formed biofilm which is critical in chronic infections.

259. P14-09. INHIBITION OF TRITRICHOMONAS FOETUS GROWTH BY BROAD-SPECTRUM ANTIBIOTICS

Maria Rosana Ramirez¹, Jorge Oyhenart²

1. Instituto de Química Básica y Aplicada del Nordeste Argentino (IQUIBA-NEA); FACENA- CCT Nordeste

2. Instituto de Ciencias de la Tierra y Ambientales de La Pampa (INCITAP). Universidad Nacional de La Pampa / Facultad De Ciencias Exactas y Naturales /; Facultad de Ciencias Naturales CONICET

mr.ramirez@conicet.gov.ar

Tritrichomonas foetus is a sexually transmitted protozoan that causes highly damaging reproductive failure in livestock, prompting some countries to initiate control programs. These programs are based on the evaluation and exclusion of individual bulls. Nitroimidazoles are effective for controlling the disease, but their use is not recommended in animals intended for food production. For this reason, one strategy is to find new therapeutic uses for existing drugs, such as antibiotics. Ciprofloxacin is a broad-spectrum antibiotic that is not known for its effect on protozoa as an inhibitor of *T. foetus* growth. Chloramphenicol inhibits protein synthesis in bacteria and may have effects on eukaryotic cells, such as inhibiting the growth of *T. foetus*. Therefore, the objective of this study was to investigate the efficacy of two broad-spectrum antibiotics, ciprofloxacin and chloramphenicol. To do this, *T. foetus* trophozoites were incubated in culture medium with serial dilutions of ciprofloxacin or chloramphenicol, and mortality was determined after 24 hours. During this period, the antibiotic ciprofloxacin eliminated all cells with an EC₅₀ of 21.5 µg/ml. Chloramphenicol produced the same effect with a maximum effective concentration (EC₅₀) of 281.0 µg/ml. The results showed effective inhibition of *T. foetus* growth at moderate concentrations of ciprofloxacin. The results showed effective inhibition of *T. foetus* growth at moderate concentrations of ciprofloxacin, whereas high concentrations of chloramphenicol are required to produce the same effect. The results were sensitive under the established experimental conditions, but evaluation under other experimental conditions and in the field is required.

260. P14-10. MECHANISMS INVOLVED IN CARDIAC I/R DYSFUNCTION IN AGING VS OVARECTOMY: ROLE OF THE MITOCHONDRIAL SODIUM-CALCIUM EXCHANGER AND OXIDATIVE STRESS

Germán Andrés Colareda¹, María Inés Ragone², Juan Manuel Lofeudo³, Romina Gisel Díaz⁴, Alicia Elvira Consolini⁵

1. Facultad de Ciencias Exactas, Universidad Nacional de La Plata; Cátedra de Farmacología de Farmacia, Laboratorio de Farmacología Experimental y Energética Cardíaca (LaFEYEC), Departamento de Ciencias Biológicas.

2. Facultad de Ciencias Exactas, Universidad Nacional de La Plata; Cátedra de Farmacología de Farmacia, Laboratorio de Farmacología Experimental y Energética Cardíaca (LaFEYEC), Departamento de Ciencias Biológicas

3. CONICET-UNLP; Centro de Investigaciones Cardiovasculares (CIC) "Doctor Horacio Eugenio Cingolani"

4. CONICET-UNLP; Centro de Investigaciones Cardiovasculares (CIC) "Doctor Horacio Eugenio Cingolani"

5. Facultad de Ciencias Exactas, Universidad Nacional de La Plata; Cátedra de Farmacología de Farmacia, Laboratorio de Farmacología Experimental y Energética Cardíaca (LaFEYEC), Departamento de Ciencias Biológicas gcolareda@biol.unlp.edu.ar

Ischemic heart disease is the most significant contributor to cardiovascular diseases in morbidity and mortality. Loss of estrogens and aging reduce ischemic cardioprotection in women. Previously, we observed that aging reduced post-ischemic recovery (PIR) in rats due to impaired SR-Ca release and NCX expression. No variations in PIR were observed in ovariectomized rats, highlighting the different mechanisms in senility versus estrogen deficiency. The aim of this work was to analyze whether oxidative stress contributes to I/R injury in aging and the role of the mitochondrial sodium-calcium exchanger (mNCX) in aging and estrogen deficiency. Methods: Ventricles (n=3) from adult female (YF), ovariectomized YF (OVX), or aged (AgF) rats were perfused inside a flow-calorimeter, and exposed to a stunning model (20'1-45'R). Maximal intraventricular pressure (P), diastolic contracture (ΔLVDP), and heat rate (Ht) were simultaneously measured, and muscle economy (P/Ht) was calculated. A group of AgF was perfused with 2 mM MPG (ROS scavenger) before I and during R. Additionally, AgF, OVX, and YF were perfused with clonazepam 10 µmol/L (to inhibit mNCX). Statistics: 2-way ANOVA: *P<0.05. Results: MPG did not modify P or P/Ht recoveries nor ΔLVDP in AgF. The inhibition of mNCX reduced P recovery (from 45.4±5.2 to 14.5±3.8%* in AgF and from 64±8.4 to 22.7±7.9%* in OVX) and P/Ht recovery, but not in YF. Conclusions: the low PIR of aging hearts does not involve ROS accumulation. In aged rats and in those ovariectomized the mNCX contributes to reduce the mitochondrial calcium overload during I/R as a mechanism of cardioprotection.

261. P14-11. ACCESSIBLE LOW-COST 3D SCAFFOLDS: SYRINGE EXTRUSION AND SEM VALIDATION

Verónica Martínez Marignac¹, Jorge Cargnelutti², Gloria Oertlin³, Silvina Richard⁴

1. Centro de Investigaciones - Universidad de Concepción del Uruguay, CONICET; IBIOGEM

2. CICYTTP; IBIOGEM

3. CICYTTP-CONICET; IBIOGEM

4. Centro de Investigaciones- Universidad de Concepcion del Uruguay -CONICET; IBIOGEM veromm99@gmail.com

Three-dimensional (3D) bioprinted matrices better recapitulate tissue microenvironments than traditional two-dimensional (2D) monolayers by promoting cell-cell contacts and physiologically relevant mass transport. We present a low-cost, syringe-extrusion approach to make porous alginate scaffolds using Pluronic F127 as a sacrificial material, and we characterized nanostructure by scanning electron microscopy (SEM). Bioinks were prepared from sodium alginate (3% w/v) and Pluronic PF127 (tested at 5.5–11% w/v). Microgels were formed by syringe extrusion (5 mL syringe) into a CaCl₂ bath (100 mM), followed by sacrificial PF127 removal at 4 °C and sequential washes (100 mM □ 5 mM CaCl₂, then PBS). Constructs were incubated at 37 °C (12 h). Samples were dehydrated through graded ethanol and imaged by SEM (PHENOM Pro-X; 540–1000x, 5–10 kV, ~10 nm resolution, WD ≈ 2.5 mm). The SEM analysis revealed interconnected porosity and nano-/micro-topographies in formulations containing 11% PF127 + 3% alginate (I4) and 5.5% PF127 + 3% alginate (II4). Removal of the sacrificial phase produced increased specific surface area and pores of 15 to 70µm, features expected to enhance cell-medium exchange by promoting

3D direct cell-cell interactions compared with 2D cultures. These structural properties are consistent with our prior observations of improved cell viability, prolonged stability (up to ~24 days under similar conditions), and more biologically relevant responses in 3D versus 2D systems. Syringe-based extrusion combined with sacrificial Pluronic yields reproducible, porous alginate scaffolds. SEM validation confirms architectures likely to improve biological fidelity relative to 2D culture while minimizing equipment and costs.

ORALES 13 - SAIC - TOXICOLOGÍA Y ECOTOXICOLOGÍA

DATE & TIME: 19/11/2025 13:00 - 14:30 H

Chairs: Noelia Miret, Marianela Lasagna

262. O13-01. URBAN AIR POLLUTION EXPOSURE SUSTAINS OXI-INFLAMMATORY RESPONSE THAT UNDERLY IMPAIRED ALVEOLAR EPITHELIUM REPAIR

Sofía Reynoso¹, Florencia Sarno², Laura Caltana³, Agustina Freire⁴, Mariana Garcés⁵, Manuela Martinefski⁶, Mayra El Zar⁷, Lourdes Cáceres⁸, Timoteo Marchini⁹, Valeria Tripodi¹⁰, Pablo Evelson¹¹, Natalia Magnani¹²

1. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.; Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.

2. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.; Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.

3. Universidad de Buenos Aires, Facultad de Medicina, Instituto de Biología Celular y Neurociencias (IBCN-UBA-CONICET), Buenos Aires, Argentina.; Instituto de Biología Celular y Neurociencias (IBCN-UBA-CONICET), Buenos Aires, Argentina.

4. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.; Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.

5. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.; Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.

6. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Tecnología Farmacéutica, Buenos Aires, Argentina.; Departamento de Tecnología Farmacéutica, Buenos Aires, Argentina.

7. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.; Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.

8. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.; Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.

9. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.; Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.

10. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Tecnología Farmacéutica, Buenos Aires, Argentina.; Departamento de Tecnología Farmacéutica, Buenos Aires, Argentina.

11. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.; Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires,

Argentina.

12. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.; Instituto de Bioquímica y Medicina Molecular Prof. Alberto Boveris (IBIMOL-UBA-CONICET), Buenos Aires, Argentina.

sreynoso@docente.fyb.uba.ar

Environmental pollution is a major health hazard that increases respiratory disease risk, contributing to global morbidity and mortality. Inhalation of particulate matter (PM) present in urban air (UA) triggers an interplay between oxidative stress and inflammation, aggravating lung injury. To investigate UA-underlying oxi-inflammatory mechanisms, mice were exposed to filtered air (FA) or UA in whole-body exposure chambers for up to 8 weeks. After UA exposure, bronchoalveolar lavage (BAL) analysis revealed elevated IL-6 ($p \leq 0.01$) and reduced IL-10 ($p \leq 0.05$), alongside increased macrophage-derived nitric oxide ($p \leq 0.05$) and neutrophil superoxide production ($p \leq 0.01$). Total BAL cell count and protein levels were also higher compared to FA ($p \leq 0.05$). To assess the oxi-inflammation impact on lung repair, mice were exposed to FA or UA for 8 weeks, followed by an injury induced by instillation of hydrochloric acid. Five days later, UA-exposed lungs displayed a more oxidizing environment, evidenced by an increased GSH/GSSG ratio ($p < 0.001$). Consistently, the redox sensitive NF- κ B, involved in inflammatory pathways, showed enhanced nuclear translocation ($p \leq 0.05$) leading to elevated TNF- α ($p \leq 0.001$) and IL-6 ($p \leq 0.01$), while IL-10 remain unchanged after UA exposure. Ultrastructural analysis showed alveolar-capillary barrier widening and epithelial alterations supporting the observed UA-increased permeability. A disrupted redox homeostasis together with a sustained inflammation delay alveolar repair mechanisms prolonging lung functional loss. Understanding these mechanisms is crucial to develop strategies to mitigate the impact of air pollution on human health.

263. O13-02. IMIDACLOPRID, AN ENDOCRINE-DISRUPTING CHEMICAL, PROMOTES ENDOMETRIOSIS-ASSOCIATED CELLULAR CHANGES VIA G PROTEIN-COUPLED ESTROGEN RECEPTOR (GPER) SIGNALING

Martina Leturia¹, Leandro Ceballos², Martina Kolesnik³, Chiara Santos⁴, Sol Buján⁵, Carolina Pontillo⁶, Noelia Miret⁷, Mariel Núñez⁸, Andrea Randi⁹, Florencia Chiappini¹⁰

1. CONICET- Universidad de Buenos Aires, Instituto de Investigaciones Biomédicas (INBIOMED), , Paraguay 2155, Piso 5, (CP 1121), CABA, Argentina; Laboratorio de Efectos Biológicos de Contaminantes Ambientales

2. CONICET- Universidad de Buenos Aires, Instituto de Investigaciones Biomédicas (INBIOMED), Laboratorio de Efectos Biológicos de Contaminantes Ambientales, Paraguay 2155, Piso 5, (CP 1121), CABA, Argentina; Universidad de Buenos Aires, Facultad de Medicina, Departamento de Bioquímica Humana, CABA, Argentina; Laboratorio de Efectos Biológicos de Contaminantes Ambientales

3. CONICET- Universidad de Buenos Aires, Instituto de Investigaciones Biomédicas (INBIOMED), Paraguay 2155, Piso 5, (CP 1121), CABA, Argentina.; Laboratorio de Efectos Biológicos de Contaminantes Ambientales

4. CONICET- Universidad de Buenos Aires, Instituto de Investigaciones Biomédicas (INBIOMED), Paraguay 2155, Piso 5, (CP 1121), CABA, Argentina; Laboratorio de Efectos Biológicos de Contaminantes Ambientales

5. CONICET- Universidad de Buenos Aires, Instituto de Investigaciones Biomédicas (INBIOMED), Paraguay 2155, Piso 5, (CP 1121), CABA, Argentina; Laboratorio de Efectos Biológicos de Contaminantes Ambientales

6. CONICET- Universidad de Buenos Aires, Instituto de Investigaciones Biomédicas (INBIOMED), Paraguay 2155, Piso 5, (CP 1121), CABA, Argentina; Laboratorio de Efectos Biológicos de Contaminantes Ambientales

7. CONICET- Universidad de Buenos Aires, Instituto de Investigaciones Biomédicas (INBIOMED), Paraguay 2155, Piso 5, (CP 1121), CABA, Argentina; Universidad de Buenos

Aires, Facultad de Farmacia y Bioquímica. Departamento de Fisicomatemática, Cátedra de Física, Junín 956, C.A.B.A., Argentina.; Laboratorio de Efectos Biológicos de Contaminantes Ambientales

8. 3Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. Departamento de Fisicomatemática, Cátedra de Física. Junín 956, C.A.B.A., Argentina.; Laboratorio de Radioisótopos

9. 1CONICET- Universidad de Buenos Aires, Instituto de Investigaciones Biomédicas (INBIOMED), Paraguay 2155, Piso 5, (CP 1121), CABA, Argentina; Universidad de Buenos Aires, Facultad de Medicina, Departamento de Bioquímica Humana, CABA, Argentina; Laboratorio de Efectos Biológicos de Contaminantes Ambientales

10. CONICET- Universidad de Buenos Aires, Instituto de Investigaciones Biomédicas (INBIOMED), Paraguay 2155, Piso 5, (CP 1121), CABA, Argentina; Universidad de Buenos Aires, Facultad de Medicina, Departamento de Bioquímica Humana, CABA, Argentina; Laboratorio de Efectos Biológicos de Contaminantes Ambientales
martinaleturia@gmail.com

Endometriosis is an estrogen-dependent disorder defined as the presence of endometrial tissue outside the uterus, which causes pelvic pain and infertility. The environmental endocrine-disrupting chemicals (EDCs) are exogenous agents that interfere with synthesis, secretion, transport, signaling, or metabolism of hormones, responsible for reproductive diseases. Endometriosis has been potentially linked to exposure to EDCs. Imidacloprid (IMI), is a neonicotinoid insecticide, that is used worldwide. Like many pesticides, IMI can act as EDC. In this study we investigate the effects of IMI exposure on changes linked to the progression of endometriosis. Stromal endometrial cells (T-HESCs) were treated with different concentrations of IMI (0.01, 0.1, 1, and 10 μ M). The results showed that IMI increased cell migration (15% and 30% at 1 and 10 μ M, scratch motility assay), invasion (46% at 10 μ M, transwell invasion assay) and proliferation (48% at 10 μ M, PCNA expression). We also analyzed the activity of matrix metalloproteinases (MMPs), crucial enzymes for migration and invasion. IMI increased the activity of both MMP-9 (17%, 26%, 23% at 0.1, 1, 10 μ M) and MMP-2 (41% and 28% at 0.01 and 1 μ M, zymography assays). Furthermore, we observed that IMI (1 and 10 μ M) induced the expression of aromatase and G protein-coupled estrogen receptor (GPER) (74%, 67%; and 62%, 71%, by Western blot). Finally, we observed that the increase in migration, invasion, and MMPs activation induced by IMI is dependent on GPER. In conclusion, our findings provide experimental evidence that exposure to IMI can induce cellular changes associated with endometriosis development.

264. O13-03. PESTICIDE EXPOSURE PROFILES IN PREGNANT WOMEN WITH COMORBIDITIES: IMPLICATIONS FOR MATERNAL-FETAL HEALTH

María Emilia Racca¹, Julieta Cepeda², María Alejandra Cardozo³, Magali Aldana Wettstein⁴, Romina Bodrone⁵, Aldo Rubén Rinesi⁶, Melina Paola Michlig⁷, María Rosa Repetti⁸, María Florencia Rossetti⁹, Jorge Guillermo Ramos¹⁰, Enrique Hugo Luque¹¹, Mónica Muñoz-de-Toro¹², María Mercedes Milesi¹³, Jorgelina Varayoud¹⁴

1. Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina. Departamento de Bioquímica Clínica, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -

2. Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -

3. Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina. Departamento de Bioquímica Clínica, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina. BLUT Laboratorios, Santa Fe, Argentina.; -

4. Instituto Nacional de Enfermedades Respiratorias "Dr. Emilio Coni"; -

5. PlusLab, San Justo, Santa Fe, Argentina.; -

6. Clínica NACER SH, Reconquista, Santa Fe, Argentina.; -

7. Programa de Investigación y Análisis de Residuos y Contaminantes Químicos (PRINARC), Facultad de Ingeniería Química, Universidad Nacional del Litoral, Santa Fe, Argentina. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina.; -

8. Programa de Investigación y Análisis de Residuos y Contaminantes Químicos (PRINARC), Facultad de Ingeniería Química, Universidad Nacional del Litoral, Santa Fe, Argentina.; -

9. Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -

10. Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina. Departamento de Bioquímica Clínica, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -

11. Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -

12. Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -

13. Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.

Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -

14. Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.

Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -

meracca@fbc.unl.edu.ar

Comorbidities during pregnancy may predispose to adverse maternal-fetal outcomes, while environmental pesticide exposure may act as an aggravating factor. We investigated the prevalence of comorbidities and their association with pesticide presence in a cohort of 82 pregnant women. Lifestyle information was collected via questionnaires, and health status data were obtained from medical records. Urinary pesticides were analyzed using a multiresidue method based on solid-phase extraction, followed by gas chromatography-tandem mass spectrometry. Comorbidities were present in 37% of participants, classified as hemostasis disorders (15%, including thrombophilia and antiphospholipid syndrome) or other comorbidities (22%, such as hypothyroidism and hypertension). Women with comorbidities showed a significantly higher prevalence of adverse outcomes in previous pregnancies (86%, $p = 0.01$), with spontaneous abortion being the most frequent (67%, $p = 0.028$). These prevalences were even higher in the hemostasis disorder group ($p < 0.05$). Lifestyle habits were similar across groups, except for daily fruit intake, which was higher among women without comorbidities ($p = 0.038$). Pesticide detection rates and levels did not differ significantly between groups. However, pesticide mixtures were more frequently detected in women with comorbidities (80%, $p = 0.02$), along with a higher number of compounds ($p = 0.04$). Increased detection of arylphenylpropionates and organosulfur compounds was also associated with comorbidities ($p = 0.046$), and pyrethroids were significantly more frequent in the hemostasis disorder group ($p < 0.001$). These findings underscore the need to further investigate the combined impact of health conditions and pesticide exposure on maternal-fetal health.

265. O13-04. PLACENTAL EPIGENETIC ALTERATIONS ASSOCIATED WITH CHLORPYRIFOS EXPOSURE DURING

PREGNANCY

Celeste Lesende¹, Azul Sanchez Cabrera², Piuque Rodriguez³, Paola Ordanza⁴, Natalia Guíñazu⁵, Silvina Sonzogni⁶

1. Centro de Investigaciones en Toxicología Ambiental y Agrobiotecnología del Comahue CITAAC-CONICET, Universidad Nacional del Comahue, Neuquén.; Laboratorio de estudios toxicológicos en humanos

2. Centro de Investigaciones en Toxicología Ambiental y Agrobiotecnología del Comahue CITAAC-CONICET, Universidad Nacional del Comahue, Neuquén.; Laboratorio de estudios toxicológicos en humanos

3. Centro de Investigaciones en Toxicología Ambiental y Agrobiotecnología del Comahue CITAAC-CONICET, Universidad Nacional del Comahue, Neuquén. Departamento de Ciencias del Ambiente, Facultad de Ciencias del Ambiente y la Salud. Universidad Nacional del Comahue, Neuquén.; Laboratorio de estudios toxicológicos en humanos

4. Instituto de Investigaciones Marinas y Costeras (IIMyC), Facultad de Ciencias Exactas y Naturales, Universidad Nacional de Mar Del Plata-CONICET; Laboratorio de Ecotoxicología y Contaminación Ambiental

5. Centro de Investigaciones en Toxicología Ambiental y Agrobiotecnología del Comahue CITAAC-CONICET, Universidad Nacional del Comahue, Neuquén. Departamento de Ciencias del Ambiente, Facultad de Ciencias del Ambiente y la Salud. Universidad Nacional del Comahue, Neuquén.; Laboratorio de estudios toxicológicos en humanos

6. Centro de Investigaciones en Toxicología Ambiental y Agrobiotecnología del Comahue CITAAC-CONICET, Universidad Nacional del Comahue, Neuquén.; Laboratorio de estudios toxicológicos en humanos celestelesende0@gmail.com

In the Alto Valle of Río Negro and Neuquén, apple and pear orchards have depended on intensive pesticide use. The pesticide chlorpyrifos (CP) was widely used, until it was banned in 2023. Studies have shown that prenatal exposure to CP may impact both maternal and fetal health, with long-term consequences. Evidence suggests that pesticides may disrupt epigenetic mechanisms, including DNA methylation and histone modifications, leading to persistent changes in gene expression that may even be transmitted to future generations. This study evaluated whether environmental CP exposure during pregnancy affected DNA methylation machinery and histone modifications in the placenta. A total of 46 placental samples from a population-based study were analyzed: 23 with CP levels above the limit of quantification (LOQ) -high CP group-, and 23 below the LOQ, -low CP group-. Gene expression of DNMT1, DNMT3A, TET1, TET2, and TET3 was assessed by qPCR, while H3K4me3 and H3K9me3 levels were measured by Western blot. Results showed a significant decrease in TET3 expression ($p=0.409$) and a trend toward downregulation of TET2 ($p=0.0735$) in the high CP group. No significant changes were detected for DNMT1, DNMT3A, or TET1 between groups. Regarding histone modifications, H3K4me3 levels were significantly reduced ($p=0.0377$) in the high CP group, while H3K9me3 remained unchanged. These findings suggest that prenatal CP exposure alters chromatin state by reducing TET enzymes and H3K4me3, both associated with active chromatin. Overall, our results support the hypothesis that CP exposure during pregnancy may induce epigenetic reprogramming linked to global chromatin silencing.

266. O13-05. CARDIAC ADAPTATIONS IN IUGR F2 FETUSES EXPOSED TO GLYPHOSATE: ALTERATIONS IN CARDIAC REMODELING AND METABOLIC PROGRAMMING

Ailín Almirón¹, Virginia Lorenz², Sebastián Di Paolo³, Milena Durando⁴, María Mercedes Milesi⁵

1. Instituto de Salud y Ambiente del Litoral (ISAL), UNL - CONICET, Argentina. Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas (FBCB) - UNL, Argentina; -

2. Instituto de Salud y Ambiente del Litoral (ISAL), UNL - CONICET, Argentina. Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas (FBCB) - UNL,

Argentina; -

3. Instituto de Salud y Ambiente del Litoral (ISAL), UNL - CONICET, Argentina.; -

4. Instituto de Salud y Ambiente del Litoral (ISAL), UNL - CONICET, Argentina. Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas (FBCB) - UNL, Argentina; -

5. Instituto de Salud y Ambiente del Litoral (ISAL), UNL - CONICET, Argentina. Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas (FBCB) - UNL, Argentina; -

ailinalmiron98@gmail.com

Intrauterine growth restriction (IUGR) is a major cause of perinatal morbidity. Growth-restricted fetuses develop characteristic cardiovascular adaptations to overcome the suboptimal intrauterine environments. These adaptations reprogram fetal development and predispose offspring to lifelong cardiovascular morbidities. We previously demonstrated that second-generation rat fetuses (F2) developed IUGR when their mothers (F1) were exposed to glyphosate-based herbicide (GBH) or glyphosate (Gly) during gestation and lactation. Our study investigated the effects of GBH or Gly exposure on cardiac development in IUGR F2 fetuses. Pregnant rats (F0) received GBH or Gly (2 mg glyphosate/kg/day) from gestational day (GD) 9 to offspring postnatal day (PND) 21. F1 females were mated at PND90, and F2 hearts were collected at GD19. We assessed relative heart weight, left ventricle morphometry, and mRNA expression of genes related to mitochondrial biogenesis (PGC1- α , NRF1), oxidative phosphorylation (ND1), cardiac metabolism (PDK4, Dio2) and remodeling (FoxO1, PINK1, Vcam1). GBH and Gly males showed increased relative heart weight. GBH fetuses exhibited reduced left ventricular wall thickness, with males displaying dilated ventricular cavities. Upregulation of PGC1- α , NRF1, and ND1 indicated increased mitochondrial biogenesis and oxidative function, particularly in GBH males. Additionally, decreased Dio2 (Gly males) and increased PDK4 (GBH females) expression suggests altered cardiac metabolism. Regarding cardiac remodeling, Vcam1 expression increased in males from both groups, indicating activation of inflammatory pathways. Gly or GBH exposure leads to sex-specific cardiac adaptations in IUGR F2 fetuses, characterized by cardiac remodeling and metabolic reprogramming. These changes suggest compensatory responses to intrauterine stress that may predispose to future cardiovascular dysfunction.

267. O13-06. HUMAN TERM PLACENTAL EXPLANTS AS AN EX VIVO MODEL: INDIVIDUAL VARIABILITY IN RESPONSE TO GLYPHOSATE

María Emilia Racca¹, Nataly de Dios², María Laura Zenclussen³, María Paula Gastiazoro⁴, Luis Gerardo⁵, Marcelo Laco⁶, Cecilia Varone⁷, María Mercedes Milesi⁸, Jorgelina Varayoud⁹

1. Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina. Departamento de Bioquímica Clínica, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -

2. Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), CONICET, Buenos Aires, Argentina.; -

3. Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina. Cátedra de Fisiología, Facultad de Ciencias Médicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -

4. Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina. Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; -

5. Sanatorio Diagnóstico, Santa Fe, Argentina; -

6. *Sanatorio Diagnóstico, Santa Fe, Argentina;* -
 7. *Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), CONICET, Buenos Aires, Argentina.;* -
 8. *Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina. Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.;* -
 9. *Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina. Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.;* -
 meracca@fbc.unl.edu.ar

Ex vivo models using human placenta are a valuable tool for studying the toxicity of environmental chemicals. This study evaluated glyphosate effects on term placental explants from cesarean deliveries (N = 3). Explants were cultured under three conditions: control, 0.01 μ M glyphosate, and 1.0 μ M glyphosate. Cellular damage and function were assessed by measuring Lactate dehydrogenase (LDH) activity and β -subunit human chorionic gonadotropin (β hCG) levels, respectively. Tissue integrity was evaluated histologically on 5 μ m sections stained with hematoxylin–eosin and periodic acid–Schiff. Molecular analysis included total protein and relative mitochondrial DNA content using real-time PCR. Statistical analysis included Two-way RM ANOVA and mixed-effects models. Differences in β hCG ($p = 0.0037$) and LDH ($p = 0.0291$) levels were primarily determined by the placenta, with glyphosate showing no global effect. Histologically, a significant interaction between placenta origin and glyphosate was observed for the villous area ($p = 0.020$), with total villous alterations influenced by both factors ($p = 0.0010$). Syncytiotrophoblast detachment and trophoblast lesions with nuclear release were significantly affected by placenta, glyphosate, and their interaction ($p < 0.05$). Basal membrane thickness decreased at low glyphosate doses ($p < 0.0001$). At the molecular level, glyphosate significantly affected total protein concentration ($p = 0.0361$), while protein content was placenta-dependent ($p < 0.01$). Mitochondrial DNA levels remained unaffected. These results suggest that glyphosate induces placental tissue damage and molecular alterations, yet the responses are strongly influenced by intrinsic biological variability among placentas, highlighting the importance of accounting for this variability in toxicological studies.

268. O13-07. COULD SPIRULINA BE USED AS A NUTRACEUTICAL PROTECTOR AGAINST CADMIUM INTOXICATION?

Emilse Sanchez¹, Maria Agustina Jofre², Gianella Melisa Leyes³, Laura V Gatica⁴, Silvina Alvarez⁵
 1. *IMIBIO SL, UNSL; Lab de Nutricion, Medio Ambiente y Metabolismo celular.*
 2. *UNSL; Lab de Nutricion, Medio Ambiente y Metabolismo Celular*
 3. *UNSL; Lab de Fisiologia*
 4. *IMIBIO SL CONICET; Lab de Nutricion, Medio Ambiente y Metabolismo celular*
 5. *IMIBIO SL CONICET, UNSL; Lab de Nutricion, medio Ambiente y metabolismo celular*
 emysilsanchez@gmail.com

Over the years, we studied Cd intoxication. It exerts its action mainly by inducing oxidative stress. Searching for protective strategies, we previously evaluated potential agents such as Soybean with promising results; however, its phytoestrogen limited their suitability, particularly in female animals. Thus, we explored Spirulina (*Arthrospira platensis*), a high nutritional value microalga, as an alternative. Amphibians provide a sensitive bioindicator and a translational biomedical research model, given their complex ontogeny and high

susceptibility to contaminants. We investigated the effects of Spirulina supplementation on Cd-intoxicated *Rhinella arenarum* tadpoles. Larvae (Gosner stage 25) were exposed for one month to sublethal Cd concentrations (0.25 and 0.5 mg/L) or to diets enriched with Spirulina (5–100%). Growth parameters (weight, body area, total length), developmental progression and hematological profile were assessed. These preliminary results showed that Cd exposure accelerated food intake, larval growth, and metamorphosis in a dose-dependent manner, and modified the blood profile, while Spirulina supplementation reduced growth and delayed metamorphosis. Interestingly, Spirulina-fed tadpoles showed increased resistance to acute Cd toxicity. These results suggest that while Cd accelerates metamorphosis as an adaptive survival strategy, Spirulina may act as a modulatory and protective agent. Spirulina under toxic conditions exacerbates the accelerated metamorphosis, synergizing Cd enhancing survival. Although preliminary, our findings suggest that Spirulina could represent a safe, accessible, and cost-effective nutritional strategy to mitigate Cd toxicity. It may offer translational benefits for human populations chronically exposed to Cd. These results support further investigation into Spirulina as a potential protective agent in environmental and clinical toxicology.

269. O13-08. EFFECT OF THE ENVIRONMENTAL CONTAMINANT IMIDACLOPRID ON THE REGULATION OF CELL GROWTH AND LIVER FUNCTION

Zahira Deza¹, Giselle Romero Caimi², Ezequiel Ridruejo³, Laura Alvarez⁴
 1. *FMED UBA; Laboratorio de Efectos Biologicos de Contaminantes Ambientales*
 2. *FMED UBA-Hospital Aleman, CABA; Laboratorio de Efectos Biologicos de Contaminantes Ambientales*
 3. *FMED UBA-CEMIC CABA; Laboratorio de Efectos Biologicos de Contaminantes Ambientales*
 4. *FMED-UBA-CONICET; Laboratorio de Efectos Biologicos de Contaminantes Ambientales*
 zahi.deza@gmail.com

Hepatocellular carcinoma is the most common liver cancer, with risk factors such as hepatitis B virus (HBV) and endocrine-disrupting environmental contaminants (EPCs) such as the neonicotinoid insecticide Imidacloprid (IMI). To evaluate the effect of Imidacloprid on the regulation of liver growth and function. Balb/c mice: IMI (0.01; 0.1; 10 mg/kg b.w.) orally for 30 days. We evaluated histology, functionality, and molecules (PCNA, TGF- β 1, caspase-3, MMPs, and tissue T3). In Huh7 and Huh7/Hbx transfected mice, IMI (0.01 and 10 μ M) was used at 4 and 24 hours to analyze deiodinase 1 (D1) mRNA, TGF- β 1 activity, metalloprotease (MMP2/9) activity, zymography, and the effect of Huh7 conditioned media (CM) with 10 μ M IMI on wound migration of EA-hy926. Mice: 0.01 mg/kg b.w. increased glycogen, vascular dilation, and connexin 43 (42%), and decreased caspase-3 (37%); 10 mg/kg b.w. decreased T3 (177%, $p > 0.01$), increased inflammatory infiltrate, caspase-3 (350%), PCNA (92%), and connexin 43 (23%). Colonies (7 days) increased IMI 0.01 μ M (56%), 0.1 μ M (28%) and decreased 1 μ M (44%) and 10 μ M (36%); 24hs: decreased PCNA (55%), β 3(CRP) (25%), TGF- β 1(WB) (63%) and increased MMP2 (55%); 4hs: increased PCNA (100%), β 3 (37%), TGF- β 1 (20%), MMP2 (200%) and D1 (103%). MC migration 4hs 0.01 μ M increased and 10 μ M decreased. Huh7/HBx IMI 24hs decreased PCNA (43%; $p > 0.01$). At 4 h, PCNA decreased (56%), TGF- β 1 mRNA (40%), D1 mRNA (103%), β 3 mRNA (49%), and MMP9 (50%). IMI in the liver alters functionality and histology, and deregulates thyroid growth and metabolism; TGF- β 1 and T3 may be involved

270. O13-09. META-ANALYSIS OF OIL-DERIVED HYDROCARBONS SHOWS DISTINCT TOXICITY IN TUMORIGENIC AND NON-TUMORIGENIC CELLS

Mariana Noelia Mardirosian¹, Mariana Lasagna², Lucía Enriquez³, Mariel Nuñez⁴, Claudia Cocca⁵, Andrés Venturino⁶
 1. *Instituto de Química y Fisicoquímica Biológicas "Prof. Alejandro C. Paladini" (UBA-CONICET). Buenos Aires, Argentina;*
 2. *Laboratorio de Radioisótopos, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Argentina.*

2. Instituto de Química y Fisicoquímica Biológicas "Prof. Alejandro C. Paladini" (UBA-CONICET). Buenos Aires, Argentina; Laboratorio de Radioisótopos, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Argentina.
3. Instituto de Química y Fisicoquímica Biológicas "Prof. Alejandro C. Paladini" (UBA-CONICET). Buenos Aires, Argentina; Laboratorio de Radioisótopos, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Argentina.
4. Instituto de Química y Fisicoquímica Biológicas "Prof. Alejandro C. Paladini" (UBA-CONICET). Buenos Aires, Argentina; Laboratorio de Radioisótopos, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Argentina.
5. Instituto de Química y Fisicoquímica Biológicas "Prof. Alejandro C. Paladini" (UBA-CONICET). Buenos Aires, Argentina; Laboratorio de Radioisótopos, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Argentina.
6. Centro de Investigaciones en Toxicología Ambiental y Agrobiotecnología del Comahue (UNCO-CONICET). Neuquén, Argentina; Laboratorio de investigaciones bioquímicas y químicas del ambiente, Universidad Nacional del Comahue, Argentina.
marianamardi@gmail.com

In recent decades, oil spills have become increasingly frequent, causing severe contamination events. Our study evaluated the toxic effects of hydrocarbons, focusing on the water-accommodated fraction of oil (WAF) and the polycyclic aromatic hydrocarbon (PAH) anthracene (ANT) on tumorigenic and non-tumorigenic cells. Experimentally, WAF decreased viability and clonogenicity in breast cancer cells (MDA-MB-231 and MCF-7), while ANT mainly reduced these parameters in non-tumorigenic MCF10-A cells. WAF also increased catalase activity in tumorigenic cells, whereas ANT reduced antioxidant activity in all cell lines, with GST showing cell-type specific responses. Multivariate analysis revealed correlations between viability markers and detoxifying enzymes. The results indicated concentration-dependent patterns: a biphasic response in tumorigenic cells exposed to WAF, and an ascending concentration-dependent response to ANT across all lines. These findings suggest that cellular sensitivity is modulated by tumorigenicity, and exposure to hydrocarbons may exacerbate malignant conditions. Additionally, we conducted a meta-analysis by integrating these results with 20 peer-reviewed studies assessing WAF, PAH, BTEX group (benzene, toluene, ethylbenzene, and xylene) and alkanes across different tissues and species. Using sensitivity distribution analysis, data were ranked according to effective concentrations for endpoints such as viability, clonogenicity, apoptosis, and genotoxicity. Surprisingly, tumorigenic cells were significantly more sensitive to hydrocarbons than non-tumorigenic cells ($p < 0.05$). Among hydrocarbons, PAH were the most toxic, followed by WAF, while BTEX and alkanes showed more heterogeneous effects. This work provides novel evidence of systematic differences in tumorigenic versus non-tumorigenic cellular responses to hydrocarbons, highlighting the value of integrating multiple biomarkers to assess toxicological risks.

ORALES 14 - SAIC - SESION ESPECIAL MULTIDISCIPLINARIA DE TRABAJOS ENVIADOS A PREMIO
DATE & TIME: 19/11/2025 13:00 - 14:30 H
Chairs: Graciela Calabrese, Giselle Peters

271. O14-01. **EFFEROCYTOSIS AND M2 MACROPHAGE POLARIZATION GENE EXPRESSION CORRELATES WITH RELAPSED AND REFRACTORY CLASSICAL HODGKIN LYMPHOMA PATIENTS: A MULTI-OMIC ANALYSIS**
Juan Quarroz Braghini¹, María Cecilia Cabral Lorenzo², Laura Kornbliht³, Mariana S. De Lorenzo⁴, Stella Maris Ranuncolo⁵, Guillermo Blanco⁶
1. Hospital de Clínicas "José de San Martín", Facultad de Medicina, Universidad de Buenos Aires; División Anatomía Patológica
2. Hospital de Clínicas "José de San Martín", Facultad de Medicina, Universidad de Buenos Aires; División Anatomía Patológica
3. Hospital de Clínicas "José de San Martín", Facultad de Me-

- dicina, Universidad de Buenos Aires; División Hematología
4. Office of Education-Rutgers New Jersey Medical School; Laboratory of Metabolism and Cancer Prevention, Department of Cell Biology & Molecular Medicine
5. Instituto de Oncología "Ángel H. Roffo", Facultad de Medicina, Universidad de Buenos Aires (UBA); Área Investigación
6. Hospital de Clínicas "José de San Martín" Facultad de Medicina Universidad de Buenos Aires (UBA); Laboratorio de Inmunotoxicología (LIT) IDEHU-CONICET
juanquarroz@gmail.com

Classical Hodgkin lymphoma (cHL) is a malignant neoplasm derived from germinal center-experienced B cells, characterized by Hodgkin-Reed-Sternberg cells (HRS) which comprise only 0.1–2% of the affected tissue, immersed in a complex microenvironment (TME). We hypothesized that efferocytosis and M2 macrophage polarization create an immunosuppressive TME, promoting HRS cell survival and treatment resistance. To test this, we performed a multi-omic analysis of a public microarray dataset from 130 cHL patients. We estimated cell type proportions using deconvolution (CIBERSORT) and grouped patients via hierarchical clustering (HC) based on a 19-gene signature related to efferocytosis and M2 macrophage function. Predictive power was evaluated by building and comparing ridge regression models to predict treatment outcomes based on cell types, the 19-gene signature, and clinical variables. Increased M2 and total macrophages fractions were significantly associated with poor outcomes ($p < 0.01$ and $p < 0.05$). HC revealed a cluster with low treatment response, high expression of efferocytosis and M2 genes, and enriched in early relapse and refractory cases. A predictive model using cell type proportions achieved an AUC of 0.83, and a hybrid model combining cell types with the 19-gene signature showed the highest predictive accuracy (AUC 0.87). Gene predictors of poor outcome included MerTK, AXL, and CD36, together with M2 macrophages and HRS cells. We conclude that the proportion of M2 macrophages, along with HRS cells, were significant predictors of poor outcome. The enrichment of efferocytosis and M2-related genes supported our hypothesis that this process is a critical immune checkpoint that promotes cHL progression and treatment failure.

272. O14-02. **TRISTETRAPOLIN (TTP/ZFP36) EXPRESSION IS ASSOCIATED WITH LOW PROLIFERATION AND ACTIVATION OF THE IL6/STAT3 PATHWAY IN LUMINAL BREAST CANCER CELLS**

Angela Lara Montero¹, Pedro Salaberry², Emilia Bogni³, Ana Laura⁴, Karina Cicinelli⁵, Noemi Jordanovski⁶, Eliana Querol⁷, Florencia Costa⁸, Mary Carrasco⁹, Daniela Maltagliatti¹⁰, Verónica Sanchotena¹¹, Laura Leguina¹², Silvia Vornetti¹³, Nicasio Cuneo¹⁴, Eva Wertheimer¹⁵, Claudia Arias¹⁶, Gabriela Acosta¹⁷, Diego Flaks¹⁸, Edith Kordon¹⁹

1. Instituto de Fisiología, Biología Molecular y Neurociencias; IFIBYNE
2. Instituto de Fisiología, Biología Molecular y Neurociencias; IFIBYNE
3. Instituto de Fisiología, Biología Molecular y Neurociencias; IFIBYNE
4. Instituto de Fisiología, Biología Molecular y Neurociencias; IFIBYNE
5. Instituto de Fisiología, Biología Molecular y Neurociencias; IFIBYNE
6. Hospital Oncológico Marie Curie; Departamento de Anatomía Patológica
7. Hospital Oncológico Marie Curie; Departamento de Anatomía Patológica
8. Hospital Oncológico Marie Curie; Departamento de Patología Mamaria
9. Hospital Oncológico Marie Curie; Departamento de Patología Mamaria
10. Hospital Oncológico Marie Curie; Departamento de Patología Mamaria
11. Hospital Oncológico Marie Curie; Departamento de Patología Mamaria
12. Hospital Oncológico Marie Curie; Departamento de

Anatomía Patológica
 13. Hospital Oncológico Marie Curie; Departamento de Anatomía Patológica
 14. Hospital Oncológico Marie Curie; Departamento de Patología Mamaria
 15. Centro de Estudios Farmacológicos y Botánicos; CE-FYBO
 16. Hospital Oncológico Marie Curie; Departamento de Patología Mamaria
 17. Hospital Oncológico Marie Curie; Departamento de Anatomía Patológica
 18. Hospital Oncológico Marie Curie; Departamento de Patología Mamaria
 19. Instituto de Fisiología, Biología Molecular y Neurociencias; IFIBYNE
 angelalaramt@gmail.com

Tristetraprolin (TTP), encoded by the ZFP36 gene, is an anti-inflammatory and tumor suppressor protein that regulates cytoplasmic mRNA degradation and modulates nuclear transcription. Its down-regulation has been reported in invasive breast cancer, particularly in basal-like compared with luminal tumors. To better define its role, we performed an integrative analysis using breast cancer samples from patients at the Marie Curie Oncologic Hospital (Argentina), together with data from TCGA, METABRIC, and CPTAC, complemented by studies in luminal breast cancer cell lines (MCF7 and T47D). We confirmed by qPCR that TTP expression is reduced in tumors compared with adjacent normal tissue, decreases with advancing clinical stage, and associates with poor prognosis in premenopausal women. We found negative correlations between TTP and the proliferation markers Ki-67 and Cyclin D1, which became stronger with tumor growth progression. Silencing ZFP36 in MCF7 cells significantly increased these markers, while GSEA revealed enrichment of cell cycle-related genes inversely correlated with TTP, supporting its antiproliferative effect. Conversely, TTP expression correlated positively with immune response-related genes, particularly IL6, and with phosphorylated STAT3 in multiple cohorts and tissues. Functional assays demonstrated that IL6 induces TTP expression through STAT3 activation, as shown by RNA-seq, real-time PCR, Western Blot, ChIP-seq, and reporter assays. Blocking STAT3 phosphorylation abrogated this induction. Together, our findings support TTP as a tumor suppressor in luminal breast cancer by limiting proliferation. However, its STAT3-dependent induction suggests a dual, context-dependent role during tumor progression, potentially reflecting differential functions in early versus advanced breast cancer and in tumor-immune system interactions.

273. O14-03. METRONOMIC CHEMOTHERAPY (MCT) WITH CYCLOPHOSPHAMIDE (CY) AND LOSARTAN (LOS) REDUCES SYSTEMIC TOXICITY ASSOCIATED WITH CONVENTIONAL MAXIMUM TOLERATED DOSE (MTD) THERAPY IN M-234p TRIPLE NEGATIVE MAMMARY ADENOCARCINOMA BEARING MICE

Eva Soto Arenilla¹, María del Pilar López², María Croce³, Camila Delfina Díaz Unzué⁴, Viviana R. Rozados⁵, O. Graciela Scharovsky⁶, Leandro E. Mainetti⁷, María José Rico⁸

1. Facultad de Ciencias Médicas, Universidad Nacional de Rosario.; Instituto de Genética Experimental, Facultad de Ciencias Médicas, Universidad Nacional de Rosario
 2. Facultad de Ciencias Médicas, Universidad Nacional de Rosario.; Instituto de Genética Experimental, Facultad de Ciencias Médicas, Universidad Nacional de Rosario
 3. Facultad de Ciencias Médicas, Universidad Nacional de Rosario.; Instituto de Genética Experimental, Facultad de Ciencias Médicas, Universidad Nacional de Rosario
 4. Facultad de Ciencias Médicas, Universidad Nacional de Rosario.; Instituto de Genética Experimental, Facultad de Ciencias Médicas, Universidad Nacional de Rosario
 5. Facultad de Ciencias Médicas, Universidad Nacional de Rosario. CONICET; Instituto de Genética Experimental, Facultad de Ciencias Médicas, Universidad Nacional de Rosario.
 6. Facultad de Ciencias Médicas, Universidad Nacional de

Rosario. CONICET; Instituto de Genética Experimental, Facultad de Ciencias Médicas, Universidad Nacional de Rosario.
 7. Facultad de Ciencias Médicas, Universidad Nacional de Rosario. CONICET; Instituto de Genética Experimental, Facultad de Ciencias Médicas, Universidad Nacional de Rosario.
 8. Facultad de Ciencias Médicas, Universidad Nacional de Rosario. CONICET.; Instituto de Genética Experimental, Facultad de Ciencias Médicas, Universidad Nacional de Rosario.
 evac-sotoa@unilibre.edu.co

Triple-negative breast cancer (TNBC) is an aggressive subtype characterized by the absence of estrogen (ER) and progesterone (PR) receptors, and low expression of HER2, limiting therapeutic options. Standard treatment involves maximum tolerated dose (MTD) chemotherapy, but it often leads to systemic toxicity and resistance. Metronomic chemotherapy (MCT), administers low doses continuously, reducing toxicity and indirect antitumor effects. Cyclophosphamide (CY), a widely used alkylating agent, and Losartan (LOS), a repositioned drug, can reduce stromal collagen, thereby improving delivery of drugs and oxygen to the tumor. We assessed the efficacy of MCT (CY+LOS), MTD, and Chemo-Switch (C-S) strategy (one MTD cycle followed by MCT) on tumor growth, metastasis, white blood cell count (WBC), and body weight in BALB/c mice challenged with M-234p breast adenocarcinoma (n=27) s.c. Groups: CONTROL, CY+LOS (25 mg/kg CY + 200 mg/kg LOS), MTD (150 mg/kg CY i.p. on days 0, 2, 4 with 21-day rest), and C-S (MTD followed by CY+LOS from day 13). The experiment had two endpoints: 1st: where CONTROL group and half of treated groups were euthanized. 2nd: where remaining mice were euthanized. Results: 1st point: All treatments significantly reduced tumor volume vs. CONTROL (P<0.05). CY+LOS maintained WBC within normal limits (P<0.05). 2nd point: Lung metastases were observed in MTD (25%) and C-S (20%), but not in CY+LOS. Only MTD caused significant weight loss (P<0.05). Conclusion: CY+LOS preserves WBC counts within the normal range, prevents metastasis, and reduces systemic toxicity compared to MTD, supporting its potential as a safer and effective alternative for TNBC treatment.

274. O14-04. GENERATION OF A MULTIDIMENSIONAL SYSTEM TO MODEL CARDIAC REGENERATION FROM MATURE CARDIOMYOCYTES DERIVED FROM HUMAN PLURIPOTENT STEM CELLS

Joaquín Smucler¹, Joaquín Etchepareborda², Julia Halek³, Denisse Saulnier⁴, Sheila Castañeda⁵, Theo Fernández Long⁶, Guadalupe Amin⁷, Alejandra Guberman⁸, Santiago Miriuka⁹, Lucía Moro¹⁰, Ariel Waisman¹¹

1. INEU-FLENI; LIAN
 2. INEU-FLENI; LIAN
 3. INEU-FLENI; LIAN
 4. INEU-FLENI; LIAN
 5. INEU-FLENI; LIAN
 6. INEU-FLENI; LIAN
 7. INEU-FLENI; LIAN
 8. IQUIBICEN-FCEN-UBA; Laboratorio de Regulación Génica en Células Madre
 9. INEU-FLENI; LIAN
 10. INEU-FLENI; LIAN
 11. INEU-FLENI; LIAN
 joaquin.smucler@gmail.com

Cardiovascular diseases constitute the leading cause of death worldwide. Unlike vertebrates such as zebrafish and newts that can completely regenerate the myocardium, the adult mammalian heart possesses an extremely limited capacity for post-ischemic regeneration, often leading to heart failure. It was recently demonstrated that neonatal mammals retain an intrinsic regenerative capacity during the first postnatal week, which is mediated by proliferation of surviving cardiomyocytes. This makes cell cycle re-entry an important therapeutic target for future regenerative therapies. This project develops a comprehensive in vitro model to study cardiac regeneration using cardiomyocytes derived from human pluripotent stem cells. First, we adapted a robust metabolic reprogramming protocol that transforms cardiomyocytes with fetal identity to a mature stage

similar to the postnatal phenotype, characterized by structural, metabolic, and functional changes. RNA sequencing analysis validated the maturation process and allowed us to identify two potential maturation specific markers, such as DES and XIRP2. Second, we demonstrated that the most common cardiac differentiation protocol generates pure populations of left ventricular cardiomyocytes, resolving a long-standing controversy in the field. Third, we developed innovative methodological tools including a cell cycle reporter cell line and a culture platform with artificial intelligence analysis to distinguish genuine proliferation from polynucleation or polyploidy. Preliminary studies with WNT pathway activators and neuregulin showed significant induction of cell cycle re-entry. This comprehensive system provides the foundation for identifying therapeutic strategies that promote human cardiac regeneration.

275. O14-05. COMMONLY-USED HERBICIDES TRIGGER STRESS AND SURVIVAL PATHWAY DISRUPTION IN HUMAN CELLS: A TRANSCRIPTOMIC AND FUNCTIONAL ANALYSIS

Calén Sansalone¹, Tomás Lorusso², Ianina Ferder³, Ezequiel Petrillo⁴, Matías Blaustein⁵, Mercedes García Carrillo⁶

1. Universidad de Buenos Aires (UBA). Facultad de Ciencias Exactas y Naturales (FCEyN). Departamento de Fisiología, Biología Molecular y Celular (DFBMC). Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3). Buenos Aires, Argentina.; Grupo de Biología de Sistemas y Filosofía del Cáncer

2. Universidad de Buenos Aires (UBA). Facultad de Ciencias Exactas y Naturales (FCEyN). Departamento de Fisiología, Biología Molecular y Celular (DFBMC). Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3). Buenos Aires, Argentina.; Grupo de Biología de Sistemas y Filosofía del Cáncer

3. Universidad de Buenos Aires (UBA). Facultad de Ciencias Exactas y Naturales (FCEyN). Departamento de Fisiología, Biología Molecular y Celular (DFBMC). Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3). Buenos Aires, Argentina.; Laboratorio DNS: Genética y Genómica de enfermedades hereditarias humanas

4. CONICET-UBA. Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE). Buenos Aires, Argentina.; Laboratorio de Fotobiología del ARN

5. Universidad de Buenos Aires (UBA). Facultad de Ciencias Exactas y Naturales (FCEyN). Departamento de Fisiología, Biología Molecular y Celular (DFBMC). Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3). Buenos Aires, Argentina. CONICET, Buenos Aires, Argentina.; Grupo de Biología de Sistemas y Filosofía del Cáncer

6. Universidad de Buenos Aires (UBA). Facultad de Ciencias Exactas y Naturales (FCEyN). Departamento de Biodiversidad y Biología Experimental (DBBE). Buenos Aires, Argentina. Universidad de Buenos Aires (UBA). Facultad de Ciencias Exactas y Naturales (FCEyN). Departamento de Fisiología, Biología Molecular y Celular (DFBMC). Instituto de Biociencias, Biotecnología y Biología Traslacional (iB3). Buenos Aires, Argentina.; Grupo de Biología de Sistemas y Filosofía del Cáncer y Grupo de Etnobiología (DBBE, FCEyN)

cnsansalone@gmail.com

An increasing body of evidence suggests that herbicides may elicit a harmful effect on human cells. This work aimed to perform a comparative analysis of the potential toxicological effects of three herbicide formulations on human cells: RoundUp (active ingredient: glyphosate), Gesaprim (active ingredient: atrazine), and Paraquat Insuagro (active ingredient: paraquat). Previous bioinformatic results revealed that herbicide-protein interaction networks were linked to the regulation of key signaling pathways involved in cell death and survival, stress response, and the maintenance of proteostasis, including the PI3K/Akt and the Unfolded Protein Response pathways. Besides, an enrichment in cancer-associated categories was detected for all herbicides. Transcriptomic analysis using the PromethION 2 sequencing platform revealed that all formulations

produced changes in alternative splicing patterns compared to the vehicle treatment (1x PBS). Moreover, paraquat induced changes in the expression of genes linked to the response to cellular stress, apoptosis, cell-cycle regulation, and proliferation. These results were confirmed experimentally: RoundUp caused an increase in pAKT Ser-473 levels, Paraquat Insuagro and Gesaprim triggered the activation of the PERK branch of the UPR as evidenced by increased ATF4 protein levels, and Paraquat Insuagro elicited the activation of the IRE1 UPR branch as evidenced by an increase in the XBP1 spliced/unspliced ratio. In the same line, confocal microscopy with fluorescent reporters experiments revealed changes in the regulation of both pathways in cells exposed to these formulations. Overall, our results indicated that herbicides can deregulate the Akt and UPR pathways, affecting proteostasis and potentially altering crucial physiological and pathological processes.

276. O14-06. YERBA MATE SHOWS ANTI-INFLAMMATORY AND CARDIOPROTECTIVE POTENTIAL THROUGH NLRP3 INHIBITION

Ignacio Barbani Moglie¹, Jazmin Kelly², Stefano Toldo³

1. Robert M. Berne Cardiovascular Research Center, University of Virginia, Charlottesville, VA, USA; Hospital Universitario Austral, Pilar, Buenos Aires, Argentina; Robert M. Berne Cardiovascular Research Center, University of Virginia

2. Robert M. Berne Cardiovascular Research Center, University of Virginia, Charlottesville, VA, USA; Robert M. Berne Cardiovascular Research Center, University of Virginia

3. Robert M. Berne Cardiovascular Research Center, University of Virginia, Charlottesville, VA, USA; Robert M. Berne Cardiovascular Research Center, University of Virginia

ignaciomoglie.ph@gmail.com

Background: NLRP3 inflammasome activation is a major contributor to systemic inflammation and cardiac dysfunction. Yerba mate (YM), a traditional South American infusion, contains bioactive compounds with reported anti-inflammatory effects. We hypothesize that YM could inhibit NLRP3 activation, reduce proinflammatory cytokine release, and preserve cardiac function under systemic inflammatory stress. Therefore, the objective of this study is to investigate YM's anti-inflammatory and cardioprotective effects in both *in vitro* and *in vivo* models. Methods: An aqueous YM extract (200 mg/mL) was prepared from commercial leaves. *In vitro*, murine J774.1 macrophages were treated with YM (100 or 500 µg/mL) for 24 hours, followed by stimulation with lipopolysaccharide (LPS) (4 µg/mL) and adenosine triphosphate (ATP) (5 mM). Supernatants were analyzed for IL-1β and IL-6 secretion using ELISA. *In vivo*, male CD1 mice were pretreated with YM (25 mg/day via oral gavage) or water for 7 days, then challenged with lipopolysaccharide (5 mg/kg, intraperitoneal). Cardiac function was evaluated by transthoracic echocardiography at baseline and 4 hours post-challenge. Results: YM significantly reduced IL-1β and IL-6 secretion in LPS/ATP-stimulated macrophages at both 100 and 500 µg/mL (****p < 0.0001), with an additional reduction between doses (**p < 0.01). *In vivo*, LPS markedly reduced left ventricular ejection fraction in controls (****p < 0.0001), whereas YM-pretreated animals preserved cardiac function (**p < 0.01). Conclusion: These findings suggest that YM exerts anti-inflammatory and cardioprotective effects through both NLRP3-dependent and independent mechanisms, likely involving NFκB pathway modulation. Further studies are required to evaluate *in vivo* cytokine release and confirm these results.

277. O14-07. SMYD2 INHIBITION AS A DUAL STRATEGY TO SUPPRESS TUMOR GROWTH AND ENHANCE ANTI-PD-1 THERAPY IN MURINE HCC

Bárbara Bueloni¹, Mariel Fusco², Esteban Fiore³, Mariana Malvicini⁴, María Jose Cantero⁵, Lucía Lamerli⁶, Mailín Casadei⁷, Brian Martinez Ruiz⁸, Catalina Atorrasagasti⁹, Florencia Mercogliano¹⁰, Guillermo Mazzolini¹¹, Juan Bayo¹²

1. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Av. Presidente Perón 1500 (B1629AJH) Pilar, Buenos Aires, Argentina; Programa de Hepatología Experimental y Terapia Génica

2. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Av. Presidente Perón 1500 (B1629AJH) Pilar, Buenos Aires, Argentina; Laboratorio de Inmunobiología del Cáncer
3. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Av. Presidente Perón 1500 (B1629AJH) Pilar, Buenos Aires, Argentina; Programa de Hepatología Experimental y Terapia Génica
4. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Av. Presidente Perón 1500 (B1629AJH) Pilar, Buenos Aires, Argentina.; Laboratorio de Inmunobiología del Cáncer
5. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Av. Presidente Perón 1500 (B1629AJH) Pilar, Buenos Aires, Argentina.; Programa de Hepatología Experimental y Terapia Génica
6. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Av. Presidente Perón 1500 (B1629AJH) Pilar, Buenos Aires, Argentina.; Programa de Hepatología Experimental y Terapia Génica
7. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Av. Presidente Perón 1500 (B1629AJH) Pilar, Buenos Aires, Argentina.; Programa de Hepatología Experimental y Terapia Génica
8. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Av. Presidente Perón 1500 (B1629AJH) Pilar, Buenos Aires, Argentina.; Programa de Hepatología Experimental y Terapia Génica
9. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Av. Presidente Perón 1500 (B1629AJH) Pilar, Buenos Aires, Argentina.; Programa de Hepatología Experimental y Terapia Génica
10. Instituto de Biología y Medicina Experimental, Consejo Nacional de Investigaciones Científicas y Tecnológicas (CONICET) Vuelta de Obligado 2490; Laboratorio de Inmunología Tumoral
11. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Av. Presidente Perón 1500 (B1629AJH) Pilar, Buenos Aires, Argentina.; Programa de Hepatología Experimental y Terapia Génica
12. Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Av. Presidente Perón 1500 (B1629AJH) Pilar, Buenos Aires, Argentina.; Programa de Hepatología Experimental y Terapia Génica
bbueloni-conicet@austral.edu.ar

Hepatocellular carcinoma (HCC) is a major cause of mortality, and novel treatments are imperative. SMYD2, a lysine methyltransferase overexpressed in several tumors, modifies histone and non-histone substrates that regulate oncogenic signaling, with emerging evidence linking it to the tumor microenvironment. However, its role in HCC remains unclear. To address this, we analyzed public and spatial transcriptomic datasets from HCC patients, assessing SMYD2 correlations through Gene Ontology and immune deconvolution. RNA-seq was performed on HuH7 cells following SMYD2 inhibition. PM299L cells with hyperactive β -catenin were used to evaluate the effects of SMYD2 inhibition on signaling pathways. Tumor-macrophage interactions were assessed in J774 macrophages exposed to Wnt modulators and tumor-conditioned media. The SMYD2 inhibitor AZ-505 was tested in orthotopic Hepa129 and PM299L models, including combination with anti-PD-1. Gene expression in tumors was analyzed by RNA-seq and qPCR, and immune infiltrate by flow cytometry. Patient datasets showed SMYD2 upregulation in tumors, inverse association with immune effector infiltration, and correlation with oncogenic programs. SMYD2 inhibition reversed these programs in HCC cells and impaired viability without affecting primary hepatocytes. AZ-505 reduced Hepa129 tumor growth, shifting gene expression toward an inflammatory profile. Mechanistically, AZ-505 downregulated Wnt/ β -catenin signaling targets, reduced Wnt ligand expression in PM299L cells and limited tumor-driven TGF- β expression in macrophages. In PM299L tumors, AZ-505 synergized with anti-PD-1 to reduce tumor burden and enhance immune response. These findings unveil SMYD2 as a central regulator of tumor pro-

gression and immunosuppression in HCC and provide rationale for its combination with immunotherapy, particularly in Wnt/ β -catenin-active tumors.

278. O14-08. ENHANCING CDK4/6 INHIBITION IN BREAST CANCER BY TARGETING PROGESTERONE RECEPTOR ISOFORM A: MECHANISMS AND STRATEGIES TO OVERCOME PALBOCICLIB RESISTANCE

Gabriela Pataccini¹, Andrés Elía², Luisa Ambrosio³, Leo Saldain⁴, Paola Rojas⁵, Silvia Inés Vanzulli⁶, Karin Villar⁷, Javier Burruchaga⁸, Florencia Torres⁹, Paula Martínez-Vázquez¹⁰, Caroline A Lamb¹¹, Victoria Fabris¹², Virginia Novaro¹³, Martin C Abba¹⁴, Sebastián Giulianelli¹⁵, Claudia Lanari¹⁶

1. Instituto de Biología y Medicina Experimental (IBYME), CONICET, CABA, Argentina; Laboratorio de carcinogénesis hormonal

2. Instituto de Biología y Medicina Experimental (IBYME), CONICET, CABA, Argentina; Laboratorio de carcinogénesis hormonal

3. Instituto de Biología y Medicina Experimental (IBYME), CONICET, CABA, Argentina; Laboratorio de carcinogénesis hormonal

4. Instituto de Biología y Medicina Experimental (IBYME), CONICET, CABA, Argentina; Laboratorio de carcinogénesis hormonal

5. Instituto de Biología y Medicina Experimental (IBYME), CONICET, CABA, Argentina; Laboratorio de carcinogénesis hormonal

6. Instituto de Biología y Medicina Experimental (IBYME), CONICET, CABA, Argentina; Laboratorio de carcinogénesis hormonal

7. Hospital de Agudos "Magdalena V de Martínez", General Pacheco, Buenos Aires, Argentina; Servicio de Mastología

8. Hospital de Agudos "Magdalena V de Martínez", General Pacheco, Buenos Aires, Argentina; Servicio de Mastología

9. Hospital de Agudos "Magdalena V de Martínez", General Pacheco, Buenos Aires, Argentina; Servicio de Patología

10. Hospital de Agudos "Magdalena V de Martínez", General Pacheco, Buenos Aires, Argentina; Servicio de Mastología

11. Instituto de Biología y Medicina Experimental (IBYME-CONICET), CABA, Argentina; Laboratorio de carcinogénesis hormonal

12. Instituto de Biología y Medicina Experimental (IBYME-CONICET), CABA, Argentina; Laboratorio de carcinogénesis hormonal

13. Instituto de Biología y Medicina Experimental (IBYME-CONICET), CABA, Argentina; Laboratorio de Proteínas Quinasas y Cáncer

14. Centro de Investigaciones Inmunológicas Básicas y Aplicadas (CINIBA), Facultad de Ciencias Médicas, Universidad Nacional de La Plata, La Plata, Buenos Aires, Argentina; Centro de Investigaciones Inmunológicas Básicas y Aplicadas (CINIBA)

15. Instituto de Biología de Organismos Marinos, IBIO-MAR-CCT CENPAT-CONICET, Argentina; Laboratorio de reproducción y biología integrativa de invertebrados marinos

16. Instituto de Biología y Medicina Experimental (IBYME-CONICET), CABA, Argentina; Laboratorio de carcinogénesis hormonal

gaby.pataccini@gmail.com

CDK4/6 inhibitors (CDK4/6-i) have significantly advanced the treatment of hormone receptor-positive breast cancer. Mifepristone is currently under investigation for tumors with a higher expression of progesterone receptor PR isoform A (PRA) relative to isoform B (PRB), termed PRA-high (PRA-H). This study evaluated the therapeutic efficacy of combining mifepristone with CDK4/6-i in PRA-H models. Mifepristone enhanced the anti-proliferative effects of palbociclib, ribociclib, and abemaciclib in PRA-expressing human breast cancer cell lines ($p < 0.0001$, $p < 0.001$ and $p < 0.05$, respectively). Co-treatment reduced proliferation through downregulation of RB phosphorylation and E2F1 expression ($p < 0.0001$ and $p < 0.01$). A direct effect of mifepristone increasing PR binding to E2F1 promot-

er was confirmed by CHIP assays. These effects were corroborated in T47D xenografts, PRA-H patient-derived tumor cultures and a PRA-H murine model. Among murine tumor lines, the 59 family was sensitive to palbociclib, while the C4 family displayed de novo resistance. Exome sequencing did not reveal recurrent mutations driving resistance although transcriptomic analysis highlighted E2F pathway enrichment in sensitive tumors and Notch signaling in resistant variants. Critically, pharmacologic inhibition of NOTCH1 restored palbociclib sensitivity in resistant C4-derived cells ($p < 0.001$). These findings elucidate the benefit of combining mifepristone with CDK4/6-i in PRA-H breast tumors and implicate the Notch pathway, particularly NOTCH1, as a modulator of resistance, highlighting a novel therapeutic target. This work supports further clinical investigation of combined CDK4/6 with PR or Notch blockade and highlights novel biomarkers for directing therapeutic strategies to overcome resistance in luminal breast cancer.

279. O14-09. WHOLE-EXOME SEQUENCING REVEALS COMPOUND HETEROZYGOUS EIF2B5 VARIANTS IN LEUKODYSTROPHY WITH VANISHING WHITE MATTER

Sofia Savy¹, Franciso A. Montes², Carola L. Grosso³, Laura E. Laróvere⁴, Silene M. Silvera-Ruiz⁵, Gerardo H. Carro⁶, Guillermo Guelbert⁷, Adriana Becerra⁸, David Morales⁹, Juan Pablo Nicola¹⁰

1. Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina; Centro de Investigaciones en Bioquímica Clínica e Inmunología - Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina.
2. Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina.; Centro de Investigaciones en Bioquímica Clínica e Inmunología - Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina.
3. Centro de Estudio de las Metabolopatías Congénitas, Hospital de Niños de la Santísima Trinidad. Córdoba, Argentina.; Cátedra de Clínica Pediátrica, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba. Córdoba, Argentina.
4. Centro de Estudio de las Metabolopatías Congénitas, Hospital de Niños de la Santísima Trinidad. Córdoba, Argentina.; Cátedra de Clínica Pediátrica, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba. Córdoba, Argentina.
5. Centro de Estudio de las Metabolopatías Congénitas, Hospital de Niños de la Santísima Trinidad. Córdoba, Argentina.; Sección de Enfermedades Metabólicas
6. Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina.; Centro de Investigaciones en Bioquímica Clínica e Inmunología - Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina.
7. Sección de Enfermedades Metabólicas, Hospital de Niños de la Santísima Trinidad. Córdoba, Argentina.; Pediatría en la sección de enfermedades metabólicas
8. Sección de Enfermedades Metabólicas, Hospital de Niños de la Santísima Trinidad. Córdoba, Argentina.; Pediatría en la sección de enfermedades metabólicas
9. Servicio de Neurología, Hospital Nuestra Señora de la Misericordia. Córdoba, Argentina.; Neurología
10. Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina.; Centro de Investigaciones en Bioquímica Clínica e Inmunología - Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina.

sofia.savy@mi.unc.edu.ar

Vanishing white matter disease is a rare autosomal recessive leukodystrophy associated with pathogenic variants in any of the five genes (EIF2B1-5) that encode subunits of the eukaryotic translation initiation factor 2B (eIF2B). Here, we present a case of a 26-year-old female patient from a non-consanguineous Amerindian Bolivian family, with clinical and neuroimaging findings suggestive of early-onset vanishing white matter disease, characterized by slowly progressive neurological deterioration in the absence of ovarian fail-

ure. Whole-exome sequencing revealed a novel pair of compound heterozygous variants in the EIF2B5 gene, confirming the diagnosis of leukodystrophy with vanishing white matter and bringing closure to a nearly 20-year diagnostic odyssey. The identified c.318A>T (p.Leu106Phe) and c.1688G>A (p.Arg563Gln) in the EIF2B5 gene were classified as pathogenic and likely-pathogenic, respectively, according to the American College of Medical Genetics and Genomics. Complementary Sanger sequencing revealed that the variants co-segregated with the phenotype in the pedigree, providing strong evidence of autosomal recessive inheritance of the disease, and enabling the molecular diagnosis of two asymptomatic sisters presenting white matter abnormalities on neuroimaging. This case underscores the heterogeneous nature of vanishing white matter disease, and emphasizes the relevance of integrating a comprehensive clinical evaluation, brain magnetic resonance imaging, and genetic studies in the diagnosis of leukodystrophies.

POSTERS 15 - SAIC - BIOLOGÍA CELULAR Y MOLECULAR 2

DATE & TIME: 19/11/2025 13:00 - 14:30 H

Chairs: Mercedes Debernardi, Flavia Piccioni, Juan Bizzotto

280. P15-13. GALECTIN-1 DRIVES THE BIOENERGETIC REPROGRAMMING OF PATIENT-DERIVED GLIOMA STEM CELLS

Luisina Belén Ripari¹, Mariana Belén Vera², Olivia Morris-Hannon³, Joaquín Pedro Merlo⁴, Gustavo Sevelever⁵, Guillermo Videla-Richardson⁶, Gabriel Adrián Rabinovich⁷

1. FLENI-CONICET; Laboratorio de Investigación Aplicada a las Neurociencias (LIAN)
2. FLENI-CONICET; Laboratorio de Investigación Aplicada a las Neurociencias (LIAN)
3. FLENI-CONICET; Laboratorio de Investigación Aplicada a las Neurociencias (LIAN)
4. IBYME-CONICET; Laboratorio de Glicomedicina
5. FLENI-CONICET; Laboratorio de Investigación Aplicada a las Neurociencias (LIAN)
6. FLENI-CONICET; Laboratorio de Investigación Aplicada a las Neurociencias (LIAN)
7. IBYME-CONICET; Laboratorio de Glicomedicina

luisina.ripari@gmail.com

Glioblastoma (GB) is the most common and lethal tumor of the central nervous system. It shows high intra- and inter-tumoral heterogeneity and a high recurrence rate, leading to a median survival of only 14 months. These aggressive features are largely driven by glioma stem cells (GSCs), which promote tumor initiation and maintenance. As in many cancers, cellular metabolism is frequently dysregulated in GB. Galectin-1 (Gal-1) is a glycan-binding lectin involved in tumor-promoting mechanisms, including cell migration, stemness, angiogenesis, and immune evasion. Using our own established patient-derived GSC lines (G02, G03, and G09) we studied the role of Gal-1 in metabolism and defined their distinct bioenergetic profiles. RNA sequencing of G09 revealed that Gal-1 increases the expression of genes related to oxidative phosphorylation and glycolysis. Seahorse assays confirmed reduced oxygen consumption rate and extracellular acidification rate upon Gal-1 loss. Interestingly, G03 showed the opposite behavior, with increased glycolysis when Gal-1 was silenced. This correlated with a significant drop in glucose uptake, suggesting a metabolic shift toward greater glycolytic activity. Using Seahorse, TMRE and MitoSOX assays, we found that G02 exhibited the highest metabolic activity, with more functional and efficient mitochondria and lower oxidative stress. Cell imaging showed a fused mitochondrial network, a state linked to enhanced oxidative phosphorylation and stress resilience, contrasting with the fragmented morphology of the other lines. Altogether, these findings demonstrate how Gal-1 shapes GSC metabolism and highlight metabolic heterogeneity among patient-derived lines, underscoring its potential as a therapeutic target and the need for personalized strategies in GB.

281. P15-14. MELATONIN PROTECTS AGAINST PARA-

QUAT-INDUCED OXIDATIVE STRESSPaloma Grimaldi¹, Santiago Charif²

1. *Universidad Argentina de la Empresa (UADE); Facultad de Ingeniería y Ciencias Exactas,*
 2. *Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) / Universidad Argentina de la Empresa (UADE); Instituto de Tecnología (INTEC), Departamento de Biotecnología, Alimentos, Agro y Ambiental (DEBAL), Facultad de Ingeniería y Ciencias Exactas*
 pagrimaldi@uade.edu.ar

Paraquat (PQ) is a commonly used and widely distributed herbicide that acts as a redox cyclor, inducing oxidative stress in cells and posing serious health risks. If not relieved or stopped, cell viability and nuclear integrity could be compromised, ultimately leading to apoptosis. This highlights the importance of exploring new and natural protective agents capable of preventing or mitigating these harmful effects. Melatonin, a hormone produced by the pineal gland in vertebrates, has demonstrated strong antioxidant properties. In line with the search for low-cost, accessible, and naturally derived antioxidants, This study aimed to evaluate potential antioxidant and protective effects of melatonin against PQ-induced cytotoxicity. CHO-K1 cells were incubated with different doses of PQ (24 hours), 50 μ M MEL (24 hours), or sequentially with PQ followed by 50 μ M MEL (each for 24 hours). Control consisted in culture medium (48h). Nuclei were stained with DAPI to evaluate damage, cell viability was estimated by Trypan blue exclusion assay and cytotoxicity was determined by MTS assay. Results were expressed as mean $\pm$ standard error of the mean (SEM). The highest concentration of PQ (1000 μ M) reduced the percentage of viable cells, while MEL alone had no notable effect. However, 1000 μ M PQ-50 μ M MEL treatment significantly improved cell viability. MTS assay results revealed a similar fashion. DAPI staining showed increased fluorescence intensity in PQ-treated cells, indicating nuclear damage, which was significantly reduced in cells under subsequent MEL treatment. In conclusion, MEL post-treatment may counteract PQ-induced cytotoxicity and apoptosis-related nuclear changes, offering a potential natural protective strategy.

282. P15-15. EFFECTS OF LUMACFTOR AND IVACFTOR ON MITOCHONDRIAL DYNAMICS IN CYSTIC FIBROSIS CELL LINES HETEROZYGOUS FOR Δ F508-CFTRCamila Dib¹, Mia Salgado², Analía Graciela Karadayian³, Adriana Gabriela López Guerra⁴, Tomás Antonio Santa Coloma⁵, Ángel Gabriel Valdivieso⁶

1. *BIOMED-UCA-CONICET; Laboratory of Cell. & Mol. Biol.*
 2. *BIOMED-UCA-CONICET; Laboratory of Cell. & Mol. Biol.*
 3. *BIOMED-UCA-CONICET; Laboratory of Cell. & Mol. Biol.*
 4. *BIOMED-UCA-CONICET; Laboratory of Cell. & Mol. Biol.*
 5. *BIOMED-UCA-CONICET; Laboratory of Cell. & Mol. Biol.*
 6. *BIOMED-UCA-CONICET; Laboratory of Cell. & Mol. Biol.*
 cdib@uca.edu.ar

Mutations in the CFTR gene causing cystic fibrosis (CF) are associated with mitochondrial abnormalities and altered mitochondrial dynamics. We previously observed increased mitochondrial fission upon cAMP stimulation of CFTR in IB3-1 CF cells. Lumacaftor (VX-809) and ivacaftor (VX-770) are the first CFTR modulators approved for CF treatment, but their efficacy in heterozygous patients is limited. To analyze the effects of VX-809 and VX-770, alone or combined, on mitochondrial morphology and function, IB3-1 (Δ F508/W1282X), S9 (IB3-1 expressing wild-type CFTR) and C38 (IB3-1 expressing truncated functional CFTR) cells were used. Cells were treated with VX-809 (10 μ M) and VX-770 (0.1 μ M) for 48 h. Cell viability was assessed by XTT assay. Mitochondrial morphology was analyzed in live cells using MitoTracker Orange and confocal microscopy. MFN1 and DRP1 expressions were measured by WB. Mitochondrial membrane potential (Ψ m) and ROS levels were measured via flow cytometry using TMRE/JC-1 and DCFH/MitoSOX, respectively. Complexes I-III activities and basal ATP were quantified spectrophotometrically and by luminescence. CFTR function was evaluated via iodide efflux using MQAE fluorescent probe. Combined VX-809 and VX-770 treatment increased mitochondrial fission

without altering MFN1 or DRP1 expression, reduced complex I-III activity and did not affect basal ATP levels or Ψ m. No improvement in CFTR function was observed. In conclusion, in heterozygous Δ F508-CF cells, combined VX-809 and VX-770 induce mitochondrial fragmentation and reduces complex I-III activity without altering bioenergetics. These effects may reflect compensatory adaptations or off-target effects of CFTR modulators. Supported by ANPCYT (PICT-2015-1031 and PICT-2020 SERIE A-03854); CONICET grants number PIP 2022-2024.

283. P15-16. FUNCTIONAL ANALYSIS OF A VUS (P.S140F) AND A PATHOGENIC (P.153X) PKP2 MUTATION ASSOCIATED WITH ARRHYTHMOGENIC CARDIOMYOPATHY IN MATURE IPSC-DERIVED CARDIOMYOCYTESMateo Lacava¹, Guadalupe Amin², Joaquín Smucler³, Ariel Waisman⁴, Lucia Moro⁵

1. *Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)*
 2. *Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)*
 3. *Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)*
 4. *Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)*
 5. *Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigación Aplicada a Neurociencias (LIAN)*
 mateolacava@gmail.com

Arrhythmogenic cardiomyopathy (ACM) is a genetic disorder characterized by the substitution of myocardium with fibrofatty tissue, resulting in ventricular dysfunction and arrhythmia. Mutations in PKP2, a protein located in the desmosomes of cardiomyocytes (CMs), are the most commonly found in patients. An in-vitro model of ACM based on PKP2 genetically edited induced pluripotent stem cells (iPSCs) was previously established. The objective of this work was to differentiate and characterize mature cardiomyocytes (MCMs) derived from three iPSCs lines: PKP2-KO with pathogenic mutation p.153X; PKP2-S140F with a variant of uncertain significance (VUS) p.S140F; and WT, wild-type isogenic control. iPSCs were differentiated into CMs with a monolayer protocol. After 21 days of differentiation, the obtained fetal-like CMs were matured by inducing metabolic transition toward fatty acid oxidation to obtain MCMs (post-natal-like CMs) by day 38. RT-qPCR analysis of MCMs derived from all lines exhibited a mature phenotype, showing an increment in TNNI3, MYL2, FABP3 and DES. However, PKP2 and CX-43 expression was altered in PKP2-S140F and PKP2-KO compared to WT. Variability in contraction rhythm (arrhythmogenesis) was assessed by video-based contraction analysis of MCMs. Both PKP2-KO and PKP2-S140F MCMs exhibited higher SDNN (Standard Deviation of Normal-to-Normal Intervals) and RMSSD (Root Mean Square of Successive Differences) values relative to WT, indicating increased irregularity in contraction periodicity. In summary, we generated MCMs from all three iPSCs lines, which enabled us to identify in-vitro manifestations of ACM in PKP2-KO (pathogenic) and PKP2-S140F (VUS) lines. Our model will provide a platform to determine the pathogenicity of other VUS variants associated with ACM.

284. P15-17. MICROBIOME AND ITS RELATIONSHIP WITH PERI-IMPLANT DISEASE. PARTIAL RESULTSJudith Palomino¹, Ada Kaarina Molinas², Gabriela Viviana Pisterna³, Edmundo D'atri⁴

1. *CIC- UNR - Especialidad de Periodoncia - Facultad Odontología de Rosario. UNR;*
 2. *Facultad Odontología Rosario*

2. CIC- UNR - Especialidad de Periodoncia - Facultad Odontología de Rosario. UNR; Facultad Odontología de Rosario
3. Especialidad de Periodoncia - Facultad Odontología de Rosario. UNR; Facultad Odontología Rosario
4. Especialidad de Periodoncia - Facultad Odontología de Rosario. UNR; Facultad Odontología de Rosario
palominoj@intramed.net

Introduction: In implant rehabilitation, technical and biological complications can arise, such as peri-implant diseases caused by oral biofilm, which produce peri-implant mucositis with progressive bone loss. Clinical diagnosis is based on bleeding, discharge upon probing, and probing depth. Identifying the oral microbiome allows the patient to receive appropriate treatment, avoiding complications and reducing the risk of potential associated systemic diseases. **Objectives:** To characterize the members of the peri-implant disease microbiome. To justify the importance of microbiological analysis as a complementary diagnostic tool. **Materials and methods or techniques used *** Samples were taken from tooth and implant surfaces with paper cones and sterile swabs, at a depth of 2 mm in the peri-implant sulcus, with a dragging motion and throughout the entire sulcus depth. The samples were cultured anaerobically at 37 ± 2°C for 4-5 days on anaerobic blood agar. **Results *** Abundant small and medium-sized cream-colored and black colonies were found on both teeth and implants. Staining and microscopic examinations showed a clear prevalence of gram-negative anaerobic bacteria. **Partial results** are presented based on the following variables: sampled area, seeding method, and macroscopic and microscopic analysis. **Conclusions:** The results obtained so far are in line with those expected according to the literature, and it is not yet possible to infer the existence of significant differences in the microbiota between healthy and diseased implants, as the study is not yet complete.

285. P15-18. PHENOTYPIC AND STRUCTURAL CHARACTERIZATION OF 3 NOVEL FGFR1 VARIANTS P.(ARG233SER), P.(HIS652PRO) AND P.(GLU715VAL) IN BOYS WITH HYPOGONADOTROPHIC HYPOGONADISM

Mariela Urrutia¹, Franco G. Brunello², Sebastián Castro³, Gabriela Sansó⁴, Paula Scaglia⁵, Lourdes Correa-Brito⁶, Romina Paula Grinspon⁷, Rodolfo Alberto Rey⁸

1. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Fisiopatología y Clínica del Desarrollo Gonadal
2. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina; Bioinformática
3. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Fisiopatología y Clínica del Desarrollo Gonadal
4. Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Genómica
5. Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Genómica
6. Unidad de Medicina Traslacional, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Genómica
7. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Fisiopatología y Clínica del Desarrollo Gonadal
8. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.; Fisiopatología y Clínica del Desarrollo Gonadal
murrutia@cedie.org.ar

FGFR1 is the most frequently affected gene in congenital Hypogonadotrophic Hypogonadism (cHH). FGFR1 is required for normal development of the gonadotropin-releasing hormone neuronal system. Patients with cHH were studied genetically identifying 3 novel FGFR1 variants. Crystal structure of wild-type FGFR1 in the variant positions were analyzed in detail.

Patient 1 presented with micropenis, pubertal delay and short stature. NGS of genomic DNA identified a heterozygous variant in FGFR1, NM_023110.2:c.699A>T; p.(Arg233Ser), classified as Likely Pathogenic according to the ACMG criteria. Crystallographic structure of FGFR1-FGF2 showed that Arg233 forms 7 bonds with residues Asp244, Gly205, Asp218, Ser219 and Arg202. Six of the residues would be lost when arginine is replaced by serine. Patient 2 had cryptorchidism and pubertal delay. NGS identified a de novo heterozygous variant FGFR1, NM_023110.2:c.1955A>C; p.(His652Pro) classified as Likely Pathogenic. In FGFR1 crystallographic structure residue His652 forms 3 hydrogen bonds with residues Asp682, Ala640 and Asp623. When His652 was replaced by proline, main chain flexibility of the protein was restricted due to the proline cyclic structure and consequently the 3 bonds would be lost. Patient 3 had cryptorchidism, micropenis, pubertal delay, hypospadias and minor congenital malformations. A heterozygous variant FGFR1, NM_023110.2:c.2144A>T, p.(Glu715Val) was detected, classified as Likely Pathogenic. Crystallographic structure of the FGFR1, Glu715 showed 2 salt bridges with Lys711 and Leu712, both would be lost when glutamate was replaced by valine. In summary, we identified 3 novel FGFR1 variants in boys with cHH and characterised the underlying 3D structural alteration destabilizing the conformational structure of the receptor.

POSTERS 15 - SAIC - TRANSDUCCIÓN DE SEÑALES

DATE & TIME: 19/11/2025 13:00 - 14:30 H

Chairs: Mercedes Debernardi, Flavia Piccioni, Juan Bizzotto

286. P15-19. MAGEB2 SHAPES NUCLEOLAR STRESS RESPONSE BY PROMOTING P53 DEGRADATION

Micaela Escalada¹, Maximiliano Silva², Candela Vidal³, Melisa Suberbordes⁴, Rocio Toppino⁵, Philippe Soubeyran⁶, Martin Monte⁷

1. Dpto. Química Biológica, FCEN-UBA. Instituto IQUIBICEN, UBA-CONICET, Buenos Aires, Argentina; Laboratorio de Oncología Molecular
2. Dpto. Química Biológica, FCEN-UBA. Instituto IQUIBICEN, UBA-CONICET, Buenos Aires, Argentina; Laboratorio de Oncología Molecular
3. Dpto. Química Biológica, FCEN-UBA. Instituto IQUIBICEN, UBA-CONICET, Buenos Aires, Argentina; Laboratorio de Oncología Molecular
4. Dpto. Química Biológica, FCEN-UBA. Instituto IQUIBICEN, UBA-CONICET, Buenos Aires, Argentina; Laboratorio de Oncología Molecular
5. Dpto. Química Biológica, FCEN-UBA. Instituto IQUIBICEN, UBA-CONICET, Buenos Aires, Argentina; Laboratorio de Oncología Molecular
6. INSERM U1068, CNRS UMR 7258, Aix-Marseille Université and Institut Paoli-Calmettes, 13288, Marseille, France; Centre de Recherche en Cancérologie de Marseille (CRCM),
7. Dpto. Química Biológica, FCEN-UBA. Instituto IQUIBICEN, UBA-CONICET, Buenos Aires, Argentina; Laboratorio de Oncología Molecular
micaela.escalada1@gmail.com

MAGE-I proteins are aberrantly re-expressed in cancer, where they contribute to oncogenic signaling networks. MageB2 is distinctive for its nucleolar localization under basal conditions and redistribution to the nucleoplasm upon nucleolar stress (NoS) induced by Actinomycin D or BMH21 treatment, thereby impairing the NoS-induced p53 response. To explore stress-specific mechanisms, we performed IP/MS to define the MageB2 interactome under basal versus NoS conditions. MageB2 displayed a dynamic interactome ($p < 0.05$), with stress-specific partners such as SMAD3, COPS6, and FBXO2, all previously linked to p53 regulation. Complementary, RNA-seq of BMH21-treated cells revealed enrichment of processes related to p53 stabilization when MageB2 was expressed. These observations support the notion that MageB2 could specifically inhibit the p53 response under NoS. Functional assays confirmed this hypothesis. RT-qPCR showed

that the induction of canonical p53 target genes (p21, bax, PUMA; $p < 0.05$) was significantly attenuated in MageB2-expressing cells. At the protein level, short-term NoS revealed reduced acetylation of p53 in the presence of MageB2. At later time points, cycloheximide chase experiments demonstrated a decreased p53 half-life during BMH-21 treatment. This effect was reversed by MG132, indicating the proteasome-dependent involvement. Treatment with the histone deacetylase inhibitor Trichostatin A rescued p53 acetylation and restored its transcriptional activity in MageB2-expressing cells, further suggesting that MageB2 represses p53 by interfering with its acetylation-dependent stabilization under NoS. Together, these findings indicate that MageB2 stress-dependent interactions and downstream effects reshape the nucleolar stress response by promoting p53 degradation, a mechanism of particular relevance in tumors expressing MageB2.

POSTERS 15 - SAIC - BIOINFORMÁTICA

DATE & TIME: 19/11/2025 13:00 - 14:30 H

Chairs: Mercedes Debernardi, Flavia Piccioni, Juan Bizzotto

287. P15-20. DEVELOPMENT OF TECHNOLOGIES FOR THE MANAGEMENT AND TRACEABILITY OF BIOLOGICAL SAMPLES

Diego Raffo¹

1. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET - FEI - División de Endocrinología, Hospital de Niños Dr. Ricardo Gutiérrez; Cultivo Celular draffo@cedie.org.ar

Implementation of technologies that facilitate information entry, detail the location and storage conditions of samples, and provide tools for data processing and analysis are essential for laboratories working with patient samples. However, these technologies are often inaccessible to the academic or public health sectors. To address this issue and provide accessible technologies for these sectors, the "Locatorapps" platform was developed. This platform has three main applications hosted on a web server: www.locatorapps.com, featuring a user and permissions system and a detailed activity log, recording all changes made to the database, including the user and the specific information modified. The "Locator" application manages biobanks, while the "Sample Manager" application creates collaborative databases. The "Sensor" application was designed to receive and process information from remote monitoring devices for laboratory equipment such as freezers, refrigerators, ultra-freezers, liquid nitrogen tanks, and/or incubators. The applications have proven highly useful, making it easier to locate samples, consolidate multiple files from different team members into one unified database accessible online, and access temperature records and alarms for laboratory equipment to safeguard samples and reagents. A platform that ensures the accessibility, traceability, and security of data and stored samples is highly valuable for any laboratory that manages patient samples.

288. P15-21. IDENTIFICATION OF PROGNOSTIC SIGNATURES OF RESISTANCE TO CYCLIN-DEPENDENT KINASE INHIBITORS IN BREAST CANCER USING ARTIFICIAL INTELLIGENCE TECHNIQUES

Aylén Avila¹, Nahuel Cesatti Laluez², Mauricio Menacho Márquez³, Luciano E Anselmino⁴

1. Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).

2. Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).

3. Facultad de Ciencias Médicas. Universidad Nacional de Rosario. CONICET.; Centro de Investigación del Cáncer de Rosario y Centro de Investigación y Producción de Reactivos Biológicos (CIC-R; CIPReB). IDICER.

4. Facultad de Ciencias Médicas. Universidad Nacional de

Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).
aylen.avila@gmail.com

Resistance to cyclin-dependent kinase inhibitors (CDKis) in hormone receptor-positive breast cancer limits their long-term efficacy despite clear clinical benefits. Identifying predictive biomarkers of resistance could refine treatment selection and improve patient outcomes. This study aimed to define prognostic signatures of CDKi resistance by analyzing gene expression profiles from sensitive and resistant breast cancer cell lines. Expression data were retrieved from the Gene Expression Omnibus using GEOquery in R, preprocessed, and subjected to differential expression analysis. Functional interpretation included over-representation and gene set enrichment analyses, while Extreme Gradient Boosting (XGBoost) was applied to identify genes predictive of the resistant phenotype. Drug repositioning was explored through the CLUE platform and NIH-LINCS L1000 Connectivity Map, prioritizing compounds with resistance-reversal potential. Key genes—CHPF2, FAM83A, SCARB1, and S100A10—emerged as central players in pathways linked to cell adhesion, migration, signaling, and metabolism. These findings indicate that resistance mechanisms extend beyond cell cycle regulation, encompassing cytoskeleton remodeling, metabolic reprogramming, and microenvironmental adaptation. Comparison of RNASeq and microarray datasets revealed partial overlaps but also distinct gene sets, underscoring the influence of technology and suggesting that multi-omic integration could enhance robustness. Drug repurposing analysis highlighted NVP-BE235 (PI3K/mTOR inhibitor) and Simvastatin (lipid metabolism modulator) as promising candidates, with complementary mechanisms potentially capable of reversing resistance.

289. P15-22. BIOINFORMATIC ANALYSIS OF GENE EXPRESSION IN NON-FUNCTIONING ADRENAL ADENOMAS

Eugenia Cespedes¹, David E. Bajicoff², María Q. López Jové³, Pablo J. Azurmendi⁴, Alejandro L. Arregger⁵

1. Instituto de Investigaciones Médicas A. Lanari IDIM UBA-CONICET; Endocrinología Experimental

2. Instituto de Investigaciones Médicas A. Lanari IDIM UBA-CONICET; Endocrinología Experimental

3. Instituto de Investigaciones Médicas A. Lanari IDIM UBA-CONICET; Endocrinología Experimental

4. Instituto de Investigaciones Médicas A. Lanari IDIM UBA-CONICET; Nefrología Experimental y Bioquímica Molecular

5. Instituto de Investigaciones Médicas A. Lanari IDIM UBA-CONICET; Endocrinología Experimental
mecespedes@hotmail.com

Introduction: Non-functioning adrenal adenomas (NFA) are the most common incidental adrenal tumors, with a prevalence of 1.4%. The study of the underlying genetic mechanisms is necessary to understand their clinical and molecular variability. Our purpose was to analyze the gene expression profile of NFA compared to normal adrenal tissue (C). Methods: The GSE10927 database from the GEO (Gene Expression Omnibus) repository, obtained by the Affymetrix Human Genome U133 Plus 2.0 Array platform, was used. Eight NFA and four C samples were analyzed using GEO2R, GEOquery, and limma (Bioconductor). The data were normalized, a differential expression analysis was performed and a Benjamini-Hochberg adjusted- $p < 0.05$ was considered significant. Functional enrichment analysis was carried out with ConsensusPathDB. Results: One hundred fourteen differentially expressed genes were identified, comprising 64 downregulated and 50 upregulated genes. Among the downregulated genes, HSD11B1, CYP19A1 and CYB5A (involved in steroid metabolism) were highlighted, as were proinflammatory chemokines (CXCL8, CCL2, CCL8 and CCL13) and TLR4. Among the upregulated genes, SQSTM1 (p62), related to autophagy and cell signaling, stood out. Functional analysis revealed alterations in steroidogenesis and immunomodulation, including leukocyte adhesion and migration. The identified genes are regulated by transcription factors related to steroidogenesis (NR3C1, RARG and RXRA)

and the inflammatory response (RELA, NFKB1, STAT3 and STAT6). Discussion: A potential dysfunction of steroid metabolic pathways was identified in NFA, associated with alterations in immune modulation, suggesting a molecular origin of this phenotype. These findings provide useful evidence for identifying diagnostic biomarkers and potential therapeutic targets.

POSTERS 16 - SAIC - MEDICINA REGENERATIVA Y NANOMEDICINA

DATE & TIME: 19/11/2025 13:00 - 14:30 H

Chairs: Maria Andrea Camilletti, Jorge Aquino

290. P16-01. DESMIN AS A MATURATION MARKER REVEALS HETEROGENEOUS DIFFERENTIATION OF HUMAN PLURIPOTENT STEM CELL-DERIVED CARDIOMYOCYTES AND PROVIDES A TOOL FOR PROTOCOL OPTIMIZATION

Denisse Saulnier¹, Joaquin Smucler², Sheila Castañeda³, Julia Halek⁴, Guadalupe Amin⁵, Alejandra Guberman⁶, Lucia Moro⁷, Ariel Waisman⁸

1. Instituto de Neurociencias (INEU-CONICET), Fundacion para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

2. Instituto de Neurociencias (INEU-CONICET), Fundacion para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

3. Instituto de Neurociencias (INEU-CONICET), Fundacion para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

4. Instituto de Neurociencias (INEU-CONICET), Fundacion para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

5. Instituto de Neurociencias (INEU-CONICET), Fundacion para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio: Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

6. IQUIBICEN, Instituto de Química Biológica - Ciencias Exactas y Naturales, UBA/CONICET; Laboratorio de Regulación Génica en Células Madre

7. Instituto de Neurociencias (INEU-CONICET), Fundacion para la Lucha contra las Enfermedades de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

8. Instituto de Neurociencias (INEU-CONICET), Fundacion para la Lucha contra las Enfermedades de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

saulnier.denisse@gmail.com

Cardiovascular diseases remain the leading cause of mortality worldwide. During postnatal maturation, cardiomyocytes (CMs) undergo profound structural and metabolic remodeling, including increased expression of Desmin (DES), a type III intermediate filament essential for CM architecture. Human induced pluripotent stem cell (hiPSC)-derived CMs provide a powerful model to study cardiac development and disease. We recently adapted a CM maturation protocol and evaluated it via RNA-seq. Analysis between immature and metabolically matured CMs revealed DES as one of the most differentially expressed genes. RT-qPCR confirmed progressive DES upregulation during maturation. Interestingly, immunofluorescence at D38 revealed heterogeneous DES expression within mature CM population, suggesting this protocol could be further improved. DES promoter analyses suggested possible involvement of enhancers responsive to PPAR α and glucocorticoids, factors incorporated into our maturation protocol. However, immunofluorescence and RT-qPCR analysis lacking PPAR α or dexamethasone revealed no appreciable changes in DES expression, indicating additional regulatory factors. Our results indicate DES could serve as a maturation marker for

CMs, something highly required in the field. Thus, we set to generate an endogenous hiPSC reporter line for Desmin fused to mScarlet3 via CRISPR/Cas9-mediated homologous recombination. Using overexpression experiments, we validated that the fusion protein displays correct localization in cardiomyocytes, demonstrating proper folding. We cloned 2 guide RNAs targeting the DES stop codon and engineered a donor plasmid to introduce mScarlet3 fusion downstream of DES. This tool will enable dynamic and quantitative assessment of DES expression, providing a refined platform to evaluate novel CM maturation strategies and improve cardiovascular disease models.

291. P16-02. BIOCOMPATIBILITY AND ADHESION ANALYSIS OF POLYCAPROLACTONE (PCL) SCAFFOLDS FOR BONE TISSUE REGENERATION

Nadín I. Calvente¹, Gastón I. Angelini Marquiani¹, Joaquín P. Camacho¹, M. Albertina Loureiro¹, María Magdalena Miró Specos², Leandro N. Monsalve^{2*}, Marcela F. Bolontrade^{1*}.

1. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET- Hospital Italiano de Buenos Aires (HIBA) - Universidad del Hospital Italiano (UHIBA), Buenos Aires, Argentina.

2. INTI Textiles - Instituto Nacional de Tecnología Industrial (INTI), Argentina.

*Equal contribution

nadin.calvente@hospitalitaliano.org.ar

Bone tissue regeneration represents a clinical challenge, as currently available materials show limitations in their osteoinductive capacity and integration with the host tissue. At present, the greatest challenge is to maintain and expand mesenchymal stem/stromal cells (MSCs) in vitro under conditions that replicate their interactions with the microenvironment, which are essential for their function. In this context, the fabrication of biocompatible scaffolds functionalized with MSCs emerges as an innovative strategy to promote bone repair. The aim of this work is to evaluate the biocompatibility and osteogenic potential of polycaprolactone (PCL) scaffolds, fabricated by electrospinning and subsequently seeded with MSCs. It also seeks to assess whether standard sterilization techniques affect cell growth. MSCs were isolated from adipose tissue obtained from the knee, and cultured in low-glucose DMEM supplemented with 1% glutamine, 1% antibiotic, and 10% FBS. A total of 5000 cells/well were seeded in a 96-well plate with a PCL membrane placed on a removable support, and their viability, adhesion, and proliferation were evaluated using microscopy and metabolic assays. The results from the images obtained show that the scaffolds exhibit an architecture compatible with cell adhesion and proliferation. The MTS assay was consistent, detecting values of 0.193 ± 0.040 (absorbance $\pm$ standard deviation) in the presence of MSCs, corresponding to a 1.5-fold increase compared to the acellular biomaterial. In conclusion, PCL scaffolds functionalized with MSCs represent a promising tool in regenerative medicine, with potential applications in bone reconstruction therapies.

292. P16-03. DEVELOPMENT OF A GELATIN-ALGINATE BIOINK FOR 3D PRINTING OF VIABLE CELL SCAFFOLDS

Exequiel David Giorgi¹, Pablo Antezana², Sofía Genovés³, Tomas Grosso⁴, Matias Ostrowski⁵, Mauricio De Marzi⁶, Martin Desimone⁷

1. Instituto de Ecología y Desarrollo Sustentable (Universidad Nacional de Luján-CONICET); Universidad Nacional de Luján, Departamento de Ciencias Básicas; FOCIS Center of Excellence - Vaccines and Immunotherapies against Infections and Cancers (VITIC); Grupo de Investigaciones Básicas y Aplicadas en Inmunología y Bioactivos

2. Universidad de Buenos Aires, IQUIFEFA-CONICET, Facultad de Farmacia y Bioquímica (FFYB); Laboratorio de Nanobiomateriales

3. Universidad de Buenos Aires, IQUIFEFA-CONICET, Facultad de Farmacia y Bioquímica (FFYB); Laboratorio de Nanobiomateriales

4. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA (INBIRS, CONICET-UBA); Laboratorio de Vesículas

Extracelulares

5. Instituto de Investigaciones Biomédicas en Retrovirus y SIDA (INBIRS, CONICET-UBA); Laboratorio de Vesículas Extracelulares

6. Instituto de Ecología y Desarrollo Sustentable (Universidad Nacional de Luján-CONICET); Universidad Nacional de Luján, Departamento de Ciencias Básicas; FOCIS Center of Excellence - Vaccines and ImmunoTherapies against Infections and Cancers (VITIC); Grupo de Investigaciones Básicas y Aplicadas en Inmunología y Bioactivos

7. Universidad de Buenos Aires, IQUIMEFA-CONICET, Facultad de Farmacia y Bioquímica (FFYB); Laboratorio de Nanobiomateriales

exequiel_giorgi@yahoo.com.ar

3D printing is a promising technology for regenerative medicine, offering the ability to create complex, customized scaffolds with tailored physical and chemical properties. A key challenge is developing bioinks that support cell viability during and after the printing process. Our goal was to create a gelatin-alginate bioink that maintains the viability of embedded HEK-293 cells. We also produced and characterized the resulting 3D-printed scaffolds. We prepared the bioink by mixing gelatin and alginate (7:3) in deionized water at 60°C for one hour. After cooling this mixture to 37°C, we incorporated HEK-293 cells. The bioink was loaded into syringes and bioprinted at 28°C. The printed scaffolds were then immersed in a 100 mM CaCl₂ solution to induce cross-linking. We evaluated the scaffolds' swelling ratio over 48 hours and measured the metabolic activity of the embedded cells using an MTT assay over the same period. The scaffolds absorbed water, as indicated by a continuous increase in mass until they began to lose structural integrity after 48 hours. Approximately 50% of the cells were viable after 24 hours, and their metabolic activity increased by approximately 25% after 48 hours. This increase suggests that the surviving cells were proliferating within the scaffold. In conclusion, we successfully developed a protocol for producing gelatin-alginate scaffolds with viable HEK-293 cells using 3D printing. The embedded cells survived and proliferated. This method provides a foundation for future work using this bioink to create tissue-specific scaffolds with improved therapeutic potential.

293. P16-04. SPHEROID CULTURE IN A MICROFLUIDIC DEVICE AS A TOOL TO STUDY CELL BEHAVIOR IN 3D

Angelini Marquiani, G. I.¹; Rizzo, M. E.¹; Calvente, N. I.¹; Loureiro, M. A.¹; Sarkisian, M.¹; Dominguez, J. S.¹; Valenzuela Alvarez, M.¹; Changuan, J.²; Lerner, B.²; Bolontrade, M.¹.

1. Laboratorio de Procesos Remodelativos y Nichos Celulares, Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET - Hospital Italiano de Buenos Aires (HIBA) - Universidad del Hospital Italiano (UHI), Buenos Aires, Argentina.

2. Centro de Ingeniería de Recubrimientos Especiales y Nanoestructuras, Facultad Regional Haedo, Universidad Tecnológica Nacional (UTN).

gaston.angelini@hospitalitaliano.org.ar

Cell culture models represent a breakthrough of basic, applied, and translational research, with monolayer cultures providing understanding into cell behavior outside the tissue context. However, the need for more physiologically relevant models led to the development of three-dimensional (3D) cultures, like spheroids, mimicking tissue architecture. The high costs of research and the limited availability of primary cells have driven the development of microfluidic systems. We designed and characterized a spheroid-forming microfluidic device (SFMD) containing 239 concave wells of three different sizes, manufactured using polydimethylsiloxane (PDMS). A total of 30,000 3T3 cells were seeded per device and cultured in standard DMEM culture medium for nine days. Images were acquired on days 1, 3, 4, 7, and 9, and analyzed with ImageJ to assess spheroid formation, number, area and morphometric parameters. The SFMD spheroid formation efficiency was 69.0% (largest wells), 58.9% (medium-sized wells), and 11.3% (smallest wells), with an overall

efficiency of 31.9%. The number of spheroids decreased over time (slope = -0.268 ± 0.061 , Mean $\pm$ SD), while the mean spheroid area progressively increased from $2051 \pm 1957 \mu\text{m}^2$ on day 1, to $2419 \pm 2166 \mu\text{m}^2$ on day 3, $2797 \pm 3318 \mu\text{m}^2$ on day 4, $2824 \pm 3118 \mu\text{m}^2$ on day 7, and reaching $4224 \pm 5093 \mu\text{m}^2$ on day 9 (Mean, $\mu\text{m}^2 \pm$ SD). These results demonstrate that the SFMD successfully generates and enables monitoring of spheroids from small cell samples, contributing with a valuable tool for studying cell behavior in tissue-like structures in vitro.

POSTERS 16 - SAIC - HEMATOLOGÍA

DATE & TIME: 19/11/2025 13:00 - 14:30 H

Chairs: Maria Sol Ruiz, Daniela Vittori

294. P16-10. LONGITUDINAL AND DYNAMIC PROFILE OF THE INTESTINAL MICROBIOME IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: PILOT EXPERIENCE IN ARGENTINA

Florencia Adriana Lohmann¹, Maria Silvina Odstroil Bobillo², Lucrecia Liliana Osés³, Letizia Yamamoto⁴, Laura Raquel Soto⁵, Marcela Alejandra Martinez von Scheide⁶, Carlos Alberto Vaccaro⁷, Jorge Alberto Alberbide⁸

1. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB), Hospital Italiano de Buenos Aires (HIBA) - Universidad del Hospital Italiano de Buenos Aires (UHIBA) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Potosí 4240, CABA (1199), Argentina.; Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB), Hospital Italiano de Buenos Aires (HIBA) - Universidad del Hospital Italiano de Buenos Aires (UHIBA) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET)

2. Servicio Hematología, Hospital Italiano de Buenos Aires (HIBA), Perón 4190, CABA (1199), Argentina.; Servicio Hematología, Hospital Italiano de Buenos Aires (HIBA)

3. Servicio Hematología, Hospital Italiano de Buenos Aires (HIBA), Perón 4190, CABA (1199), Argentina.; Servicio Hematología, Hospital Italiano de Buenos Aires (HIBA)

4. Sección Inmunología, Hospital Italiano de Buenos Aires (HIBA), Perón 4190, CABA (1199), Argentina.; Sección Inmunología, Hospital Italiano de Buenos Aires (HIBA)

5. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB), Hospital Italiano de Buenos Aires (HIBA) - Universidad del Hospital Italiano de Buenos Aires (UHIBA) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Potosí 4240, CABA (1199), Argentina.; Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB), Hospital Italiano de Buenos Aires (HIBA) - Universidad del Hospital Italiano de Buenos Aires (UHIBA) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET)

6. Investigación e Innovación tecnológica - Departamento de Informática en Salud, Hospital Italiano de Buenos Aires (HIBA), Perón 4190, CABA (1199), Argentina.; Investigación e Innovación tecnológica - Departamento de Informática en Salud, Hospital Italiano de Buenos Aires (HIBA)

7. Servicio de Coloproctología, Hospital Italiano de Buenos Aires (HIBA), Perón 4190, CABA (1199), Argentina. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB), Hospital Italiano de Buenos Aires (HIBA) - Universidad del Hospital Italiano de Buenos Aires (UHIBA) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Potosí 4240, CABA (1199), Argentina.; Servicio de Coloproctología, Hospital Italiano de Buenos Aires (HIBA)

8. Servicio Hematología, Hospital Italiano de Buenos Aires (HIBA), Perón 4190, CABA (1199), Argentina.; Servicio Hematología, Hospital Italiano de Buenos Aires (HIBA)

florencia.lohmann@hospitalitaliano.org.ar

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a life-saving treatment for hematologic disorders, but prognosis is often limited by graft-versus-host disease and infections, major causes of early mortality. The intestinal microbiota plays a central role in post-transplant patient evolution, yet evidence from Latin American populations remains limited. This study aimed to charac-

terize intestinal microbiota dynamics in adult allo-HSCT recipients in Argentina, assessing longitudinal changes versus controls and identifying outcome-related microbial biomarkers. We prospectively analyzed 24 adult allo-HSCT recipients at Hospital Italiano de Buenos Aires (2021–2024), with healthy volunteers as controls. Fecal samples were collected at days 0, +15, and +100post-allo-HSCT. The V4 region of the 16S rRNA gene was sequenced. Data analysis comprised phylogenetic reconstruction, assessment of alpha and beta diversity, and multivariate analyses (PERMANOVA). Redundancy analysis (RDA) and canonical correspondence analysis (CCA) were applied to link microbial profiles with clinical variables. Alpha diversity declined at day +15 ($p < 0.01$) and partially recovered by day +100, while beta diversity shifted over time ($p = 0.001$). Longitudinal profiling revealed fluctuations; *Enterococcus* correlated with adverse outcomes, whereas *Blautia* stability was associated with favorable prognosis, *Roseburia* and *Faecalibacterium*, both recognized as butyrate-producing genera, were also identified. At day +100post-allo-HSCT, patient microbiota remained distinct from controls, with persistent depletion of *Bacteroides* and *Faecalibacterium*. This first longitudinal study of post-allo-HSCT gut microbiota in Argentina highlights prognostic microbial signatures, provides a foundation for transplantation-related microbiome research, and represents an initial step toward disentangling post-transplant complications and guiding future microbiota-targeted strategies in Latin American populations.

295. P16-11. ANDROGEN RECEPTOR EXPRESSION IN PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMC) OF PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA

Luisa Gaydou¹, Julieta Cepeda², Ma Alejandra Cardozo³, Adriana Follonier⁴, Jorge Guillermo Ramos⁵

1. FBCB. ISAL CONICET - UNL; Departamento de Bioquímica Clínica y cuantitativa, Facultad de Bioquímica y Cs. Biológicas, UNL. Instituto de Salud y Ambiente del Litoral, CONICET - UNL

2. ISAL CONICET - UNL; Instituto de Salud y Ambiente del Litoral, CONICET - UNL

3. FBCB. ISAL CONICET - UNL; Departamento de Bioquímica Clínica y cuantitativa, Facultad de Bioquímica y Cs. Biológicas, UNL. Instituto de Salud y Ambiente del Litoral, CONICET - UNL

4. FBCB. ISAL CONICET - UNL; Departamento de Bioquímica Clínica y cuantitativa, Facultad de Bioquímica y Cs. Biológicas, UNL. Instituto de Salud y Ambiente del Litoral, CONICET - UNL

5. FBCB. ISAL CONICET - UNL; Departamento de Bioquímica Clínica y cuantitativa, Facultad de Bioquímica y Cs. Biológicas, UNL. Instituto de Salud y Ambiente del Litoral, CONICET - UNL

lgaydou@fbc.unl.edu.ar

Chronic Lymphocytic Leukemia (CLL) is the most common leukemia in our society. Given that males present higher disease incidence and worse prognosis than females, the role of sex steroids in CLL has been studied. Previously, we evidenced lower mRNA expression of androgenic enzymes 5 alpha reductase (5 α -R) 1 and 3, both regulated by the androgen receptor (AR), in CLL PBMC compared to healthy controls (HC). The aim of this work was to evaluate expression of AR variants (ARVs) in CLL mononuclear cells and its correlation with androgenic enzymes. PBMC from HC (males, HM, 19; females, HF, 7) and CLL patients (males, CLLM, 12; females, CLLF, 9), ages 40 - 85, were isolated from whole blood using Ficoll gradient. RNA was obtained with Trizol reagent and reverse transcribed to cDNA. Primers were designed for ARVs listed in NCBI. Real-Time PCR was performed using L19 as housekeeping gene. Statistical analysis was carried out using R software. We established transcript presence of four ARVs in CLL PBMCs, with lower expression levels of AR-FL compared to HC ($p < 0.001$). We evidenced a positive correlation in CLLM between 5 α -R 3 and AR-FL (cor: 0,675; $p < 0,05$), and between 5 α -R 1 and 5 α -R 3 (cor: 0,787; $p < 0,01$), both absent in HCM. This suggests an altered androgenic pathway in CLL PBMCs. It remains unclear whether these alterations are cause or consequence of this illness, if they relate to disease severity, or

whether they reflect new mechanistic pathways that could be potential therapeutic targets.

296. P16-12. CONDITIONED MEDIA FROM ERYTHROPOIETIN-TREATED ERYTHROID CELLS DOWNREGULATE HEPICIDIN USING A CALCIUM-DEPENDENT MECHANISM IN THE HEPG2 CELL LINE

Romina Maltaner¹, María Eugenia Chamorro², Edgardo Stephano Carabajal³, Daniela Cecilia Vittori⁴

1. Instituto del Departamento de Química Biológica de la Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (IQUIBICEN, CONICET-UBA); Laboratorio de Eritropoyetina en la Fisiología Celular

2. Instituto del Departamento de Química Biológica de la Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (IQUIBICEN, CONICET-UBA); Laboratorio de Eritropoyetina en la Fisiología Celular

3. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Laboratorio de Eritropoyetina en la Fisiología Celular

4. Instituto del Departamento de Química Biológica de la Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (IQUIBICEN, CONICET-UBA); Laboratorio de Eritropoyetina en la Fisiología Celular
remaltaneri@qb.fcen.uba.ar

Systemic iron (Fe) homeostasis is essential for hemoglobin production. Upon erythropoietin (Epo) stimulation, bone marrow erythroblasts secrete erythroferrone (ERFE), which downregulates liver hepcidin (Hep) expression thus favoring Fe release from intracellular stores. The aim of our work was to investigate the action mechanisms responsible for Hep suppression using ERFE-containing conditioned media (CM) obtained from Epo-treated erythroleukemia K562 cells. Previously, we demonstrated that Epo (10 U/mL) increases ERFE expression and secretion in K562 cells. Here we report that CM from Epo-treated K562 cells reduced Hep mRNA in the human hepatocyte HepG2 cell line (6 h) compared to CM from untreated cells (RT-qPCR; a.u.: CM-C=1; **CM-Epo=0.47 $\pm$ 0.1; Mann-Whitney, ** $p < 0.01$). JAK2 kinase inhibitor AG490 (50 μ M) did not affect Hep suppression by CM-Epo, suggesting no involvement of the classical signaling pathways elicited by Epo ($n=3$). ERFE belongs to the adiponectin protein family, which regulates metabolism via calcium (Ca) signaling. Hep mRNA was significantly up-regulated by Ca entry (a.u.: C=1; 1 μ M A23187 ionophore=2.3 $\pm$ 0.5; Mann-Whitney, * $p < 0.05$, $n=4$). CM-Epo (15 min) enhanced intracellular Ca levels in HepG2 cells (Fluo-4, AM; a.u.: CM-C=1; *CM-Epo=1.7 $\pm$ 0.4; Mann-Whitney, * $p < 0.05$, $n=3$). Experiments with Ca chelator EGTA (1 mM) showed that Ca influx is necessary for the inhibition of Hep expression by CM-Epo (a.u.: *CM-C=1; CM-Epo=0.36 $\pm$ 0.1; *CM-E+EGTA=0.95 $\pm$ 0.2; Kruskal Wallis-Dunn, * $p < 0.05$ vs CM-E, $n=6$). Interestingly, Epo (20 U/mL, 6 h) reduced Hep mRNA directly in HepG2 cells without activating Ca signaling. Our results highlight the fact that ERFE-containing CM can suppress Hep expression in HepG2 cells through a Ca-dependent mechanism.

297. P16-13. POTENTIAL VALUE OF THE NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A PROGNOSTIC MARKER IN MYELOFIBROSIS

David Eduardo Bajicoff¹, Ana Claudia Glembotsky², Rosana Fernanda Marta³, Nora Paula Goette⁴, Evana Paredes⁵, Laureano Julian Kamiya⁶, Paola Roxana Lev⁷, Geraldine De Luca⁸, Paula Graciela Heller⁹

1. Instituto de Investigaciones Medicas Alfredo Lanari. Unidad ejecutora IDIM, UBA CONICET; Hematología Investigación

2. Instituto de Investigaciones Medicas Alfredo Lanari. Unidad ejecutora IDIM, UBA CONICET; Hematología Investigación

3. Instituto de Investigaciones Medicas Alfredo Lanari. Unidad ejecutora IDIM, UBA CONICET; Hematología Investigación

4. Instituto de Investigaciones Medicas Alfredo Lanari; Laboratorio Central

5. Instituto de Investigaciones Medicas Alfredo Lanari. Unidad ejecutora IDIM, UBA CONICET; Hematología Investigación

6. Instituto de Investigaciones Medicas Alfredo Lanari. Unidad ejecutora IDIM, UBA CONICET; Hematología Investigacion
 7. Instituto de Investigaciones Medicas Alfredo Lanari. Unidad ejecutora IDIM, UBA CONICET; Hematología Investigacion
 8. Instituto de Investigaciones Medicas Alfredo Lanari. Unidad ejecutora IDIM, UBA CONICET; Hematología Investigacion
 9. Instituto de Investigaciones Medicas Alfredo Lanari. Unidad ejecutora IDIM, UBA CONICET; Hematología Investigacion
 davidabajocoff@gmail.com

Polycythemia vera (PV), essential thrombocythemia (ET) and myelofibrosis (MF) are myeloproliferative neoplasms driven by clonal myeloid proliferation. Advanced MF is characterized by inflammation, ineffective hematopoiesis leading to cytopenias and adverse prognosis. The neutrophil-to-lymphocyte ratio (NLR) is an inflammatory biomarker reflecting innate versus adaptive immunity. It is associated with increased thrombotic risk in ET and PV although its role in MF remains uncertain. Our aim was to determine whether the NLR is altered in MF and its association with clinical, molecular and inflammatory parameters. The NLR ratio was elevated in MF patients (n=45) compared to controls, $P<0.0001$, without differences versus PV and ET, which also displayed elevated NLR. The NLR did not differ according to the mutational status nor thrombotic history. However, MF patients in higher risk categories (DIPSS score) showed lower NLR compared to those in lower risk groups ($P<0.05$), revealing that NLR decreases upon disease progression. MF patients with lower NLR showed higher frequency of clinical complications, such as anemia ($P<0.01$), circulating blasts ($P<0.05$) and thrombocytopenia, alongside higher inflammation (CRP and IL-6 levels, $P<0.05$) and tumor burden (cell-free DNA, $P<0.05$ and LDH, $P=0.08$). Low NLR showed a trend towards shorter survival. In conclusion, although myeloid proliferation results in elevated NLR in MF, it declines along disease progression, probably due to inflammation-induced ineffective myelopoiesis leading to cytopenias and worse outcome. Unlike other diseases where high NLR indicates risk, in MF low NLR marks adverse outcomes. The potential value of low NLR as a prognostic marker in MF deserves further study.

298. P16-14. EFFECT OF ERYTHROPOIETIN ON HEPICIDIN REGULATION IN A PROINFLAMMATORY AND HYPOXIC ENVIRONMENT IN MACROPHAGES

Ailén Macarena Gomez Romano¹, Romina Maltaner², Alcira Nesse³, Daniela Cecilia Vittori⁴, María Eugenia Chamorro⁵

1. Departamento de Química Biológica. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Eritropoyetina en la Fisiología Celular

2. Instituto del Departamento de Química Biológica de la Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (IQUIBICEN, CONICET-UBA); Eritropoyetina en la Fisiología Celular

3. Instituto del Departamento de Química Biológica de la Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (IQUIBICEN, CONICET-UBA); Eritropoyetina en la Fisiología Celular

4. Instituto del Departamento de Química Biológica de la Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (IQUIBICEN, CONICET-UBA); Eritropoyetina en la Fisiología Celular

5. Instituto del Departamento de Química Biológica de la Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (IQUIBICEN, CONICET-UBA); Eritropoyetina en la Fisiología Celular

maca.gomez.romano@gmail.com

Iron (Fe) is an essential mineral for cellular survival, and macrophages are responsible for recycling most of the body's iron. Produced in hepatocytes and macrophages, Hepcidin (Hep) regulates Fe availability by binding to ferroportin, the only known Fe exporter, and inducing its degradation. While Hep regulation has been extensively studied in hepatocytes, the signaling pathways controlling its expression in macrophages remain poorly understood. In this study, we analyzed the effect of erythropoietin (Epo) on Hep expression in macrophages under pro-inflammatory and hy-

poxic conditions. Using THP-1 monocytic cells differentiated into macrophages, we assessed Hep mRNA levels by RT-PCR. Epo treatment (160 ng/mL, 6 h) significantly reduced Hep expression (a.u.: Control=0.42±0.08; **Epo=0.16±0.05, ** $P<0.01$, n=10). These results were confirmed by RT-qPCR. Under inflammatory conditions induced by IL-6, evidenced by an increase in ROS levels (fluorometry using the DCFH-DA probe), Hep mRNA levels significantly increase, whereas co-treatment with Epo did not alter them (RT-PCR, a.u.: Control=0.30±0.04; *IL-6=0.47±0.06; *Epo=0.14±0.06; IL-6+Epo=0.41±0.09, * $P<0.05$ vs. C, n=4). In a chemically-induced hypoxic environment generated with CoCl₂ (100 μ M, 24 h), a reduction in Hep levels was observed, while co-treatment with Epo resulted in an even greater decrease (RT-PCR, a.u.: Control=0.32±0.05; *CoCl₂=0.14±0.04; *Epo=0.15±0.08; **CoCl₂+Epo=0.06±0.02, * $P<0.05$ and ** $P<0.01$ vs. C, n=4). These results may indicate a reduced sensitivity to Epo in inflammatory conditions, which could reflect a state of functional resistance in macrophages. On the other hand, this supports the idea that Epo and hypoxia may converge on shared regulatory mechanisms controlling Hep expression in macrophages.

299. P16-15. RESISTANCE TO ERYTHROPOIETIN DUE TO A PROINFLAMMATORY ENVIRONMENT IN THE REGULATION OF IRON BIOAVAILABILITY BY HEPICIDIN

Edgardo Stephano Carabajal¹, María Eugenia Chamorro², Ailén Macarena Gómez Romano³, Daniela Cecilia Vittori⁴, Romina Eugenia Maltaner⁵

1. Departamento de Química Biológica. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Eritropoyetina en la Fisiología Celular.

2. Instituto del Departamento de Química Biológica de la Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (IQUIBICEN, CONICET-UBA); Eritropoyetina en la Fisiología Celular.

3. Departamento de Química Biológica. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; Eritropoyetina en la Fisiología Celular.

4. Instituto del Departamento de Química Biológica de la Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (IQUIBICEN, CONICET-UBA); Eritropoyetina en la Fisiología Celular.

5. Instituto del Departamento de Química Biológica de la Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (IQUIBICEN, CONICET-UBA); Eritropoyetina en la Fisiología Celular.

edgardouba49@gmail.com

Anemia associated with chronic inflammatory pathologies is linked to the induction of hepcidin (Hep) by interleukin 6 (IL-6), which limits iron (Fe) availability. Although treatment with Fe and erythropoietin (Epo) usually corrects anemia, approximately one-third of patients present therapeutic resistance. The aim of this work was to evaluate Hep mRNA regulation in response to IL-6 and to generate an inflammatory model in the HepG2 hepatocyte cell line to study a possible mechanism of resistance to Epo involving its receptor EpoR. To this end, an IL-6 concentration-response curve (24 h) was performed in HepG2 cells. Hep induction peaked at 20 ng/mL (RT-qPCR; a.u.: C=1; 10 ng/mL=0.5±0.3; *20 ng/mL=3.9±1.3; 50 ng/mL=1.2±0.6; Kruskal Wallis-Dunn, * $p<0.05$ vs C, n=5), accompanied by an increase in intracellular Fe(III) (colorimetric assay; a.u.: C=1; *IL-6=3.9±1.3; Mann-Whitney, * $p<0.05$, n=3) and no morphological changes. Epo (20 U/mL, 6 h) failed to decrease Hep expression in HepG2 cells preincubated with IL-6 (20 ng/mL, 24 h), in comparison with Epo alone (RT-qPCR; a.u.: C=1; *Epo=0.6±0.2; *IL-6=3.6±1.3; IL-6+Epo=3.4±2.2; Kruskal Wallis-Dunn, * $p<0.05$ vs C, n=4), which suggests resistance. EpoR mRNA expression was measured under the same conditions. The highest induction was observed with IL-6, although coinubation with Epo decreased it (RT-qPCR; a.u.: C=1; Epo=1.5±0.4; *IL-6=4.2±1.1; IL-6+Epo=1.5±0.4; Kruskal Wallis-Dunn, * $p<0.05$ vs C, n=3). These results show that Epo could not counteract the proinflammatory induction of Hep achieved with IL-6. EpoR modulation under these conditions suggests a mechanism that could contribute to treatment

resistance in patients with inflammatory anemia.

300. P16-16. INFLUENCE OF *Ligaria cuneifolia* ("Argentine mistletoe") INFUSION ON LIPID PROFILE AND PLASMA FACTORS OF ERYTHROCYTE AGGREGATION IN DYS-LIPIDEMIC PATIENTS

Martín Perez¹, Mariana Ferrero², Leda Urli³, Diego Crosetti⁴, Juan Alonso⁵, Jose Gonzalez⁶, Bruno Wienzbicki⁷, Cecilia Dobrecky⁸, Daniel De Vuono⁹, Marcelo Wagner¹⁰, Rodolfo Leiva¹¹, Cristina Carnovale¹², Alejandra Luquita¹³

1. Facultad de Ciencias Médicas. Universidad Nacional de Rosario; Laboratorio de Biología Sanguínea - Cátedra de Biofísica FCM - UNR.

2. Facultad de Ciencias Médicas. Universidad Nacional de Rosario; Laboratorio de Biología Sanguínea - Cátedra de Biofísica FCM - UNR.

3. Facultad de Ciencias Médicas. Universidad Nacional de Rosario; Laboratorio de Biología Sanguínea - Cátedra de Biofísica FCM - UNR.

4. Facultad de Ciencias Médicas. Universidad Nacional de Rosario; Laboratorio de Biología Sanguínea - Cátedra de Biofísica FCM - UNR.

5. Facultad de Ciencias Médicas. Universidad Nacional de Rosario; Laboratorio de Biología Sanguínea - Cátedra de Biofísica FCM - UNR.

6. Facultad de Ciencias Médicas. Universidad Nacional de Rosario; Laboratorio de Biología Sanguínea - Cátedra de Biofísica FCM - UNR.

7. Facultad de Ciencias Médicas. Universidad Nacional de Rosario; Laboratorio de Biología Sanguínea - Cátedra de Biofísica FCM - UNR.

8. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.; Cátedra de Farmacobotánica - Facultad de Farmacia y Bioquímica UBA.

9. Hospital Provincial del Centenario; Laboratorio Central del Hospital Provincial del Centenario

10. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.; Cátedra de Farmacobotánica - Facultad de Farmacia y Bioquímica UBA.

11. Hospital Provincial del Centenario, Rosario.; Servicio de Cardiología - Hospital Provincial del Centenario, Rosario.

12. CONICET; IFISE - Facultad de Ciencias Bioquímicas y Farmacéuticas, UNR

13. Facultad de Ciencias Médicas. Universidad Nacional de Rosario; Laboratorio de Biología Sanguínea - Cátedra de Biofísica FCM - CIUNR

tinchox8@gmail.com

Ligaria cuneifolia (Lc) is traditionally used to improve blood fluidity and reduce plasma cholesterol. Objectives: to analyze the effect of Lc infusion on plasma cholesterol (Cho) and plasma factors influencing erythrocyte aggregation in dyslipidemic patients. Methods: Fourteen patients (50 ± 15 years) from the Cardiology Service, Hospital Provincial Centenario, received lyophilized Lc extract in tea bags three times per week for 28 days. Baseline (C) and after treatment (TLc) blood samples were collected. Measurements included: Plasma total Cho (TCho), HDLCho and LDLCho, colorimetrically; Serum C-reactive protein (CRP), Triglycerides (TG) and Fibrinogen (FB) by enzymatic methods and in whole blood erythrocyte aggregation velocity (EAV) by optical densitometry and erythrocyte sedimentation rate (ESR) by Westergren. Statistical analysis was performed with the Wilcoxon test. Results: Median values (95% CI) were: TCho, C: 242 (205–250) vs TLc: 232 (180–261), ns; HDLCho, C: 67 (51–86) vs TLc: 75 (53–83), ns; LDLCho, C: 185 (140–203) vs TLc: 168 (101–181)*; TG (mg/dl): C: 80 (66–343), TLc: 102 (42–118) ns; FB (mg/dl): C: 300 (190–410), TLc: 237 (187–359)*; ESR (mm/1sth): C: 10 (2–67), TLc: 7 (2–32) ns PCR (mg/dl): C: 1,20 (0,6–6,7), TLc: 1,25 (0,6–1,09) ns; EAV: C: 0,49 (0,3–1,13), TLc: 0,44 (0,26–1,09)**; (**p< 0,01 and *p< 0,05 vs. C; ns: non significative vs C). Conclusion: Lc significantly reduced LDLCho without altering TCho, HDLCho, CRP, ESR or TG. Furthermore, Lc treatment significantly decreased FB, the main pro-aggregatory plasma protein, thereby lowering EAV and improving blood fluidity.

ORALES 15 - SAIC - INMUNOLOGÍA E INFLAMACIÓN

DATE & TIME: 19/11/2025 15:00 - 16:30 H

Chairs: Maria Florencia Mercogliano, Silvana Gazzaniga

301. O15-01. INFLAMMATORY BIOMARKERS IN SALIVA AND THEIR ASSOCIATION WITH HANGOVER SEVERITY IN YOUNG SOCIAL DRINKERS

Analia Karadayian¹, Evi C van Oostrom², Laura A Tijs³, Auroa JAE van de Loo⁴, Joris C Verster⁵

1. Institute for Biomedical Research (BIOMED), National Scientific and Technical Research Council (CONICET), Argentina. School of Medical Sciences, Pontifical Catholic University of Argentina (UCA), Buenos Aires, Argentina.; Laboratory of Cellular and Molecular Biology

2. Utrecht University, Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacology, Utrecht, The Netherlands.; Division of Pharmacology

3. Utrecht University, Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacology, Utrecht, The Netherlands.; Division of Pharmacology

4. Utrecht University, Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacology, Utrecht, The Netherlands.; Division of Pharmacology

5. Utrecht University, Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacology, Utrecht, The Netherlands. Swinburne University of Technology, Centre for Mental Health and Brain Sciences, Melbourne, Australia. Cognitive Neurophysiology, Department of Child and Adolescent Psychiatry, Faculty of Medicine, TU Dresden, Germany; Division of Pharmacology

analiakaradayian@uca.edu.ar

Increasing evidence suggests that immune activation contributes to the pathogenesis of alcohol hangover. This study investigated whether salivary immune biomarkers correlate with hangover severity. A naturalistic study was conducted among 15 healthy social drinkers (18–30 years old), including both an alcohol day and an alcohol-free control day. Saliva samples were collected, and hangover severity was assessed hourly between 09:30 and 15:30 on a 0–10 scale. Concentrations of interleukin (IL)-1 β , IL-6, IL-8, and tumor necrosis factor alpha (TNF- α) were determined. Spearman's correlations were calculated between the change in biomarker concentrations (alcohol minus control day) and hangover severity, with bootstrapping (B = 10,000) applied to compute bias-corrected and accelerated 95% confidence intervals (BCa 95% CI). Significant associations were found for IL-1 β at 12:30 with hangover severity at 12:30 (r = 0.708, BCa 95% CI = 0.174–0.954), 13:30 (r = 0.574, CI = 0.061–0.878), and 14:30 (r = 0.684, CI = 0.281–0.925). IL-6 at 12:30 correlated with severity at 12:30 (r = 0.515, CI = 0.112–0.774), 13:30 (r = 0.480, CI = 0.076–0.753), and 14:30 (r = 0.563, CI = 0.183–0.807). TNF- α concentrations at 11:30 and 12:30 showed significant correlations with later hangover severity up to 15:30 (r = 0.516–0.674). In contrast, IL-8 showed no significant associations. These findings demonstrate that salivary inflammatory biomarkers correlate with alcohol hangover severity, supporting immune involvement in its pathology.

302. O15-02. IMMUNOMODULATORY EFFECTS OF ANTI-OXIDANT NATURAL EXTRACTS IN MONOCYTES AND LPS-ACTIVATED MONOCYTES

Laura Montaldo¹, BendeZú Llerson², Liliana Noemí Guerra³, Mauricio De Marzi⁴

1. Universidad Nacional de Lujan; GIBAIB-Laboratorio de Inmunología

2. Universidad Nacional de Lujan; GIBAIB-Laboratorio de inmunología-

3. Universidad Nacional de Lujan; INEDES-CONICET GIBAIB-Laboratorio de inmunología

4. Universidad Nacional de Lujan; INEDES-CONICET GIBAIB-Laboratorio de inmunología
laura.montaldo24@gmail.com

Previously, we demonstrated that an aqueous extract of *Baccharis articulata* exhibits anti-proliferative and anti-inflammatory effects, correlating with increment IL-10 levels in PMA-induced monocyte-derived macrophages. Additionally, *Citrus sinensis* extract (orange-Cs) and *Peumus boldus* extract (boldo-Pb) displayed high antioxidant capacity. Here, we evaluated Cs and Pb immunomodulatory effects in resting monocytes (Mo) and LPS-activated monocytes (LPS-Mo). Cs and Pb were obtained through aqueous extraction (1h, 37°C). Bioactive compounds were identified via HPLC. Total polyphenol content (TPC, mg/mL) was determined by the Folin-Ciocalteu method, and total flavonoid level (mg/mL) was assessed via aluminum chloride assay. Cytotoxicity was evaluated using MTT assay, while cytokine production (IL-1 β , IL-8, and IL-10, pg/mL) was measured by ELISA. HPLC analysis identified high gallic acid concentrations, as well as other phenolics like benzoic and caffeic acids. TPC in Cs and Pb was 0.07 ± 0.02 and 0.20 ± 0.00 , respectively. Flavonoids were significantly ($p < 0.01$) higher in Pb (1.30 ± 0.02) than in Cs (0.82 ± 0.02). No significant differences in cell viability were observed in Mo or LPS-Mo after treatments. Both extracts reduced, although not significantly, IL-1 β levels compared to non-treated Mo (Moc). Pb significantly decreased IL-8 ($p < 0.05$) (3.83 ± 0.79 [Mo+Pb] vs 10.48 ± 0.49 [Moc]). In LPS-Mo-treated cells, Cs and Pb significantly increased IL-10 secretion ($p < 0.05$), compared to non-treated cells (0.37 ± 0.01 [Mo-LPS+Cs], 0.27 ± 0.04 [Mo-LPS+Pb], 0.16 ± 0.01 [non-treated-Mo-LPS]). Antioxidant extracts had similar phenolic profiles. They reduced pro-inflammatory cytokine secretion in Mo and showed an anti-inflammatory response in LPS-Mo by stimulating IL-10 release.

303. O15-03. ANTITUMOR AND IMMUNE EFFECTS OF NIRAPARIB AND ANTI-PD-1 IN AN ASCITIC HR-DEFICIENT OVARIAN CANCER MOUSE MODEL

Florencia Menay¹, Gonzalo Gonzalez², Ginnete Moyano³, Kevin Madauss⁴, Florencia Cayrol⁵, Helena Sterle⁶, Vanesa Gottifredi⁷, Graciela Cremaschi⁸

1. Instituto de Investigaciones Biomédicas (BIOMED) UCA-CONICET; Laboratorio de Neuroinmunomodulación y Oncología Molecular
 2. Instituto de Investigaciones Biomédicas (BIOMED) UCA-CONICET; Laboratorio de Neuroinmunomodulación y Oncología Molecular
 3. Instituto Leloir; Laboratorio de Ciclo Celular y Estabilidad Genómica
 4. Laboratorio GlaxoSmithKline (GSK)
 5. Instituto de Investigaciones Biomédicas (BIOMED) UCA-CONICET; Laboratorio de Neuroinmunomodulación y Oncología Molecular
 6. Instituto de Investigaciones Biomédicas (BIOMED) UCA-CONICET; Laboratorio de Neuroinmunomodulación y Oncología Molecular
 7. Instituto Leloir; Laboratorio de Ciclo Celular y Estabilidad Genómica
 8. Instituto de Investigaciones Biomédicas (BIOMED) UCA-CONICET; Laboratorio de Neuroinmunomodulación y Oncología Molecular
- florenciamenay@uca.edu.ar

Ovarian cancer is one of the deadliest malignancies in women, due to its aggressiveness, late diagnosis, and limited treatment options. Although PARP inhibitors have improved outcomes, resistance frequently develops, highlighting the need for combination strategies. Using a dHR (p53/BRCA2) ID8 preclinical model of ovarian cancer ascites, which recapitulates key features of human disease, we aimed to investigate how Niraparib (Nira) and anti-PD-1 therapy, alone or in combination, modulate antitumor immunity and impact therapeutic response. We found that treatment with Nira, either alone or in combination with anti-PD1, significantly decreased ascites volume ($p < 0.001$) and total cell count ($p < 0.001$). While Nira increased ($p < 0.05$) systemic dendritic cells, it reduced ($p < 0.05$) their proportion in ascites, without affecting other immune cell populations within the tumor microenvironment. These results suggest that Nira may not strongly affect antitumor immune response, and its effect on tumor growth may be main-

ly cytotoxic, potentially mediated by synthetic lethality in dHR cells. On the other hand, anti-PD-1 treatment enhanced the antitumor immune response by increasing effector CD8⁺ T-cells ($p < 0.05$), reducing MDSCs ($p < 0.05$) and increasing dendritic cells ($p < 0.05$) in ascites. In the spleen, it decreased exhausted CD8⁺ T-cells ($p < 0.01$), independently of Nira treatment, suggesting that anti-PD-1 may facilitate the immune-mediated elimination of tumor cells, including those that escape the direct drug-induced cytotoxicity. These findings provide preclinical evidence supporting the combination of Nira and anti-PD-1 as a promising therapeutic approach in dHR ovarian cancer, with Nira eliciting cytotoxic effects in dHR cells and anti-PD-1 enhancing antitumor immunity by reducing immunosuppression.

304. O15-04. THYROID HORMONE-DRIVEN MODULATION OF CYTOKINES SHAPES IMMUNE RESPONSE AND LUNG METASTASIS IN BREAST CANCER

Gonzalo Gonzalez¹, Florencia Menay², Johana Diaz Albuja³, Maria Mercedes Debernardi⁴, Lucero Alvarado⁵, Maria Alejandra Paulazo⁶, Cinthia Rosembli⁷, Florencia Cayrol⁸, Graciela Cremaschi⁹, Helena Sterle¹⁰

1. Instituto de Investigaciones Biomédicas (BIOMED) - UCA - CONICET; Laboratorio de neuroinmunomodulación y oncología molecular
 2. Instituto de Investigaciones Biomédicas (BIOMED) - UCA - CONICET; Laboratorio de neuroinmunomodulación y oncología molecular
 3. Instituto de Investigaciones Biomédicas (BIOMED) - UCA - CONICET; Laboratorio de neuroinmunomodulación y oncología molecular
 4. Instituto de Investigaciones Biomédicas (BIOMED) - UCA - CONICET; Laboratorio de neuroinmunomodulación y oncología molecular
 5. Instituto de Investigaciones Biomédicas (BIOMED) - UCA - CONICET; Laboratorio de neuroinmunomodulación y oncología molecular
 6. Instituto de Investigaciones Biomédicas (BIOMED) - UCA - CONICET; Laboratorio de neuroinmunomodulación y oncología molecular
 7. Instituto de Investigaciones Biomédicas (BIOMED) - UCA - CONICET; Laboratorio de neuroinmunomodulación y oncología molecular
 8. Instituto de Investigaciones Biomédicas (BIOMED) - UCA - CONICET; Laboratorio de neuroinmunomodulación y oncología molecular
 9. Instituto de Investigaciones Biomédicas (BIOMED) - UCA - CONICET; Laboratorio de neuroinmunomodulación y oncología molecular
 10. Instituto de Investigaciones Biomédicas (BIOMED) - UCA - CONICET; Laboratorio de neuroinmunomodulación y oncología molecular
- gonzalezgonzalo4e@gmail.com

The relationship between thyroid status and breast cancer progression remains incompletely understood. We have previously reported that hyperthyroid mice bearing 4T1 breast cancer tumors exhibited an increased primary tumor growth rate, whereas hypothyroid mice developed slower-growing tumors but a higher number of lung metastases. Our aim was to further evaluate the impact of thyroid status on lung metastasis formation in this model, by investigating the composition of the immune microenvironment in the lungs and the production of cytokines and chemokines both in primary tumors and in the lungs. For this, female Balb/c mice were treated with thyroxine for 4 weeks (hyperthyroid), with propylthiouracil (PTU) for 2 weeks (hypothyroid), or with PTU plus daily doses of triiodothyronine (T3) to revert hypothyroidism. Mice were then orthotopically inoculated with 4T1 cells, and after 21 or 35 days, tumors and lungs were excised and analyzed. Hyperthyroid mice displayed a higher proportion of cytotoxic T, NK, and B cells ($p < 0.05$) in the lungs along with higher IFN- γ and IL-2 levels ($p < 0.05$), indicating a more cytotoxic microenvironment. In contrast, lungs of hypothyroid mice displayed elevated levels of CCL5, CCL17, and CCL22 ($p < 0.05$), which were reverted by T3 treatment and are associated with increased immunosuppression. Tumors

from hyperthyroid mice also secreted higher levels of CXCL1, CCL5, CCL17, and CCL22 ($p < 0.05$), suggesting an immunosuppressive intratumoral milieu that may contribute to increased tumor growth. Together, these findings highlight the dual role of thyroid hormones in shaping local and systemic immune responses that differentially affect breast cancer growth and metastasis.

305. O15-05. OXIDATIVE STRESS AND INFLAMMATION IN THE ANTERIOR PITUITARY GLAND UPON EXPOSURE TO CONDITIONED MEDIUM FROM SPLENIC MACROPHAGES: AN EX VIVO MODEL OF POLYCYSTIC OVARY SYNDROME

Mendoza GV¹, Figueroa MF², SANDRA E. GOMEZ MEJIBA³, DARIO C RAMIREZ⁴, MIRIAN FORNERIS⁵

1. Facultad de Química, Bioquímica y Farmacia (UNSL).

San Luis, Argentina

2. Facultad de Química, Bioquímica y Farmacia (UNSL).

San Luis, Argentina

3. IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.

4. IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.

5. Facultad de Química, Bioquímica y Farmacia (UNSL).

San Luis, Argentina

gise.mza10@gmail.com

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrinological disease characterized by hyperandrogenism and infertility. Previously, we demonstrated an immune-endocrine interaction through the action of splenic macrophage-conditioned medium (SpM-CM) with the anterior pituitary (AP) of rats with polycystic ovary (AP-PCO). In this study, we hypothesize that myeloperoxidase (MPO), inducible nitric oxide synthase (iNOS) and proinflammatory cytokines promote inflammation and oxidative stress in AP in a rat model of PCO. Thus, our aim was to test whether incubation with SpM-CM can change the expression and activity of MPO, iNOS and proinflammatory cytokines in the AP of PCO (PCO-AP) and control (C-AP) rats. We induced PCO in adult rats with estradiol valerate (2 mg/rat i.m.). Then, we incubated PCO-AP and C-AP with either RPMI medium (baseline) or SpM-CM from PCO rats. In AP homogenates, we measured MPO and iNOS, as well as chlorotyrosine- and nitrotyrosine-modified proteins, by ELISA. The expression of MPO and iNOS in the APs was also assessed by RT-PCR. Compared with those in the C-AP group, the nitrotyrosine and chlorotyrosine levels in the PCO-AP group increased MPO after incubation with baseline media. No difference was observed in either C-AP or PCO-AP when incubated with PCO-SpM-CM. The release of TNF α and IL-6, as well as their mRNA levels, was greater in PCO-AP than in C-AP. Our results are consistent with a link between MPO and increased inflammation in AP, with subsequent oxidative damage and dysfunction likely exacerbated by the androgenic environment in our rat model of PCO.

306. O15-06. ECHINOCOCCUS GRANULOSUS ANTIGENS ACTIVATE DIFFERENT METABOLIC PATHWAYS AND INDUCE OXIDATIVE STRESS IN BONE MARROW-DERIVED DENDRITIC CELLS

Maia Chop¹, Gianluca Demare², Ágata Cevey de Laforé³, Christian Rodríguez Rodríguez⁴

1. CONICET, Universidad Nacional de Mar del Plata; Lab 1

2. Universidad Nacional de Mar del Plata; Lab 1

3. CONICET, Universidad Nacional de Mar del Plata; Lab 1

4. CONICET, Universidad Nacional de Mar del Plata; Lab 1

maiachop@gmail.com

Background: Foreign antigens can activate dendritic cells, inducing a metabolic shift from oxidative phosphorylation (OXPHOS) to glycolysis, which is closely related to cell status and the type of immune

response elicited. This study aimed to determine whether purified laminar layer (pLL) or hydatid fluid (HF) isolated from *Echinococcus granulosus* cysts can alter cellular metabolism. Methods: Bone marrow-derived dendritic cells (BMDCs) were obtained from CF-1 mice. Metabolic gene expression was analyzed using RT-qPCR. Confocal microscopy and FACS were used to measure oxidative stress levels. Results: HF-stimulated cells showed increased expression of genes related to glycolysis and the pentose phosphate pathway, such as gapdh, hk2 and g6pd, respectively ($n=3$, $*p < 0.05$, $**p < 0.01$, HF vs. CTRL). Conversely, pLL-stimulated BMDCs exhibited induction of OXPHOS-related genes, such as cs and idh2 and an increase in the amino acid and fatty acid transporters slc1a5 and cpt1a respectively ($n=3$, $*p < 0.05$, $***p < 0.001$, $****p < 0.0001$ pLL vs. CTRL). The presence of superoxide anions was measured using a DHE probe. Both antigens revealed a significant increase in O₂- in stimulated cells ($n=3$, $p < 0.0001$, HF or pLL vs. CTRL). Reactive oxygen species (ROS) levels were assessed using H2DCF-DA, indicating that HF-stimulated cells produced higher ROS levels than pLL-stimulated cells ($n=3$, $p < 0.0001$, HF vs. CTRL; $p < 0.05$, pLL vs. CTRL). Nitric oxide production was measured using DAF-FM diacetate, which showed an increase only in HF-stimulated BMDCs ($p < 0.01$, HF vs. control). Conclusion: *E. granulosus* antigens differentially activate metabolic pathways and induce oxidative stress, potentially impairing cellular function and affecting anti-parasitic immune responses.

307. O15-07. CELL-FREE SUPERNATANT FROM B. LACTIS INL1 MODULATES IMMUNE CELL FUNCTION AND INFLUENCES COLORECTAL CANCER CELL VIABILITY

Pedro Carriere¹, María Belen Novoa Díaz², Cintia Birkens-tok³, Natalia Calvo⁴, Gabriela Sica⁵, Gabriel Vinderola⁶, Quentin Boussau⁷, Judith Bruyere⁸, Diego Cattoni⁹, Claudia Gentili¹⁰

1. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)

2. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)

3. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)

4. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)

5. Departamento de Ciencias de la Salud, UNS, Bahía Blanca, Argentina. Departamento de Biología, Bioquímica y Farmacia, UNS, Bahía Blanca, Argentina.; Laboratorio de Bacteriología y Micología

6. Universidad Nacional del Litoral (UNL), Santa Fe, Argentina.; INLAIN (CONICET-UNL)

7. Centro de Biología Estructural, CNRS-UM-INSERM, Montpellier, Francia.; Grupo de Biología Sintética

8. Centro de Biología Estructural, CNRS-UM-INSERM, Montpellier, Francia.; Grupo de Biología Sintética

9. Centro de Biología Estructural, CNRS-UM-INSERM, Montpellier, Francia.; Grupo de Biología Sintética

10. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.; INBIOSUR (CONICET-UNS)

pedro.carriere@uns.edu.ar

Probiotic-derived metabolites have emerged as promising agents for modulating immune responses and shaping the tumor microenvironment. In this study, we evaluated whether the cell-free supernatant (CFS) of *Bifidobacterium animalis* subsp. *lactis* INL1 (*B. lactis* INL1) (agreement UNS-UNL N°REC-1092496-2), a strain isolated from breast milk, can modulate events associated with these effects. Initially, THP-1 monocytic cells, either undifferentiated or differentiated into macrophage-like cells using phorbol 12-myristate 13-acetate (PMA), were used to assess phagocytic capacity following pre-treatment with *B. lactis* INL1. Using a gentamicin protection assay with *E. coli* Nissle 1917 constitutively expressing the red fluorescent pro-

tein mKate (EcN-mKate) as the phagocytic target, we observed that PMA-differentiated THP-1 cells exhibited enhanced phagocytic uptake of EcN-mKate following exposure to CFS. This was confirmed by light microscopy and drop-CFU assays. Additionally, we evaluated phagocytosis in Peripheral Blood Mononuclear Cells (PBMCs) isolated from healthy donors, observing a comparable increase in their phagocytic index. We next investigated whether CFS exposure altered the cytokine profile of THP-1 cells and PBMCs. Using a multiplex immunoassay, we found that pre-treatment with CFS under LPS-induced inflammatory conditions modulated the release of key immune cytokines, including IL-6, IL-1 β , and IL-10, while others, such as TNF- α and CCL2 showed no significant changes. These effects were cell-type-specific. Finally, conditioned media obtained from THP-1 cells and PBMCs pre-treated with CFS and exposed to LPS reduced the viability of colorectal carcinoma MC38 cells. This suggests that immune cell function and immune-tumor cell interactions may be modulated by metabolites derived from *B. lactis* INL1.

308. O15-08. Antibodies against Respiratory Syncytial Virus Dynamics in the Context of COVID19 pandemics in children from Buenos Aires

Pablo Pakciarz¹, Julia Dvorkin², Gonzalo Guíñazu³, Pilar Sorgente⁴, Daniela Parada⁵, Damián Alvarez-Paggi⁶, Mauricio Caballero⁷

1. Universidad Nacional de San Martín.; Centro Infant de Medicina Traslacional (CIMeT)
 2. Universidad Nacional de San Martín, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Centro Infant de Medicina Traslacional (CIMeT)
 3. Universidad Nacional de San Martín; Centro Infant de Medicina Traslacional (CIMeT)
 4. Universidad Nacional de San Martín.; Centro Infant de Medicina Traslacional (CIMeT)
 5. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires.; Instituto de Cálculo
 6. Universidad Nacional de San Martín, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Centro Infant de Medicina Traslacional (CIMeT)
 7. Universidad Nacional de San Martín, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Centro Infant de Medicina Traslacional (CIMeT)
- ppakciarz@iib.unsam.edu.ar

Respiratory syncytial virus (RSV) is a major health threat to children worldwide. COVID-19 disrupted RSV seasonality affecting the burden and severity of RSV-related acute lower respiratory illness (ALRI). To evaluate the relationship between RSV seroprevalence in children under five years and the burden of hospitalizations in Buenos Aires in 2022-2023 compared to pre-pandemic, we conducted a multicenter, retrospective cohort study, using lower respiratory tract infections (LRTI) hospitalization data from 2018-2023 across 4 hospitals. We also collected serum samples during 2020-2023 and pre-pandemic samples from serum biobanks to investigate changes in RSV antibody titers, including their neutralizing capacity within age subgroups. 12907 LRTI hospitalizations were recorded, 4284 RSV-positive cases. Pediatric intensive care unit (PICU) admissions increased significantly in the post-pandemic period (26.68% in 2022-2023 vs 12.50% in 2018-2019), both groups with similar comorbidities. The mean age of patients admitted to PICU was also higher (9.13 vs 7.38 months). We found a reduction in seropositivity and RSV-specific IgG geometric mean titers (GMT) between 7 and 36 months during 2020-2022, with recovery to pre-pandemic values in 2023. Moreover, we observed that the neutralizing capacity of the sera in this age group across the years is low compared to those younger than 6 or older than 36 months, and even 40% of the tested sera were not neutralizing. The unusual situation caused by the COVID-19 pandemic has generated an ideal context to understand RSV dynamics of community seroprevalence and hospitalization, previewing the potential impact of the RSV immunization strategy on the burden of RSV-ALRI.

309. O15-09. IMMUNOGENICITY AND INTRINSIC ADJUVANT PROPERTIES OF A VIRUS-LIKE PARTICLE VACCINE

PLATFORM

Daniela Romina Montagna¹, María Florencia Todero², Mercedes Pastorini³, Mercedes Alemán⁴, Sandra Goñi⁵, Cristina Borio⁶, Alejandra Duarte⁷

1. 1-Instituto de Química y Fisicoquímica Biológicas (IQUI-FIB), Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, UBA-CONICET.; Laboratorio de glicobiología tumoral
 2. Fundación H.A Barceló, Buenos Aires, Argentina; Cátedra de Anatomía Patológica, Facultad de Odontología, UBA.;
 3. Universidad Nacional de Quilmes (UNQ); Laboratorio de Virus Emergentes
 4. Academia Nacional de Medicina.; IMEX-CONICET
 5. Universidad Nacional de Quilmes (UNQ); Laboratorio de Virus Emergentes
 6. Universidad Nacional de Quilmes (UNQ).; Laboratorio de Virus Emergentes
 7. INIGEM-UBA-CONICET, Hospital de Clínicas José de San Martín.; Laboratorio de Diabetes y metabolismo.
- daniela.r.montagna@gmail.com

The emergence of SARS-CoV-2 variants and other viruses underscores the need for continued development of adaptable and durable vaccines. Platforms with efficient antigen presentation and intrinsic adjuvant properties are key to next-generation vaccines. This study evaluates a Virus-Like Particle (VLP) platform derived from the Junín virus as a flexible system for this purpose. We engineered VLPs to display the receptor-binding domain (RBD) of SARS-CoV-2 and assessed the subsequent immune response in a murine model. BALB/c and C57BL/6 mice were immunized with VLPs-RBD on day 0, with boosters on days 14 and 30. Spleens, lymph nodes, and serum samples were collected at different time points. Immunological markers were evaluated by flow cytometry. Our results demonstrate that VLPs significantly enhanced the expression of MHC class I and II molecules and the costimulatory marker CD86 on bone marrow-derived dendritic cells. This, along with elevated IL-6 and TNF- α cytokines in vivo, confirms the platform's intrinsic adjuvant effect. Immunized mice exhibited superior activation and proliferation of both CD4⁺ and CD8⁺ T cells, characterized by elevated secretion of IFN- γ and IL-2. Furthermore, the platform induced robust memory cell populations, including central (CD44+CD62L+) and effector (CD44+CD62L-) memory T cells, alongside key memory B cell subsets, significantly increased B220⁺ CD19⁺ CD45⁺ B cells in spleen and lymph nodes, along with a higher percentage of IgG⁺ cells. These findings establish that this VLP platform functions as a potent, self-adjuvating system that drives a comprehensive and durable immune response, marking it as a promising tool against evolving viral pathogens.

POSTERS 17 - SAIC - FIRST-TIME PRESENTERS 3

DATE & TIME: 19/11/2025 15:00 - 16:30 H

Chairs: Carolina Sétula, Mailín Casadei, Gastón Pascual, Gisela Mazaira

310. P17-17. INHIBITION OF CERAMIDE SYNTHESIS ATTENUATES MICROGLIAL REACTIVITY IN EXPERIMENTAL ALZHEIMER'S DISEASE

Melina Bellotto¹, Martín Ignacio Carrera², Melisa Bentivegna³, Carlos Javier Pomilio⁴, Nicolas Gonzalez Perez⁵, Soledad Porte Alcon⁶, Flavia Eugenia Saravia⁷, Juan Beauquis⁸

1. IBYME; Neurobiología del envejecimiento
 2. IBYME; Neurobiología del envejecimiento
 3. IBYME; Neurobiología del envejecimiento
 4. IBYME; Neurobiología del envejecimiento
 5. IBYME; Neurobiología del envejecimiento
 6. IBYME; Neurobiología del envejecimiento
 7. IBYME; Neurobiología del envejecimiento
 8. IBYME; Neurobiología del envejecimiento
- melinabellotto@gmail.com

Alzheimer's disease (AD) is the primary cause of dementia and is characterized by extracellular amyloid plaques accompanied

by inflammation and glial reactivity. Ceramides, membrane lipids that mediate inflammation, may contribute to neurodegeneration and glial reactivity in AD. Our aim was to study the effects of inhibiting ceramide synthesis pathways on microglial activation using familial AD model PDAPP-J20 mice and microglial cell cultures. Eight-month-old female PDAPP-J20 mice were treated i.p. with Myriocin (an inhibitor of serine-palmitoyl transferase [SPT], the de novo ceramide synthesis pathway) or GW4869 (an inhibitor of neutral sphingomyelinase 2 [nSMase2]) for 3 weeks. Brain immunofluorescence revealed that Myriocin treatment increased hippocampal amyloid pathology, indicating disease worsening, while GW4869 reduced amyloid burden and microglial activation. In vitro, BV2 microglia exposed to amyloid beta for 2 hours showed increased nuclear translocation of NF- κ B, a pro-inflammatory transcription factor ($p < 0.001$ vs. control). Co-treatment with GW4869 or Myriocin significantly reduced NF- κ B nuclear translocation ($p < 0.001$ and $p < 0.01$ vs. amyloid), but cambinol, another nSMase2 inhibitor, did not. Our findings demonstrate that inhibition of ceramide synthesis via nSMase2 attenuates amyloid pathology and microglial activation, highlighting this pathway as a promising therapeutic target in AD. Conversely, inhibiting the de novo ceramide synthesis pathway may exacerbate the pathology. These results underscore the critical role of ceramide metabolism in AD pathogenesis and inflammation.

311. P17-18. LOW-DOSE EXPOSURE TO A GLYPHOSATE-BASED HERBICIDE DISRUPTS UTERINE DECIDUALIZATION AND IMPAIRS PREGNANCY OUTCOMES IN WISTAR RATS

Lucila Mijno¹, Ramiro Alarcón², Valentín Fernandez Schamzenpach³, Gabriela Anahí Bressan⁴, María Laura Zenclussen⁵, Virginia Lorenz⁶, Paola Inés Ingaramo⁷

1. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; Fisiopatología Ambiental

2. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; Fisiopatología Ambiental

3. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; Fisiopatología Ambiental

4. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; Fisiopatología Ambiental

5. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; Endocrinología y Carcinogénesis

6. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; Fisiopatología Ambiental

7. Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral - Consejo Nacional de Investigaciones Científicas y Técnicas, Santa Fe, Argentina; Fisiopatología Ambiental lucilamijno@gmail.com

Strong evidence indicates that glyphosate-based herbicides (GBHs) have endocrine disrupting properties with potential implications on reproductive function. Here, we investigated whether a low dose of a GBH disrupt female reproductive performance and fetal development in Wistar rat, as well as the underlying mechanistic pathways involved. Female pups received saline solution (control) or GBH (0.2 mg/kg/day) by sc. injection on postnatal days 1, 3, 5 and 7. From postnatal day 90, females were mated with proven fertility males. One group of pregnant rats was euthanized on gestational day (GD) 19 to assess fertility outcomes and developmental parameters (fetal length and weight and placental weight).

Another group was evaluated on GD9 to study possible alterations in decidualization at the implantation sites (IS). On the IS, mRNA expression of progesterone receptor (PR), Vegf, Angpt2, Cox-2 and IL-10 were quantified using RT-qPCR. In addition, nestin and PR were assessed by immunohistochemistry. On GD19, females of GBH group exhibited increased postimplantation losses and decreased fetal length. To elucidate the pathways involved in the embryo losses, IS were analysed. Decreased PR (mRNA and protein) and reduced expression (mRNA) of angiogenic markers Vegf and Angpt2 was observed in the GBH group. Nestin expression did not show changes while the diameter of blood vessels was altered in GBH rats. Regarding the inflammatory state, while Cox-2 was decreased, IL-10 was increased in GBH treated rats. In conclusion, exposure to a low dose of a GBH impaired gestational parameters and disrupted decidualization mechanisms which may contribute to embryos loss.

312. P17-19. CHRONIC EXPOSURE TO URBAN AIR IN THE CITY OF BUENOS AIRES ALTERS REDOX METABOLISM IN MICE CEREBELLUM

Octavio Diana¹, Agustina Freire², Sofia Reynoso³, Silvia Alvarez⁴, Natalia Magnani⁵, Mariana Garces⁶, Pablo Andres Evelson⁷

1. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica.; Cátedra de Química General e Inorgánica

2. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica.; Cátedra de Química General e Inorgánica

3. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica.; Cátedra de Química General e Inorgánica

4. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica.; Cátedra de Química General e Inorgánica

5. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica.; Cátedra de Química General e Inorgánica

6. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica.; Cátedra de Química General e Inorgánica

7. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica.; Cátedra de Química General e Inorgánica

octavio.diana@alumnos.fybb.uba.ar

Several studies have identified the Central Nervous System (CNS) as a target after the exposure to air pollution. Particulate matter (PM) present in urban air (UA) has been linked to the adverse health effects associated with neurodegenerative and neurodevelopmental disorders. However, the pathways underlying physiopathological mechanisms remain unclear. Therefore, the aim of this study was to investigate the toxicological mechanisms triggered by UA exposure in the cerebellum, focusing on redox metabolism and neuroinflammation markers. BALB/c mice were exposed for 4 weeks to UA (UA, n=10) from a high-traffic area in Buenos Aires, or filtered air (FA, n=10) as a control, using whole-body exposure chambers. After the exposure period, the cerebellum was isolated, and the glutathione redox cycle enzymes were analyzed. UA exposure induced a 50% increase in glutathione S-transferase activity (FA=0.09±0.01 μ mol/min/mg protein. $p < 0.05$) and a 70% decrease in glutathione peroxidase activity (FA=0.015±0.001 μ mol/min/mg protein. $p < 0.05$) compared to FA, with no changes in glutathione reductase. Additionally, superoxide dismutase and catalase activities decreased by 40% (FA=23±1 USOD/mg protein $p < 0.01$) and 30% (FA=1.01±0.05 pmol/mg protein $p < 0.05$), respectively. After UA exposure oxidative damage to proteins was evidenced by a 40% increase in carbonyl groups content (FA=2.0±0.3 nmol/mg protein $p < 0.05$). Regarding cerebellum neuroinflammation, no differences were found between experimental groups in the assessed cytokines levels (IL-6, IL-10 and TNF- α). These findings suggest that UA exposure affects redox metabolism in cerebellum promoting oxidative damage that might play a key role in the mechanisms of neuronal injury induced by air pollution.

313. P17-20. ANALYSIS OF TOXICITY INDUCED BY THE COMMERCIAL FORMULATION OF MANCOZEB (FMZ) IN A549 CELLS

Melisa Romina Dominguez¹, Nancy Andrioli², Gabriela Chau-fan³

1. *Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, UBA; Laboratorio de Enzimología, Estrés y Metabolismo (LEEM)*
2. *Departamento de Biodiversidad y Biología Experimental, Facultad de Ciencias Exactas y Naturales, UBA; Grupo de Investigación en Biología Evolutiva (GIBE)*
3. *Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, UBA; Laboratorio de Enzimología, Estrés y Metabolismo (LEEM)*
melissardominguez@gmail.com

Fungicides are widely used in the production of fruits and vegetables, raising concerns about their potential toxic effects on the human population. One of the most commonly applied fungicides is mancozeb, whose commercial formulation (FMZ) includes adjuvants that may influence its toxicity. The A549 cell line, derived from human pulmonary epithelium, provides a suitable model to evaluate toxic effects related to the respiratory tract. The aim of this study was to analyze the cytotoxicity and oxidative stress induced by FMZ in the A549 cell line. The lethal concentration 50 (LC50) was determined as 62.97 $\mu\text{g/mL}$, with NOAEL and LOAEL concentrations of 20 $\mu\text{g/mL}$ and 40 $\mu\text{g/mL}$, respectively. These values were comparable to those reported for pure mancozeb (MZ), suggesting a similar cytotoxicity profile and indicating that the adjuvants do not significantly increase toxicity. Subcytotoxic concentrations (10, 20, and 30 $\mu\text{g/mL}$) were selected to evaluate oxidative stress biomarkers. The activities of catalase (CAT), superoxide dismutase (SOD), glutathione S-transferase (GST), and the content of reduced glutathione (GSH) were measured. An increasing trend was observed in SOD activity and GSH content, along with a decrease in GST activity as the concentration increased. These findings suggest that, although FMZ toxicity does not differ from that of the active ingredient, its formulation may modulate the cellular oxidative response.

314. P17-21. MOLECULAR OXYGEN DOES NOT MEDIATE IGG-AGGREGATION INDUCED BY CU(II)/ASCORBIC ACID MIXTURE BUT RENDERS THE AGGREGATE INSENSITIVE TO METAL CHELATION-MEDIATED SOLUBILIZATION

Agustín Bautista Silva¹, Lila Lopez Montañana², Juan Ignacio Bellida³, Guadalupe Pagano⁴, Federico Marino⁵, Ludmila Moyano Libertini⁶, Leonella Ariana Danzi⁷, Iara Puertas⁸, Maximiliane Wissler⁹, María Laura Facio¹⁰, Margarita Martínez Sarraquie¹¹, Alejandra Cimato¹², Marisa Gabriela Repetto¹³, Christian Martín Saporito Magriña¹⁴

1. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Estrés oxidativo y agregados proteicos*
2. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Estrés oxidativo y agregados proteicos*
3. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Estrés oxidativo y agregados proteicos*
4. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Estrés oxidativo y agregados proteicos*
5. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Estrés oxidativo y agregados proteicos*
6. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Estrés oxidativo y agregados proteicos*
7. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Estrés oxidativo y agregados proteicos*
8. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Estrés oxidativo y agregados proteicos*
9. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Estrés oxidativo y agregados proteicos*
10. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica; Bioquímica clínica - INFIBIOQ*
11. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, IBIMOL; Estrés oxidativo y agregados proteicos*
12. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, IBIMOL; Estrés oxidativo y agregados proteicos*
13. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, IBIMOL; Estrés oxidativo y agregados proteicos*
14. *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, IBIMOL; Estrés oxidativo y agregados proteicos*

agus10102020@gmail.com

Cu(II) induces the aggregation of IgG, an effect strongly potentiated by ascorbic acid (AA) but not observed in proteins such as albumin. Considering that free Cu(II) ions and high concentrations of AA are present in plasma, this phenomenon may be relevant in modulating the concentration of circulating protein aggregates. The aim of this work is to understand the mechanism driving this process. Results: Cu(II)-induced IgG aggregation, observed as increased opalescence (405nm), is significantly enhanced by AA and other reducing agents such as N-acetylcysteine, cysteine, and dithionite ($p < 0.001$), whereas the presence of the reducing agent alone does not induce aggregation. The aggregated fraction consists of monomeric, dimeric, and multimeric IgG species detected by SDS-PAGE. Dimeric and multimeric aggregates are degraded by β -mercaptoethanol into 25 and 50 kDa fragments. The O_2 consumption rate of the Cu(II)/AA system at pH 7.4 decreases significantly in the presence of IgG ($p < 0.001$). Aggregate formation is reduced by 60% with EDTA or GSH ($p < 0.001$), while under O_2 depletion by dithionite, metal chelation completely abolishes opalescence ($p < 0.001$). These results indicate that reducing agents potentiate IgG aggregation in the presence of Cu(II) through the formation of Cu(I), independently of O_2 -derived species, since dithionite also induces aggregation. Nonetheless, O_2 is implicated in the generation of irreversible aggregates: when induced with AA, aggregates resist EDTA dissolution, whereas those generated under O_2 -depleted conditions dissolve completely upon metal chelation. Together, these findings reveal a novel redox-dependent mechanism by which Cu(II) and reductive agents promote IgG aggregation whereas O_2 determines the reversibility of the process.

315. P17-22. BNCT FOR PANCREATIC TUMORS: IN VITRO STUDIES AND BORON UPTAKE MEDIATED BY GB-10 IN AN IN VIVO ORTHOTOPIC PANCREATIC TUMOR MODEL

Mayra Rotchtein¹, Yago Dores Dores², Mónica A. Palmieri³, Verónica A. Trivillín⁴, María Silvina Olivera⁵, Agustina M. Portu⁶, Paula Curotto⁷, Paula Ramos⁸, Silvia Thorp⁹, Eduardo Cafferata¹⁰, Marcela A. Garabalino¹¹, Carla B. Rodríguez¹², Andrea Monti Hughes¹³

1. *Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Depto Radiobiología*
2. *Comisión Nacional de Energía Atómica (CNEA), Argentina; LANAIP*
3. *Departamento de Biodiversidad y Biología Experimental (DBBE), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (UBA), CABA, Argentina; Departamento de Biodiversidad y Biología Experimental (DBBE)*
4. *Comisión Nacional de Energía Atómica (CNEA); Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; Div. Patología de la Radiación, Depto Radiobiología*
5. *Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Depto BNCT*
6. *Comisión Nacional de Energía Atómica (CNEA), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; Div Radiomicrobiología, Depto Radiobiología*
7. *Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Haces RA-3*
8. *Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Haces RA-3*
9. *Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; División Instrumentación y Dosimetría*
10. *Fundación Instituto Leloir, CONICET, Argentina; Laboratorio de terapia molecular y celular*
11. *Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Depto Radiobiología*
12. *Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina; Div Bioquímica Nuclear, Depto Radiobiología*
13. *Comisión Nacional de Energía Atómica (CNEA), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; Div. Patología de la Radiación, Depto Radiobiología*
mayra.rotchtein@comunidad.ub.edu.ar

Pancreatic ductal adenocarcinoma is an aggressive type of cancer with limited and toxic therapies. Novel treatments are needed to control the tumor while preserving the surrounding structures and organs. Boron Neutron Capture Therapy (BNCT) combines preferential tumor uptake of 10-B compounds and neutron irradiation. The aim of this study is to evaluate the cytotoxic effect of BNCT mediated by GB-10 (sodium decahydrodecaborate) as boron compound in hamster pancreatic tumor cells (HapT1) and to perform GB-10 biodistribution studies to evaluate the therapeutic potential of GB-10/BNCT in an in vivo orthotopic tumor model. Cells in exponential growth phase and previously incubated with GB-10 (50 ppm) were irradiated with neutrons at 1, 3 and 5 Gy. A non-irradiated control was included (0 Gy). Survival fraction (SF) was obtained by clonogenic assays. For GB-10 biodistribution studies, HapT1 cells (5x105) were injected beneath the capsule of the pancreas, in the splenic lobe (T0) (2 animals). GB-10 (50 mg B/kg) was injected intravenously, 14 days after inoculation. Blood, tumor, pancreas, stomach, spleen, intestine and kidney were analyzed by ICP-OES and neutron autoradiography. GB-10/BNCT induced a significant cell survival decrease at 3 and 5 Gy (SF=0.12±0.02 and 0.040±0.004, respectively). Tumor absolute boron concentration values were around 10 ppm and tumor-to-normal pancreas ratio was 1.2. Theoretically, these values would not be therapeutically useful but our previous studies in a hamster oral cancer model showed similar results with significant therapeutic effect and slight induced radio-toxicity. Based on these studies GB-10/BNCT could be a potential effective therapy for pancreatic tumors.

316. P17-23. PRECLINICAL STUDIES OF BORON NEUTRON CAPTURE THERAPY (BNCT) FOR THE TREATMENT OF CUTANEOUS MELANOMA

Estanislao Pavlik¹, Susana Nieves², Marina Carpano³, Antonella Pastini⁴, Luciano Parodi⁵, Florencia Nataly Navarro⁶, Juan Manuel Longhino⁷, José Gómez Escalante⁸, Érica Rojas Bilbao⁹, Pablo Menéndez¹⁰, Karen Morrison¹¹, Michael Torgov¹², Kendall Morrison¹³, María Alejandra Dagrosa¹⁴

1. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Centro Oncológico de Medicina Nuclear
2. Instituto de Oncología "Ángel H. Roffo" Facultad de Medicina, Universidad de Buenos Aires; Centro Oncológico de Medicina Nuclear.

3. Comisión Nacional de Energía Atómica; Radiobiología

4. Instituto de Oncología "Ángel H. Roffo" Facultad de Medicina, Universidad de Buenos Aires; Centro Oncológico

5. Comisión Nacional de Energía Atómica; División Bioterio

6. Comisión Nacional de Energía Atómica; RA6

7. Comisión Nacional de Energía Atómica; RA6

8. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Departamento de Patología.

9. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Dirección de Área Diagnóstico Departamento de Patología

10. Instituto de Oncología "Ángel H. Roffo" Facultad de Medicina, Universidad de Buenos Aires; Dirección de Área Terapia Radiante y Medicina Nuclear

11. TAE Life Sciences, Santa Monica, California 90404, United States; Drug Development Division,

12. TAE Life Sciences, Santa Monica, California 90404, United States; Drug Development Division

13. TAE Life Sciences, Santa Monica, California 90404, United States; Drug Development Division

14. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Centro Oncológico de Medicina Nuclear estaanipavlik@gmail.com

Introduction: Clinical trials of boron neutron capture therapy (BNCT) using borophenylalanine (BPA) were performed in Argentina for human patients with melanoma. In order to optimize BNCT, two new

boron compound (TAE Life Science): a phenylalanine dipeptide (TC440) and an analogues of L-tyrosine (TC220), were evaluated. Materials and Methods: NIH nude mice implanted with the human melanoma line (Mel J) were injected ip with BPA (30g/L), TC220 and TC440 (90g/L) in a volume of 300 µL (CICUAL-CNEA on 08/2024_V2). Biodistribution and irradiation studies were performed in two different stages. Twenty five animals were divided in the following groups: 1) Control: without treatment; 2) NCT: irradiated with the neutron beam only; 3) BNCT I: BPA plus neutrons; 4) BNCT II: TC 400 plus neutrons and 5) BNCT III: TC 220 plus neutrons. Irradiation was performed in RA 6 (Flux=2.8 x108 n/cm 2.sec) for 37 min. The follow up was carried out for 30 days and histologic and IHC for CD133 (ab278053, Abcam) were carried out at day 7. Results: Biodistribution showed a peak of boron of 26-28 µg/g of tissue with a tumor/blood ratio of 4 for TC440 at 4 h post injection while BPA showed a peak of 15 ppm at 2 h. Complete BNCT demonstrated tumor growth inhibition for the three compounds, being 1.5 and 2.5 times greater for TC440 and TC220 respectively respect to BPA. No CD133 positive cells were found for BNCT. Conclusion: BNCT to melanoma using the new borated compounds showed a therapeutic advantage over BPA.

317. P17-24. EFFECTS OF ACSL4 INHIBITION ON THE AGGRESSIVENESS OF COLON CANCER CELLS

Valentina Celine Bulian¹, Ludmila Gutierrez², Luciano Martin Quevedo³, Silvana Nudler⁴, Ana Fernanda Castillo⁵, Ulises Daniel Orlando⁶

1. Instituto de Investigaciones Biomédicas (INBIOMED UBA-CONICET); HRDC

2. Instituto de Investigaciones Biomédicas (INBIOMED UBA-CONICET); HRDC

3. Instituto de Investigaciones Biomédicas (INBIOMED UBA-CONICET); HRDC

4. Instituto de Investigaciones Biomédicas (INBIOMED UBA-CONICET); HRDC

5. Instituto de Investigaciones Biomédicas (INBIOMED UBA-CONICET); HRDC

6. Instituto de Investigaciones Biomédicas (INBIOMED UBA-CONICET); HRDC
valenbuli@hotmail.com

The transition from adenoma to adenocarcinoma in colorectal cancer (CRC) is characterised by the accumulation of mutations in key genes such as APC, KRAS, TP53 and SMAD4, leading to deregulation of multiple cellular pathways. Among the processes involved, alterations in arachidonic acid (AA) metabolism are linked to overexpression of enzymes such as cyclooxygenase-2 (COX-2) and 5-lipoxygenase (5-LOX), together with activation of pro-tumoural pathways including AKT/mTOR and WNT/β-catenin. In this context, the enzyme acyl-CoA synthetase 4 (ACSL4), which participates in AA metabolism, is upregulated during adenoma-to-adenocarcinoma progression. Bioinformatic analyses of CRC patient samples confirmed a significant increase in ACSL4, COX-2 and 5-LOX in primary tumours. The aim of this study was to evaluate the impact of combined inhibition of ACSL4, COX-2 and 5-LOX, together with inhibitors of the mTOR and WNT pathways, on cellular functions such as proliferation and migration in CRC cell lines. SW480, Caco-2, DLD-1 and T84 cells, which display differential enzyme expression and pathway activation, were used. Expression of ACSL4, COX-2, 5-LOX and components of the mTOR and WNT/β-catenin pathways was analysed by western blot. Cell proliferation was assessed by MTT assays after treatment with the ACSL4 inhibitor PRGL493, alone or combined with ibuprofen (COX-2 inhibitor), zileuton (5-LOX inhibitor), rapamycin (mTOR inhibitor) and XAV939 (WNT inhibitor). Preliminary results showed that PRGL493 in combination with these drugs significantly reduced proliferation and migration compared with single treatments (p< 0.5–0.01), suggesting a synergistic effect and supporting ACSL4 as a therapeutic target in CRC cells.

318. P17-25. CYTO- AND GENOTOXICITY OF A TEBUCO-NAZOLE-BASED FORMULATION IN A549 CELLS

Stefan Zylbersztein¹, Gastón Piccinini², Nancy Andrioli³, Gabriela Chauhan⁴

1. *Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, UBA; Laboratorio de Enzimología, Estrés y Metabolismo (LEEM)*
2. *Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, UBA; Laboratorio de Enzimología, Estrés y Metabolismo (LEEM)*
3. *Departamento de Biodiversidad y Biología Experimental, Facultad de Ciencias Exactas y Naturales, UBA; Grupo de Investigación en Biología Evolutiva (GIBE)*
4. *Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, UBA; Laboratorio de Enzimología, Estrés y Metabolismo (LEEM)*
stefan.zylb@gmail.com

Tebuconazole (TB) is a widely used agricultural fungicide, with reported toxic effects such as neurotoxicity, immunotoxicity, reproductive toxicity, and carcinogenicity. This study evaluated the cytotoxicity and genotoxicity of a commercial TB formulation (Trigal 43% w/v) in A549 cells (human pulmonary epithelium) exposed to different concentrations of the formulation. Cell viability was assessed using the MTT assay within a range of 1.075 to 516 $\mu\text{g/mL}$ of the TB formulation (FTB), yielding an LC50 of 44.33 $\mu\text{g/mL}$ (95% CI: 40.67–48.53 $\mu\text{g/mL}$). The NOAEL was 4.3 $\mu\text{g/mL}$ and the LOAEL 10.75 $\mu\text{g/mL}$. Based on these results, concentrations lower than 10.75 $\mu\text{g/mL}$ were selected for the cytokinesis-block micronucleus (CBMN) assay to evaluate micronuclei (MNI) frequency in binucleated cells. No significant differences were observed in the nuclear division index ($p=0.4$), indicating no cytotoxicity at the tested concentrations. However, MNI frequency showed a significant increase in treated groups compared to the control ($p<0.05$). In conclusion, this FTB at subcytotoxic concentrations induces genotoxic damage in A549 cells, underscoring the need for further research on commercial fungicide formulations due to their potential health risks.

319. P17-26. REGULATION OF LIPID METABOLISM BY GLUCOCORTICOIDS

- Florencia Santaromita¹, Francisco D. Rosa², Juliana L. Bernacchia³, María Florencia Quintanilla⁴, Alejandra G. Palma⁵, Natalia Paladino⁶, Monica A. Costas⁷, María Fernanda Rubio⁸
1. *IDIM UBA-CONICET; Lab. Biología Molecular y Apoptosis*
 2. *IDIM UBA-CONICET; Lab. Biología Molecular y Apoptosis*
 3. *IDIM UBA-CONICET; Lab. Biología Molecular y Apoptosis*
 4. *IDIM UBA-CONICET; Lab. Biología Molecular y Apoptosis*
 5. *IDIM UBA-CONICET; Lab. Biología Molecular y Apoptosis*
 6. *Universidad Nacional de Quilmes; Laboratorio de Cronobiología*
 7. *IDIM UBA-CONICET; Lab. Biología Molecular y Apoptosis*
 8. *IDIM UBA-CONICET; Lab. Biología Molecular y Apoptosis*
santaromitaflor@gmail.com

Glucocorticoids (GCs) are natural anti-inflammatory agents that regulate lipid metabolism in adipocytes. They are involved in metabolic adaptation and their action on the adipose tissue is complex since the lipid release or storage depends on the physiological or pathological state of the tissue. It is proposed that different GC concentrations can alter the balance between lipolysis and lipogenesis. This study evaluated the effect of two doses of glucocorticoid dexamethasone (Dx) on mammary adipose tissue explants from female mice. We measured glycerol secretion in murine mammary gland AT conditioned media after 48 h with Dx5 or Dx500. The high dose (500 nM) reduced adipocyte size and increased glycerol secretion, indicating a lipolytic profile. However, no significant changes were seen in cell size or glycerol secretion with the low dose (5 nM). We also performed a total extraction of lipids from the tissue. At 5 nM Dx, an increase in lipid content was observed, but with 500 nM although a decrease in total lipid content was observed, it was not statistically significant. Additionally, the expression of 11 β -hydroxysteroid dehydrogenase type 1 (11 β -HSD1) was analyzed. This enzyme converts inactive cortisone into active cortisol at the tissue level and we observed that 11 β -HSD1 expression increased with higher GC doses. These results suggest that there is a differential modulation in the lipolysis/lipogenesis balance dependent on the dose of dexamethasone, with a lipolytic profile at high doses that would be enhanced

by the in situ conversion of cortisone.

320. P17-27. METFORMIN RESTORES COGNITIVE FUNCTION, MICROGLIAL HOMEOSTASIS AND SENESCENCE IN EXPERIMENTAL MODELS OF BRAIN AGING

Facundo Dallo¹, Nicolas Gonzalez Perez², Valentina Saud³, Soledad Porte Alcón⁴, Melina Bellotto⁵, Melisa Bentivegna⁶, Martín Carrera⁷, Jéssica Presa⁸, Juan Beauquis⁹, Flavia Saravia¹⁰, Carlos Pomilio¹¹

1. *IByME (CONICET) - Depto de Química Biológica (FCEyN-UBA); Laboratorio de Neurobiología del Envejecimiento*
2. *IByME (CONICET) - Depto de Química Biológica (FCEyN-UBA); Laboratorio de Neurobiología del Envejecimiento*
3. *IByME (CONICET) - Depto de Química Biológica (FCEyN-UBA); Laboratorio de Neurobiología del Envejecimiento*
4. *IByME (CONICET) - Depto de Química Biológica (FCEyN-UBA); Laboratorio de Neurobiología del Envejecimiento*
5. *IByME (CONICET) - Depto de Química Biológica (FCEyN-UBA); Laboratorio de Neurobiología del Envejecimiento*
6. *IByME (CONICET) - Depto de Química Biológica (FCEyN-UBA); Laboratorio de Neurobiología del Envejecimiento*
7. *IByME (CONICET) - Depto de Química Biológica (FCEyN-UBA); Laboratorio de Neurobiología del Envejecimiento*
8. *IByME (CONICET) - Depto de Química Biológica (FCEyN-UBA); Laboratorio de Neurobiología del Envejecimiento*
9. *IByME (CONICET) - Depto de Química Biológica (FCEyN-UBA); Laboratorio de Neurobiología del Envejecimiento*
10. *IByME (CONICET) - Depto de Química Biológica (FCEyN-UBA); Laboratorio de Neurobiología del Envejecimiento*
11. *IByME (CONICET) - Depto de Química Biológica (FCEyN-UBA); Laboratorio de Neurobiología del Envejecimiento*
facundodallo@hotmail.com

Brain aging is a multifactorial process characterized by neuroinflammation, oxidative stress and mitochondrial dysfunction that progressively compromise synaptic plasticity and increase vulnerability to neurodegenerative disease. We tested whether metformin (MET), a widely used drug to treat diabetes, with reported geroprotective and neuroprotective properties, attenuates age-associated cognitive decline and dysfunctional microglial activation using complementary in vivo and in vitro models. Male C57BL/6 aged mice (9 and 16 months old) received intraperitoneal MET (320 mg/kg) or saline buffer three times weekly during the last three weeks of life. MET-treated aged mice exhibited reduced anxiety-like behavior (evaluated by Open field test) and improved spatial memory (across Novel Object Location and Barnes maze tests). In parallel, BV2 microglial cells were exposed 24 h to increasing concentrations of ferric ammonium citrate (FAC) to model brain iron accumulation (a process closely linked to aging and a potent driver of microglial dysfunction). MET (0.2 mM) was added during the final hour of treatment. FAC induced senescence-associated changes in BV2 cells that were attenuated by MET, including decreased immunoreactivity of the senescence marker p21 and reduced nuclear enlargement associated with senescence. Together, these findings suggest that metformin can improve cognitive performance, reduce senescence-associated alterations, and restore microglial homeostasis in experimental models of brain aging, supporting its potential as a therapeutic strategy to counteract neuroinflammation and age-related cognitive decline.

321. P17-28. SYNERGISTIC EFFECTS OF DKC1 INHIBITION AND PACLITAXEL TO IMPROVE THERAPEUTIC STRATEGIES FOR TRIPLE-NEGATIVE BREAST CANCER

María del Pilar Casco¹, Roman Nicolas Vilarullo², María Candelaria Mares Ahlers³, Vanesa Gottifredi⁴, Lara Balcone⁵, Julian Maggio⁶, Diego Luis Mengual Gómez⁷, Daniel Eduardo Gomez⁸, Romina Gabriela Armando⁹

1. *Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional*
2. *Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional*
3. *Fundación Instituto Leloir; Instituto de Investigaciones Bioquímicas de Buenos Aires*
4. *Fundación Instituto Leloir; Instituto de Investigaciones*

Bioquímicas de Buenos Aires

5. *Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional*

6. *Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional*

7. *Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional*

8. *Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional*

9. *Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional*

pilicasco98@gmail.com

Tumor cells have an unlimited replicative potential, principally due to telomerase activity, which depends on the assembly of many components. Dyskerin pseudouridine synthase 1 (DKC1) is one of them and it is overexpressed in triple-negative breast cancer (TNBC) and associated with poor prognosis. In previous works, we developed a novel DKC1 inhibitor, R1D2-10, targeting the interaction between the telomerase's RNA template and DKC1. R1D2-10 already demonstrated powerful antitumoral activity in various in vitro essays. In this study, we investigated whether combining paclitaxel (PTX) with R1D2-10 enhances the antitumoral effects while reducing required PTX dosages.

The research was conducted using two different TNBC cell lines in high- and low-density proliferation assays. The combination demonstrated synergistic effects, showing dose-dependent cytotoxicity and a decrease in colony formation. Regarding cell cycle regulation, we found that the combined treatment increased the population of cells in both G2/M and Sub-G1 phases. These results align with the qPCR results, which showed higher expression of cell cycle arrest makers, such as p21. We also evaluated the effect on apoptosis and found an increase in caspase 3/7 activity, followed by an upregulation of the pro-apoptotic gene expression ratio bax/bcl-xl. Lastly, this increase in apoptosis was not accompanied by DNA damage or replication stress. These results are promising, considering that combining R1D2-10 with PTX may provide an effective therapeutic strategy to reduce dose-related toxicity while enhancing chemotherapy effects in TNBC.

322. P17-29. EFFECTS OF DIET AND SEX ON PHYSICAL PARAMETERS, LIPID PROFILE, AND BLOOD GLUCOSE IN YOUNG RATS OF BOTH SEXES

Adriana Pietrelli¹, Adriana Pietrelli², Jone Iriondo Darriba³, Rayk Patricio De Souza⁴, Ricardo Orzuza⁵, Nora Paglia⁶

1. *University of Business and Social Sciences (UCES). School of Health Sciences. Buenos Aires, Argentina.; Dept of Basic Research*

2. *Universidad de Ciencias Empresariales y Sociales (UCES); Dept de Inv Básica y Bioterio*

3. *Universidad de Ciencias Empresariales y Sociales (UCES); Dept Investigación Básica y Bioterio*

4. *Universidad de Ciencias Empresariales y Sociales (UCES); Dept Inv Básica y Bioterio*

5. *Universidad de Ciencias Empresariales y Sociales (UCES); Dpt de Inv Básica y Bioterio*

6. *Universidad de Ciencias Empresariales y Sociales (UCES); Dpt Inv Básica y Bioterio*

adrianapietrelli@gmail.com

The aim of this study was to evaluate the effect of two normocaloric commercial diets and sex on physical and physiological parameters in Wistar rats. The qualitative-quantitative composition and metabolizable energy of each diet, C or G, were obtained from nutritional labels. Females (n=12) and males (n=12) were randomized into C (n=6) vs. G (n=6). The study began at 30 days of age (prepubescent) and ended at 3 months (adulthood). Body weight and food and water intake were measured over 10 weeks. Prior to the endpoint, serum samples were collected for lipid profile and glucose determinations. Using metabolic cages, feces, urine, and 24-hour food and water intake were also obtained. Sexual differences in body weight were observed regardless of diet. From the onset of sexual maturity, animals consumed more diet C than

diet G. Both sex and diet affected triacylglycerol (TG) and HDL cholesterol levels. A significant positive correlation (68%) between blood glucose and TG was detected only in males. Daily food intake was influenced by diet type and modulated by sex. Males fed with diet C drank more water than the other rats and excreted twice as much urine. The results demonstrate that diet composition and sex can modify feeding behavior and caloric homeostasis. This suggests the need to consider age, sex, and purpose (maintenance, experimentation, or reproduction) when selecting a diet for laboratory animals.

323. P17-30. BENCHMARKING TRANSCRIPTOMIC ANALYSIS STRATEGIES TO DEVELOP A ROBUST GENE SIGNATURE FOR PROSTATE CANCER

Nicolas Nahuel Crespi¹, Eden Korniansky², Lucas Abbate³, Elba Vazquez⁴, Javier Cotignola⁵, Geraldine Gueron⁶, Juan Bizzotto⁷

1. *Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Buenos Aires, Argentina - CONICET, Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina- Universidad Argentina de la Empresa (UADE), Instituto de Tecnología (INTEC), Buenos Aires C1073AAO, Argentina; Laboratorio de Inflamación y Cáncer*

2. *Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Buenos Aires, Argentina - CONICET, Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina- Universidad Argentina de la Empresa (UADE), Instituto de Tecnología (INTEC), Buenos Aires C1073AAO, Argentina; Laboratorio de Inflamación y Cáncer*

3. *Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Buenos Aires, Argentina - CONICET, Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer*

4. *Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Buenos Aires, Argentina - CONICET, Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer*

5. *Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Buenos Aires, Argentina - CONICET, Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer*

6. *Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Buenos Aires, Argentina - CONICET, Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina; Laboratorio de Inflamación y Cáncer*

7. *Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica, Buenos Aires, Argentina - CONICET, Universidad de Buenos Aires, Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Buenos Aires, Argentina - Universidad Argentina de la Empresa (UADE), Instituto de Tecnología (INTEC), Buenos Aires C1073AAO, Argentina; Laboratorio de Inflamación y Cáncer*

crespi.nicolasnahuel@gmail.com

Gene expression signatures can be pivotal in guiding treatment decisions for prostate cancer (PCa). Advances in RNA-seq technology, coupled with the growing availability of transcriptomic datasets, offer an unprecedented opportunity to develop and test machine learning (ML) models for biomarker discovery. To leverage this, robust pipelines for data processing and harmonization are essential precursors. In this study, we benchmarked strategies for data curation, pro-

cessing, and normalization across four large-scale, publicly available PCa datasets (n=478). Using logistic regressions we filtered and combined candidates into a 7-gene signature to predict disease progression. Thereafter, we assessed how different data handling strategies impact predictive models. Logistic regression analyses showed a significant association between higher signature scores and disease progression across all three independent validation datasets. In addition, we found that both z-score and reference gene scaling significantly improved the gene signature's performance during external validation (unscaled AUC: 0.46, z-score scaling AUC: 0.72, reference gene scaling AUC: 0.76), thereby enhancing model robustness. Furthermore, our results show that pseudoalignment-based quantification provides a fast and reproducible approach for processing RNA-seq data while maintaining rigorous quality control. Principal Component Analysis revealed that sequencing alignment percentage was a major source of inter-sample variability. In summary, we established a workflow to benchmark data processing strategies and used it to create a novel gene signature that enhances prognostic accuracy in PCa. These findings highlight the critical importance of rigorous bioinformatic methods in developing reliable prognostic models to guide clinical decision-making.

POSTERS 18 - SAIC - SISTEMA RESPIRATORIO

DATE & TIME: 19/11/2025 17:00 - 18:30 H

Chairs: Verena Franco Riveros, Gabriela Marina Prendes, Mariano Schuman

324. P18-13. IMPACT OF SEVERE RSV INFECTION IN INFANCY ON RECURRENT WHEEZING DURING CHILDHOOD

Pilar A. Sorgente¹, Pablo H. Pakciarz², Julia Dvorkin³, Damian Alvarez Paggi⁴, Mauricio T. Caballero⁵

1. Centro INFANT de Medicina Traslacional (CIMEt), Universidad de San Martín (UNSAM), Buenos Aires, Argentina.

2. Centro INFANT de Medicina Traslacional (CIMEt), Universidad de San Martín (UNSAM), Buenos Aires, Argentina.

3. Centro INFANT de Medicina Traslacional (CIMEt), Universidad Nacional de San Martín (UNSAM), Buenos Aires, Argentina; Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina.

4. Centro de Rediseño e Ingeniería de Proteínas (CRIP), Universidad Nacional de San Martín (UNSAM), Buenos Aires, Argentina; Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina.

5. Centro INFANT de Medicina Traslacional (CIMEt), Universidad Nacional de San Martín (UNSAM), Buenos Aires, Argentina; Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina.
psorgente@unsam.edu.ar

Background: Respiratory syncytial virus (RSV) has been implicated in the development of recurrent wheezing and asthma, particularly in vulnerable pediatric populations. Longitudinal data from socio-economically disadvantaged settings is essential to understand the long-term consequences of RSV-related lower respiratory tract infections (LRTIs). **Methods:** We conducted a multicenter, prospective cohort study involving 1,128 infants under 12 months of age without medical insurance in Buenos Aires. Participants were categorized as either healthy controls or cases with severe LRTI (RSV-positive or RSV-negative). Monthly physician assessments were performed to diagnose wheezing episodes. Long-term follow-up was achieved in over 70% of the cohort for up to six years. **Results:** In the first year, 57% of infants (n = 642) experienced wheezing. The cumulative incidence of recurrent wheezing (RW) was significantly higher in the RSV group (24.7%) compared to healthy controls (17%; p = 0.003). Wheezing and RW diagnoses decreased across all groups over time. Infants with RSV-related RW were younger (RR 3.01; 95% CI: 1.5–7.0), more likely to be premature (RR 2.54; 95% CI: 1.2–5.2), and more often required mechanical ventilation during RSV-LRTI (RR 1.84; 95% CI: 1.0–3.2) than non-RSV wheezers. **Conclusion:** Wheezing episodes declined notably after the first three years of life. Children with recurrent wheezing and asthma diagnoses in the RSV subgroup exhibited distinct clinical risk profiles compared to those with other severe viral LRTIs and healthy controls. These findings

underscore the importance of targeted surveillance and early intervention strategies in high-risk pediatric populations.

POSTERS 18 - SAIC - SISTEMA CARDIOVASCULAR

DATE & TIME: 19/11/2025 17:00 - 18:30 H

Chairs: Verena Franco Riveros, Gabriela Marina Prendes, Mariano Schuman

325. P18-14. CARDIOMYOCYTE MITOTIC CATASTROPHE IN HUMAN ACUTE MYOCARDIAL INFARCTION

María del Rosario Bauzá¹, Araceli Castro², Roberto René Favaloro³, Carlos Adolfo Vigliano⁴, Rubén Laguens⁵

1. Instituto de Medicina Traslacional, Trasplante y Bioingeniería (IMETTyB)- Universidad Favaloro- CONICET; Laboratorio de Medicina Regenerativa Cardiovascular

2. Instituto de Medicina Traslacional, Trasplante y Bioingeniería (IMETTyB)- Universidad Favaloro- CONICET; Laboratorio de Medicina Regenerativa Cardiovascular

3. Hospital Universitario Fundación Favaloro; Departamento de Cirugía Cardiovascular y Trasplante

4. Hospital Universitario Fundación Favaloro; Departamento de Patología

5. Hospital Universitario Fundación Favaloro; Departamento de Patología

mdelosariobauza@gmail.com

Introduction: Acute myocardial infarction (AMI) causes extensive cardiomyocyte loss through necrosis and apoptosis, followed by scar formation and ventricular remodeling which impairs cardiac function. Although cardiomyocytes can re-enter the cell cycle, this process is often abnormal, leading to multinucleation and polyploidy. Mitotic catastrophe (MC), a mechanism that eliminates cells with defective mitosis, has been described mainly in cancer, but its role in AMI remains unclear. We aimed to investigate whether cardiomyocytes undergo MC 7–13 days after AMI and to assess the co-expression of cell cycle and apoptotic markers as evidence of this phenomenon. **Methods:** Cardiac tissues from 14 AMI patients (7–13 days post-event) and controls were analyzed by histology and immunohistochemistry. Cell cycle markers (Ki67, pH3, Cyclin B1, Aurora Kinase B, PCNA) and apoptosis-related proteins (p53, caspase-3, C9, ubiquitin, Bcl-2) were quantified. **Results:** Histology revealed multinucleation, micronucleation, and bizarre polyploid nuclei in peri-infarction cardiomyocytes, absent in controls. Ki67 positivity was observed in 11.27% of cardiomyocytes, pH3 in 4.38%, Cyclin B1 in 0.88%, PCNA in 6.23%, and Aurora Kinase B in 0.28%. Apoptotic markers included p53 (1.48%), caspase-3 (2.88%), ubiquitin (2.47%), Bcl-2 (5.71%), and C9 (20.02%). Double staining confirmed co-expression of Ki67 with caspase-3 or C9, demonstrating simultaneous proliferation attempts and apoptosis in cardiomyocytes. **Conclusion:** Cardiomyocytes in peri-infarction areas show morphological and molecular features of MC, characterized by abnormal nuclei and co-expression of proliferative and apoptotic markers. These findings suggest that MC contributes to cardiomyocyte loss and adverse remodeling after AMI, representing a potential therapeutic target.

326. P18-15. CARDIAC OXIDATIVE STRESS MODULATION BY CANNABIS OILS WITH DIFFERENT THC: CBD RATIOS AND TERPENES IN AN EXPERIMENTAL MODEL OF METABOLIC SYNDROME

Camila Luz Filippa¹, Maria Eugenia D'Alessandro², Maria Eugenia Oliva³

1. Facultad de Bioquímica y Ciencias Biológicas. Universidad Nacional del Litoral. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina.; Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición.

2. Facultad de Bioquímica y Ciencias Biológicas. Universidad Nacional del Litoral. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina.; Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición

3. Facultad de Bioquímica y Ciencias Biológicas. Universi-

dad Nacional del Litoral. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina.; Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición.
camilaflippa@hotmail.com

Metabolic Syndrome (MS) is characterized by a cluster of metabolic alterations, such as central obesity, dyslipidemia, hypertension, and insulin resistance, which are closely associated with increased oxidative stress. Previous studies from our group have demonstrated that cannabis oils (CO) attenuate reactive oxygen species (ROS) production, inflammation, and liver damage. However, their effects on cardiac tissue remain poorly understood, representing a strategic area for further research. Objective: To evaluate the impact of full-spectrum CO, with different THC:CBD ratios and terpene profiles, on cardiac oxidative stress in male Wistar rats with MS induced by a sucrose-rich diet (SRD). Materials and Methods: Male Wistar rats were fed for 3 weeks with the following diets: a) Reference Diet (RD); b) SRD; c) SRD+CBD (CO rich in CBD); d) SRD+THC (CO rich in THC); e) SRD+CBD:THC (1:1 CBD:THC). COs were administered noninvasively using an oral syringe at a dose of 1.5 mg/kg body weight/day. Serum parameters (GOT and CK-MB), redox status (ROS, TBARS, GSH), and antioxidant enzyme activities (CAT, GR, GPx, GST) were determined. Results: CO significantly reduced serum GOT and CK-MB levels, demonstrating a cardioprotective effect. At the cardiac level, administration of the different oils decreased ROS, TBARS levels and GST enzyme activity, while increasing both GSH content and antioxidant enzyme activities (CAT, GR and GPx). These modifications may be associated with the activation of Nrf2-regulated pathways, suggesting a potential mechanism of action. Conclusion: Cannabis oils may represent a promising therapeutic strategy to counteract cardiac oxidative stress associated with MS.

327. P18-16. EFFECTS OF AN IN VITRO MODEL OF ATHEROSCLEROSIS IN ENDOTHELIAL CELLS

Daiana Martire Greco¹, Guadalupe Amin², veronica landoni³, Gabriela Fernandez⁴, Lucia moro⁵

1. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurodegenerativas (FLENI); Laboratorio de Investigaciones aplicadas a Neurociencias (LIAN)

2. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurodegenerativas (FLENI); Laboratorio de Investigaciones aplicadas a Neurociencias (LIAN)

3. Instituto de Medicina experimental. IMEXCONICET; Laboratorio de procesos inflamatorios

4. Instituto de Medicina experimental. IMEXCONICET; Laboratorio de procesos inflamatorios

5. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurodegenerativas (FLENI); Laboratorio de Investigaciones aplicadas a Neurociencias (LIAN)

daianamartire@hotmail.com

The endothelium regulates vascular tone, barrier function, and immune cell recruitment. In atherosclerosis (AT), it becomes dysfunctional through loss of nitric oxide, and increased adhesion molecule expression, promoting inflammation. Beyond these mechanisms, endothelial cells release as paracrine mediators miRNAs that influence cardiomyocytes, thereby modulating key processes such as inflammation, lipid metabolism, contributing to increased atherosclerotic damage. In these sense, the aim of this work was to study the expression of different miRNAs released by the endothelium in an in vitro model of atherosclerosis using HMEC as a source of endothelial cells. TNF- α (10 and 40 ng/ml) and LPS were used as a stimulus of AT to endothelium for 24 hs. We observed that the viability of HMEC with the treatment of TNF α decreased with a dose dependent response (number of cells dyed with cristal violet Control: 30 $\pm$ 2, TNF α (10 mg/ml): 17 $\pm$ 3, TNF α (40 mg/ml); 5 $\pm$ 1). We also observed that miRNA 126 increased its expression five times with the treatment of TNF 40 mg/ml related to Control cells measured by qPCR (log

expresión miRNA Control: 1 $\pm$ 0.5 vs TNF 40mg/ml:6 $\pm$ 0,1). Treatment with LPS decreased the expresión of miRNA126 compared to Control HMEC (log expresión miRNA Control: 1 $\pm$ 0.5 vs LPS: 0.3 $\pm$ 0,01, p>0.05) Also, we differentiated induced pluripotent stem cell to endothelial cells to study miRNAs in a modelo of AT. In conclusión we observed that the treatment of TNF 40 mg/ml decreased the viability of HMEC and increased the expresión of miRNA 126 in a model of AT

328. P18-17. EVALUATION OF THE RISK-BENEFIT RATIO OF THROMBOLYTICS IN STROKE BASED ON DOOR-TO-NEEDLE TIME IN A PUBLIC HOSPITAL

Pablo Roberto Manjarín¹, Patricia Mariana Delnero², Jorge Alejandro Aimar³, Carlos Hurtado⁴, Guillermo Alberto Keller⁵

1. Hospital General de Agudos Donación Francisco J. Santojanni, Departamento de Urgencias; Comité de Investigación

2. Hospital General de Agudos Donación Francisco J. Santojanni, Departamento de Urgencias; Comité de Investigación

3. Universidad de Buenos Aires, Facultad de Medicina; Centro Universitario de Canabís Medicinal

4. Hospital General de Agudos Donación Francisco J. Santojanni, Departamento de Urgencias; Comité de Investigación

5. Universidad de Buenos Aires - Facultad de Medicina, Centro de Vigilancia y Seguridad de Medicamentos; Laboratorio de Medicina Personalizada y Data Mining
pmanjarin@farmacologia.com.ar

Background: The implementation of rapid thrombolytic therapy in stroke makes it possible to obtain greater benefit with lower risk of complications. Purpose: To evaluate the safety and effectiveness and their relationship throughout the implementation of a door-to-needle time reduction program. Methods: We retrospectively analyzed stroke cases admitted to the hospital during the initial 8 months of the program, considering the number of thrombolysis sessions performed, indications and contraindications for each case, clinical comorbidities, and complications. Results: Of a total of 110 patients admitted for stroke, 47 arrived late, 25 were stroke mimics, meanwhile only 38 presented in a timely manner for thrombolysis (34.5%). Of these, 14 had contraindications. The remaining 24 patients underwent thrombolysis with alteplase. Initial imaging and laboratory studies were performed in all cases, but laboratory results were not expected before starting thrombolytic therapy. No patient developed hemorrhagic complications related to bleeding. Of those receiving treatment, 20 patients (83%) showed significant improvement in their neurological symptoms. There was evidence of improved efficacy parameters over time (60% at baseline vs. 83% at end), which was significantly related ($P < 0.032$) to the number of trained personnel in the area for early detection and rapid protocol activation. Conclusions: Our retrospective, single-center experience study shows that shortening treatment times based on training and instruction in the use of thrombolytics improves therapeutic outcomes with safety based on early identification of patients.

329. P18-18. NEUROCARDIAC PROTECTION BY DONEPEZIL AND NEBIVOLOL AGAINST INJURY INDUCED BY TRANSIENT CEREBRAL ISCHEMIA/REPERFUSION IN A MOUSE MODEL

Ignacio Barbieri¹, Verena Franco-Riveros², Suin Kim³, Sol Hernández Cicalé⁴, Alelí Silva del Puerto⁵, Sofía Giménez⁶, Christian Höcht⁷, Federico Penas⁸, Bruno Buchholz⁹

1. Universidad de Buenos Aires. Facultad de Medicina.; Instituto de Fisiopatología Cardiovascular (INFICA).

2. Universidad de Buenos Aires. Facultad de Medicina.; Instituto de Fisiopatología Cardiovascular (INFICA).

3. Universidad de Buenos Aires. Facultad de Medicina.; Instituto de Fisiopatología Cardiovascular (INFICA).

4. Universidad de Buenos Aires. Facultad de Medicina.

5. Departamento de Microbiología, Parasitología e Inmunología; Instituto de Investigaciones Biomédicas en Retrovirus y Sida (INBIRS)

6. Universidad de Buenos Aires, Facultad de Ciencias Veterinarias.

7. Universidad de Buenos Aires. Facultad de Farmacia y

Bioquímica.; Departamento de Farmacología.

8. Universidad de Buenos Aires. Departamento de Microbiología, Parasitología e Inmunología.; Instituto de Investigaciones Biomédicas en Retrovirus y Sida (INBIRS).

9. Universidad de Buenos Aires. Facultad de Medicina.; Instituto de Fisiopatología Cardiovascular (INFICA).
ibarbieri@fmed.uba.ar

Objective: Cardiac electrical and contractile alterations complicate the clinical course of stroke. We aimed to evaluate the protective effects of donepezil (DPZ) and nebivolol (NBV) on cerebral infarct size (IS), left ventricular dysfunction, and electrocardiographic abnormalities induced by cerebral ischemia (I) and reperfusion (R). **Methods:** Male FVB mice underwent 1h cerebral ischemia followed by 24h reperfusion. DPZ (2 mg/kg, s.c.) enhances parasympathetic tone, while NBV (10 mg/kg, i.p.) provides selective β_1 -blockade. Neurological and cardiac outcomes were assessed by infarct size, neurological score, survival, ECG, and echocardiography. **Results:** IS was $34.6 \pm 3.3\%$ in I/R, $26.7 \pm 3.8\%$ in I/R+DPZ (NS vs. I/R), and $11.9 \pm 2.3\%$ in I/R+NBV ($p < 0.0001$ vs. I/R). NBV improved neurological score at 24hR. Survival was 43.3% in I/R, 50.0% with DPZ, and 72.7% with NBV. Both DPZ and NBV preserved ejection fraction ($75.8 \pm 1.1\%$ and $71.2 \pm 1.9\%$, respectively) compared with I/R ($67.7 \pm 1.5\%$). QTc prolonged at 1hI in I/R (143.0 ± 4.1 ms vs. baseline 125.6 ± 3.3 ; $p < 0.01$), prevented by DPZ (132.6 ± 2.0 vs. 124.0 ± 4.5 ; NS) and NBV (143.5 ± 4.5 vs. 137.4 ± 3.4 ; NS). At 24hR, QTc further increased in all groups ($p < 0.01$ vs. baseline). Tp-Te also increased during R in I/R (35.2 ± 1.6 vs. 26.9 ± 1.2 ms; $p < 0.01$), I/R+DPZ (47.1 ± 3.3 vs. 32.6 ± 3.4 ; $p < 0.0001$), and I/R+NBV (49.3 ± 3.1 vs. 33.8 ± 2.0 ; $p < 0.01$). NBV prevented the fall in connexin-43 expression, while both drugs attenuated the increase in IL-1 β . **Conclusion:** NBV reduces infarct size, improves neurological outcomes, and increases survival after cerebral I/R. Both DPZ and NBV prevent systolic dysfunction and attenuate depolarization/repolarization abnormalities during ischemia, although not during reperfusion.

330. P18-19. COBALT CHLORIDE PROMOTES CATECHOLAMINES OXIDATION. DOES IT HAVE PHYSIOLOGICAL IMPLICATIONS?

Christopher Gutierrez¹, Agustina Mansisidor², Santiago Gullino³, Matías Ramírez⁴, Tomás Little⁵, Rocío Castilla⁶

1. Instituto Alberto C. Taquini de Investigaciones en Medicina Traslacional (IATIMET), Universidad de Buenos Aires - CONICET.; Mecánica y fisiología cardiovascular

2. Instituto Alberto C. Taquini de Investigaciones en Medicina Traslacional (IATIMET), Universidad de Buenos Aires - CONICET.; Mecánica y fisiología cardiovascular

3. Instituto Alberto C. Taquini de Investigaciones en Medicina Traslacional (IATIMET), Universidad de Buenos Aires - CONICET.; Mecánica y fisiología cardiovascular

4. Instituto Alberto C. Taquini de Investigaciones en Medicina Traslacional (IATIMET), Universidad de Buenos Aires - CONICET.; Mecánica y fisiología cardiovascular

5. Instituto Alberto C. Taquini de Investigaciones en Medicina Traslacional (IATIMET), Universidad de Buenos Aires - CONICET.; Mecánica y fisiología cardiovascular

6. Instituto Alberto C. Taquini de Investigaciones en Medicina Traslacional (IATIMET), Universidad de Buenos Aires - CONICET.; Mecánica y fisiología cardiovascular
cpag13@hotmail.com

Our laboratory previously demonstrated that CoCl₂, a hypoxia-mimetic agent, exerts cardioprotective effects in adult and infant rat hearts by limiting calcium overload through inhibition of calcium currents. In the heart, CoCl₂ decreases calcium currents, whereas in arteries it has been reported to increase them. Given the close relationship between vascular processes and cardiac function, we investigated its effects on arterial reactivity. CoCl₂ did not alter basal tone or maximal contraction induced by catecholamines but progressively reduced tension, a phenomenon not previously reported. Therefore, our aim was to identify the mechanism underlying this reduction and its physiological implications. Thoracic aortas from adult male Wistar rats were dissected into 3-mm

rings and mounted in organ baths under isometric tension. After stabilization, rings were exposed to 230 μ M CoCl₂ for 5 min and then subjected to catecholamine stimulation, with or without CoCl₂ presence. The reduction in catecholamine-induced tension by CoCl₂ was not modified by calcium supplementation, adrenergic receptor selectivity, or nitric oxide synthase inhibition. Endothelium removal abolished the effect. Conditioned media from rings incubated with catecholamines and CoCl₂ failed to induce contraction when reapplied, suggesting catecholamine inactivation. Ascorbic acid attenuated the effect, methylene blue assays confirmed the generation of an oxidant media, and spectrophotometry demonstrated adrenalinine oxidation. Importantly, human serum abolished the phenomenon, and the effect was reversible upon CoCl₂ washout. Arterial pressure remained unchanged after CoCl₂ perfusion in vivo model. In conclusion, CoCl₂ promotes catecholamine oxidation ex vivo in an endothelium-dependent manner. While this mechanism does not compromise hemodynamic safety in vivo.

331. P18-20. EXPLORING THE CARDIOPROTECTIVE POTENTIAL OF STEVIOSIDE UNDER FASTING CONDITIONS: THE ROLE OF AKT IN AN EX VIVO ISCHEMIA-REPERFUSION MODEL

Victoria Mestre Cordero¹, María de las Mercedes Fernández Pazos², Federico Joaquín Reznik³, Romina Hermann⁴, María Gabriela Marina Prendes⁵

1. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.; CONICET - Universidad de Buenos Aires, Instituto de Química y Metabolismo del Fármaco (IQUIMEFA). Buenos Aires, Argentina.

2. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.; CONICET - Universidad de Buenos Aires, Instituto de Química y Metabolismo del Fármaco (IQUIMEFA). Buenos Aires, Argentina.

3. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.

4. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.; CONICET - Universidad de Buenos Aires, Instituto de Química y Metabolismo del Fármaco (IQUIMEFA). Buenos Aires, Argentina.

5. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.; CONICET - Universidad de Buenos Aires, Instituto de Química y Metabolismo del Fármaco (IQUIMEFA). Buenos Aires, Argentina.

vicky.mestrecordero@gmail.com

Stevioside, a glycoside from *Stevia rebaudiana* Bertoni, has been described as cardioprotective in ischemia-reperfusion (Is-Rs) models, partly through Akt activation and mitochondrial preservation. In this study, we aimed to evaluate the effects of oral stevioside (S, 168 mg/kg/day, 15 days) under fasting conditions, a metabolic state where fatty acid oxidation predominates; and to investigate the role of Akt using the inhibitor wortmannin (W, 100 nM) 15 min before Is. Female Sprague-Dawley rats were used prior 24h-fasting. Isolated hearts were subjected to Is-Rs in a Langendorff system. Cardiac mechanical function and infarct size were determined. Mitochondria were isolated in pre-ischemic and post-Is-Rs states and were functionally evaluated. ANOVA, $n=6$ /group. Preliminary results indicate that stevioside-treated hearts (SF) exhibited a faster recovery of rate-pressure product at 5 min reperfusion compared with controls (CF and CF+W), although this effect was transient. Wortmannin delayed this recovery. No significant differences were found in other functional parameters or infarct size. Tissue ATP decrease after Is-Rs was less marked in SF relative to its pre-ischemic state. Mitochondrial ATP synthesis showed no group differences after Is-Rs. Mitochondrial complex I activity was lower in SF and SF+W compared with CF pre-ischemic, but was not further reduced after Is-Rs, while CF showed a tendency to decline. Mitochondrial calcium retention capacity supported by succinate was higher

in CF+W, SF and SF+W both pre- and post-Is-Rs ($p<0.05$). Membrane potential showed substrate- and state-dependent changes. In conclusion, stevioside induced an early but transient functional benefit under fasting, with possible involvement of Akt.

332. P18-21. IMPACT OF FASTING ON ISCHEMIC POSTCONDITIONING: ¿IS AMP ACTIVATED PROTEIN KINASE (AMPK) INVOLVED?

María de las Mercedes Fernández Pazos¹, Victoria Evangelina Mestre Cordero², Violeta Gómez Peracca³, Lucía Saffer⁴, Federico Joaquín Reznik⁵, María Gabriela Marina Prendes⁶, Romina Hermann⁷

1. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.; CONICET - Universidad de Buenos Aires, Instituto de Química y Metabolismo del Fármaco (IQUIMEFA). Buenos Aires, Argentina.

2. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.; CONICET - Universidad de Buenos Aires, Instituto de Química y Metabolismo del Fármaco (IQUIMEFA). Buenos Aires, Argentina.

3. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.; CONICET - Universidad de Buenos Aires, Instituto de Química y Metabolismo del Fármaco (IQUIMEFA). Buenos Aires, Argentina.

4. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.; CONICET - Universidad de Buenos Aires, Instituto de Química y Metabolismo del Fármaco (IQUIMEFA). Buenos Aires, Argentina.

5. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.; CONICET - Universidad de Buenos Aires, Instituto de Química y Metabolismo del Fármaco (IQUIMEFA). Buenos Aires, Argentina.

6. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.; CONICET - Universidad de Buenos Aires, Instituto de Química y Metabolismo del Fármaco (IQUIMEFA). Buenos Aires, Argentina.

7. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.; CONICET - Universidad de Buenos Aires, Instituto de Química y Metabolismo del Fármaco (IQUIMEFA). Buenos Aires, Argentina. mechifp92@gmail.com

In previous studies, we analyzed the role of AMPK in the beneficial effects of ischemic postconditioning (IPostC) in rats fed ad libitum. IPostC increased contractile function recovery, decreased infarct size, and preserved mitochondrial ultrastructure and function. These effects were reversed by AMPK inhibition. Since the clinical outcomes of IPostC have been controversial, further exploration of possible influential factors is needed. The aim of this study was to evaluate the effects of IPostC in Langendorff-perfused hearts from previously fasted (24 hours) rats subjected to ischemia(I) - reperfusion(R), and the involvement of AMPK in these effects. Isolated hearts from fasted female Sprague-Dawley rats (220-270g) were subjected to 25 min I-60 min R. IPostC (6 cycles, 10 sec R-10 sec I) was carried out at the onset of R. Compound C (CC, 20 μ M), an AMPK inhibitor, was added during the first 5 min of R. Contrary to the results from rats fed ad libitum, IPostC had no effect on systolic function recovery. However, CC increased left ventricular end-diastolic pressure in the first 5 minutes of R ($p<0.05$ vs. Control, IPostC). Additionally, neither IPostC nor CC had any effect on infarct size and tissular ATP content. Mitochondrial ultrastructure was preserved by IPostC, and the addition of CC had no significant effect. Activity of mitochondrial complexes I-III, II-III and IV was not affected by IPostC or CC. These findings suggest that fasting abolishes most of the cardio-

protective effects of IPostC and that AMPK is not implicated in this response under such metabolic conditions.

ORALES 16 - SAIC - BIOLOGÍA CELULAR Y MOLECULAR 2

DATE & TIME: 20/11/2025 9:00 - 10:30 H

Chairs: Virginia Vanasco, Analía Karadayan

333. O16-01. BEYOND PARP INHIBITION: THE CONTRIBUTION OF NIRAPARIB'S OFF-TARGETS TO ITS CYTOTOXIC EFFECT IN TUMOR CELLS

María Candelaria Mares Ahlers¹, Ginette Moyano², Florencia Menay³, Helena Sterle⁴, Florencia Cayrol⁵, Gracielra Cremaschi⁶, Kevin Madauss⁷, Verónica Okraine⁸, Sara Miranda⁹, Sebastian Omar Siri¹⁰, Vanesa Gottifredi¹¹

1. Fundación Instituto Leloir; Ciclo Celular y Estabilidad Genómica

2. Fundación Instituto Leloir; Ciclo Celular y Estabilidad Genómica

3. Instituto de Investigaciones Biomédicas, UCA, CONICET; Instituto de Investigaciones Biomédicas

4. Instituto de Investigaciones Biomédicas, UCA, CONICET; Instituto de Investigaciones Biomédicas

5. Instituto de Investigaciones Biomédicas, UCA, CONICET; Instituto de Investigaciones Biomédicas

6. Instituto de Investigaciones Biomédicas, UCA, CONICET; Instituto de Investigaciones Biomédicas

7. GlaxoSmithKline, Oncology R&D, London, United Kingdom.; GlaxoSmithKline, Oncology R&D

8. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires- CONICET; Ciclo Celular y Estabilidad Genómica

9. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires- CONICET; Ciclo Celular y Estabilidad Genómica

10. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires- CONICET; Ciclo Celular y Estabilidad Genómica

11. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires- CONICET; Ciclo Celular y Estabilidad Genómica

cmars@leloir.org.ar

Synthetic lethality (SL) is a therapeutic strategy that combines genetic and pharmacological factors to induce selective tumor cell death while sparing normal cells. Breast and ovarian cancers often display homologous recombination (HR) repair deficiencies, impairing their ability to repair DNA double-strand breaks (DSBs). This vulnerability is exploited with Poly (ADP-Ribose) Polymerase inhibitors (PARPi), which stabilize PARP-DNA complexes and promote DSB accumulation, ultimately leading to SL in HR-deficient cells. Four PARPis, including olaparib and niraparib, have been approved for ovarian cancer. Notably, niraparib also shows efficacy in HR-proficient tumors, suggesting additional mechanisms beyond PARP inhibition. Unlike other PARPis, niraparib inhibits additional intracellular kinases. Here, we evaluated the contribution of one such off-target (OT) to the cytotoxic effect of niraparib. Using established and primary ovarian cancer cultures, our findings align with clinical data reporting niraparib as more effective than olaparib, particularly in HR-proficient cellular models. We tested the cytotoxic effect of a combination between the PARPis niraparib (or olaparib) with such OT inhibitor (OTi) comparing it with individual treatments. Cell numbers after niraparib + OTi were comparable to niraparib treatment, whereas olaparib was less effective than olaparib + OTi. Similar results were observed in patient-derived cultures. Additionally, the knockdown of niraparib's OT by shRNA further supported its role in cytotoxicity. In conclusion, olaparib-mediated PARP inhibition reduces cell numbers and can be enhanced by niraparib's OTi. In contrast, niraparib shows no additive effect, suggesting its cytotoxicity may depend on simultaneous inhibition of PARP and its OT.

334. O16-02. DIFFERENTIAL UBIQUITINATION REGULATION BY THE CANCER-TESTIS ANTIGENS MAGEB2 AND MA-

GEA9

Candela Vidal¹, Micaela Escalada², Melisa Suberbordes³, Maximiliano Silva⁴, Rocio Toppino⁵, Philippe Soubeyran⁶, Martín Monte⁷

1. IQUIBICEN; Oncología molecular

2. IQUIBICEN; Oncología molecular

3. IQUIBICEN; Oncología Molecular

4. IQUIBICEN; Oncología molecular

5. IQUIBICEN; Oncología Molecular

6. Université and Institut Paoli-Calmettes, Marseille, France.; Centre de Recherche en Cancérologie de Marseille (CRCM)

7. IQUIBICEN; Oncología molecular

canduvidal7@gmail.com

The MAGE-I family belongs to the cancer-testis antigens, which are aberrantly expressed in tumors and play critical roles in oncogenesis. MAGE proteins have been reported to bind and enhance RING-type E3 ubiquitin ligases activity. To explore their impact on ubiquitination, we performed global ubiquitinome profiling using two different MAGE members. MAGEA9 ubiquitinome was analyzed in HN30 Flag-MAGEA9 inducible cells, whereas MAGEB2 was studied in HCT116 Flag-MAGEB2 inducible cells. Bioinformatic analyses revealed significant global changes in ubiquitination ($p < 0.05$). MAGEA9 regulated 509 proteins, predominantly decreasing ubiquitination (541 proteins less ubiquitinated, 38 more ubiquitinated). In contrast, MAGEB2 affected 304 proteins, with a more balanced outcome: 173 proteins showed increased ubiquitination and 131 decreased ubiquitination. These findings suggest, for the first time, that MAGE proteins can regulate ubiquitin ligase activity in both positive and negative directions, controlling distinct biological processes. Besides, only 39 proteins were shared on both datasets, correlating to MAGEA9 and MAGEB2 interactome data, were among the ubiquitin-related interactors they only share the E3 ubiquitin ligase HUWE1 and a ubiquitin-specific protease USP7. For MAGEB2, additional mass spectrometry analyses in HCT116 WT and MAGEB2-KO cells revealed that seven proteins were both upregulated and more ubiquitinated in the presence of MAGEB2, suggesting non-degradative ubiquitination. Conversely, two proteins were over-ubiquitinated and downregulated at protein levels, suggesting MAGEB2-dependent targeting for proteasomal degradation. Together, these results uncover the ability of MAGEB2 and MAGEA9 to govern ubiquitination dynamics as a new mechanism through which MAGE proteins may contribute to tumor progression.

335. O16-03. GENETIC VARIANT INTERPRETATION BASED SOLELY ON PROTEIN CHANGES MASKS SPLICING DEFECTS IN THE SODIUM IODIDE SYMPORTER-CODING PRE-MESSENGER RNA

Natalia Silvina Muñoz¹, Sofía Savy², Valentina Ricci³, Mariano Martín⁴, Gerardo Hernán Carro⁵, Francisco Andrés Montes⁶, Romina Celeste Geysels⁷, Victoria Peyret⁸, Ana María Masini-Repiso⁹, Mariana Lorena Tellechea¹⁰, Juan Pablo Nicola¹¹

1. Centro de Investigaciones en Bioquímica Clínica e Inmunología, Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina; Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina

2. Centro de Investigaciones en Bioquímica Clínica e Inmunología, Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina.; Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina.

3. Centro de Investigaciones Endocrinológicas Dr. César Bergadá, Consejo Nacional de Investigaciones Científicas y Técnicas (CEDIE-CONICET), Buenos Aires, Argentina.; División de Endocrinología, Hospital de Niños Dr. Ricardo Gutiérrez, Buenos Aires, Argentina

4. Centro de Investigaciones en Bioquímica Clínica e Inmunología, Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina; Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina

5. Centro de Investigaciones en Bioquímica Clínica e Inmunología, Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina; Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina

6. Centro de Investigaciones en Bioquímica Clínica e Inmunología, Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina; Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina

7. Centro de Investigaciones en Bioquímica Clínica e Inmunología, Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina; Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina

8. Centro de Investigaciones en Bioquímica Clínica e Inmunología, Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina; Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina

9. Centro de Investigaciones en Bioquímica Clínica e Inmunología, Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina.; Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina

10. Centro de Investigaciones Endocrinológicas Dr. César Bergadá, Consejo Nacional de Investigaciones Científicas y Técnicas (CEDIE-CONICET), Buenos Aires, Argentina; División de Endocrinología, Hospital de Niños Dr. Ricardo Gutiérrez, Buenos Aires, Argentina

11. Centro de Investigaciones en Bioquímica Clínica e Inmunología, Consejo Nacional de Investigaciones Científicas y Técnicas (CIBICI-CONICET), Córdoba, Argentina; Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina nataliasilvina.munoz@mi.unc.edu.ar

Genetic variants associated with congenital hypothyroidism are frequently interpreted solely at the protein level, overlooking their potential impact on pre-mRNA processing. Exonic variants—including synonymous, missense, or nonsense changes—may alter or create cryptic motifs recognized by the splicing machinery. Since splicing-altering variants contribute substantially to human disease, their systematic evaluation and the prediction of splicing defects are particularly relevant. In this study, we analyzed reported SLC5A5 variants associated with congenital hypothyroidism using bioinformatic tools to predict central and auxiliary elements involved in NIS pre-mRNA splicing. The variants c.970-3C>A and c.1315_1329del were predicted to disrupt donor and acceptor splice sites, respectively. Variants c.572A>G, c.749G>T, c.809T>A, c.1157T>G, c.1183G>A, and c.1593C>G were predicted to generate cryptic splice sites, in agreement with experimental evidence supporting the deleterious effect of c.1593C>G. Furthermore, variants c.1106A>T, c.1628G>A, and c.1679C>T were predicted to affect auxiliary splicing elements, whereas c.371G>A and c.1183G>A showed no predicted impact on NIS pre-mRNA splicing, consistent with functional assays. Overall, 36% of the analyzed variants were predicted to compromise NIS pre-mRNA splicing. These findings demonstrate that a substantial proportion of pathogenic SLC5A5 variants exert their effect through splicing defects rather than direct protein alteration. Our results underscore the importance of functional studies for accurate variant annotation and for assessing the pathogenicity of novel variants with respect to pre-mRNA splicing, prior to attributing their effect to protein-level changes.

336. O16-04. ISOLATION AND CHARACTERIZATION OF PRIMARY CULTURES FROM ASCITIC FLUID OF PATIENTS FOR FUNCTIONAL TESTING AND EVALUATION OF SENSITIVITY TO POLY (ADP-RIBOSE) POLYMERASE (PARP) INHIBITORS

Ginette Moyano¹, Candelaria Mares Alhers², Florencia Menay³, Glenda Ernst⁴, Jorgelina Nelly Real⁵, Ernesto Korb-

enfeld⁶, Branda Iglesias⁷, Kevin Madauss⁸, Helena Sterle⁹, Florencia Cayrol¹⁰, Graciela Cremaschi¹¹, Vanesa Gottifredi¹²

1. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires, CONICET; Ciclo celular y estabilidad genómica
 2. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires, CONICET; Ciclo celular y estabilidad genómica
 3. Instituto de Investigaciones Biomédicas, UCA, CONICET
 4. Hospital Británico, Buenos Aires, Argentina; Hospital Británico
 5. Hospital Británico, Buenos Aires, Argentina; Hospital Británico
 6. Hospital Británico, Buenos Aires, Argentina; Hospital Británico
 7. GlaxoSmithKline, Oncology R&D, London, United Kingdom; GlaxoSmithKline, Oncology R&D
 8. GlaxoSmithKline, Global Health R&D, Upper Providence, PA, United States; GlaxoSmithKline, Global Health R&D
 9. Instituto de Investigaciones Biomédicas, UCA, CONICET; Instituto de Investigaciones Biomédicas
 10. Instituto de Investigaciones Biomédicas, UCA, CONICET; Instituto de Investigaciones Biomédicas
 11. Instituto de Investigaciones Biomédicas, UCA, CONICET; Instituto de Investigaciones Biomédicas
 12. Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires, CONICET; Ciclo celular y estabilidad genómica
- gmoyano@leloir.org.ar

High-grade serous ovarian carcinoma (HGSOC) is the most common subtype of epithelial ovarian cancers (EOC), accounting for about 70% of cases. Approximately 50% of HGSOCs are associated with deficiencies in the homologous recombination (HR) DNA repair pathway, often caused by mutations in genes such as Breast Cancer 1 (BRCA1) or Breast Cancer 2 (BRCA2). This impaired DNA repair mechanism is referred to as "homologous recombination deficiency" (HRD). However, HRD can also arise from other genetic or epigenetic events, a phenotype collectively known as "BRCAness." Poly (ADP-ribose) polymerase inhibitors (PARPi) exploit these defects, selectively inducing tumor cell death. Advanced stages of ovarian cancer are frequently associated with the accumulation of ascitic fluid in the abdominal cavity, which contains both cellular and acellular components. Clinically, once surgically removed, ascitic fluid is discarded. However, in this project, it represents a valuable source of patient-derived tumor cells. These cells were used to validate results obtained with established commercial cell lines. After developing a protocol to generate primary cultures from ascites-derived tumor cells, we evaluated their sensitivity to the PARPi niraparib and olaparib. In vitro assays performed with established primary cultures allowed us to characterize key biomarkers of this tumor type, including HR status, p53, and CK7, using Western blotting and immunofluorescence. The generation of primary ovarian cancer cultures from ascitic fluid provides a more clinically relevant biological model to assess the effects of PARPi and their potential correlation with molecular markers, in contrast to conventional commercial cell lines.

337. O16-05. LRP1 AND ENERGY METABOLISM AS MARKERS OF PROGRESSION IN PAPILLARY THYROID CARCINOMA OF OVERWEIGHT AND OBESE PATIENTS

Antonella Lombardi¹, Marcela Díaz², Agustín Fernando Santiago Campos Londero³, Demian Slodki⁴, Bladimiro Americo Lenis⁵, Matilde Cortabarría⁶, Rafael José Argüello⁷, Pablo Alberto Romagnoli⁸, Gustavo Alberto Chiabrando⁹, Leonel Malacrida¹⁰, Marta Alicia Toscano¹¹, Javier Roberto Jaldin Fincati¹²

1. Hospital Dr. Arturo Oñativia; Unidad de Conocimiento Traslacional Hospitalaria-Dr. Arturo Oñativia (CONICET)
2. Institut Pasteur-Montevideo; Unidad de Bioimagenología Avanzada
3. Centro de Investigación en Medicina Traslacional Severo M. Amuchástegui (IUCBC-CONICET); Laboratorio de Enfer-

medades Crónicas No Transmisibles

4. Hospital Dr. Arturo Oñativia; Unidad de Conocimiento Traslacional Hospitalaria-Dr. Arturo Oñativia (CONICET)
 5. Hospital Dr. Arturo Oñativia; Unidad de Conocimiento Traslacional Hospitalaria-Dr. Arturo Oñativia (CONICET)
 6. Institut Pasteur-Montevideo; Unidad de Bioimagenología Avanzada
 7. Centre d'immunologie de Marseille Luminy (CNRS-Marseille-Francia); Dendritic cell Biology
 8. Centro de Investigación en Medicina Traslacional Severo M. Amuchástegui (IUCBC-CONICET); Laboratorio de Enfermedades Crónicas No Transmisibles
 9. Centro de Investigación en Medicina Traslacional Severo M. Amuchástegui (IUCBC-CONICET); Laboratorio de Enfermedades Crónicas No Transmisibles
 10. Institut Pasteur-Montevideo; Unidad de Bioimagenología Avanzada
 11. Hospital Dr. Arturo Oñativia; Unidad de Conocimiento Traslacional Hospitalaria-Dr. Arturo Oñativia (CONICET)
 12. Hospital Dr. Arturo Oñativia; Unidad de Conocimiento Traslacional Hospitalaria-Dr. Arturo Oñativia (CONICET)
- antilomb@gmail.com

Thyroid carcinoma (TC) is the most common endocrine malignancy worldwide. In parallel, the prevalence of overweight and obesity has markedly increased, both recognized as risk factors for TC. Chronic low-grade inflammation, insulin resistance, oxidative stress, and hormonal alterations are proposed mechanisms underlying this association. Within this context, the low-density lipoprotein receptor-related protein 1 (LRP1), a transmembrane protein involved in energy metabolism and metabolic syndrome, has been implicated in tumor progression. Our aim was to investigate the role of LRP1 and energy metabolism as potential prognostic markers in papillary thyroid carcinoma (PTC). Using an in vitro model with Nthy-ori 3-1 (normal thyroid) and TPC-1 (PTC) cell lines, flow cytometry and immunofluorescence analyses revealed differential expression and localization of LRP1, suggesting distinct functions in normal versus tumor cells. Metabolic profiling by SCENITH showed predominant glycolytic dependence in both lines; however, tumor cells activated alternative energetic pathways when glycolysis and oxidative phosphorylation were inhibited. In histological samples from patients categorized by body mass index (BMI), hyperspectral microscopy distinguished between normal thyroid and tumor tissues across all BMI groups, with overweight cases exhibiting the most pronounced spectral shifts, indicative of altered tissue composition. Moreover, LRP1 distribution varied according to BMI and tissue compartment, with increased expression observed in tumor cells from obese patients. Taken together, these findings suggest that LRP1 expression and energy metabolism may be influenced by BMI. Further studies are needed to clarify their relevance as potential markers and to better understand their role in TC progression in the context of obesity.

338. O16-06. NITRONE LQB122 IS AN NRF2 AGONIST AND REDUCES OBESITY-ASSOCIATED METABOLIC RISK LINKED TO NEUTROPHILIC INFLAMMATION

Inalen Del V. Chacon¹, Carla F. Guzman², Florencia S. Barrera³, Jonathan M. Ramirez⁴, Rivero, L⁵, Morales, I.⁶, Barberis, S.⁷, Toledo, F.⁸, Vega Hissi, Eg⁹, Garro, J.c.¹⁰, Dias, A.¹¹, Costa, D.¹², Costa P.¹³, Santillan, Ld L¹⁴, Dario C. Ramirez¹⁵, Sandra E. Gomez Mejiba¹⁶

1. IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.
2. IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.
3. IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University

of San Luis, San Luis, 5700-San Luis, Argentina.

4. IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.

5. IMIBIO-CCT-SL-CONICET; Food Science Laboratory CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina

6. IMIBIO-CCT-SL-CONICET; Food Science Laboratory CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina

7. IMIBIO-CCT-SL-CONICET; Food Science Laboratory CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.

8. IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, San Luis, 5700-San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.

9. IMIBIO-CCT-SL-CONICET; Medicinal Chemistry Laboratory. CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.

10. IMIBIO-CCT-SL-CONICET; Medicinal Chemistry Laboratory. CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.

11. Federal University of Rio de Janeiro, Rio de Janeiro, Brazil.; Department of Biochemistry, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil.

12. Federal University of Rio de Janeiro, Rio de Janeiro, Brazil.; Department of Biochemistry, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil.

13. Federal University of Rio de Janeiro, Rio de Janeiro, Brazil.; Department of Biochemistry, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil.

14. IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.

15. IMIBIO-CCT-SL-CONICET; Laboratory of Experimental and Translational Medicine, CONICET-San Luis & National University of San Luis, 5700 San Luis, Argentina. Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.

16. IMIBIO-CCT-SL-CONICET; Laboratory of Nutrition and Experimental Therapeutics CCT-San Luis, National University of San Luis, San Luis, 5700-San Luis, Argentina.

inachacon55@gmail.com

Obesity, caused by a chronic positive energy balance, leads to increased levels of free fatty acids (FFAs), which causes neutrophilic inflammation in several tissues, and macrophage activation, which contributes to obesity-associated metabolic risk. In this study, we investigated the potential of nitron compounds as modulators of adipose tissue dysfunction, focusing on the activation of the Nrf2 pathway, a master regulator of oxidative stress, adipogenesis and inflammation. Using molecular modeling tools, among other nitrones, LQB122 was shown to exhibit significant affinity for Keap1, an Nrf2 regulatory protein, whose interaction energy is similar to that of sulforaphane. Pairs of structures known as parallel and opposite were compared, and the opposite forms were found to display a higher affinity, attributed to a greater number of hydrogen bonds and π -type interactions, suggesting that small structural modifications could optimize the activity of these compounds. LQB122 had no toxic effects and promoted adipogenesis in the 3T3-L1 cell line, suggesting activation of the Nrf2 pathway. This nitron also decreased hepatic and systemic neutrophilic inflammation in a mouse model of diet-induced obesity. Biochemical assays and in vitro assays in A549 cells further confirmed that LQB122—and to a lesser extent DMPO—scavenges hypochlorite, potentially interfering with neutrophilic inflammation. These results position LQB122 as a promising structural platform for the design of new drugs to reduce neutrophilic inflammation and

obesity-associated metabolic risk.

339. O16-07. ROLE OF FKBP51 IN CELL SURVIVAL AND GENE EXPRESSION REGULATION IN HEK293 CELLS

Valentina Hansen¹, Gisela Mazaira², Martina Villanueva³, Mario Galigniana⁴, Alejandra Erlejman⁵

1. IQUIBICEN; Laboratorio de Biología Celular y Molecular

2. IQUIBICEN; Laboratorio de Biología Celular y Molecular

3. IQUIBICEN; Laboratorio de Biología Celular y Molecular

4. IBYME; Laboratorio de Receptores Nucleares

5. IQUIBICEN; Laboratorio de Biología Celular y Molecular
valenhansen99@gmail.com

FKBP51 protein, an immunophilin (IMM) that binds to FK506, was originally identified as a regulator of steroid receptor activity, and is now recognized as a modulator of multiple transcription factors, including NF- κ B. FKBP51 is overexpressed in several types of cancer, contributing to tumorigenesis and chemoresistance. Conversely, its inhibition has been associated with an improved response to anti-tumor therapies. This work aimed to investigate the global effects of FKBP51 on cell survival. In our previous studies, we generated a stable HEK293 cell line overexpressing FKBP51 (HEK 51+) and observed a significant increase in cell proliferation compared to wild-type cells, while FKBP51 silencing reversed this effect. Furthermore, FKBP51 overexpression conferred protection against cell death induced by hydrogen peroxide and staurosporine. To further explore the molecular mechanisms underlying these effects, we performed gene expression microarray analysis. We identified 28 upregulated and 15 downregulated genes associated with FKBP51 overexpression. Functional enrichment analysis (GO and KEGG) revealed a strong impact on cell adhesion, and Wnt signalling pathways were notably affected, suggesting that FKBP51 may influence key processes involved in cellular remodeling and tumor progression. In conclusion, we demonstrate that FKBP51 regulates genes involved in critical signalling pathways, related to our previous findings where this IMM promotes cell proliferation and enhances survival under cytotoxic conditions. We propose that FKBP51 regulates processes linked to tumor development and progression, supporting its potential relevance in cellular biology and deserving further investigation.

340. O16-08. SWIMMING AGAINST THE CURRENT: DESIGN AND TESTING OF A CITOTOXIC STRATEGY THAT DEPRIVES CANCER CELLS OF CHROMOSOME INSTABILITY

Lilen Ivonne Caimi¹, Sofia Venerus Arbilla², Yiovana Verónica Okraina³, Ginette Moyano⁴, Ariel Isaac Abramovici Blasco⁵, Vanesa Gottifredi⁶, Nicolás Calzetta⁷

1. Fundación Instituto Leloir - Instituto de Investigaciones Bioquímicas de Buenos Aires (IIBBA-CONICET); Laboratorio de Estabilidad Genómica y Ciclo Celular

2. Fundación Instituto Leloir - Instituto de Investigaciones Bioquímicas de Buenos Aires (IIBBA-CONICET); Laboratorio de Estabilidad Genómica y Ciclo Celular

3. Fundación Instituto Leloir - Instituto de Investigaciones Bioquímicas de Buenos Aires (IIBBA-CONICET); Laboratorio de Estabilidad Genómica y Ciclo Celular

4. Fundación Instituto Leloir - Instituto de Investigaciones Bioquímicas de Buenos Aires (IIBBA-CONICET); Laboratorio de Estabilidad Genómica y Ciclo Celular

5. Fundación Instituto Leloir - Instituto de Investigaciones Bioquímicas de Buenos Aires (IIBBA-CONICET); Laboratorio de Estabilidad Genómica y Ciclo Celular

6. Fundación Instituto Leloir - Instituto de Investigaciones Bioquímicas de Buenos Aires (IIBBA-CONICET); Laboratorio de Estabilidad Genómica y Ciclo Celular

7. Fundación Instituto Leloir - Instituto de Investigaciones Bioquímicas de Buenos Aires (IIBBA-CONICET); Laboratorio de Estabilidad Genómica y Ciclo Celular

lcaimi@leloir.org.ar

Chk1 inhibitors (Chk1i) are being investigated in clinical trials for their ability to induce cell death (CD) in cancer cells. Similarly to other approved therapies, their action also generates replicative stress

(RS) and chromosome instability (CIN). The latter can function as a promoter of chemoresistance. We have previously demonstrated that CD induced by Chk1 inhibition is molecularly independent from CIN, which suggests that therapeutic efficacy could be maximized while avoiding or delaying the potential for chemoresistance in the residual cell population. This work aimed to identify pharmacological combinations that promote CIN-free CD after Chk1 inhibition and to evaluate if this appearance and separation of phenotypes is exclusive to this context or if it extends to other clinically relevant checkpoint kinases like Wee1 and ATR. We successfully identified a candidate with the potential to prevent CIN caused by Chk1i without affecting CD. Results were corroborated by inhibiting other actors of its M-phase signaling pathway. Furthermore, it was demonstrated that this dissociation of phenotypes (CD without CIN) is specific to Chk1 inhibition, not occurring in the same way when the inhibited checkpoint kinase is Wee1 or ATR. Our data indicate that the appropriate combination of drugs can favor CIN-free CD post-Chk1i. This effect is specific to Chk1 inhibition and is not observed with the inhibition of other evaluated checkpoint kinases. This highlights the potential of Chk1-targeted therapies to maximize anti-tumor efficacy and prevent or delay the appearance of resistance. These data will allow us to advance to analysis in preclinical models.

341. O16-09. ANALYTICAL, CLINICAL, AND REGULATORY VALIDATION OF A NOVEL SIMPLIFIED MOLECULAR DIAGNOSTIC KIT FOR CONGENITAL CHAGAS DISEASE

Larocca L¹, Russo Y², Roa E², Leonardi S², Romero V², Maidana Kuleszka MN², Lopez I², Reynaga N², Pallotto S³, Zago MP², Carrillo C¹

1. Instituto de Ciencia y Tecnología Dr. César Milstein (Mils-tein-CONICET)

2. Unidad de Conocimiento Traslacional, Hospital Público Materno-Infantil (UCT-HPMI), Salta

3. Neokit SAS

ccarrillo@centromilstein.org.ar

Neonatal Chagas disease is a public health problem in Argentina, with an incidence of approx 1,100 infected newborns annually. Despite mandatory notification (Chagas Law N°26.281), effective diagnostic coverage is below 25% due to the reduced sensitivity or high operational complexity of conventional methods. We therefore developed a simplified molecular test to detect *Trypanosoma cruzi* (the etiological agent) in neonates from birth. The test is based on Loop-Mediated Isothermal Amplification (LAMP), targeting a repetitive region of the *T. cruzi* genome (satellite sequence). Operational simplification focused on streamlining both sample handling and result interpretation. Analytical and clinical validation were performed following international regulatory guidelines. The test utilizes a liquid or dried blood spot sample, bypassing nucleic acid extraction. Pre-treatment and Amplification Mixes (stored at 4°C and handled at room temperature -INPI Patent P190102073) are presented in droppers, avoiding pipette use. The procedure requires only a heat-block, taking under 100 minutes in three simple steps: i-Pre-treatment (sample + Lysis Solution, 8min-98°C); ii-Amplification (sample inoculated into an amplification tube with Amplification Mix - violet color, 90min-64°C); iii-Visual Reading (violet: negative; blue: positive). The test demonstrated an analytical sensitivity of 10 femtograms of DNA or one parasite per reaction, with 100% inclusivity (recognizing all six *T. cruzi* Discrete Typing Units) and 100% exclusivity. Clinical validation (n=125 samples, Hospital Público Materno-Infantil, Salta) showed 92% sensitivity, 97% specificity, and 96% overall accuracy. This performance led to recent regulatory approval by ANMAT (PM 2576-03). The kit's performance, simplicity, and affordability facilitate early, decentralized newborn Chagas diagnosis.

POSTERS 19 - SAIC - TOXICOLOGÍA Y ECOTOXICOLOGÍA

DATE & TIME: 20/11/2025 9:00 - 10:30 H

Chairs: Mariana Mardirosian, Natacha Piloni

342. P19-01. PESTICIDES CHLORPYRIFOS AND CYPERMETHRIN ENHANCE BREAST CANCER CELL PROLIFER-

ATION INVOLVING ESTROGEN RECEPTOR ALPHA: EXPERIMENTAL AND COMPUTATIONAL EVIDENCE

Lucía Enriquez¹, Mariana Lasagna², Mariana Mardirosian³, Rocío Natalia Cardozo⁴, Mariel Núñez⁵, Pablo Power⁶, Danilo Ceschin⁷, Claudia Cocca⁸

1. Instituto de Química y Físicoquímica Biológicas "Prof. Alejandro C. Paladini" (UBA-CONICET).; Laboratorio de Radioisótopos, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.

2. Instituto de Química y Físicoquímica Biológicas "Prof. Alejandro C. Paladini" (UBA-CONICET).; Laboratorio de Radioisótopos, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.

3. Instituto de Química y Físicoquímica Biológicas "Prof. Alejandro C. Paladini" (UBA-CONICET).; Laboratorio de Radioisótopos, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.

4. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.; Laboratorio de Radioisótopos, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.

5. Instituto de Química y Físicoquímica Biológicas "Prof. Alejandro C. Paladini" (UBA-CONICET).; Laboratorio de Radioisótopos, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.

6. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.; Cátedra de Microbiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.

7. Centro de Investigaciones en Medicina Traslacional "Severo Amuchástegui" (CIMETSA-CONICET).; Instituto Universitario de Ciencias Biomédicas de Córdoba

8. Instituto de Química y Físicoquímica Biológicas "Prof. Alejandro C. Paladini" (UBA-CONICET).; Laboratorio de Radioisótopos, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.

lunenriquezgen@gmail.com

Exposure to endocrine disruptors (EDs) has been linked to the breast cancer (BC) etiology. Chlorpyrifos (CPF) and cypermethrin (CPM) are widely used pesticides, both individually and in commercial mixtures. We previously demonstrated that CPF promotes estrogen receptor (ER)-dependent proliferation in MCF-7 BC cells. Aims: assess the clonogenic capacity of CPF and CPM individually and in combination in MCF-7 cells; predict CPF and CPM binding to ERα by in silico molecular docking; identify BC-associated genes potentially modulated by ED exposure through public database bioinformatic analysis. MCF-7 cells were exposed to serial concentrations of CPM (0.05-50μM) and CPF+CPM combinations for clonogenic assays (n=3). Molecular docking simulation evaluated pesticide binding to ERα. Toxicogenomics databases were analyzed to identify overlapping genes between BC pathways and ED exposure. CPM concentration higher than 50μM reduced cell viability, while lower concentrations (0.05-5μM) increased clonogenicity. The combination of 0.5μM CPF + 5μM CPM produces the greatest enhancement in colony formation compared to individual treatment (p<0.001), indicating synergistic effects. Molecular docking revealed that both pesticides bind to the same ERα ligand-binding domain with favorable binding energies. Bioinformatic analysis identified ESR1, ESR2, CCND1 and TP53 as genes of interest for subsequent studies. These findings demonstrate that CPF+CPM act enhancing BC cell proliferation through ER-mediated pathways. The identified target genes provide candidates for mechanistic studies. Our results suggest that exposure to these pesticides may have greater BC risk than individual compounds, which justify further investigation of pesticide mixture effects in cancer development.

343. P19-02. URBAN AIR POLLUTION TRIGGERS GLIAL ACTIVATION AND CYTOKINE INCREASE IN MICE OLFACTORY BULB

Agustina Freire¹, Octavio Diana², Sofia Reynoso³, Jorge Goldstein⁴, Silvia Alvarez⁵, Natalia Magnani⁶, Pablo Evelson⁷, Mariana Garcés⁸

1. Instituto de Bioquímica y Medicina Molecular (IBIMOL,

- CONICET); Cátedra de Química General e Inorgánica, Facultad de Farmacia y Bioquímica, UBA.
2. Instituto de Bioquímica y Medicina Molecular (IBIMOL, CONICET); Cátedra de Química General e Inorgánica, Facultad de Farmacia y Bioquímica, UBA.
3. Instituto de Bioquímica y Medicina Molecular (IBIMOL, CONICET); Cátedra de Química General e Inorgánica, Facultad de Farmacia y Bioquímica, UBA.
4. CONICET- Universidad de Buenos Aires. Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO).; Facultad de Medicina, Universidad de Buenos Aires.
5. Instituto de Bioquímica y Medicina Molecular (IBIMOL, CONICET); Cátedra de Fisicoquímica, Facultad de Farmacia y Bioquímica, UBA.
6. Instituto de Bioquímica y Medicina Molecular (IBIMOL, CONICET); Cátedra de Química General e Inorgánica, Facultad de Farmacia y Bioquímica, UBA.
7. Instituto de Bioquímica y Medicina Molecular (IBIMOL, CONICET); Cátedra de Química General e Inorgánica, Facultad de Farmacia y Bioquímica, UBA.
8. Instituto de Bioquímica y Medicina Molecular (IBIMOL, CONICET); Cátedra de Química General e Inorgánica, Facultad de Farmacia y Bioquímica, UBA.
- agustinafreire@gmail.com

Several epidemiological studies suggest the brain as a target of particulate matter (PM) present in air pollution. It is suggested that inflammation and oxidative stress are the main mechanisms leading to adverse health effects. Herein, we aimed to study the inflammatory response caused by urban air (UA) pollution on the olfactory bulb (OB), focusing on the evaluation of cytokine release and microglia activation. BALB/c mice (8 weeks old) were exposed to filtered air (FA, control group) or UA in whole-body chambers located in a polluted area of Buenos Aires city for up to 4 weeks. To determine whether adverse effects were reversible, a 4-week washout (WO) period with FA exposure was included. Inflammatory mediators, including IL-6 mRNA, IL-1 β mRNA, TNF- α mRNA, IL-6, TNF α , and IL-10, were significantly elevated after UA exposure ($p < 0.05$) while iNOS expression was increased as well ($p < 0.01$). Regarding glial activation, UA increased Iba-1 and GFAP expression and decreased MBP levels ($p < 0.001$). When assessing reversibility, WO significantly decreased GFAP expression compared to UA ($p < 0.01$). Similarly, Iba-1 expression was reduced in WO animals compared with UA ($p < 0.01$). However, TNF- α , IL-6, and IL-10 levels remained elevated in WO mice compared to FA ($p < 0.01$). These results indicated that neuroinflammation involves the infiltration of immune cells and activation of microglia and astrocytes, which can lead to neurotoxicity in polluted environments. The recovery process following the washout period may have a lag, thus indicating persistent inflammation that can hinder healing.

344. P19-03. ENZYMATIC AND MITOCHONDRIAL ALTERATIONS IN ENDOTHELIAL CELLS EXPOSED TO NON-CYTOTOXIC CONCENTRATIONS OF ORGANOPHOSPHATES

- Mario Besarón¹, Ema Kohen², Milagros Mariani de Camas Quinteros³, María del Carmen Martínez⁴, Silvina Gazzaniga⁵
1. Escuela ORT Argentina; QB63/QB66 Biología Tumoral y Mecanismos de Toxicidad por Xenobióticos
2. Escuela ORT Argentina; QB63/QB66 Biología Tumoral y Mecanismos de Toxicidad por Xenobióticos
3. Escuela ORT Argentina; QB63/QB66 Biología Tumoral y Mecanismos de Toxicidad por Xenobióticos
4. Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; QB63/QB66 Biología Tumoral y Mecanismos de Toxicidad por Xenobióticos
5. Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; QB63/QB66 Biología Tumoral y Mecanismos de Toxicidad por Xenobióticos
- abelardo.sztrum@ort.edu.ar

Organophosphates (OPs) are chemical compounds commonly used as pesticides, which act as inhibitors of the enzyme acetylcholinesterase (AChE). Their well-known adverse effects are mainly focused on the central nervous system. Nonetheless, this enzyme is also present in non-neural tissues as the vascular endothelium and, there is limited evidence regarding the potential damage/dysfunction caused by OPs on endothelial cells (EC). Thus, the aim of this study is to comparatively evaluate the effect of two OPs at non-cytotoxic concentrations on EC in vitro in terms of enzymes acetylcholinesterase (AChE) and carboxylesterases (CES), respectively. Cytotoxicity of fenitrothion (FNT; 0.01-10 μ M) and clorpyrifos (CPF; 0.01-300 μ M) on EC were assessed by crystal violet (CV) and MTT assays. AChE and CES activities were quantified spectrophotometrically in cell lysates after 48 h-treatment. For FNT, no significant reduction in viability respect to control cells was observed at any concentration with either method, except at 10 μ M, where a significant decrease of $\approx 65\%$ (CV) and $\approx 80\%$ (MTT) suggested potential mitochondrial dysfunction. Similarly, CPF showed no cytotoxicity up to 150 μ M CPF by MTT; however MTT reduction was approximately 70% for 70 μ M CPF ($p < 0.05$), indicating impaired mitochondrial activity. FNT IC₅₀ for AChE activity was 0.133 μ M CPF and for CES activity was 0.026 μ M. Meanwhile, for CPF, IC₅₀ for AChE activity was 18.63 μ M CPF and for CES activity was 20 μ M. In conclusion, this study allows us the selection of non-cytotoxic concentrations of both OP to evaluate their impact on esterase inhibition in the functional performance of ECs.

345. P19-04. EVALUATION OF CITOTOXIC EFFECTS OF BIS-MUTH MOFS ON GRAM-NEGATIVE AND GRAM-POSITIVE BACTERIA

Hinojosa Vera Kathleen F¹, Cáceres Caludia S², Gómez Germán E³, Stege Patricia W⁴

1. UNSL; Laboratorio de medicina Experimental y Traduccional, IMIBIO-SL-CONICET-UNSL
2. UNSL; Área de Microbiología e Inmunología, Universidad Nacional de San Luis.
3. UNSL; Instituto de Investigaciones en Tecnología Química (INTEQUI)
4. UNSL; Área de Química Analítica. Laboratorio Nanotecnología y BioMedicina Regenerativa IMIBIO-SL-CONICET-UNSL
- kat17hv@gmail.com

Metal-organic frameworks (MOFs) are porous, crystalline materials resulting from the self-assembly of metal ions and organic ligands. Their high structural and functional versatility, together with the possibility of incorporating biologically active metal ions, makes them attractive candidates for biomedical applications, particularly as antimicrobial agents. In this work, the antibacterial properties of two bismuth compounds were evaluated: [Bi₂(1,4-NDC)₃·2DMF] (Bi-9) and [Bi₂(2,6-NDC)₃(1,10-phen)₂] (Bi-11). Antibacterial activity was assessed by Mueller-Hinton agar diffusion assays and by monitoring bacterial growth in liquid culture (Mueller-Hinton) using optical density (OD) measurements. Sulfamethoxazole was used as a control for *Escherichia coli*, and vancomycin was used for *Staphylococcus aureus*. Additionally, a bismuth salt [(BiO)₂CO₃] was included as a reference to discriminate the contribution of the metal ion in solution. In *E. coli*, both Bi-9 and Bi-11 exhibited comparable behavior to the bismuth salt, with no significant differences compared to the positive control. In contrast, *S. aureus* showed a marked reduction in OD in the presence of both MOF and the salt, indicating an increased susceptibility of Gram-positive bacteria to these bismuth-based systems. Importantly, OD reflects turbidity and total biomass but does not distinguish between viable and non-viable cells. Therefore, although the results suggest a promising inhibitory effect of bismuth MOFs, further studies (colony forming unit counts and viability assays) will be required to clarify whether their action is primarily bacteriostatic or bactericidal.

346. P19-05. EARLY-LIFE CHLORPYRIFOS EXPOSURE: AN ENDOCRINE DISRUPTOR THAT DELAYS MAMMARY GLAND DEVELOPMENT

Rocío Natalia Cardozo¹, Lucía Enriquez², Giselle Fainberg³, Mariana Mardirosian⁴, Claudia Cocca⁵, Marianela Lasagna⁶, Mariel Nuñez⁷

1. UBA. Buenos Aires, Argentina.; Laboratorio de Radioisótopos, FFYB,

2. UBA-CONICET. Buenos Aires, Argentina; Lab de Radioisótopos, FFYB/Lab. de Contaminantes Ambientales y trastornos endócrinos, IQUIFIB

3. UBA. Buenos Aires, Argentina; Lab. de Radioisótopos, FFYB

4. UBA-CONICET. Buenos Aires, Argentina; Lab de Radioisótopos, FFYB/Lab. de Contaminantes Ambientales y Trastornos Endócrinos, IQUIFIB.

5. UBA-CONICET. Buenos Aires, Argentina; Lab de Radioisótopos, FFYB/Lab. de Contaminantes Ambientales y Trastornos Endócrinos, IQUIFIB.

6. UBA-CONICET. Buenos Aires, Argentina; Lab. de Radioisótopos, FFYB/Lab. de Contaminantes Ambientales y Trastornos Endócrinos, IQUIFIB.

7. UBA-CONICET. Buenos Aires, Argentina; Lab. de Radioisótopos, FFYB/Lab. de Contaminantes Ambientales y Trastornos Endócrinos, IQUIFIB.

natyrocardozo@gmail.com

We have previously demonstrated that chlorpyrifos (CPF) acts as an endocrine disruptor. Exposure to environmental toxicants during critical windows of susceptibility can negatively influence normal mammary gland development. Aim: To determine if environmentally relevant concentrations of CPF (NOAEL: 0.1 mg/kg/day – CPF 0.1 and ADI: 0.001 mg/kg/day – CPF 0.001) could affect normal mammary gland (MG) development in female Sprague-Dawley rat offspring exposed in utero from gestation to weaning. We evaluated developmental parameters using whole mounts and histopathological analysis of MG at postnatal days (PND) 21, 55 and 90. PCNA and ER α expression were determined by immunohistochemistry. At PND 21, MG showed decreased lateral growth and increased distance between MG4 and MG5 ($p < 0.05$ CPF 0.001 vs C), and a reduced number of terminal end buds (TEBs) ($p < 0.05$ CPF 0.1 vs C). Histological analysis revealed a decrease in glandular area and in periglandular fibrous stroma ($p < 0.01$ and $p < 0.05$ CPF 0.001 vs C, respectively). At PND 55, MG had a greater number of TEBs and higher PCNA expression ($p < 0.05$ CPF 0.001 vs C; $p < 0.01$ CPF 0.1 vs C) and ER α expression diminished ($p < 0.05$ CPF 0.001 vs C). By PND 90, MGs showed increased ER α expression ($p < 0.05$ CPF 0.1 vs C). Conclusion: Our results demonstrate that exposure to CPF during early windows of susceptibility induces a developmental delay in the MG of female rats.

347. P19-06. EPIDEMIOLOGICAL SITUATION OF SCORPIONISM IN THE CITY OF LA RIOJA BETWEEN 2022 AND 2023

María Eugenia de la Vega¹, María del Carmen Díaz Ariza², Bizzotto, Cristian³, Melina Milagros Carabajal⁴, Gabriela Narena Cuello⁵, Rocío María de las Nieves Gorriti⁶, Vidal Carrasco Lourdes⁷, Stewart, María Gabriela del Valle⁸

1. IUCS Fundación Barceló -sede La Rioja; CyT

2. IUCS Fundación Barceló; CyT

3. Epidemiología Ministerio Salud Publica La Rioja; artrópodos interés sanitario del Ministerio Salud Publica-La Rioja

4. IUCS Fundación Barceló -sede La Rioja; CyT

5. IUCS Fundación Barceló -sede La Rioja; CyT

6. IUCS Fundación Barceló -sede La Rioja; CyT

7. IUCS Fundación Barceló -sede La Rioja; CyT

8. IUCS Fundación Barceló -sede La Rioja; CyT

mariaeugeniadlavega@gmail.com

Scorpionism represents a significant public health issue, with approximately 1.5 million cases reported globally each year and a fatality rate of 3%. This study analyzes the epidemiological profile of scorpion stings in La Rioja capital between 2022 and 2023, employing a prospective, quantitative descriptive approach. It encompasses species identification, clinical data collection, and educational outreach to healthcare personnel. The primary objective is to characterize the epidemiological situation of scorpionism in the region. Specific goals include identifying medically relevant scorpion

species, documenting sting incidents and responsible species, recording clinical manifestations in children under 15, and promoting awareness among health professionals regarding clinical management and reporting. A total of 384 cases were reviewed. The 6-10 age group exhibited the highest incidence. In 2023, 53.2% of cases were male; in 2022, 49.7%. Lower limbs were the most affected site in 2022 (46.8%), while 45.9% of 2023 cases lacked anatomical data. Pain was the most frequently reported symptom (18.1% in 2022; 15.9% in 2023), though symptom data were missing in most cases. Accident location and context were also poorly documented. Antivenom was rarely required: 4.5% of patients over 10 years in 2022 and 5.3% of children aged 6-10 in 2023 received it. A major limitation was the high rate of incomplete reporting forms 77% in 2022 and 86% in 2023 impeding species identification and contextual analysis. Improved documentation and enhanced clinical awareness are essential to strengthen care protocols and epidemiological surveillance in scorpionism cases

POSTERS 19 - SAIC - ENDOCRINOLOGÍA

DATE & TIME: 20/11/2025 9:00 - 10:30 H

Chairs: Mariel Nuñez, Hugo Ortega

348. P19-07. DECIPHERING FOXA2 CONTRIBUTION TO HUMAN PITUITARY DIFFERENTIATION AND CONGENITAL HYPOPITUITARISM USING IPSC-BASED MODELS

Gonzalo Tomás Chirino Felker¹, María Inés Pérez Millán², Sheila Castañeda³, Federico Zabalegui⁴, Guadalupe Amin⁵, Alicia Belgorosky⁶, Marta Ciaccio⁷, María Isabel Di Palma⁸, Elisa Vaiani⁹, Ariel Waisman¹⁰, Santiago Miriuka¹¹, Lucía Natalia Moro¹², María Andrea Camilletti¹³

1. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

2. Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE), Universidad de Buenos Aires (UBA-CONICET); Laboratorio de Genética Molecular en Endocrinología

3. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

4. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

5. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

6. Servicio de Endocrinología del Hospital de Pediatría S.A.M.I.C. Prof. Dr. Juan P. Garrahan; Consejo Nacional Científico Tecnológico, Buenos Aires, Argentina (CONICET); .

7. Servicio de Endocrinología del Hospital de Pediatría S.A.M.I.C. Prof. Dr. Juan P. Garrahan; .

8. Servicio de Endocrinología del Hospital de Pediatría S.A.M.I.C. Prof. Dr. Juan P. Garrahan; .

9. Servicio de Endocrinología del Hospital de Pediatría S.A.M.I.C. Prof. Dr. Juan P. Garrahan; .

10. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

11. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

12. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a Neurociencias (LIAN)

13. Instituto de Neurociencias (INEU-CONICET), Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI); Laboratorio de Investigaciones Aplicadas a

Neurociencias (LIAN)
gonzalofelker1@gmail.com

Congenital hypopituitarism (CH) is a complex genetic disorder caused by impaired pituitary function and hormone production. Forkhead Box A2 (FOXA2) is a pioneer transcription factor essential for the development of the node and notochord, pancreas, and brain. Heterozygous FOXA2 variants were identified in Argentine patients with CH, but the pathogenesis remains unclear. We sought to define FOXA2 function and evaluate candidate variants using an in vitro pituitary differentiation model. We generated two human induced pluripotent stem cell (hiPSC) lines: FOXA2+/Ser229* hiPSCs, reprogrammed from PBMCs of a CH patient with craniofacial malformations carrying heterozygous nonsense FOXA2 c.686C>T (p.Ser229*), and FOXA2KO hiPSCs by CRISPR-Cas9. Both lines were validated as pluripotent and, with wild-type hiPSCs, underwent a 15-day, 2D pituitary induction protocol. Differentiation was assessed by RT-qPCR for key pituitary genes (PITX1/2, HESX1, OTX2, SOX2, SIX1) and candidate FOXA2 interactors (including GLI), plus SOX2 immunofluorescence. Over 15 days, preliminary data showed that all three lines progressed toward a pituitary lineage, with no differences in lineage markers between wild-type and FOXA2-deficient cells. Nonetheless, trends were detected: PITX2, TFAP2A, and SIX1 tended to be lower in FOXA2-deficient lines, whereas SOX2 and FOXA2 homolog FOXA1 tended to be higher. At the pituitary stage, FOXA2-deficient cells showed increased SOX2, a pituitary stem-cell marker, suggesting delayed or impaired formation of functional pituitary progenitors. Future work will extend differentiation to hormonal stages. These data provide the first in vitro characterization of pituitary differentiation in patient-derived and CRISPR-edited FOXA2-deficient hiPSCs, establishing a model to dissect how FOXA2 variants contribute to CH.

349. P19-08. ESTRONE COUNTERACTS OXIDATIVE STRESS IN RAT UTERUS UNDER OBESITY

María I. Valle, Virginia L. Massheimer
Instituto de Ciencias Biológicas y Biomédicas del Sur (INBIO-SUR), CONICET-Universidad Nacional del Sur (UNS). Departamento de Biología, Bioquímica y Farmacia. UNS. Bahía Blanca. Argentina

We have previously reported uterus is a target tissue of estrone (E1) action, one of the major estrogens produced by ovaries. In this work we evaluated the mechanism of action of the steroid on the regulation of uterine oxidative stress induced by obesity. Uterine explants isolated from Wistar rats bilaterally ovariectomized fed with high-fat diet (obese rats) were in vitro exposed to E1 for 4 h, and immediately after nitric oxide (NO) and hydrogen peroxide (H_2O_2) release were measured. PD98059 and LY294002 compounds were employed as MEK/ERK and PI3K/Akt inhibitors respectively. Indeed equilin (100–10 μ M), an 17 β -HSD inhibitor, was used to prevent conversion of E1 to estradiol. After E1 treatment (0.1–50 nM), Ut slices exhibited an enhancement in nitric oxide synthesis (27–130% above control, $P < 0.001$), and a reduction in H_2O_2 production (10–40% below control, $P < 0.01$), with the maximal effect observed at 10 nM E1. Estradiol (10 nM) exhibited similar action. The preincubation with the inhibitors PD98059 or LY294002 suppressed the reduction in ROS release elicited by the hormone. However the antagonists did not altered the stimulatory action on E1 on NO production (84; 110; 90% above each control, E1; E1+PD, E1+LY respectively; $p < 0.01$). The presence of Equilin, at all concentrations tested, not modify E1 modulatory action either on NO or H_2O_2 release, suggesting that E1 acts by its own, and not through conversion to estradiol. In summary, in obese uterus, E1 per se exhibited an antioxidative effect through a mechanism of action that partially involved MEK/ERK and PI3K/Akt signaling transduction pathways.

350. P19-09. EFFECT OF CHRONIC STRESS EXPOSURE ON DIABETES INCIDENCE IN NOD/SHIL TJ MICE. ROLE OF GUT MICROBIOTA AND INTESTINAL PERMEABILITY

Laura Wydra¹, Maria Silvia Bianchi², Miriam Ruth Wald³, Ana Maria Genaro⁴, Mara Roxana Rubinstein⁵
1. *Instituto de investigaciones Biomédicas (UCA-CONICET);*

Laboratorio Psiconeuroendocrinoinmunología
2. *Instituto de Biología y Medicina Experimental (CONICET);*
Laboratorio de Neuroendocrinología
3. *Instituto de investigaciones Biomédicas (UCA-CONICET);*
Laboratorio Psiconeuroendocrinoinmunología
4. *Instituto de investigaciones Biomédicas (UCA-CONICET);*
Laboratorio Psiconeuroendocrinoinmunología
5. *Instituto de investigaciones Biomédicas (UCA-CONICET);*
Laboratorio Psiconeuroendocrinoinmunología
laurasofiaWydra@gmail.com

Introduction: Type 1 diabetes (T1D) is an autoimmune disease characterized by impaired insulin secretion. Psychosocial factors and unbalanced gut microbiota contribute to T1D development. The aim of this work is to determine the role of chronic stress in T1D development and the mechanisms involved by evaluating the microbiological and immunological profiles of the gut microbiota. Methods: Two-month-old NOD/ShiLtJ mice (a spontaneous model of T1D) were subjected to CS through the application of aleatory and unpredictable stressors. Results: Female mice exposed to CS showed increased diabetes incidence ($p < 0.05$), while in males, CS only increased the insulinitis score. Therefore, the study continued using only female mice. Corticosterone levels were increased in animals exposed to CS ($p < 0.05$). To determine microbiota alterations, genomic DNA was extracted from fecal samples. 16S bacteria, 16S Bacteroidetes and 16S Firmicutes (the most abundant phyla of gut microbiota) were measured by qPCR. At 30 days of CS, an increase in 16S Firmicutes was found in mice not exposed to CS that later became diabetic ($p < 0.05$). At 90 days of CS, only a decrease in 16S Bacteroidetes was observed in animals exposed to CS regardless of later diabetic development ($p < 0.05$). Mice exposed to CS that later became diabetic exhibited increased intestinal permeability ($p < 0.05$) as well as altered TGF- β and IL-17a expression in the mesenteric lymph node ($p < 0.05$). Conclusion: These results demonstrate that CS plays a role in the development of T1D. Studying the involved mechanisms revealed changes in gut microbial composition and increased intestinal permeability, promoting an immune imbalance.

351. P19-10. THYROTROPIN RECEPTOR ACTIVATING VARIANTS RESPONSIBLE FOR NONAUTOIMMUNE NEONATAL HYPERTHYROIDISM

Valeria F. Garzón¹, Noelia Dujovne², Ailen S. Borgononi³, Natalia Gazek⁴, Maricel Molina⁵, Ariel M. Gallo⁶, Héctor M. Targovnik⁷, Carina M. Rivolta⁸
1. *Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Microbiología, Inmunología, Biotecnología y Genética/Cátedra de Genética.; Laboratorio de Genética Molecular Tiroidea*
2. *Hospital de Pediatría JP Garrahan - Buenos Aires, Argentina; Servicio de Endocrinología*
3. *Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Microbiología, Inmunología, Biotecnología y Genética/Cátedra de Genética. Buenos Aires, Argentina; Laboratorio de Genética Molecular Tiroidea*
4. *Hospital de Pediatría JP Garrahan - Buenos Aires, Argentina; Servicio de Endocrinología*
5. *Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Microbiología, Inmunología, Biotecnología y Genética/Cátedra de Genética. Buenos Aires, Argentina; Laboratorio de Genética Molecular Tiroidea*
6. *Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Microbiología, Inmunología, Biotecnología y Genética/Cátedra de Genética. Buenos Aires, Argentina; Laboratorio de Genética Molecular Tiroidea*
7. *Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Microbiología, Inmunología, Biotecnología y Genética/Cátedra de Genética. Buenos Aires, Argentina; Laboratorio de Genética Molecular Tiroidea*
8. *Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Microbiología, Inmunología, Biotecnología y Genética/Cátedra de Genética. CONICET-Universidad de Buenos Aires. Instituto de Inmunología, Genética y Metabolismo (INIGEM), Buenos Aires, Argentina*

na.; Laboratorio de Genética Molecular Tiroidea
valeriafarzon@gmail.com

Nonautoimmune congenital hyperthyroidism caused by activating germline variants in the thyrotropin receptor (TSHR) gene is a rare disorder which shows a persistent and severe hyperthyroidism. Clinical manifestations might occur from the fetus and cause tachycardia, arrhythmia, intrauterine growth retardation and premature birth. There are 2 types of activating TSHR germline variants. One is familial nonautoimmune hyperthyroidism (FNAH), an autosomal dominant disorder, and the other is sporadic nonautoimmune hyperthyroidism (SNAH), caused by de novo variants. Compared to FNAH, SNAH tends to occur at a younger age and present more severe clinical symptoms. To date, a total of 18 activating variants in the TSHR have been reported in patients with SNAH and 31 activating variants, in patients with FNAH. 2 patients with clinical and biochemical data compatible with nonautoimmune neonatal hyperthyroidism were analyzed in the present study. Genomic DNA was isolated from blood cells of the patients and parents and all exons of the TSHR gene, including the flanking intronic regions, were amplified by PCR. Each amplified fragment were sequenced with the Taq polymerase-based chain terminator method. In Patient 1, sequence analysis revealed a de novo, heterozygous and germinal activating variant: c.1897G>C; p.Asp633His. In Patient 2, a de novo heterozygous and germinal variant c.1515C>A; p.Ser505Arg was identified. In silico studies were performed to elucidate a correlation between structural disturbances and putative functional commitment. If diagnosis and treatment are delayed, nonautoimmune congenital hyperthyroidism may cause irreversible complications such as mental retardation. Therefore, early molecular diagnosis and prompt treatment with genetic counseling are necessary.

352. P19-11. RETROSPECTIVE AND LONGITUDINAL STUDY OF METABOLIC CHANGES IN USERS OF MASCULINIZING HORMONE THERAPY IN CÓRDOBA, ARGENTINA

Agostina Santi¹, Eugenia Estario², Lorena Saletti³, Claudia G. Pellizas⁴, Dana M. Negretti Borgia⁵

1. Hospital Córdoba. Córdoba Capital, Argentina.; Servicio de Endocrinología.

2. Hospital Córdoba. Córdoba Capital, Argentina.; Servicio de Endocrinología

3. Centro de Investigaciones y Estudios sobre Cultura y Sociedad (CIECS). Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET)- Universidad Nacional de Córdoba (UNC). Córdoba Capital, Argentina.; Desigualdades de género, salud pública y violencias de género

4. Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas (FCQ), UNC. Córdoba Capital, Argentina/ Centro de Investigaciones en Bioquímica Clínica e Inmunología (CIBICI), CONICET-UNC. Córdoba Capital, Argentina.; Mecanismos celulares y moleculares involucrados en la acción de las hormonas tiroideas sobre células dendríticas y su impacto en la inmunidad adaptativa

5. Centro de Investigaciones y Estudios sobre Cultura y Sociedad (CIECS). Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET)- Universidad Nacional de Córdoba (UNC). /Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas (FCQ), UNC. Córdoba Capital, Argentina.; Salud Integral Trans, Travesti y No Binario agostina.santi@unc.edu.ar

Gender-transition hormone therapy (HT) is used by more than 70% of transgender, travesti, and non-binary individuals. Masculinizing HT (MHT) involves the administration of testosterone, which suppresses ovarian hormones and promotes male phenotypic characteristics. Although hormonal and hematological biomarkers are commonly monitored, scientific evidence regarding the associated metabolic changes remains limited and, at times, contradictory. The aim of this study was to evaluate changes in physical and biochemical parameters related to metabolism in MHT users over a one-year period. A retrospective analysis included 33 patients from the Endocrinology Service of Hospital Córdoba (Argentina) between 2020 and 2024. Baseline values were compared with those obtained after

twelve months of treatment using a paired t-test. As a result, after one year of MHT, total testosterone ($p<0.0001$) and bioavailable testosterone ($p<0.0001$) increased, while estradiol ($p=0.0085$) and prolactin ($p=0.0013$) decreased. Weight ($p=0.0024$) and body mass index ($p=0.0026$) increased, with no significant changes in fasting glucose ($p=0.2197$). The lipid profile showed increases in total cholesterol ($p=0.0196$), LDL cholesterol ($p=0.0132$), and triglycerides ($p=0.0292$), with a decrease in HDL cholesterol ($p=0.0407$). Liver enzymes also increased: GOT ($p=0.0025$), GPT ($p=0.0076$), and GGT ($p=0.0013$). Hematocrit and hemoglobin increased within clinically expected ranges. In summary, MHT effectively achieves hormonal and hematologic targets within clinical guidelines. However, the observed metabolic alterations, including changes in lipid and liver enzyme levels, highlight the importance of comprehensive follow-up and monitoring in this population. Furthermore, these findings reinforce the need to establish population-specific reference values to optimize clinical care and prevent complications.

POSTERS 20 - SAIC - LATE-BREAKING ABSTRACTS

DATE & TIME: 20/11/2025 9:00 - 10:30 H

Chairs: Martin Codegnone, Agustin Yaneff, Roxana Peroni

353. P20-01. ORGANOLEPTIC OPTIMIZATION OF DISPERSIBLE GRANULES: TOWARD IMPROVED THERAPEUTIC ADHERENCE IN PEDIATRIC TUBERCULOSIS

Laura Carolina Luciani Giacobbe¹, Patricia Sierra², Josefina Aylen Accendere³, Marcela Lilian Martinez⁴, María Eugenia Olivera⁵

1. Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba y Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, CONICET.; GIT Farma. Laboratorio 210, Edificio de Ciencias II, Haya de la Torre y Medina Allende, Córdoba, Argentina. CP: X5000HUA

2. Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba y Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, CONICET.; GIT Farma. Laboratorio 210, Edificio de Ciencias II, Haya de la Torre y Medina Allende, Córdoba, Argentina. CP: X5000HUA

3. Facultad de Ciencias Químicas, Universidad Nacional de Córdoba; Laboratorio 210, Edificio de Ciencias II, Haya de la Torre y Medina Allende, Córdoba, Argentina. CP: X5000HUA

4. Facultad de Ciencias Exactas, Físicas y Naturales, Universidad Nacional de Córdoba e Instituto Multidisciplinario de Biología Vegetal (IMBIV), CONICET; Cátedra de Química Orgánica, Av. Vélez Sarsfield 1611, X5016GCA Córdoba, Argentina.

5. Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba y Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, CONICET.; GIT Farma. Laboratorio 210, Edificio de Ciencias II, Haya de la Torre y Medina Allende, Córdoba, Argentina. CP: X5000HUA

lluciani@unc.edu.ar

Pediatric tuberculosis remains a therapeutic challenge, mainly due to the poor acceptability of currently available oral formulations, affected by the bitter taste of active pharmaceutical ingredients. To improve treatment adherence, we developed an alternative formulation in the form of dispersible granules incorporating an innovative organoleptic correction system suitable for pediatric use. The objective was to evaluate the ability of the test formulation to mask the bitter taste in comparison with the commercial (reference) formulation. An affective acceptability study was conducted in 40 healthy adult volunteers, following a protocol approved by the Ethics Committee (CIEIS HNC, UNC; Acta III; N°208/2021). Each participant evaluated both randomly coded formulations using a five-point hedonic scale and a 0–100% visual analogue scale, then ranked them according to overall preference. Qualitative observations were also recorded. Data were analyzed using Wilcoxon or

paired Student's t-tests, as appropriate ($p < 0.05$). Results showed significant differences in favor of the test formulation ($p < 0.001$, paired Wilcoxon) in both scales. A total of 92.3% of participants preferred the innovative formulation, describing it as sweeter and more pleasant, with a lower perception of bitterness. Comments highlighted a fruity profile and rapid attenuation of bitterness, although visual appearance was suggested for improvement. In conclusion, the test formulation exhibited significantly superior organoleptic properties compared to the commercial reference, suggesting enhanced acceptability that could translate into improved therapeutic adherence in pediatric patients with tuberculosis.

354. P20-02. IMPACT OF CDK5 LOSS ON PARAQUAT-INDUCED METABOLIC ACTIVITY AND CELL DEATH IN HUMAN INDUCED PLURIPOTENT STEM CELL- DERIVED NEURAL STEM CELLS AND NEURONS

Mayra Alexa López¹, Sofía Mucci², Gustavo Sevelev³, María Érida Scassa⁴, Leonardo Romorini⁵, Analia Czerniczyniec⁶

1. FLENI, B1625XAF, Belén de Escobar, Provincia de Buenos Aires, Argentina.; Laboratorio de Investigación Aplicada a Neurociencias, Instituto de Neurociencias, Fundación Para La Lucha Contra Las Enfermedades Neurológicas de La Infancia (LIAN-INEU, Fleni-CONICET)

2. FLENI, B1625XAF, Belén de Escobar, Provincia de Buenos Aires, Argentina.; Laboratorio de Investigación Aplicada a Neurociencias, Instituto de Neurociencias, Fundación Para La Lucha Contra Las Enfermedades Neurológicas de La Infancia (LIAN-INEU, Fleni-CONICET)

3. FLENI, B1625XAF, Belén de Escobar, Provincia de Buenos Aires, Argentina.; Laboratorio de Investigación Aplicada a Neurociencias, Instituto de Neurociencias, Fundación Para La Lucha Contra Las Enfermedades Neurológicas de La Infancia (LIAN-INEU, Fleni-CONICET)

4. FLENI, B1625XAF, Belén de Escobar, Provincia de Buenos Aires, Argentina.; Laboratorio de Investigación Aplicada a Neurociencias, Instituto de Neurociencias, Fundación Para La Lucha Contra Las Enfermedades Neurológicas de La Infancia (LIAN-INEU, Fleni-CONICET)

5. FLENI, B1625XAF, Belén de Escobar, Provincia de Buenos Aires, Argentina.; Laboratorio de Investigación Aplicada a Neurociencias, Instituto de Neurociencias, Fundación Para La Lucha Contra Las Enfermedades Neurológicas de La Infancia (LIAN-INEU, Fleni-CONICET)

6. FLENI, B1625XAF, Belén de Escobar, Provincia de Buenos Aires, Argentina.; Laboratorio de Investigación Aplicada a Neurociencias, Instituto de Neurociencias, Fundación Para La Lucha Contra Las Enfermedades Neurológicas de La Infancia (LIAN-INEU, Fleni-CONICET)

mayraalexalopez1@gmail.com

Impact of CDK5 Loss on Paraquat-induced metabolic activity and cell death in human induced pluripotent stem cell- derived neural stem cells and neurons. Paraquat (PQ) is one of the most widely used herbicides worldwide, and its neurotoxic mechanisms involve excessive production of reactive oxygen species (ROS) and mitochondrial dysfunction. In a previous study, we demonstrated that PQ exposure (50 μ M, 24 h) induced cell death in human induced pluripotent stem cell (hiPSC)-derived neurons, associated with mitochondrial impairment and dysregulation of mitochondrial dynamics. In contrast, hiPSC- derived neural stem cells (NSCs) preserved viability by enhancing glycolytic pathways. Cyclin- dependent kinase 5 (CDK5), initially described as a classical CDK, is a proline-directed serine/threonine kinase activated by interaction with the regulatory subunits p35 and p39, which are predominantly expressed in the nervous system. CDK5 regulates neuronal migration, cytoskeletal dynamics, synaptic function, and vesicular transport. However, under neurotoxic conditions such as oxidative stress or mitochondrial dysfunction, p35 is cleaved to p25 and p10. The resulting CDK5/p25 complex is more stable, can translocate to the nucleus, and aberrantly phosphorylates proteins associated with neurodegenerative diseases, including Parkinson's disease. The aim of this work was to evaluate PQ neurotoxicity in hiPSC-derived NSCs and neurons deficient in CDK5 (FN2.1 CDK5^{-/-}). Cells were exposed to PQ (50

μ M, 24 h), and metabolic activity and cell viability were assessed. PQ treatment reduced metabolic activity by 75% in hiPSC- derived NSCs and 50% in hiPSC-derived neurons. However, trypan blue and propidium iodide exclusion assays revealed no significant reduction in cell viability

355. P20-03. GESTATIONAL EXPOSURE TO POLYETHYLENE MICROPLASTICS AND BISPHENOL F IMPAIRS REPRODUCTIVE AND METABOLIC OUTCOMES IN RATS

Almirón Ailín¹, Lorenz Virginia², González César³, Lell Brune-lla⁴, Giecco Agustina⁵, Trejo Delfina⁶, Sager Candela⁷, Blettler Martín⁸, Adur Javier⁹, Attademo A. Maximiliano¹⁰, Durando Milena¹¹, Milesi M. Mercedes¹²

1. Instituto de Salud y Ambiente del Litoral (ISAL), Universidad Nacional del Litoral (UNL) - CONICET, Argentina.

Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas (FBCB) - UNL, Argentina.; -

2. Instituto de Salud y Ambiente del Litoral (ISAL), Universidad Nacional del Litoral (UNL) - CONICET, Argentina.

Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas (FBCB) - UNL, Argentina.; -

3. Laboratorio de Microscopía Aplicada a Estudios Moleculares y Celulares (LMAE), Facultad de Ingeniería - Universidad Nacional de Entre Ríos (FI - UNER), Argentina.; -

4. Instituto de Salud y Ambiente del Litoral (ISAL), Universidad Nacional del Litoral (UNL) - CONICET, Argentina.; -

5. Instituto de Salud y Ambiente del Litoral (ISAL), Universidad Nacional del Litoral (UNL) - CONICET, Argentina.; -

6. Instituto de Salud y Ambiente del Litoral (ISAL), Universidad Nacional del Litoral (UNL) - CONICET, Argentina.; -

7. Instituto de Salud y Ambiente del Litoral (ISAL), Universidad Nacional del Litoral (UNL) - CONICET, Argentina.; -

8. Laboratorio de Microscopía Aplicada a Estudios Moleculares y Celulares (LMAE), Facultad de Ingeniería - Universidad Nacional de Entre Ríos (FI - UNER), Argentina. Instituto de Investigación y Desarrollo en la Bioingeniería y Bioinformática (IBB), UNER - CONICET, Argentina.; -

9. Laboratorio de Microscopía Aplicada a Estudios Moleculares y Celulares (LMAE), Facultad de Ingeniería - Universidad Nacional de Entre Ríos (FI - UNER), Argentina. Instituto de Investigación y Desarrollo en la Bioingeniería y Bioinformática (IBB), UNER - CONICET, Argentina.; -

10. Laboratorio de Ecotoxicología, FBCB, UNL - CONICET, Argentina.; -

11. Instituto de Salud y Ambiente del Litoral (ISAL), Universidad Nacional del Litoral (UNL) - CONICET, Argentina.

Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas (FBCB) - UNL, Argentina.; -

12. Instituto de Salud y Ambiente del Litoral (ISAL), Universidad Nacional del Litoral (UNL) - CONICET, Argentina.

Cátedra de Fisiología Humana, Facultad de Bioquímica y Ciencias Biológicas (FBCB) - UNL, Argentina.; -

ailinalmiron98@gmail.com

The increasing accumulation of microplastics (MPs) in the environment, together with their recent detection in human placentas, has raised concerns about their potential impact on human health, and especially during a stage as sensitive as pregnancy. Moreover, plasticizing additives such as bisphenol F (BPF) may act as endocrine disruptors. In this context, the present study aimed to evaluate the impact of MPs or BPF on the reproductive health and fetal development in pregnant Wistar rats. Dams were orally exposed from gestational day (GD) 1 to GD18 to vehicle (control group), polyethylene MPs (50 mg/kg/day), or BPF (10 μ g/kg/day). Maternal body weight (BW) gain and food intake were monitored at two-days intervals along pregnancy. At necropsy (GD19), maternal glycemia was assessed and a fertility test was performed to determine the number of corpora lutea, and the implantation and resorption sites. Additionally, fetal and placental weights were recorded. Finally, fetal livers were examined for the presence of MPs by fluorescence microscopy. Dams exposed to MPs or BPF showed decreased BW gain throughout gestation. Moreover, MPs exposure reduced maternal food intake. In both MPs- and BPF-exposed groups, pre-implan-

tation embryo losses and glycemia were increased compared with controls. MPs were detected in fetal liver from MPs-exposed group, evidencing placental translocation. No significant changes were observed in fetal or placental weights. These findings suggest that oral exposure to polyethylene MPs or BPF during gestation impaired reproductive performance and induced nutritional and metabolic alterations. Ongoing research will bring light on the mechanisms underlying these effects.

356. P20-04. DIAGNOSIS OF HEREDITARY BREAST AND OVARIAN CANCER: FIRST COHORT STUDY IN SALTA

Ana Sol Fachini¹, Camila Ximena Peñalva², Sofía de La Fuente³, Andrea Quispe⁴, Ivanna Lopez⁵, Nora Reynaga⁶, José Dipierri⁷, Pablo Isa⁸, Nicolás Trigo⁹, Carlos David Brunque¹⁰, Marisol Delea¹¹, Ramiro Poma¹², María Paola Zago¹³

1. Hospital Público Materno Infantil de Salta; Unidad de Conocimiento Traslacional Hospitalaria-CONICET

2. Hospital de Alta Complejidad El Calafate - SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

3. Hospital de Alta Complejidad El Calafate - SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica

4. Hospital Público Materno Infantil de Salta; Unidad de Conocimiento Traslacional Hospitalaria - CONICET

5. Hospital Público Materno Infantil de Salta; Unidad de Conocimiento Traslacional Hospitalaria - CONICET

6. Hospital Público Materno Infantil de Salta; Unidad de Conocimiento Traslacional Hospitalaria - CONICET

7. Hospital Público Materno Infantil de Salta; -

8. Hospital Público Materno Infantil de Salta; Unidad de Conocimiento Traslacional Hospitalaria - CONICET

9. Argenyx

10. Hospital de Alta Complejidad El Calafate - SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

11. Hospital de Alta Complejidad El Calafate - SAMIC; Unidad de Conocimiento Traslacional Hospitalaria Patagónica - CONICET

12. Hospital Público Materno Infantil de Salta; Unidad de Conocimiento Traslacional Hospitalaria - CONICET

13. Hospital Público Materno Infantil de Salta; Unidad de Conocimiento Traslacional Hospitalaria - CONICET

sof9297@gmail.com

Hereditary breast and ovarian cancer (HBOC) syndrome is primarily associated with pathogenic variants in BRCA1/2, including genetics variants and copy number variants (CNVs), although other genes may also be involved. A retrospective study was conducted on 26 patients with clinically suspected HBOC treated at the Hospital Publico Materno Infantil. Inclusion criteria were diagnosis before the age of 50 and a family history of breast or ovarian cancer. NGS was initially performed focusing on HBOC-related genes, and MLPA was applied to patients with negative results to detect large BRCA1/2 rearrangements. Among the clinical variables considered, we included age at diagnosis and tumor subtype, among others. Using a genomic diagnostic strategy (NGS and/or MLPA), 4/26 patients (15.4%) were found to carry pathogenic or likely pathogenic variants in the MSH2 and BRCA1/2 genes, including 2 CNVs. In addition, 4 VUS (15.4%) were identified, distributed as follows: ATM (3/26) and POT1 (1/26). No variants were detected in 18/26 patients (69.2%). The mean age at diagnosis was 37 years, and 21% of tumors were classified as triple negative. These findings from the first cohort studied in Salta highlight the importance of incorporating genomic and cytogenomic analyses into the diagnostic approach. This study demonstrates the feasibility of implementing genetic testing in a public hospital and underscores the need for complementary methodologies to optimize the detection of pathogenic variants. Expanding this approach to larger cohorts will help refine diagnostic and therapeutic strategies and support the development of more equitable screening programs for hereditary breast and ovarian cancer.

357. P20-05. LUPEOL AS A NATURAL INHIBITOR OF CLOSTRIDIODES DIFFICILE SPORE GERMINATION

Florencia Antonella Musso¹, Franco Caram², Fernando Trejo³, Pablo Fernando Pérez⁴, Alan Talevi⁵, Carolina Bellera⁶, María Belén Faraoni⁷

1. INQUISUR - CONICET - UNS; Laboratorio de Productos Naturales y Análogos Bioactivos (PRONABIO)

2. CONICET, Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP); Laboratorio de Investigación y Desarrollo de Bioactivos (LIDeB)

3. Centro de Investigación y Desarrollo en Ciencia y Tecnología de los Alimentos (CIDCA) - CONICET- UNLP- CIC; Instituto de Ciencias de la Salud. Universidad Nacional Arturo Jauretche

4. CONICET- UNLP- CIC; Centro de Investigación y Desarrollo en Ciencia y Tecnología de los Alimentos (CIDCA)

5. CONICET, Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP); Laboratorio de Investigación y Desarrollo de Bioactivos (LIDeB)

6. CONICET, Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP); Laboratorio de Investigación y Desarrollo de Bioactivos (LIDeB)

7. INQUISUR - CONICET - UNS - CIC; Laboratorio de Productos Naturales

florencia.musso@uns.edu.ar

Triterpenes, particularly the lupane-type, are promising natural products due to their medicinal properties (e.g., antidiabetic, anti-inflammatory, antiarthritic, antioxidant, and anti-infective effects). Research focuses on assigning biological activity and obtaining these compounds for biological validations. This work aimed to: 1) select triterpene inhibitors of the germination of the nosocomial pathogen *Clostridioides difficile* in silico, 2) optimize their isolation and purification and, 3) verify their in vitro activity. An in-silico screening based on machine learning identified lupeol as a potential inhibitor of *C. difficile* spore germination. This prompted further improvements in the isolation and purification of lupeol from *Chuquiraga erinacea* ethanolic extracts using column chromatography with AgNO₃ (10%) impregnated flash silica and mobile phase gradients (CH₂Cl₂: MeOH). The in vitro anti-germinant activity was tested on spores of two *C. difficile* strains (VPI 10463 and ALCD3) stimulated with the germinant taurocholate in the presence or not of lupeol at different concentrations. The proportions of bright (non-germinated) and dark (germinated) spores relative to the total number of spores was microscopically evaluated. The optimized method significantly improved lupeol yield by 37.5% while reducing solvent use. In vitro assays using strains VPI 10463 and ALCD3, demonstrated anti-germinant activity of lupeol at 500 µM. Specifically, the proportion of non-germinated spores remained high in the presence of lupeol (79% in ALCD3 and 66% in VPI 10463), whereas values in controls without lupeol were 33% and 13%, respectively. Improvement of lupeol purification and its demonstrated anti-germinant activity support its development as a new antimicrobial therapeutic.

358. P20-06. STUDYING NEDP1 DELETION ACROSS BIOLOGICAL MODELS: FROM DECREASED SURVIVAL UPON STRESS IN INVERTEBRATES TO ALTERED ERYTHROPOIESIS, LIVER FIBROSIS AND PERINATAL LETHALITY IN MICE

Ivana Marcela Linenberg¹, Sebastian Giusti², Mariana Erdozia³, Nara Muraro⁴, Luciana F Godoy⁵, Martin Jofré⁶, Daniel Hochbaum⁷, Damian Refojo⁸

1. IBioBA-CONICET-MPSP; Neurobiología Molecular

2. IBioBA-CONICET-MPSP; Neurobiología Molecular

3. IBioBA-CONICET-MPSP; Neurobiología Molecular

4. IBioBA-CONICET-MPSP; Neurobiología del sueño

5. CEBBAD-UMAI-CONICET; Biología del Desarrollo

6. CEBBAD-UMAI-CONICET; Biología del Desarrollo

7. CEBBAD-UMAI-CONICET; Biología del Desarrollo

8. IBioBA-CONICET-MPSP; Neurobiología Molecular

ivanamlinen@gmail.com

Nedd8 belongs to the Ubiquitin-like protein family. Like Ubiquitin, Nedd8 covalently binds to its target proteins through a conjugation cascade mediated by specific enzymes, a process called neddylation. This modification is reversible and controlled by two deneddylases: the COP9 signalosome, which removes Nedd8 from Cullins—the best-characterized substrates—and Nedp1, the main protease responsible for deneddylating non-Cullin proteins. The physiological significance of Nedp1, and of non-Cullin neddylation in general, has long been debated. Using transgenic invertebrate models, we demonstrate that the loss of function of Nedp1 orthologue negatively affects survival in *D. melanogaster* and that Nedp1 confers resistance to both *D. melanogaster* and *C. elegans* upon stress conditions. In mice, Nedp1 deletion proved essential for viability, as knockout (KO) mice displayed perinatal lethality. Many Nedp1 KO embryos exhibited hepatic abnormalities like multifocal necrosis, increased fibrosis, and mRNA upregulation of fibrotic and inflammatory markers. Furthermore, RT-qPCR analysis revealed profound downregulation of erythroid regulators (Gata1, Tal1, Klf1, Bcl11a) and their targets involved in hemoglobin synthesis and membrane organization (Hbb-b, Ahsp, Slc4a1, Ermap), consistent with severe anemia and disrupted erythropoiesis. We show for the first time that Nedp1 is essential in a murine model, indicating its biological relevance in mammals. These findings contribute to understanding the physiological relevance of neddylation in general and of Nedp1, in particular, across diverse contexts and models.

359. P20-07. N-GLYCOSYLATION MODULATES THE INTERACTION OF THE GLIOBLASTOMA ASSOCIATED PROTEINS DDR1 AND IGF1R

Gretel Magali Ferreira¹, Jeremías Omar Castillo², Selene Rojo³, Valeria Inés Segatori⁴, Mariano Rolando Gabrì⁵

1. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional

2. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional

3. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional

4. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional

5. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional

maguiferreira2@gmail.com

Glioblastoma is the most aggressive and common primary brain tumor in adults, characterized by high invasiveness, therapy resistance and poor prognosis. The Discoidin Domain Receptor Tyrosine Kinase 1 (DDR1) and the Insulin-like Growth Factor 1 Receptor (IGF1R) are reported as heavily glycosylated membrane proteins, frequently overexpressed in glioblastoma and associated with tumor progression. DDR1 is activated upon binding to its natural ligand, collagen, or triggered by crosstalk with other receptors promoting extracellular matrix remodeling and cell migration. Conversely, IGF1R promotes proliferation, survival and resistance to apoptosis. The potential crosstalk between them is described; however the influence of glycosylation in modifying this interaction remains uncharacterized. The aim of this work is to evaluate the role of N-glycosylation in this interaction. In first place, by protein coimmunoprecipitation we confirmed the physical interaction between DDR1 and IGF1R using the high-grade glioblastoma cell line A172. Complementary immunofluorescence assays revealed DDR1 activation and nuclear translocation following IGF1 stimulation, suggesting functional receptor crosstalk and a potential feedback loop. Interestingly, the IGF1R/DDR1 interaction was reduced following treatment with Swainsonine, an inhibitor of hybrid and complex-type N-glycosylation. Moreover, this treatment also decreased IGF1-induced cell migration, indicating that glycosylation is critical for IGF1R activation and the subsequent downstream motility signaling. These results provide novel insights and, for the first time, highlight the critical role of N-glycans in regulating the interaction between DDR1 and IGF1R, as well as their crosstalk in glioblastoma.

360. P20-08. CROSS-SECTIONAL ANALYSIS OF THE INSTI-

TUTIONAL RARE DISEASE REGISTRY: PRELIMINARY DESCRIPTIVE COHORT IN ARGENTINA

Ana Braslavsky, Marcelina Carretero, Marcelo Martín Serra, Soledad Kleppe, Marcela Alejandra Martínez Von Scheidt, Emiliano Rossi, Ignacio Martín Bluro, María Eugenia Knorre, Ana Laura Miceli, María Julieta Argüero, Lucila Bayarri, Claudio Alberto Salvador Parisi, Rocío Celeste Moreno Rodríguez, María Adela Aguirre, Erika Bárbara Brulc, María Soledad Saez, Andrea Laura Paissan, Guillermo Alonso, Guadalupe Amparo Geli, Romina Inés Armando, Juan Ignacio Appendino, Roberta Amelia Calvano, Diego Andresik, Ernestina Angarola, Pablo Andrés Lobos, Luisa Chantada, Laura Noelia Bono, María Lourdes Posadas-Martínez

Hospital Italiano; HI/IMTIB

ana.braslavsky@hospitalitaliano.org.ar

Background: Rare diseases (RD) are individually uncommon but collectively significant, representing a major clinical and public health challenge. In Argentina, systematic data collection across RD remains limited. Aim: To describe demographic and clinical characteristics of patients included in an Institutional Rare Disease Registry at a university hospital in Buenos Aires. Methods: We conducted a cross-sectional study including all patients enrolled up to September 2025 in a REDCap-based RD registry. Diagnoses were coded using Orphacode. Descriptive analyses were performed in STATA 13. Results: A total of 1,359 patients from 15 diseases across 9 RD units were included, listed in descending order of frequency: Amyloidosis, Congenital adrenal hyperplasia due to 21-hydroxylase deficiency, Sarcoidosis, Phacomatoses, Eosinophilic gastrointestinal disorders, Pulmonary arterial hypertension, Inborn errors of immunity, Wilson disease, and Hirschsprung disease. Median age at symptom onset was 54 years [interquartile range (IQR) 33.5–71.4], with equal sex distribution. Forty-five percent (N=609) were Hispanic or Caucasian. Sixty-four percent (N=870) had postnatal symptom onset, and a similar proportion (64%, N=878) received a postnatal diagnosis. Median time from symptom onset to diagnosis was 6 months (IQR 1–20). Forty-one percent (N=555) received specific treatment, and 15% (N=201) died. Conclusions: This registry consolidates data from multiple RD units and highlights the heterogeneity of conditions observed in a single referral centre. These findings provide the basis for future longitudinal analyses. Given the recent implementation, this study represents a preliminary report based on ongoing data collection and expansion.

361. P20-09. CHLORPYRIFOS AND CYPERMETHRIN PROMOTE EPITHELIAL-MESENCHYMAL TRANSITION AND STEMNESS IN HUMAN ENDOMETRIAL CANCER CELLS

Giselle Fainberg¹, Marianela Lasagna², Lucía Enriquez³, Rocío Natalia Cardozo⁴, José Luis Rangel⁵, Florencia Chiappini⁶, Mariana Mardirosian⁷, Alicia Klecha⁸, Claudia Cocca⁹, Mariel Núñez¹⁰

1. Laboratorio de Radioisótopos, Cátedra de Física, FFyB, UBA; Instituto de Investigaciones Farmacológicas (ININFA), UBA-CONICET; Laboratorio de Contaminantes ambientales y trastornos endócrinos

2. Laboratorio de Radioisótopos, Cátedra de Física, FFyB, UBA; Instituto de Investigaciones Farmacológicas (ININFA), UBA-CONICET; Laboratorio de Contaminantes Ambientales y Trastornos Endócrinos

3. Laboratorio de Radioisótopos, Cátedra de Física, FFyB, UBA; Instituto de Investigaciones Farmacológicas (ININFA), UBA-CONICET; Laboratorio de Contaminantes Ambientales y Trastornos Endócrinos

4. Laboratorio de Radioisótopos, Cátedra de Física, FFyB, UBA; Instituto de Investigaciones Farmacológicas (ININFA), UBA-CONICET; Laboratorio de Contaminantes Ambientales y Trastornos Endócrinos

5. Laboratorio de Radioisótopos, Cátedra de Física, FFyB, UBA; Laboratorio de Contaminantes Ambientales y Trastornos Endócrinos

6. Departamento de Bioquímica Humana, FMed. UBA; Laboratorio de Efectos Biológicos de Contaminantes Ambientales

7. *laboratorio de Radioisótopos, Cátedra de Física, FFyB, UBA; Instituto de Investigaciones Farmacológicas (ININFA), UBA-CONICET; Laboratorio de Contaminantes Ambientales y Trastornos Endócrinos*
8. *Laboratorio de Radioisótopos, Cátedra de Física, FFyB, UBA; ---*
9. *Laboratorio de Radioisótopos, Cátedra de Física, FFyB, UBA; Instituto de Investigaciones Farmacológicas (ININFA), UBA-CONICET; Laboratorio de Contaminantes Ambientales y Trastornos Endócrinos*
10. *Laboratorio de Radioisótopos, Cátedra de Física, FFyB, UBA; Instituto de Investigaciones Farmacológicas (ININFA), UBA-CONICET; Laboratorio de Contaminantes Ambientales y Trastornos Endócrinos*
giselfainberg@gmail.com

Background: Chlorpyrifos (CPF) and cypermethrin (CPM) are insecticides extensively used in agricultural and domestic settings. We previously demonstrated that both compounds induce proliferation in human endometrial cells through an ER α -dependent mechanism. **Aim:** To investigate whether CPF and CPM promote epithelial-mesenchymal transition (EMT) and enrichment of stemness-like phenotypes in ECC-1 endometrial cancer cells under short- and long-term exposure conditions. **Methods:** ECC-1 cells were exposed to CPF (0.05 and 25 μ M) or CPM (0.05 and 50 μ M) for 48 h or 20 d. Cell migration was assessed by wound-healing assay. Vimentin expression and β -actin subcellular localization were analyzed by immunofluorescence (48 h). Clonogenic and tumorsphere formation assays were performed after both exposure periods. **Results:** CPF 0.05 μ M and CPM 0.05 and CPM 50 μ M significantly increased migration ($p < 0.001$). All concentrations enhanced vimentin expression and β -actin polymerization foci. Short-term exposure showed that CPF 0.05 μ M promoted first-generation tumorsphere formation ($p < 0.05$), while CPM 0.05 μ M increased second-generation tumorspheres ($p < 0.01$). After 20 d to exposure, only CPM 0.05 μ M enhanced clonogenicity, whereas CPF 0.05 and CPF 25 μ M increased both first- and second-generation tumorspheres ($p < 0.001$). CPM 0.05 μ M selectively increased second-generation tumorspheres ($p < 0.001$). **Conclusion:** Environmentally relevant concentrations of CPF and CPM promote cell migration, EMT-related changes, and stemness enrichment in ECC-1 cells. These findings suggest that exposure to these insecticides may contribute to cellular dedifferentiation processes, acting as potential risk factors for endometriosis or endometrial cancer.

362. P20-10. BIDIRECTIONAL INTERACTION BETWEEN CIRCADIAN SYSTEM AND METASTATIC DEVELOPMENT IN MICE

Guido Hokama¹, Ignacio Aiello², Ignacio Miguel³, Camila Sena⁴, Diego Golombek⁵, Carla Finkielstein⁶, Natalia Paladino⁷
 1. *Universidad Nacional de Quilmes; Laboratorio de Cronobiología*
 2. *Fralin Biomedical Research Institute; Integrated Cellular Responses Laboratory*
 3. *Universidad Nacional de Quilmes; Laboratorio de Cronobiología*
 4. *Universidad Nacional de Quilmes; Laboratorio de Cronobiología*
 5. *Universidad de San Andrés; Laboratorio Interdisciplinario del Tiempo y la Experiencia (LITERA)*
 6. *Fralin Biomedical Research Institute; Integrated Cellular Responses Laboratory*
 7. *Universidad Nacional de Quilmes; Laboratorio de Cronobiología*
 hokamaguido@gmail.com

Most physiological and behavioral functions exhibit daily rhythms synchronized with the light-dark (LD) cycle. Shift and night work desynchronize biological rhythms, promoting cancer development. Previously, we reported in a non-metastatic murine melanoma model that chronic jet-lag (CJL, 6-hour advance of the LD cycle every 2 days) increases tumor growth rate and disrupts rhythms in im-

mune parameters. Here, we evaluated a metastatic murine melanoma, which induces lung metastasis, in two circadian desynchronization models: CJL and Per2bdrn1 mutant mice. We observed an increased metastatic development in both desynchronized mice. Regarding immune system, we found daily patterns in lung macrophage levels under LD: M1 (pro-inflammatory) cells peak at the late night, while M2 (anti-inflammatory) peak at the early night. These patterns were disrupted in desynchronized mice. On another hand, the deregulation of clock-related parameters has been observed in cancer patients, therefore we evaluated if metastasis development alters body rhythms. We observed a disruption in temperature rhythms and a decrease in the strengths of locomotor activity rhythms. These findings show a bidirectional interaction between circadian system and metastatic process: circadian desynchronization promotes metastatic development, maybe in part through immune system modulation, while the circadian system itself gets worse during tumor progression which could initiate a vicious cycle that facilitates tumor growth. These results are relevant to design chrono-immunotherapies, since their success could depend on the patient's circadian desynchronization state and the daily patterns of the immune target.

363. P20-11. LACTOBIONIC ACID REVERSES DEHP-INDUCED OXIDATIVE STRESS IN MAMMARY ADENOCARCINOMA CELLS

Pablo Pérez¹, Tamara Silva², Florencia Vera³, Ideal Negri⁴, Jorge Mukdsi⁵, Silvina Gutiérrez⁶
 1. *Facultad de Ciencias Médicas-UNC. INICSA-CONICET; Centro de microscopía electrónica*
 2. *Facultad de Ciencias Médicas- UNC; Centro de microscopía electrónica.*
 3. *Facultad de Ciencias Médicas- UNC; Centro de microscopía electrónica*
 4. *Hospital Nacional de Clínicas- FCM-UNC; Servicio de patología*
 5. *Facultad de Ciencias Médicas- UNC; Centro de microscopía electrónica*
 6. *Facultad de Ciencias Médicas- UNC. INICSA-CONICET; Centro de microscopía electrónica*
 pabloperrez@cmeffcm.uncor.edu

The di(2-ethylhexyl) phthalate (DEHP) is an anthropogenic endocrine disruptor correlated with risk factors for endocrine pathologies, including breast cancer. Although its action is linked to hormonal deregulation, recent studies suggest that phthalate exposure also induces oxidative stress. Our objective was to evaluate whether DEHP induces oxidative toxicity and promotes tumor progression in mammary adenocarcinoma cells, and to explore the use of lactobionic acid (LAC) as a mitigating strategy. LMM3 cells (murine mammary adenocarcinoma) were treated for 24h with DEHP (0.5 and 1 μ M), alone or in co-administration with LAC (1mM). ROS production was quantified with the DCF-DA probe by flow cytometry and immunofluorescence. Acridine orange staining was performed to determine damage and acidic vesicle accumulation. Additionally, the expression of ki67 and MMP-2 was evaluated by immunofluorescence. Exposure to DEHP significantly increased ROS production in a dose-dependent manner (48% and 81% for 0.5 and 1 μ M, respectively), as well as cellular damage and acidic vesicle accumulation. DEHP 0.5 μ M induced cell proliferation showing values of 67.66 $\pm$ 1.0% vs. control 49.8 $\pm$ 2.8% and increased the expression of the metalloproteinase MMP-2 at both concentrations. LAC co-administration reversed the induction of ROS, reduced MMP-2 expression to basal levels, and mitigated the proliferation induction by DEHP. These findings suggest that DEHP promotes mammary tumor progression by inducing oxidative stress, proliferation, and invasion, and that lactobionic acid could reverse these effects, validating its potential as a mitigating strategy.

POSTERS 21 - SAIC - ONCOLOGÍA 3

DATE & TIME: 20/11/2025 9:00 - 10:30 H

Chairs: Alejandro Nicola Candia, Constanza Arriola Benítez, Pedro Carriere

364. P21-01. NORCANTHARIDIN SUPPRESSES TUMOR GROWTH, RECURRENCE, AND CSC-DRIVEN METASTASIS IN TRIPLE-NEGATIVE BREAST CANCER

Lizeth Aixa Ariza Bareño¹, Andrés Bechis², Diego Javier Britz Neira³, Luciana Cañonero⁴, María Giselle Peters⁵, Laura B. Todaro⁶, Alejandro Urtreger⁷

1. Instituto de Oncología Ángel H Roffo; Área de investigación, Departamento de Biología Celular

2. Instituto de Oncología Ángel H Roffo; Área de investigación, Departamento de Biología Celular

3. Instituto de Oncología Ángel H Roffo; Área de investigación, Departamento de Biología Celular

4. Instituto de Oncología Ángel H Roffo; Área de investigación, Departamento de Biología Celular

5. Instituto de Oncología Ángel H Roffo; Área de investigación, Departamento de Biología Celular

6. Instituto de Oncología Ángel H Roffo; Área de investigación, Departamento de Biología Celular

7. Instituto de Oncología Ángel H Roffo; Área de investigación, Departamento de Biología Celular

lisa19111@hotmail.com

Triple-negative breast cancer (TNBC) is an aggressive subtype lacking hormone receptors and HER2 overexpression, leaving patients without targeted therapies. Norcantharidin (NCTD), a natural derivative of cantharidin, has demonstrated antitumor effects in several malignancies but remains underexplored in TNBC. Here, we investigated its therapeutic potential using both in vitro and in vivo approaches. NCTD showed potent antiproliferative activity in TNBC cell lines (MDA-MB231, HS578T, 4T1), with IC50 values ranging from 15 to 56 μ M, and induced apoptosis and autophagy, as confirmed by flow cytometry, fluorescence microscopy, and Western blot. In vivo, systemic administration (2.5-3.75 mg/kg) significantly reduced tumor size, suppressed local recurrence, and decreased metastasis ($p < 0.05$). Histological analyses showed more differentiated epithelial-like morphology, defined tumor borders, and a marked reduction in Ki67 (~50% vs. ~80% in controls), supporting its antiproliferative effect. Importantly, NCTD suppressed CSC-driven metastasis in vivo, indicating direct CSC targeting, as evidenced by impaired oncosphere formation in vitro. To enhance treatment effectiveness, we conducted combination studies with doxorubicin or paclitaxel, which showed additive rather than synergistic effects. These findings suggest that the clinical potential of NCTD relies on its activity as a single agent, where it maintains remarkable efficacy. Altogether, our results establish NCTD as a promising therapeutic candidate for TNBC, particularly due to its ability to suppress tumor growth, prevent recurrence, and modulate CSC biology. Further research is required to elucidate the molecular mechanisms underlying its activity.

365. P21-02. CHLORPYRIFOS AND TAMOXIFEN CO-PRE-TREATMENT PROMOTES STEM-LIKE PHENOTYPE AND UPREGULATION OF ANTI-ESTROGEN THERAPY RESISTANCE MARKERS IN ERA BREAST CANCER CELLS

Marianela Soledad Lasagna¹, Lucía Enriquez², Mariana Mardirosian³, Rocio Natalia Cardozo⁴, Gabriela Martín⁵, Power Pablo⁶, Mariel Núñez⁷, Cocca Claudia⁸

1. UBA-CONICET; Instituto de Química y Fisicoquímica Biológicas "Prof. Alejandro C. Paladini"

2. UBA-CONICET; Instituto de Química y Fisicoquímica Biológicas "Prof. Alejandro C. Paladini"

3. UBA-CONICET; Instituto de Química y Fisicoquímica Biológicas "Prof. Alejandro C. Paladini"

4. UBA-CONICET; Laboratorio de Radioisótopos, Cátedra de Física, Facultad de Farmacia y Bioquímica

5. UBA-CONICET; Laboratorio de Radioisótopos, Cátedra de Física, Facultad de Farmacia y Bioquímica

6. UBA-CONICET; Departamento de Microbiología, Inmunología y Biotecnología, Facultad de Farmacia y Bioquímica

7. UBA; Laboratorio de Radioisótopos, Cátedra de Física, Facultad de Farmacia y Bioquímica

8. UBA-CONICET; Instituto de Química y Fisicoquímica

Biológicas "Prof. Alejandro C. Paladini"
marianelalasagna86@gmail.com

Endocrine therapy (ET) is the first-line treatment for hormone receptor positive breast cancer but about 30% of patients develop resistance. The loss of estrogen receptor α (ER α) expression is critical in this process. Histone deacetylase 1 (HDAC1) interacts with ER α and suppresses its transcriptional activity. Chlorpyrifos (CPF), is an endocrine disruptor pesticide that promotes a stemness phenotype and triggers molecular mechanisms involved in ET resistance. The goal of this study is to assess whether CPF induces tamoxifen (TAM) resistance by modulating RE α expression through HDAC1 regulation. We analyzed public databases of breast cancer patients and performed in vitro experiments using the MCF-7 cell line. We evaluated whether the co-pretreatment with CPF (0.05 or 50 μ M) and TAM (0.5 μ M) modulates stemness and ET resistance markers. We found that CPF+TAM selects cells that exhibit increased clonogenicity ($p < 0.001$), enhanced mammosphere-forming ability ($p < 0.01$), and upregulates the stemness markers CD44 ($p < 0.001$), NANOG ($p < 0.001$) and POU5F1 ($p < 0.001$) while decreasing CD24 ($p < 0.001$) in cells grown in monolayer. This subpopulation shows higher levels of mRNA and elevated protein expression of RE α ($p < 0.01$) and HDAC1 ($p < 0.01$). Finally, we identified a resistance and stemness marker signature induced by CPF+TAM that closely resembles the profile observed in the dataset of patients who acquired tamoxifen resistance. Our findings show that CPF promotes an undifferentiated basal-like cell phenotype that contributes to TAM resistance, reinforcing the need for global restrictions to safeguard public health.

366. P21-03. EXPRESSION OF AR, FGF2 AND WNT6 IN LUMINAL B BREAST CANCER SUBSETS: IMPLICATIONS FOR MIFEPRISTONE RESISTANCE

Marcela Coianis¹, Virginia Figueroa², Silvia Vanzulli³, Leo Saldain⁴, Paola Rojas⁵, Claudia Lanari⁶, Caroline Lamb⁷

1. Instituto de Biología y Medicina Experimental (IBYME), CONICET, Argentina; Carcinogénesis hormonal

2. Instituto de Biología y Medicina Experimental (IBYME), CONICET, Argentina; Carcinogénesis hormonal

3. Instituto de Biología y Medicina Experimental (IBYME), CONICET, Argentina; Carcinogénesis hormonal

4. Instituto de Biología y Medicina Experimental (IBYME), CONICET, Argentina; Carcinogénesis hormonal

5. Instituto de Biología y Medicina Experimental (IBYME), CONICET, Argentina; Carcinogénesis hormonal

6. Instituto de Biología y Medicina Experimental (IBYME), CONICET, Argentina; Carcinogénesis hormonal

7. Instituto de Biología y Medicina Experimental (IBYME), CONICET, Argentina; Carcinogénesis hormonal

marcelacoianis@hotmail.com

Breast cancer is clinically classified by estrogen receptor alpha (ER) and progesterone receptor (PR) status, with PR comprising PRA and PRB isoforms. According to the prevailing PR isoform, tumors are categorized as PRA-high (PRA-H) or PRB-high (PRB-H), the latter associated with resistance to mifepristone (antiprogesterin). We previously demonstrated in cell lines that PRB-H models exhibit elevated nuclear fibroblast growth factor 2 (FGF2), androgen receptor (AR), and WNT6 expression relative to PRA-H. Both PRB-H and ER+PR- subsets are included within luminal B tumors which are also linked to adverse outcomes. This study aimed to validate these findings in human ER+ breast cancer samples and assess associations among AR, FGF2, and WNT6 expression. Using immunohistochemistry, we found AR levels significantly higher in ER+PR- and PRB-H tumors compared to PRA-H ($p = 0.01$ and $p = 0.02$, respectively), with a rising trend in ER+PR+ versus ER+PR-. Notably, nuclear AR and FGF2 showed a positive correlation in PRB-H tumors. In samples with $\geq 5\%$ nuclear FGF2, AR levels were elevated in both PRB-H ($p = 0.05$) and ER+PR- ($p = 0.04$) groups. Western blot confirmed this association across ER+ subtypes ($p = 0.006$). WNT6 expression was also enriched in PRB-H and ER+PR- tumors compared to PRA-H. Our findings reveal that ER+PR- and PRB-H tumors consistently exhibit higher or trending higher levels of AR, nuclear FGF2, and

WNT6. These results provide evidence for exploring therapeutic strategies targeting AR and WNT signaling in ER+PR-AR+ and ER+PRB-H AR+ tumor subsets.

367. P21-04. HER INHIBITION REDUCES VIABILITY IN TRIPLE-NEGATIVE BREAST CANCER CELLS LINES, INCLUDING GROWTH INHIBITION OF CANCER STEM CELL

Diego Javier Britez Neira¹, Andrés Bechis², Lizeth Aixa Ariza Bareño³, Luciana Cañonero⁴, Tabatha Aylen Barlaro⁵, Alejandro Jorge Urtreger⁶, Laura Beatriz Todaro⁷

1. Instituto de Oncología "Ángel H. Roffo"; Área de Investigación, Biología Celular
 2. Instituto de Oncología "Ángel H. Roffo"; Área de Investigación, Biología Celular
 3. Instituto de Oncología "Ángel H. Roffo"; Área de Investigación, Biología Celular
 4. Instituto de Oncología "Ángel H. Roffo"; Área de Investigación, Biología Celular
 5. Instituto de Oncología "Ángel H. Roffo"; Área de Investigación, Biología Celular
 6. Instituto de Oncología "Ángel H. Roffo"; Área de Investigación, Biología Celular
 7. Instituto de Oncología "Ángel H. Roffo"; Área de Investigación, Biología Celular
- djbritezneira@gmail.com

The human epidermal growth factor receptors (HER) are a family of tyrosine kinases that play a crucial role in breast cancer progression. Lapatinib, a dual HER1 and HER2 tyrosine kinase inhibitor, is currently used for advanced HER2-positive breast cancer. Since we previously observed HER2 expression in cancer stem cells (CSCs) from some triple-negative and HER2-negative breast cancer cell lines, this study aimed to analyze the effect of HER inhibition on various tumor cell models and their CSC population. Treatment with Lapatinib significantly reduced cell viability in triple-negative breast cancer models (human HS578T and murine 4T1, LM38-LP), as well as in human hepatocellular carcinoma (Huh7) and prostate cancer (PC3) cell lines. Lapatinib also induced growth inhibition in oncospheres (CSC-enriched cultures) derived from HS578T and LM38-LP cells. Comparing the monoclonal antibodies Trastuzumab and Cetuximab effects, only Lapatinib and Cetuximab significantly reduced cell viability and oncosphere renewal. To evaluate the co-treatment effect with Lapatinib and the cellular differentiation agent all-trans retinoic acid (ATRA) on CSCs viability, we measured aldehyde dehydrogenase (ALDH) activity by flow cytometry and performed Hoechst efflux assays in the HS578T cell line. We observed a decrease in both CSC markers, particularly when HS578T cells received the combined treatment compared with either treatment alone. In addition, we observed a reduction in oncospheres diameters in 4T1, HS578T and HCC70 cell lines. These findings highlight the potential for repositioning Lapatinib as a therapeutic option beyond HER2-positive breast cancer, emphasizing its effect on the stem cell population.

368. P21-05. PRECLINICAL EVALUATION OF CELLULOSE-DERIVED MOLECULES AS NOVEL ANTICANCER AGENTS IN BREAST CANCER

Luciana Cañonero¹, Aldana M. Schey², Lizeth Ariza Bareño³, Andrés Bechis⁴, Diego Britez Neira⁵, Florencia Cámpora⁶, Beatriz E. Pava Gómez⁷, Ariel M. Sarotti⁸, Alejandra Suarez⁹, María Inés Mangione¹⁰, Rolando Spanevello¹¹, Marcela Villaverde¹², Laura B. Todaro¹³, Alejandro J. Urtreger¹⁴

1. Instituto de Oncología "A. H. Roffo", Universidad de Buenos Aires.; Área de Investigación, Biología celular y tumoral
2. Instituto de Oncología "A. H. Roffo", Universidad de Buenos Aires.; Área de Investigación, Biología celular y tumoral
3. Instituto de Oncología "A. H. Roffo", Universidad de Buenos Aires.; Área de Investigación, Biología celular y tumoral
4. Instituto de Oncología "A. H. Roffo", Universidad de Buenos Aires.; Área de Investigación, Biología celular y tumoral
5. Instituto de Oncología "A. H. Roffo", Universidad de Buenos Aires.; Área de Investigación, Biología celular y tumoral
6. Facultad de Ciencias Bioquímicas y Farmacéuticas, Uni-

versidad Nacional de Rosario-CONICET; Instituto de Química de Rosario

7. Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario-CONICET; Instituto de Química de Rosario

8. Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario-CONICET; Instituto de Química de Rosario

9. Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario-CONICET; Instituto de Química de Rosario

10. Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario-CONICET; Instituto de Química de Rosario

11. Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario-CONICET; Instituto de Química de Rosario

12. Instituto de Oncología "A. H. Roffo", Universidad de Buenos Aires; Área de Investigación, Unidad de Transferencia Genética

13. Instituto de Oncología "A. H. Roffo", Universidad de Buenos Aires; Área de Investigación, Biología celular y tumoral

14. Instituto de Oncología "A. H. Roffo", Universidad de Buenos Aires; Área de Investigación, Biología celular y tumoral

lucianacanono@gmail.com

Breast cancer is the leading cause of cancer-related deaths among women, highlighting the urgent need for novel therapies. Levoglucosenone, obtained from soybean husk pyrolysis, exhibits antiproliferative activity in breast cancer cells. Based on this scaffold, we synthesized derivatives to enhance its efficacy. Among more than twenty candidates, compounds 59A and 58A showed significantly lower IC50 values than the original compound ($4.76 \pm 2.1 \mu\text{M}$ and $3.99 \pm 1.3 \mu\text{M}$ vs. $12.23 \pm 0.5 \mu\text{M}$ in LM3 cells). Both induced apoptosis, reaching up 20.2% and 29.7% in LM3 cells and 34.4% and 48.9% in Hs57T cells for 58A and 59A, respectively. In vivo, systemic administration (4 mg/kg) reduced tumor growth, with stronger effects observed for 59A, consistent with its in vitro potency. In addition, the development of lung metastases was also reduced (median 8 [1-48], median 0 [0-5], and median 0.5 [0-4] for control, 59A, and 58A, respectively). Since both derivatives increased glucose consumption and lactate production ($p < 0.05$), we tested combinations with metabolic modulators. A clear synergistic effect was observed only with 2-deoxy-D-glucose (2-DG), confirmed by Chou-Talalay method (CI1), while their association with cisplatin consistently resulted in synergistic interactions (CI<1). Based on our findings, levoglucosenone derivatives 59A and 58A display strong antitumor activity, reduce metastatic potential, and enhance the effects of cisplatin and 2-DG. These findings highlight their translational relevance and support further preclinical evaluation as promising candidates for breast cancer therapy.

369. P21-06. PROAPOPTOTIC AND ANTIMIGRATORY EFFECTS OF THE COMBINATION OF APIGENIN AND GEFITINIB IN BREAST CANCER CELLS

Belen Berin¹, Julieta Cebón², Ana Sotelo³, Fernando Domínguez⁴, Viviana Blank⁵, María Troncoso⁶, Johanna Miquet⁷

1. Instituto de Química y Físicoquímica Biológicas (IQUI-FIB); Endocrinología molecular y carcinogénesis
 2. Instituto de Química y Físicoquímica Biológicas (IQUI-FIB); Endocrinología molecular y carcinogénesis
 3. Instituto de Química y Físicoquímica Biológicas; Endocrinología molecular y carcinogénesis
 4. Instituto de Química y Físicoquímica Biológicas (IQUI-FIB); Endocrinología molecular y carcinogénesis
 5. Instituto de Química y Físicoquímica Biológicas (IQUI-FIB); Oncología y transducción de señales
 6. Instituto de Química y Físicoquímica Biológicas (IQUI-FIB); Glicobiología tumoral
 7. Instituto de Química y Físicoquímica Biológicas (IQUI-FIB); Endocrinología molecular y carcinogénesis
- beleneliana30@gmail.com

New targets for breast cancer treatment are being investigated, including the epidermal growth factor receptor (EGFR). Gefitinib is an EGFR inhibitor that has been proposed for the treatment of certain types of breast cancer. Apigenin is a natural flavone shown to modulate EGFR expression and activation and to exert anticancer effects in different cell lines. The objective of the present work was to evaluate the proapoptotic and antimigratory effects of gefitinib and apigenin, alone or in combination, in MDA-MB-231 (triple negative) and MCF-7 (luminal A) breast cancer cells. Acridine orange/ethidium bromide staining examined under a fluorescent microscope was used to evaluate apoptosis (only in MCF-7 cells). Cell migration was assessed by the scratch assay in both cell lines. Results were analyzed by ANOVA. Treatment with apigenin or gefitinib at two concentrations (5 and 10 μ M) induced apoptosis in MCF-7 cells. When the drugs were combined at equimolar combination, the effects on apoptosis were significantly higher than those of the drugs alone ($n=5$, $p<0.05$). For scratch assays, the drugs were used at low concentrations (0.2, 1 and 2 μ M) that proved not to affect cell growth. In both cell lines, the migration was lower in cells treated with the combination than in cells treated with the drugs alone, attaining statistical significance only for the lower concentration tested ($n=4-5$, $p<0.05$). In conclusion, the combination of apigenin with gefitinib had positive interaction on the proapoptotic and antimigratory effects in breast cancer cells, supporting its potential use as new therapy for breast cancer.

370. P21-07. RHEUMATOLOGICAL ADVERSE EVENTS IN IMMUNE-CHECKPOINT INHIBITORS TREATED ONCOLOGICAL PATIENTS. FIVE YEARS FOLLOW-UP

María Victoria Collado¹, María Natalia Gandur², Anabela Llanos³, Silvana Cugliari⁴, Mónica Castro⁵, Viviana Cuartero⁶, Valeria Cáceres⁷, Inés Califano⁸, Alejandra Baez⁹, Romina Cozzani¹⁰, Marcela Serrano¹¹, Marta Zerga¹², Stella Maris Ranuncolo¹³

1. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Servicio de Reumatología.
 2. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Unidad Funcional Clínica Urológica
 3. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Unidad Funcional de Sarcomas y Melanomas
 4. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Departamento de Hematología.
 5. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Unidad Funcional de Tórax.
 6. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Unidad Funcional de tumores Digestivos.
 7. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Unidad Funcional Tumores Femeninos
 8. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Servicio de Endocrinología
 9. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Departamento de Neurología.
 10. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Departamento de Dermatología
 11. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Departamento de Enfermería.
 12. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Departamento de Clínica Oncológica.
 13. Instituto de Oncología "Ángel H. Roffo". Facultad de Medicina. UBA.; Área Investigación.
- vicollado1978@gmail.com

454 patients were treated during 2019-2024. 100/454 received ICI [51 Male, Md (range) 55.4 (15-72) years old, 49 female 58.4 (14-81)], 44 had renal carcinoma, 28 melanoma, 10 bladder, 7 breast, 6 lung, 5 other cancers. 80/100 patients developed IMAEs, being 54/80 (68%) rIMAEs (36/54 associated with non-rheumatological IMAEs) and 25/80 (32%) developed non-rheumatological IMAEs exclusively. The most frequent IMAE was diarrhea (22). Among the rEAIM were arthralgia (20), arthritis (13), rheumatic polymyalgia (9), classified as grade 1 (23), grade 2 (24), grade 3 (25), grade 4

(6), grade 5 (2). The response to the IMAEs treatment was complete (57), partial (15) and no response (8) (2 of them died). Out of the 80 patients who developed IMAEs 38 (47%) were able to continue the ICI-therapy meanwhile 22 (27%) had to transitory discontinue the treatment and 20 (25%) had to permanently suspend it. Out of 44 renal cancer, 32/44 (72%) suffered IMAEs, being 50% rheumatological. 10/44 patients had previous autoimmune diseases and 50% of them suffered symptoms exacerbation during the ICI-therapy, but all of them were able to continue the treatment. Out of 28 melanoma patients 25/28 (89%) developed IMAEs being all of them rheumatological. The appropriate management of these IMAEs is important in order to secure the ICI therapy continuity and to improve the oncological patients' prognosis.

371. P21-08. HSP90 AS A BAD PROGNOSIS INDICATOR FOR BREAST CANCER PATIENTS: AN IN VITRO COMBINATION THERAPY AND BIOINFORMATIC APPROACH

Iara S. Santa Cruz¹, Mara Belotti¹, Malen Confalonieri¹, Florencia Delgado Rizzi², Mario D. Galigniana¹
 1. IBYME; Receptores Nucleares
 2. IFIBIO-Houssay, Fac. Medicina-UBA; Neurociencias de Sistemas
 iarasofiasantacruz@gmail.com

Hsp90 stabilizes the active conformation of cognate client proteins already exhibiting a stable tertiary structure, among them, steroid receptors and several oncoproteins. Cancer cells are dependent on chaperones given their elevated proteotoxic stress. Hsp90 inhibitors are chemotherapeutic agents that show strong effects in all hallmarks of cancer. Therefore, it is considered a promising molecular target for cancer treatment. High levels of HSP90 inhibition, leading to HSF1 activation, may enable malignancy in cancer and stromal cells. In this work we evaluate the effect of low concentrations of HSP90 inhibitor geldanamycin (GA) in combination with docetaxel (DTX) or tamoxifen (TAM) in two breast cancer cell lines: MDA-MB-231 and MCF7 respectively. Combination therapies with low concentrations of GA in this in vitro models indicate a promising therapeutic efficacy allowing for the same reduction in cell viability with lower concentrations of GA, which could help reduce unwanted side-effects. We also performed a bioinformatic analysis of TC-GA-BRCA transcriptome data (total of 1,098 cases), which showed that breast cancer patients with higher HSP90 expression have worse prognosis than patients with lower levels of HSP90. In addition, when this group of patients were treated with hormone therapy or radiotherapy, exhibited less life expectancy than patients treated with other treatments. This may indicate that high levels of HSP90 may be involved in resistance to hormonal and radiation therapy. Further molecular studies may help elucidate the mechanism behind the HSP90-heterocomplex regulation and its role on therapy resistance

372. P21-09. PI3K/AKT PATHWAY SUBTYPE-SPECIFIC ACTIVATION IN BREAST CANCER

Maira Garay^{*1}, Azul Muiño^{*2}, Micaela Vivanco³, Andrea Werbach⁴, Claudia Lanari⁵, Paola De Luca⁶, Federico Waisberg⁷, Virginia Novaro⁸, Florencia Cascardo⁹
 1. Instituto de Biología y Medicina Experimental (IBYME) - CONICET (*, contribuyeron de igual manera); Laboratorio de Proteínas Quinasas y Oncología Molecular
 2. Instituto de Biología y Medicina Experimental (IBYME) - CONICET (*contribuyeron de igual manera); Laboratorio de Proteínas Quinasas y Oncología Molecular
 3. Instituto de Biología y Medicina Experimental (IBYME) - CONICET; Laboratorio de Proteínas Quinasas y Oncología Molecular
 4. Instituto de Biología y Medicina Experimental (IBYME) - CONICET; Laboratorio de Proteínas Quinasas y Oncología Molecular
 5. Instituto de Biología y Medicina Experimental (IBYME) - CONICET; Laboratorio de Carcinogénesis Hormonal
 6. Instituto de Biología y Medicina Experimental (IBYME) - CONICET; Laboratorio de Proteínas Quinasas y Oncología

Molecular

7. Instituto Alexander Fleming (IAF) Buenos Aires, Argentina; Centro Mamario IAF

8. Instituto de Biología y Medicina Experimental (IBYME) - CONICET; Laboratorio de Proteínas Quinasas y Oncología Molecular

9. Instituto de Biología y Medicina Experimental (IBYME) - CONICET; Laboratorio de Proteínas Quinasas y Oncología Molecular

maagaray@gmail.com

The PI3K/AKT signaling is aberrantly activated in more than 50% of breast tumors, making PI3K and AKT attractive therapeutic targets. This study aimed to characterize expression and activation profiles of pathway components across luminal and HER2-positive breast cancer (BC) subtypes. Transcriptomic analysis of TCGA-BRCA data revealed significantly higher AKT1 and lower AKT2 expression in PAM50 HER2 tumors compared with Luminal A and Luminal B. HER2 tumors displayed an increased AKT1/AKT2 ratio and a negative correlation between isoform expression ($r = -0.42$; $p < 0.01$). Consistently, proteomic analysis of CPTAC data showed elevated AKT1 and reduced AKT2 protein levels in HER2 tumors ($n = 14$) compared with Luminal A ($n = 57$) and B ($n = 17$). While luminal tumors demonstrated a positive correlation between AKT1 and AKT2 proteins ($r = 0.24$; $p < 0.05$), no significant association was detected in HER2 tumors. Phosphoproteomic evaluation of CPTAC data indicated subtype-specific phosphorylation of AKT1 and AKT2, along with significantly increased phosphorylation of the downstream ribosomal protein S6 in HER2 tumors. Complementary analysis in an Argentinian cohort of early-stage BC patients showed that HER2-positive tumors ($n = 24$) exhibited a higher proportion of cells with nuclear AKT1, AKT2, and phosphorylated S6 compared with ER/PR-positive tumors ($n = 132$). Ongoing studies in luminal and HER2 BC cells aim to define the contribution of each AKT isoform within these subtypes. These findings reveal subtype-dependent expression and activation of PI3K/AKT components, underscoring their potential as prognostic biomarkers and for therapeutic stratification in BC.

373. P21-10. MECHANISMS OF RADIORRESISTANCE INDUCED BY RADIOTHERAPY IN ANAPLASIC THYROID CANCER

Susana Nieves¹, Antonella Pastini², Aldana Schey³, Estanislao Pavlik⁴, Pablo Vallecorsa⁵, Luciano Rossich⁶, Alfonsina Barrios⁷, Giselle Peters⁸, Stella Ranúnculo⁹, Pablo Menéndez¹⁰, Alejandro Urtreger¹¹, María Alejandra Dagrosa¹²

1. Comisión Nacional de Energía Atómica; Centro Oncológico de Medicina Nuclear. Instituto de Oncología "Ángel Roffo".

Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

2. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Ciudad Autónoma de Buenos Aires, Argentina; Centro Oncológico de Medicina Nuclear. Instituto de Oncología "Ángel Roffo". Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

3. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Áreas Investigación Terapia Radiante y Medicina Nuclear; Patología. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Argentina

4. Facultad de Ciencias Exactas y de la Ingeniería, Universidad Favaloro (UF). Ciudad Autónoma de Buenos Aires, Argentina; Centro Oncológico de Medicina Nuclear. Instituto de Oncología "Ángel Roffo". Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

5. Comisión Nacional de Energía Atómica; Centro Oncológico de Medicina Nuclear. Instituto de Oncología "Ángel Roffo". Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

6. Comisión Nacional de Energía Atómica; División de Radiodosimetría Biológica, Departamento de Mediciones Dosimétricas, Gerencia Seguridad Radiológica y Nuclear. Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

7. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Áreas Investigación Terapia Radiante y Medicina Nuclear; Patología. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Dirección de Terapia Radiante y Medicina Nuclear. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina

7. Instituto de Oncología "Ángel Roffo". Facultad de Medicina.

Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Áreas Investigación Terapia Radiante y Medicina Nuclear; Patología. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Argentina

8. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Ciudad Autónoma de Buenos Aires, Argentina;

Área de Investigación Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Argentina

9. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Ciudad Autónoma de Buenos Aires, Argentina;

Área de Investigación Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Argentina

10. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Dirección de Terapia Radiante y Medicina Nuclear. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina

11. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Ciudad Autónoma de Buenos Aires, Argentina; Área de Investigación Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Argentina

12. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Ciudad Autónoma de Buenos Aires, Argentina; Centro Oncológico de Medicina Nuclear. Instituto de Oncología "Ángel Roffo". Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina

susanaisabelnievas@gmail.com

Introduction: Anaplastic thyroid cancer (ATC) is an extremely aggressive form of thyroid cancer, known for its resistance to conventional therapies. After surgery, X-ray radiation therapy (XRT) and boron neutron capture therapy (BNCT) can be applied. Previously we have described a persistent number of oncospheres and an increase of the expression of some genes of TGF beta/ SMAD pathway which could reflect resistance and DNA repair after irradiation Objective: evaluate the activation of TGF beta/Smad pathway and the cancer stem cells (CSC) behavior after two different radiotherapies modalities. Methodology: Human ATC cells (8505C) were divided into the following groups: 1) Control (untreated); 2) X-rays; 3) NCT (neutron thermal irradiation); and 4) BNCT (irradiated with thermal neutrons and ¹⁰Boronophenylalanine). Cells were irradiated at 3 Gy. Gene and protein expression were analyzed after 2 h for NANOG and OCT-4, TGFbeta, Smad 2 and Smad 7 by RT-qPCR and immunocytochemistry. Induced cell death was studied by flow cytometry with propidium iodide and annexin V. Results: BNCT-treated monolayers showed lower pluripotency gene expression and fewer oncospheres than other treatments ($p < 0.001$). TGF beta and Smad 7 proteins were higher in all irradiated groups, indicating DNA repair. Furthermore, at 72 h BNCT showed ~49% apoptosis, nearly double than the other treatments. Conclusions: Despite radiotherapy, CSCs persistence and TGF beta/SMAD pathway activation may contribute with ATC radorresistance

374. P21-11. SELECTIVE ARTERIAL INJECTION OF MICROSPHERES IN RATS AND DISTRIBUTION IN RENAL CAPILLARY BED

Clara Sanchez Terrero¹, Silvia Vornetti², Juan Mazzaferri³, Luciano Parodi⁴, Johanna Martinez⁵, Natalia soledad Dominguez⁶, Andrés Vidal⁷, Miguel O Prado⁸, Gisela Rutty Solá⁹, Ana Cristina Zarlenga¹⁰, Jorge Cardoso Cúneo¹¹

1. Comisión Nacional de Energía Atómica; Centro Oncológico de Medicina Nuclear del Instituto Roffo (UBA-CNEA), Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina

2. Policlínico del docente, Lavalle 1974 C1051, CABA, Argentina; Servicio de Anatomía Patológica

3. Instituto de Oncología Ángel H. Roffo, Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina; Área diagnóstico por imágenes

4. Comisión Nacional de Energía Atómica, Centro Atómico Ezeiza, Cam. Real Presbítero González y Aragón 15, B1802 Ezeiza, Provincia de Buenos Aires, Argentina; División Bioterio

5. Policlínico del docente, Lavalle 1974 C1051, CABA, Argentina; Servicio de Anatomía Patológica
6. Instituto de Oncología Ángel H. Roffo, Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina; Área diagnóstico por imágenes
7. Comisión Nacional de Energía Atómica, Centro Atómico Ezeiza, Cam. Real Presbítero González y Aragón 15, B1802 Ezeiza, Provincia de Buenos Aires, Argentina; División Bioterio
8. Comisión Nacional de Energía atómica, Centro Atómico Bariloche, Av. Bustillo 9500, R8402AGP, S.C. de Bariloche, Argentina.; Departamento de Materiales Nucleares
9. Comisión Nacional de Energía Atómica; Centro Oncológico de Medicina Nuclear del Instituto Roffo (UBA-CNEA), Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina
10. Comisión Nacional de Energía Atómica; Centro Oncológico de Medicina Nuclear del Instituto Roffo (UBA-CNEA), Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina
11. Instituto Oncológico Ángel H. Roffo. (UBA) Av. San Martín 5481, C1417DTB, Buenos Aires, Argentina; Fundación José A. Balseiro, Centro Atómico Ezeiza, Cam. Real Presbítero González y Aragón 15, B1802 Ezeiza, Argentina; Servicio de Cirugía Gastroenterológica; Centro Oncológico de Medicina Nuclear del Instituto Roffo
clarasanchez@cnea.gov.ar

The Bariloche Atomic Centre produces microspheres (MS) for Chemo (CE) and radioembolization (RE). The Nuclear Medicine Oncology Centre, Ángel Roffo Institute (UBA-CNEA), studies characterization, vehiculization and their intravascular distribution in experimental models. The aim of this work is to determine the minimal calliper of needles for intraarterial injections and assess the microspheres distribution in a rat capillary bed. Materials and methods. MS for CE and RE (25-45µm) were used. In vitro. The passage of MS through 27-31 G needles was evaluated. In vivo. Wistar rats of 250-300g (Ezeiza Atomic Centre) were used under general anaesthesia. By median laparotomy, the abdominal aorta and both renal arteries were dissected. Selective vascular clamping and trans-aortic injection into left renal artery (unclamping after injection) of: 10mg CE-MS (n=4) or 40mg RE-MS (n=4) with patent blue (50%) using a 30G needle. Euthanasia and renal ablation were performed; samples were conserved in formalin 10% for histological analysis for CE-MS and X-ray detection for radiopaque RE-MS with digital mammograph. Results. In vitro. Both MS were successfully delivered through 27-30G needles without clogging. In vivo. The renal selectivity was confirmed by blue coloration. Histological analysis showed the absence of MS in renal pelvis, few MS in the medullar area, and more MS in the cortical area, inside renal intertubular arterioles. Radiological images demonstrated vascular filling of the entire renal artery tree. Conclusion. Both MS were correctly injected and successfully delivered using a 30G needle, as they were detected in the renal cortical area, embedded in arterioles.

375. P21-12. COMPARATIVE OXIDATIVE STRESS RESPONSES AS INDICATORS OF RADIOSENSITIVITY IN HUMAN CELL LINES

Laura Mazzitelli Fuentes¹, Enio Lima Jr², Marcelo Vasquez Mansilla³, Lara Negrin⁴, Elin Winkler⁵, Roberto D. Zysler⁶, Mariana Raineri⁷

1. Institute of Nuclear Technologies for Health Foundation (INTECNUS), National Atomic Energy Commission (CNEA), San Carlos de Bariloche, Argentina.; Laboratorio de Radiobiología
2. Institute of Nanoscience and nanotechnology (CNEA-CO-NICET) & Department of Magnetism and Magnetic Materials, San Carlos de Bariloche, Argentina.; Resonancias Magnéticas
3. Institute of Nanoscience and nanotechnology (CNEA-CO-NICET) & Department of Magnetism and Magnetic Materials, San Carlos de Bariloche, Argentina.; Resonancias Magnéticas
4. Institute of Nuclear Technologies for Health Foundation (INTECNUS), National Atomic Energy Commission (CNEA), San Carlos de Bariloche, Argentina.; Radiobiología

5. Institute of Nanoscience and nanotechnology (CNEA-CO-NICET) & Department of Magnetism and Magnetic Materials, San Carlos de Bariloche, Argentina.; Resonancias Magnéticas
6. Institute of Nanoscience and nanotechnology (CNEA-CO-NICET) & Department of Magnetism and Magnetic Materials, San Carlos de Bariloche, Argentina.; Resonancias Magnéticas
7. Institute of Nanoscience and nanotechnology (CNEA-CO-NICET) & Department of Magnetism and Magnetic Materials, San Carlos de Bariloche, Argentina.; Resonancias Magnéticas
laumazzitellifuentes@gmail.com

Ionizing radiation and iron oxide nanoparticles (IONPs) exert cytotoxic effects mainly through the generation of reactive oxygen species (ROS). While radiation produces ROS via water radiolysis, IONPs catalyze Fenton-like reactions, converging in oxidative stress-mediated cell damage. This study aimed to investigate whether intrinsic oxidative stress markers or nanoparticle-induced toxicity could predict radiosensitivity across different human cell lines. Radiosensitivity was evaluated by clonogenic survival after X-ray exposure (0, 2, and 4 Gy) in four cell lines: Ln229 (glioblastoma), A375 (melanoma), HEK293 (embryonic kidney), and T47D (breast carcinoma). The ranking observed was: Ln229 > A375 > HEK293 > T47D. Basal oxidative stress was assessed in untreated cells through three complementary assays: dichlorofluorescein diacetate (DCF-DA) for intracellular ROS, thiobarbituric acid reactive substances (TBARS) for lipid peroxidation, and thiol quantification (DTNB) for antioxidant status. These intrinsic redox profiles did not show a consistent correlation with the radiosensitivity ranking. In contrast, toxicity induced by IONPs revealed a strong agreement with radiosensitivity. When exposed to magnetite nanoparticles, Ln229 cells displayed the highest susceptibility, followed by A375, HEK293, and T47D, mirroring the clonogenic results. These findings suggest that nanoparticle-induced toxicity reflects radiosensitivity profiles more reliably than basal oxidative stress markers. This correlation highlights the potential of nanoparticle assays as a rapid and practical approach to anticipate tumor radiosensitivity, offering a complementary tool for radiobiology research and therapeutic planning.

376. P21-13. DESMOPRESSIN MODULATION OF THE NEURO-ENDOCRINE PHENOTYPE IN AN AGGRESSIVE PROSTATE CANCER MODEL

Nadia Safronchik¹, Martina Buset², Paula Alejandra Sacca³, Juan Garona⁴, Daniel Fernando Alonso⁵, Noelia Paula Di Giorgio⁶, Giselle Vanina Ripoll⁷

1. Departamento en Ciencia y Tecnología. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional
2. Departamento en Ciencia y Tecnología. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional
3. Instituto de Biología y Medicina Experimental (IBY-ME)-CONICET; Laboratorio de Química de Proteoglicanos y Matriz Extracelular
4. Departamento en Ciencia y Tecnología. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional
5. Departamento en Ciencia y Tecnología. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional
6. Departamento en Ciencia y Tecnología. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional
7. Departamento en Ciencia y Tecnología. Universidad Nacional de Quilmes; Centro de Oncología Molecular y Traslacional
nadiasafronchik@gmail.com

Prostate cancer (PCa) is the second cause of cancer-related death in males worldwide. While manageable in its early stages, standard androgen deprivation therapy often can induce

castration-resistant PCa (CRPC), which is associated with epithelial-mesenchymal transition (EMT), metastasis and neuroendocrine differentiation, resulting in more aggressive tumors. Our group has investigated desmopressin (dDAVP), a vasopressin analog peptide, with antiproliferative, antiangiogenic, and antimetastatic effects in various tumor models, including CRPC. Based on this evidence, our aim was to evaluate the effects of dDAVP on aggressive phenotype of PC-3 cells, a prostate adenocarcinoma cell line expressing NE markers. RT-qPCR analysis of EMT-associated gene expression, including VIM, CDH2, TWIST1, CDH1 and SDC1, revealed that 7-day dDAVP treatment was not enough to modulate EMT PC-3 cells. Additionally, sensitivity to the chemotherapeutic agent cisplatin was studied in PC-3 cells incubated with dDAVP for 13 days, showing an impairment in cisplatin IC50 from dDAVP treated cells. This suggests that the combination could allow lower doses of cisplatin without compromising therapeutic efficacy. Furthermore, the interaction with the vascular endothelium was analyzed by assessing the response of human microvascular endothelial cells (HMEC-1) to PC-3 cells conditioned medium (CM) treated or untreated with dDAVP, evaluating the in vitro cell migration. CM from untreated PC-3 cells slightly increased migration compared with control (without CM). Notably, CM from dDAVP-treated PC-3 cells reduced significantly cell migration ($p < 0.01$ vs CM untreated PC-3 cells). Altogether, these results emphasize the potential of dDAVP as a multi-faceted antitumor agent modulating CRPC aggressiveness.

377. P21-14. ROLE OF VOLTAGE-GATED PROTON CHANNEL (Hv1) ON INTRACELLULAR pH AND ENERGETIC METABOLISM OF T-CELL LYMPHOID NEOPLASMS

Finochietto Paulina¹, Veronica Milesi², Clara Ventura³

1. Instituto de Estudios Inmunológicos y Fisiopatológicos (IIFP), UNLP, CONICET, asociado CIC PBA, Facultad de Ciencias Exactas, La Plata, Argentina; Laboratorio de Canales Iónicos

2. Instituto de Estudios Inmunológicos y Fisiopatológicos (IIFP), UNLP, CONICET, asociado CIC PBA, Facultad de Ciencias Exactas, La Plata, Argentina; Laboratorio de Canales Iónicos

3. Instituto de Estudios Inmunológicos y Fisiopatológicos (IIFP), UNLP, CONICET, asociado CIC PBA, Facultad de Ciencias Exactas, La Plata, Argentina; Laboratorio de Canales Iónicos

paufinochietto@gmail.com

T-cell neoplasms include T-cell Acute Lymphoblastic Leukemia (T-ALL) and Peripheral T-cell Lymphomas (PTCLs), which differ in their origin, biology, and response to antimetabolite therapies. Metabolic reprogramming involves H⁺ overproduction, highlighting intracellular pH (pHi)-regulating proteins, such as the voltage-gated proton channel (Hv1). We investigated Hv1 expression (RNASeq, Cancer Cell Line Encyclopedia-CCLE), and function (patch-clamp) in T-ALL- and PTCL-derived cells, and examined the effects of Hv1 inhibition on cell viability (trypan blue exclusion assay), pHi (BCE-CF-AM dye), mitochondrial membrane potential (TMRM dye) and ROS production (DCF-2DA dye). RNASeq analysis (CCLE) revealed higher HVCN1 expression in T-ALL- versus PTCL-derived cells ($p < 0.05$). Patch-clamp recordings demonstrated Hv1-mediated currents in Jurkat (T-ALL) but not Karpas299 (PTCL) cells ($p < 0.01$). Consistently, Hv1 inhibition (Cl-GBI, 30-100 μ M) induced an acute intracellular acidification only in Jurkat cells ($p < 0.05$). However, at longer times (48h), 10 μ M Cl-GBI induced cytoplasmic acidification ($p < 0.05$) in both cell lines, which showed a concentration-dependent loss of viability ($p < 0.05$). Notably, after that time, only Karpas299 cells revealed ROS accumulation ($p < 0.05$) and mitochondrial hyperpolarization ($p < 0.05$), suggesting distinct mechanisms of response to Hv1 inhibition. Finally, RNASeq analysis revealed higher glycolytic (GLUT1, PKM, MCT4) and hypoxia-related (HIF1A, HIF2A, ARNT) gene expression in PTCL- compared to T-ALL-derived cells ($p < 0.05$). Consistently, Karpas299 cells presented higher basal lactate release and ROS content ($p < 0.05$) compared to Jurkat cells. In summary, Hv1 contributes to the survival of T-ALL and PTCL cells, although through different mechanisms that require further investigation.

ORALES 17 - SAIC - FARMACOLOGÍA

DATE & TIME: 20/11/2025 13:00 - 14:30 H

Chairs: Analía Reines, Ana Sahores

378. O17-01. PRECLINICAL SAFETY COMPARATIVE ASSESSMENT OF A BIOSIMILAR TO ITS ORIGINATOR TERIPARATIDE

Pablo A. Souto, Ma. Noelia Olivera, Virginia Pelagatti, Jorge Mosquera, Néstor R. Lago

Gemabiotech SAU, Buenos Aires, Argentina; Estudios Pre-clínicos y Clínicos.

psouto@amegabiotech.com

psouto@amegabiotech.com

Introduction: Teriparatide is the N-terminal fragment of endogenous human PTH, synthesized using recombinant DNA technology. It has identical bone and renal actions to PTH, stimulating bone formation. Objective: To compare the toxicity, safety, local tolerance, and immunogenicity of the test product (Forsil) with the reference teriparatide (Forteo, Eli Lilly) and to evaluate its bone effects in an in vivo model. Methods: 32 adult Wistar rats, divided into three groups, received 28 subcutaneous injections of 40 mg/kg/day of Forsil, Forteo® or placebo once daily. An anatomic-pathological study of 12 organs was carried out, including macroscopy and microscopy, local tolerance and clinical laboratory. Immunogenicity was evaluated using an adapted ELISA. A histomorphometric study was conducted to assess cortical and trabecular bone parameters in the femur. The results were analyzed using a one-way non-parametric ANOVA, followed by a Tukey post-test when significant differences were found. Results: No significant differences were observed in biochemical parameters. No presence of anti-teriparatide antibodies was found in the animals that received teriparatide. No significant lesions were observed in the anatomic-pathological study. No signs attributable to toxicity were observed belonging to the three treatment groups. The teriparatide treatment resulted in increased trabecular thickness, while the number of trabeculae and the marrow space decreased, along with a slight increase in cortical thickness. These changes, associated with an increase in bone mass, were similar between the test product and the reference product. Conclusions: Biosimilarity in toxicity/safety, local tolerance and immunogenicity was demonstrated between Gemabiotech's teriparatide and the originator.

379. O17-02. BIOINFORMATICS APPROACH TO HEPATO-TOXICITY IN PORPHYRIAS MEDIATED BY PORPHYRIN TRANSPORTERS AND DRUGS

Priscila Ayelén Pagnotta¹, Johanna Zuccoli², Viviana Melito³, Victoria Parera⁴, Ana María Buzaleh⁵

1. Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, UBA / Instituto de Biología y Medicina Experimental (IBYME); Laboratorio de Glicomedicina

2. Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín; Laboratorio del metabolismo del Hemo. Porfirias humanas y en animales

3. Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, UBA / Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín; Laboratorio del metabolismo del Hemo. Porfirias humanas y en animales

4. Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín; Laboratorio del metabolismo del Hemo. Porfirias humanas y en animales

5. Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP), UBA-CONICET, Hospital de Clínicas José de San Martín / Universidad Favaloro; Laboratorio del metabolismo del Hemo. Porfirias humanas y en animales

priscila.pagnotta@gmail.com

Porphyrias are metabolic diseases caused by failures in Heme biosynthesis. Acute Intermittent Porphyria (AIP) is of genetic origin,

while Porphyria Cutanea Tarda (PCT) can be genetic or acquired. In both cases, a hepatotoxic context influences for disease manifestation, with symptoms due to precursors and porphyrins accumulation. We previously observed that genetic variants in xenobiotic transporters and drug metabolizing systems and also their expression levels could be linked to drug-mediated manifestation of AIP and PCT-HIV association. The aim was to analyze in silico the association between porphyrin transporters and porphyrinogenic or antiretroviral drugs. The transporters ABCG2, ABCB6, TSPO, TSPO2, SLC46A1, and FLVCR1 were investigated. Allele frequencies varied depending on the geographic region (gnomAD), highlighting the importance of local studies. No reports of associations between porphyrinogenic drugs and genetic variants of ABCB6, TSPO, TSPO2, SLC46A1, and FLVCR1 were observed (ClinPGx). ABCG2 genetic variants are associated with toxicity or differential metabolism of six porphyrinogenic drugs and three antiretrovirals. Furthermore, treatment with protease inhibitors generates changes in the gene expression levels of SLC46A1 and TSPO compared to non-nucleoside reverse transcriptase inhibitors (GSE44228; GEO-NCBI). Similarly, gene expression of some transporters is altered in liver models treated with porphyrinogenic drugs such as rifampicin or isoniazid (GEO-NCBI). We conclude that a metabolic and pharmacological communication network might exist between porphyrin transporters, antiretrovirals, and porphyrinogenic drugs that contributes to the hepatotoxic state favoring PCT and AIP triggering. The study of these systems provides a framework for pharmacogenetic, and personalized medicine tailored to the needs of each patient.

380. O17-03. PRE-CLINICAL PHARMACOKINETICS EVALUATION OF A TERIPARATIDE BIOSIMILAR DEVELOPED IN ARGENTINA

Jorge Mosquera, Pablo A. Souto, Virginia Pelagatti, Ma. Noelia Olivera, Néstor R. Lago
Gemabiotech SAU, Buenos Aires, Argentina; Estudios Pre-clínicos y Clínicos
jmosquera@amegabiotech.com

Introduction: Gemabiotech teriparatide Forsil is a biosimilar that has demonstrated equivalence to the reference product Forteo® (Eli Lilly), through a comprehensive series of comparative physicochemical studies. **Objective:** To compare the pharmacokinetic profile of Test-Teriparatide with the reference product in rats at a single and repeated -doses. **Methods:** Male and female Wistar rats were divided into two groups: Forsil and Forteo. In the single-dose pharmacokinetics study, the animals received a single subcutaneous dose of teriparatide (40 µg/kg/day). In the repeated-dose PK study, they received 28 subcutaneous injections. Plasma quantification of teriparatide was performed using a validated sandwich ELISA technique. The AUC_{0-t} was estimated by the trapezoidal rule using non-compartmental methods. C_{max} and T_{max} were obtained from the Concentration vs. Time curves. AUC_{0-t}, the concentration at the time of the last extraction and the elimination rate constant were used to calculate AUC_{0-inf}. The difference in the logarithmic transformation of each parameter was assessed using the T-test for independent samples, and the comparison of means was carried out by constructing the respective 90% CI (limited range 80-125%). **Results:** All obtained values were similar for the Test and Reference products, in both single-dose and repeated-dose assays. All values were into the established pharmacokinetic range for biosimilarity. **Conclusion:** The pharmacokinetic behavior of Forsil and Forteo were comparable, supporting the biosimilarity between both products.

381. O17-04. THE SYNTHETIC PROGESTIN MEDROXYPROGESTERONE ACETATE EXHIBITS OPPOSITE AND POTENTIALLY BENEFICIAL ACTIONS ON VASCULAR AND BONE TISSUES

Pablo Cutini, Sabrina Cepeda, Maria Ivone Valle, Virginia Massheimer, Marisa Sandoval
Instituto de Ciencias Biológicas y Biomédicas del Sur (INBIO-SUR), CONICET- Universidad Nacional del Sur (UNS). Departamento de Biología, Bioquímica y Farmacia. UNS. Bahía Blanca, Argentina.; Laboratorio de Investigaciones Endocrinas Básicas y Clínicas (LIEByC)

phcutini@gmail.com

Cardiovascular and bone diseases often coexist in postmenopausal women. The mechanisms involved in vascular calcification (VCa) include impaired endothelial function and osteogenic transdifferentiation of vascular smooth muscle cells (VSMC). Hormone replacement therapy combined with progestins such as medroxyprogesterone acetate (MPA) emerged as a therapeutic option in prevention of cardiovascular diseases. The specific actions of MPA on both VCa and osteoblastogenesis were investigated. Primary cultures of endothelial cells (EC), VSMC and preosteoblasts isolated from female Wistar rats were used. In order to induce osteogenic transdifferentiation, VSMC were cultured for 21 days in osteogenic medium. Treatment of VSMC with 1 nM MPA in OM, significantly reduced ALP activity (33% vs. control, $p < 0.02$), extracellular matrix calcium content (93% vs. control, $p < 0.02$) and calcified nuclei formation (59% vs. control, $p < 0.02$). Pretreatment with a PgR antagonist (1 µM RU486), completely reversed these actions. The involvement of the androgen receptor (AR) was ruled out, since the presence of 10 nM flutamide (AR antagonist), did not affect the action of the progestin. Treatment of EC with 1 nM MPA stimulated cell migration (395% vs. control, $p < 0.001$, 96 h, wound healing assay). On bone tissue, 15 days of treatment with 1 nM MPA induced osteoblastic differentiation: MPA markedly increased ALP activity, mineralization, and secretion of VEGF (84%, 21%, and 42% vs. control, respectively, $p < 0.02$) through a mechanism involving PgR participation. In conclusion, MPA exhibits opposite and potentially beneficial actions in bone and vascular tissues: an anti-osteogenic effect by inhibiting CaV, and a pro-osteogenic effect

382. O17-05. COMPARATIVE ANALYSIS OF THE BIOLOGICAL ACTIVITY OF DIFFERENT G-CSF ANALOGS ON THE MOBILIZATION AND DIFFERENTIATION OF MURINE BONE MARROW CELL PRECURSORS

Lucas Nahuel Laserna¹, Nicolas Seveso², Larisse Domingos Pecanha³, Azul Caporaso Ruiz⁴, Lourdes Materazzi⁵, Melany Elizabeth Lombardi⁶, Roberto Alejandro Diez⁷, María Gabriela Lombardi⁸

1. Centro de Estudios Farmacológicos y Botánicos (CEFy-BO)-CONICET, Universidad de Buenos Aires, Facultad de Medicina, Segunda cátedra de Farmacología; Oncoinmunología molecular

2. Centro de Estudios Farmacológicos y Botánicos (CEFy-BO)-CONICET, Universidad de Buenos Aires, Facultad de Medicina, Segunda cátedra de Farmacología; Oncoinmunología Molecular

3. Centro de Estudios Farmacológicos y Botánicos (CEFy-BO)-CONICET, Universidad de Buenos Aires, Facultad de Medicina, Segunda cátedra de Farmacología; Oncoinmunología Molecular

4. Centro de Estudios Farmacológicos y Botánicos (CEFy-BO)-CONICET, Universidad de Buenos Aires, Facultad de Medicina, Segunda cátedra de Farmacología; Oncoinmunología Molecular

5. universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Química Biológica; Inmunofarmacología, IQUIBICEN

6. Centro de Estudios Farmacológicos y Botánicos (CEFy-BO)-CONICET, Universidad de Buenos Aires, Facultad de Medicina.; Bioterio Central de Fmed

7. Universidad de Buenos Aires, Facultad de Medicina.; Segunda cátedra de Farmacología

8. Centro de Estudios farmacológicos y Botánicos (CEFy-BO)-CONICET, Universidad de Buenos Aires, Facultad de Medicina, Segunda Cátedra de Farmacología; Oncoinmunología Molecular

lasernalucas@gmail.com

Granulocyte colony-stimulating factor (G-CSF) is a cytokine that promotes both the growth and maturation of neutrophil progenitor cells and their mobilization into peripheral blood. In clinical practice, three recombinant G-CSF proteins are used: lenograstim (L: eukaryotic glycosylation), filgrastim (F: non-glycosylated), and

peg-filgrastim (P: non-glycosylated and pegylated, with longer half-life). Comparisons are limited, but it is accepted that they act as full agonists of the G-CSF receptor and show equivalent clinical efficacy. Since contradictory reports have emerged, the aim of this study is to compare the capacity of these G-CSF analogs on the mobilization and differentiation of murine bone marrow precursors. We used a cytopenia model induced by a single dose of cyclophosphamide (300 µg/g) in 12-week-old CD-1 mice. After 4 days, animals received either no treatment or G-CSF analogs: F or L for 4 consecutive days or P as a single dose (300 ng/g, N=6). G-CSF analogs significantly increased the number of circulating neutrophils (CD117+) compared with control ($p<0.05$), which was also confirmed by blood smear analysis of treated mice. In addition, L decreased bone marrow cell counts /bone compared with the other analogs, while significantly increasing the percentage of neutrophils in the leukocyte formula compared with control ($p<0.05$). Our findings indicate that G-CSF analogs have comparable ability to mobilize hematopoietic precursors into peripheral blood, suggesting that this effect does not depend on eukaryotic glycosylation. However, the group treated with L showed differences in bone marrow cell counts and circulating neutrophil levels, probably reflecting differences in response kinetics.

383. O17-06. USE OF BENZODIAZEPINES AND Z-DRUGS IN OLDER ADULTS AFFILIATED TO A SOCIAL SECURITY INSTITUTE. CHACO-CORRIENTES, 2024

Paula Malgor, Rocío Cardozo, Lila Almirón, María Teresa Rocha, Isabel Hartman, Lorena dos Santos
School of Medicine, National University of the Northeast, Corrientes, Argentina.; Pharmacology
paulitamalgor@gmail.com

Benzodiazepines (BZD) and Z-drugs (zolpidem, zopiclone, eszopiclone) are useful for the short-term treatment of anxiety and insomnia and are widely prescribed in older adults (OA). Objective: To characterize the prescription of BZD and Z-drugs in OA affiliated to a social security system in Chaco and Corrientes. Design: Observational, descriptive, cross-sectional study. All outpatient dispensations made in 2024 to affiliated OA (≥ 60 years) were analyzed. Variables: sex, type and amount of prescribed drug, Defined Daily Dose per 1,000 inhabitants per day (DDD/1,000/day), according to World Health Organization criteria for drug utilization studies. Out of a total of 34,605 dispensations, 3,542 (10.2%) corresponded to BZD and Z-drugs. Age range: 60–91 years; female sex: 60 %. Average consumption (DDD/1,000/day): 37.33, meaning that 37.33 out of every 1,000 affiliates use these drugs. The most prescribed according to DDD/1,000/day were clonazepam (18.65), alprazolam (11.45), and zolpidem (3.18). A high level of BZD and Z-drug consumption was observed, particularly among women, with clonazepam and alprazolam being the most frequently used. Their use in OA has been associated with an increased risk of falls and fractures (especially hip fractures), memory impairment, dementia, dependence and withdrawal. Strategies for gradual deprescription and the promotion of non-pharmacological therapeutic alternatives should be implemented.

384. O17-07. DIFFERENTIAL SENSITIVITY OF TRPC AND ORAI-MEDIATED CALCIUM ENTRIES TO SKF-96365

Julieta Mansilla Ricartti, Sebastian Susperreguy
Instituto de Investigaciones Biomedicas (BIOMED), UCA.; Lab. de Función y Farmacología de Canales Iónicos
julieta.mansillaricartti@gmail.com

Background and Purpose: SKF-96365 is commonly used as a broad-spectrum inhibitor of calcium entry, originally identified as a ROCE blocker and later shown to inhibit ORAI1-STIM1-mediated SOCE. However, its selectivity for TRPC versus ORAI channels remains unclear. Experimental Approach: To dissect SKF-96365's selectivity, we assessed its effects on SOCE and ROCE in wild-type and TRPC hepta-KO mouse embryonic fibroblasts (MEFs), as well as TRPC-mediated OAG-induced calcium entry in HEK293 cells expressing TRPC3, TRPC6, or TRPC7. Additional assays were performed in HEK293 cells expressing muscarinic receptor M5 (M5R).

IC₅₀ values were determined across all conditions. Key Results: SKF-96365 inhibited Tg-induced SOCE similarly in wild-type and TRPC hepta-KO MEFs, with IC₅₀ values around 4–5 µM, confirming its primary action on ORAI channels. Comparable inhibition was observed for CCh-activated ROCE in TRPC-deficient cells. In contrast, OAG-activated TRPC3/6/7 currents were only weakly inhibited, with IC₅₀ values exceeding 100 µM. Notably, TRPC-mediated calcium entry was unaffected by CRAC channel blockers or ORAI co-expression, reinforcing its independence from SOCE mechanisms. Conclusions and Implications: Our results show that ORAI-mediated SOCE is ~25-fold more sensitive to SKF-96365 than TRPC-mediated pathways. GSK-7975A further confirmed ORAI selectivity by blocking SOCE without affecting TRPC channels. These findings clarify SKF-96365's pharmacological profile and highlight the need for concentration-aware interpretation in calcium signaling studies, particularly in the context of CRAC channel-related disorders.

385. O17-08. REPRODUCTIVE AND DEVELOPMENTAL SAFETY OF THE ARVAC CG CANDIDATE VACCINE: A PRE-CLINICAL STUDY IN RATS

María Florencia Beltramino¹, Fátima Belén Gasser², Enrique Rebelindo³, Candela Simonetto⁴, Paula Taborda⁵, Natalia Salvetti⁶, Juliana Cassataro⁷, Karina Pasquevich⁸, Hugo Héctor Ortega⁹, María Eugenia Baravalle¹⁰

1. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Esperanza, Santa Fe.; Centro de Medicina Comparada.

2. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Esperanza, Santa Fe.; Centro de Medicina Comparada.

3. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Esperanza, Santa Fe.; Centro de Medicina Comparada.

4. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Esperanza, Santa Fe.; Centro de Medicina Comparada.

5. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Esperanza, Santa Fe.; Centro de Medicina Comparada.

6. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Esperanza, Santa Fe.; Centro de Medicina Comparada.

7. Instituto de Investigaciones Biotecnológicas, Universidad Nacional de San Martín (UNSAM), San Martín, Buenos Aires, Argentina.; laboratorio de inmunología, enfermedades infecciosas y desarrollo de vacunas.

8. Instituto de Investigaciones Biotecnológicas, Universidad Nacional de San Martín (UNSAM), San Martín, Buenos Aires, Argentina.; laboratorio de inmunología, enfermedades infecciosas y desarrollo de vacunas.

9. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Esperanza, Santa Fe.; Centro de Medicina Comparada.

10. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Esperanza, Santa Fe.; Centro de Medicina Comparada.

florencia.beltramino@icivet.unl.edu.ar

ARVAC CG is a recombinant protein-based vaccine against COVID-19, developed and produced in Argentina. It has demonstrated a satisfactory safety profile and elicits a robust neutralizing antibody response in preclinical and clinical studies. This study evaluated the effects of ARVAC CG on reproduction and development in rats, assessing reproductive indices and offspring from the par-

ent generation (G0) through weaning of the next generation (G1). Twelve male and female Wistar rats (4 weeks old) were used. The treated group received intramuscular ARVAC CG (50µg), while the control group received saline. Males were given three doses; females received two doses before mating and two during gestation. Reproductive indices (number of pregnant females, mating and pregnancy indices, gestation days, litter size, and offspring survival rate) were assessed, along with offspring physical and neurological development. Body weight, macroscopic findings, and hematological parameters were evaluated in both G0 and G1 animals. No differences in body weight, physical or neurological development were detected ($p>0.05$). Only litter size was significantly higher in the control group ($p<0.05$), but within normal colony ranges. Necropsies showed no macroscopic abnormalities. Hematological parameters in G0 were comparable between groups. In G1, treated males had higher white blood cell, granulocyte, and monocyte counts ($p<0.05$), and treated females had increased white blood cell and granulocyte counts ($p<0.05$); however, all values remained within reference ranges for the colony. These findings indicate that ARVAC CG administration does not produce clinically relevant adverse effects on reproduction or offspring development in this rat model.

- 386. O17-09. IN VITRO EVALUATION OF THE CYTOTOXIC AND GENOTOXIC EFFECTS OF BSY2 IN CHO-K1 CELLS**
 Fátima Gasser¹, Belkis Marelli², María Sol Renne³, María Florencia Beltramino⁴, Milagros Burgui⁵, Marcos Oggero⁶, Hugo Ortega⁷, María Eugenia Baravalle⁸
 1. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral), Universidad Nacional del Litoral (UNL)- Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Centro de Medicina Comparada
 2. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral), Universidad Nacional del Litoral (UNL)- Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Centro de Medicina Comparada
 3. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral), Universidad Nacional del Litoral (UNL)- Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Centro de Medicina Comparada
 4. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral), Universidad Nacional del Litoral (UNL)- Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Centro de Medicina Comparada
 5. Biosynaptica SA; Centro Biotecnológico del Litoral, FBCB, UNL, CONICET, FBCB.
 6. Biosynaptica SA; Centro Biotecnológico del Litoral, FBCB, UNL, CONICET, FBCB.
 7. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral), Universidad Nacional del Litoral (UNL)- Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Centro de Medicina Comparada
 8. Instituto de Ciencias Veterinarias del Litoral (ICIVET Litoral), Universidad Nacional del Litoral (UNL)- Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Centro de Medicina Comparada
 fatima.gasser@icivet.unl.edu.ar

BSY2 is a novel EPO-based neurotherapeutic candidate under preclinical development that exhibits neuroprotective and neuroplastic effects without hematopoietic effects, representing a promising therapy for central nervous system (CNS) disorders. The objective of this study, conducted within the context of regulatory preclinical safety evaluation, was to assess the in vitro cytotoxic and genotoxic effects of BSY2 in the CHO-K1 cell line. Cytotoxicity was assessed using the MTT assay at BSY2 concentrations ranging from 0.2-47 µg/ml, with doxorubicin and mitomycin C as positive controls. Apoptosis and caspase-3 activation were analyzed by flow cytometry using FITC-Annexin V and FITC-DEVD-FMK at 0.34 µg/ml of BSY2. Genotoxicity was evaluated by the micronucleus, comet, and γH2AX assays at 0.34 µg/ml of BSY2, with bleomycin and hydrogen peroxide as positive controls. The concentration of 0.34µg/ml of BSY2 was selected as a representative concentration based on the absence of cytotoxicity and biological relevance.

The results showed that BSY2 did not affect CHO-K1 proliferation at any tested concentrations. Levels of early and late apoptosis, necrosis, and caspase-3 activation were similar to those observed in the negative control ($p>0.05$). Genotoxic endpoints, including micronucleus frequency, DNA damage (% DNA in tail), and γH2AX expression, also showed no significant differences compared with the negative control ($p>0.05$). In conclusion, BSY2 did not induce cytotoxic or genotoxic effects in CHO-K1 cells under the tested conditions. These findings, obtained within the framework of regulatory preclinical safety studies, support its favorable safety profile and highlight its potential as a therapeutic candidate for CNS disorders.

POSTERS 22 - SAIC - METABOLISMO Y NUTRICIÓN 2
DATE & TIME: 20/11/2025 13:00 - 14:30 H
Chairs: Romina Higa, María Noel Galardo, Carolina Caniffi

387. P22-13. IMPACT OF INTERMITTENT FASTING ON GLYCEMIC CONTROL AND B-CELL FUNCTION IN MALE C57BL/6N MICE

Andrea Scelza Figueredo¹, Ingrid Pensado Evans², Miranda Sol Orellano³, Carolina Sétula⁴, Andrea M. Sanchez-Okse-
 niuk⁵, Luz Andreone⁶, Marcelo J. Perone⁷

1. Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIMT-CONICET-Univ. Austral), Pilar, Argentina.
 2. Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIMT-CONICET-Univ. Austral), Pilar, Argentina.
 3. Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIMT-CONICET-Univ. Austral), Pilar, Argentina.
 4. Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIMT-CONICET-Univ. Austral), Pilar, Argentina.
 5. Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIMT-CONICET-Univ. Austral), Pilar, Argentina.
 6. Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIMT-CONICET-Univ. Austral), Pilar, Argentina.
 7. Facultad de Ciencias Biomédicas, Universidad Austral, Pilar, Argentina.; Laboratorio de Inmuno-Endocrinología, Diabetes y Metabolismo, Instituto de Investigaciones en Medicina Traslacional (IIMT-CONICET-Univ. Austral), Pilar, Argentina.
- giusceselza@gmail.com

Intermittent fasting (IF) is a promising nutritional intervention for weight loss and metabolic health, although its effects on pancreatic islets and β cells remain incompletely understood. We aimed to evaluate whether the beneficial health effects of IF are associated with preserved islet phenotype and improved β-cell function in mice. Male C57BL/6N mice (8 weeks-old) were fed ad libitum (AL) or subjected to IF (3:2 regimen: fasting every other day with two days of AL each week) for 13 weeks. Mice were sacrificed at 21 weeks of age, while an additional group of 8-week-old mice served as young controls. Body weight and glucose homeostasis were monitored. Pancreases were analyzed histologically, and glucose-stimulated insulin secretion (GSIS) was assessed in isolated islets. IF improved glucose tolerance ($p<0.0001$ vs. AL) and insulin sensitivity ($p<0.05$ vs. AL) accompanied by a 5–10% reduction in body weight. Moreover, IF reduced mean pancreatic islet area ($p<0.05$ vs. AL) and increased their insulin immunoreactivity ($p<0.005$ vs. AL). IF also enhanced the islet expression of Sestrin1 ($p<0.02$ vs. AL) and Sestrin2 ($p<0.0005$ vs. AL), suggesting activation of adaptive stress responses against oxidative stress. β-cells from IF islets enhanced insulin secretion in response to glucose ($p<0.05$ vs. AL). Our results

indicate that the IF regimen tested improves glucose homeostasis, yielding pancreatic islet biochemical and morphological parameters comparable to those of young mice. We concluded that IF is a nutritional intervention with the potential to preserve β -cell health.

388. P22-14. EFFECTS OF FRUCTOSE-INDUCED METABOLIC SYNDROME ON BONE REPAIR

Nahuel Wanionok¹, María Silvina Molinuevo², Lucas Streckwa-ll³, Juan Manuel Fernandez⁴, Antonio Desmond McCarthy⁵

1. Dpto. Cs. Biológicas, Fac. Cs. Exactas, Universidad Nacional de La Plata; Laboratorio de Investigaciones en Osteopatías y Metabolismo Mineral

2. Dpto. Cs. Biológicas, Fac. Cs. Exactas, Universidad Nacional de La Plata; Laboratorio de Investigaciones en Osteopatías y Metabolismo Mineral

3. Dpto. Cs. Biológicas, Fac. Cs. Exactas, Universidad Nacional de La Plata; Laboratorio de Investigaciones en Osteopatías y Metabolismo Mineral

4. Dpto. Cs. Biológicas, Fac. Cs. Exactas, Universidad Nacional de La Plata; Laboratorio de Investigaciones en Osteopatías y Metabolismo Mineral

5. Dpto. Cs. Biológicas, Fac. Cs. Exactas, Universidad Nacional de La Plata; Laboratorio de Investigaciones en Osteopatías y Metabolismo Mineral
nahuelwanionok@biol.unlp.edu.ar

Introduction: Metabolic Syndrome (MetS) is a heterogeneous and multifactorial disorder associated with an increased risk of cardiovascular diseases. Currently, incidence of MetS is growing widely due to sedentary lifestyles and a high intake of fats and sugars. Preclinical and clinical studies have reported a negative correlation between MetS and bone tissue integrity and repair; however, a consensus remains elusive, likely due to the variability observed among individuals with MetS. **Materials and Methods:** Young male Wistar rats were randomly assigned to two groups (n=5). One group received 20% fructose in their drinking water, while the control group received water alone, for three months. One month prior to euthanasia, a 1 mm circular craniotomy defect was surgically created in the right parietal bones of all animals. Following euthanasia, blood samples were collected, and parietal bones were dissected and processed for histomorphometry and immunohistochemistry to evaluate accumulation of carboxy-methyl-lysine, a prevalent advanced glycation end-product (AGE). Humeral bone marrow-derived mesenchymal stem cells (BMSCs) were also isolated to assess their osteogenic potential. **Results:** Metabolic syndrome (MetS) was induced through oral fructose treatment. MetS significantly decreased newly formed bone in calvarial defects, indicating impaired mesenchymal-dependent bone repair. Furthermore, MetS increased AGE accumulation in bone tissue and reduced the osteogenic potential of BMSCs by decreasing alkaline phosphatase activity, collagen production, and extracellular calcium deposition. **Conclusion:** MetS, induced by oral administration of fructose for three months, impairs mesenchymal bone repair in rats, possibly due to elevated AGE accumulation in bone tissue.

389. P22-15. PRENATAL STRESS ALTERS HEPATIC LIPID AND ENERGY METABOLISM IN MALE BALB/C MICE

Sofía Quiroga¹, Mara Garrido², Luz Acevedo³, Roxana Rubinstein⁴, Ana María Genaro⁵, Adriana Laura Burgueño⁶

1. Instituto de Investigaciones Biomédicas. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) - Pontificia Universidad Católica Argentina.; Laboratorio de Psiconeuroendocrinoinmunología

2. Instituto de Investigaciones Biomédicas. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) - Pontificia Universidad Católica Argentina.; Laboratorio de Psiconeuroendocrinoinmunología

3. Instituto de Investigaciones Biomédicas. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) - Pontificia Universidad Católica Argentina.; Laboratorio de Psiconeuroendocrinoinmunología

4. Instituto de Investigaciones Biomédicas. Consejo Nacio-

nal de Investigaciones Científicas y Técnicas (CONICET) - Pontificia Universidad Católica Argentina.; Laboratorio de Psiconeuroendocrinoinmunología

5. Instituto de Investigaciones Biomédicas. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) - Pontificia Universidad Católica Argentina.; Laboratorio de Psiconeuroendocrinoinmunología

6. Instituto de Investigaciones Biomédicas. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) - Pontificia Universidad Católica Argentina.; Laboratorio de Psiconeuroendocrinoinmunología
sofiaquiroya93@gmail.com

Prenatal stress (PS) and a high-fat diet (HFD) intake independently contribute to the development of metabolic diseases. We previously reported a decrease in Sirt1 mRNA expression in visceral adipose tissue due to PS in BALB/c male mice. After HFD, PS animals showed increased glucose, insulin levels and adipokines gene expression in visceral adipose tissue. The liver is the main organ responsible for lipid metabolism; any dysfunction can lead to metabolic disorders related to lipid storage. Here, we analyze the impact of PS and HFD on liver mRNA expression in male and female BALB/c mice. We examined liver expression in genes that regulate lipid and energy metabolism and are related to metabolic diseases. Pregnant mice were exposed to movement restriction stress (or not) for 2 hours/day between GD14 and 21. Their offspring consumed standard or HFD for 24 weeks. We examined the expression of Pgc1 α , Ppara and Sirt1 mRNA, and associated genes, using qPCR. In PS-males, we observed a rise in body weight*, triglyceride***, and total cholesterol*** levels with increased inflammation (Socs3***). Along with decreased expression of genes involved in metabolic diseases (Pgc1 α **, Ppara***, and Sirt1***) and in lipid metabolism (Mtp*** and ApoB***). Similar disturbances were observed in non-PS males fed a HFD and in females under a HFD, regardless of prenatal treatment. We propose that PS-male mice appear to be more susceptible to an increased risk of hepatic fat accumulation, even without HFD. *p<0.05, **p<0.01 and ***p<0.001 PS vs NPS (standard diet).

390. P22-16. ASTAXANTHIN ALLEVIATES ALTERED HEPATIC LIPID METABOLISM AND OXIDATIVE STRESS IN ANIMALS FED A HIGH-SUCROSE DIET

Matías Rodrigo Vargas¹, María del Rosario Ferreira², Paola Inés Ingaramo³, Pablo Agustín Collins⁴, María Eugenia D'Alessandro⁵

1. Facultad de Bioquímica y Cs. Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina.; Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición

2. Facultad de Bioquímica y Cs. Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición

3. Facultad de Bioquímica y Cs. Biológicas, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina; Instituto de Salud y Ambiente del Litoral (ISAL)

4. Universidad Nacional del Litoral- Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Santa Fe, Argentina.; Departamento de Acuicultura, COE INTA Ángel Gallardo (EEA Rafaela)

5. Facultad de Bioquímica y Cs. Biológicas, Universidad Nacional del Litoral, Santa Fe, Argentina. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).; Laboratorio de Estudio de Enfermedades Metabólicas relacionadas con la Nutrición
mrvargas@fbcb.unl.edu.ar

The aim of the present study was to analyze the effects of an extract rich in Astaxanthin (ASTX) -a potent antioxidant- obtained from decapod crustaceans (*Dilocarcinus pagel*) from the Paraná River basin on disturbed liver lipid metabolism and oxidative stress in rats fed a high-sucrose diet (HSD). Male Wistar rats were fed for 90 days

with: 1- a standard commercial rodent diet (RD), 2- a HSD, 3-RD or 4-HSD supplemented with an extract rich in ASTX (HSD+ASTX). The rats were given orally either ASTX (10 mg/kg body weight/day in sunflower oil) or the vehicle. We analyzed in the liver: (1) NAFLD activity score (NAS), triglyceride content, carnitine palmitoyltransferase-1 (CPT-1), fatty acid synthase (FAS), acetyl-CoA carboxylase (ACC), glucose-6-phosphate dehydrogenase (G6PDH), and malic enzyme (ME) activities, and (2) reactive oxygen species (ROS), reduced glutathione (GSH) levels, catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR), glutathione-S-transferase (GST) enzyme activities. Data were analyzed by two-way ANOVA and Newman Keuls post-hoc. Compared with HSD-fed rats, animals fed HSD+ASTX showed reduced NAS and triglyceride content, increased CPT-1 and reduced ME activities. FAS, ACC and G6PDH were increased in both groups. These changes were accompanied by reduced ROS levels and an increase in CAT and GST. GPx and GR were reduced in both groups. GSH levels were similar to RD-fed group. The RD+ASTX group showed no significant difference with the RD group. This study suggests that ASTX obtained from freshwater crustaceans has beneficial effects against altered liver lipid metabolism and oxidative stress in HSD-fed rats.

391. P22-17. CIRCULATING BIOMARKERS FOR EARLY DETECTION OF CARDIO-METABOLIC RISK

Alejandra Duarte¹, Mailén Rojo², Andrea Millán³, Hernán Pérez⁴, Gustavo Frechtle⁵

1. Instituto de Inmunología, Genética y Metabolismo (INI-GEM). Universidad de Buenos Aires - CONICET.; Laboratorio de Diabetes y Metabolismo

2. Instituto de Inmunología, Genética y Metabolismo (INI-GEM). Universidad de Buenos Aires - CONICET.; Laboratorio de Diabetes y Metabolismo

3. Instituto de Inmunología, Genética y Metabolismo (INI-GEM). Universidad de Buenos Aires - CONICET.; Laboratorio de Diabetes y Metabolismo

4. Servicio de Nutrición - Hospital de Clínicas José de San Martín, Universidad de Buenos Aires. Instituto de Inmunología, Genética y Metabolismo (INIGEM). Universidad de Buenos Aires - CONICET.; Laboratorio de Diabetes y Metabolismo

5. Instituto de Inmunología, Genética y Metabolismo (INI-GEM). Universidad de Buenos Aires - CONICET. Servicio de Nutrición - Hospital de Clínicas José de San Martín, Universidad de Buenos Aires.; Laboratorio de Diabetes y Metabolismo

ales_duarte@hotmail.com

Metabolic diseases are highly prevalent chronic conditions that necessitate more precise diagnostic and therapeutic strategies, its important search for sensitive, non-invasive biomarkers for early detection. Epigenetic research has identified microRNAs (miRNAs), which are small non-coding RNAs, as key regulators in gene expression and as promising biomarkers for diagnosis and risk stratification. Furthermore, evaluating the patient's mitochondrial status is crucial for understanding disease mechanisms and developing personalized treatment. In this work we evaluate the level of circulating of miRNA and circulating mitochondrial DNA (mtDNA-c) as possible biomarkers of cardio metabolic risk. Our study evaluated by real time PCR the levels of miRNA-122, highly expressed in the liver, in individuals with T2D, obesity without diabetes, and metabolically healthy controls. We found that miRNA-122 expression was significantly higher in the T2D group compared to controls. Furthermore, subjects with obesity showed an intermediate elevation of miRNA-122, suggesting it could be an early marker of metabolic dysfunction before a diabetes diagnosis. Moreover, we analyzed the levels of mtDNA-c as a reflection of cellular stress and mitochondrial dysfunction, traditionally studied as a systemic inflammation biomarker, could serve as a molecular tool to stratify cardio-metabolic risk. Our results showed that mtDNA-c is elevated in obesity and positively correlates with blood glucose, HbA1c, and HOMA index. In this work we demonstrate that the analysis of miRNA-122 and

mtDNA-c could be used as biomarkers of metabolic dysfunction. These results support the development of precision medicine strategies, improving prevention, early diagnosis, and therapeutic intervention in cardiometabolic diseases.

392. P22-18. OMEGA-3 SUPPLEMENTATION MODULATES HEPATIC FATTY ACID METABOLISM BUT NOT INFLAMMATION IN TRANSITION DAIRY COWS

Gino Storani¹, Angeli Emmanuel², Pablo Matias Roskopf³, Sabrina C Rosina⁴, Hugo H Ortega⁵, Eloy E Salado⁶, Gustavo J Hein⁷

1. ICiVet-Litoral (UNL-CONICET); Laboratorio de Biología Celular y Molecular Aplicada,

2. ICiVet-Litoral (UNL-CONICET); Laboratorio de Biología Celular y Molecular Aplicada

3. Estación Experimental Agropecuaria, INTA, Rafaela, Santa Fe

4. Facultad de Ciencias Veterinarias, Universidad Nacional del Litoral; Laboratorio de Biología Celular y Molecular Aplicada

5. ICiVet-Litoral (UNL-CONICET); Laboratorio de Biología Celular y Molecular Aplicada

6. Estación Experimental Agropecuaria, INTA, Rafaela, Santa Fe

7. ICiVet-Litoral (UNL-CONICET); Laboratorio de Biología Celular y Molecular Aplicada

gino.storani@icivet.unl.edu.ar

The transition period, from 21 days before calving to 21 days postpartum, is marked by systemic pro-inflammation and negative energy balance (NEB), which compromise both health and productivity in dairy cows. This study evaluated whether dietary omega-3 fatty acid supplementation modulates hepatic inflammation and enzymes involved in fatty acid metabolism during this vulnerable phase. In the omega-3 group (O3G; n = 18), cows received calcium salts of fish and linseed oils at 0.4 kg dry matter (DM)/cow/day prepartum (-21 to calving) and 0.65 kg DM/cow/day postpartum (0 to +21 days). The control group (CG; n = 18) was fed an isoenergetic diet in which the omega-3 supplement was replaced with ground corn (0.8 and 1.3 kg DM/cow/day pre- and postpartum, respectively). Liver biopsies were performed at -21, +7, and +21 days relative to calving. Targets included interleukin-6, tumor necrosis factor alpha, nuclear factor kappa B activation, 3-hydroxy-3-methylglutaryl-CoA synthase, and mitochondrial carnitine palmitoyltransferase 1 were quantified by Western blot. Results showed a significant increase in hepatic 3-hydroxy-3-methylglutaryl-CoA synthase abundance in O3G cows compared with controls (p 0.05). These findings suggest that omega-3 supplementation during the transition period does not markedly alter hepatic inflammatory status but may enhance fatty acid metabolism, as reflected by increased HMG-CoA synthase levels. Additional studies are needed to determine the physiological implications of this adaptation.

393. P22-19. MATERNAL NUTRITIONAL STATUS AND BREAST MILK INTAKE

Silvina Mariela Vidueiros¹, Ricardo Wright², Cristián Nápoli³, Cristina Possidoni⁴, Gerardo Weisstaub⁵, Anabel Pallaro⁶

1. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Nutrición; -

2. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Nutrición; -

3. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Nutrición; -

4. Hospital Sagrado Corazón de Jesús de Basavilbaso, Entre Ríos; -

5. Instituto de Nutrición y Tecnología de los Alimentos (INTA), Chile; -

6. Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Nutrición; -

simavidu@ffyb.uba.ar

Early infant nutrition is crucial for development and health. WHO recommends exclusive breastfeeding for the first six months, continu-

ing up to two years. The aim of this study was to determine breast milk intake (BMIn) in Argentina and Chile using the gold standard deuterium isotope dilution method and to relate it to the nutritional status of the mother. Seventy-one mother-infant pairs from Argentina and Chile were studied. A dose of deuterium oxide was given to the mothers, and saliva samples from both were collected to measure isotopic enrichment with an FTIR spectrometer. From this data, BMIn and the intake of water from other sources (IWOS) were calculated using an algorithm. Breastfeeding was classified as exclusive or non-exclusive based on the IWOS. Statistical analyses used Kruskal-Wallis and chi-squared tests to determine differences. Although maternal overweight was higher in Chile (65.4%) than in Argentina (47.4%), the difference was not significant. A total of 73.9% of the infants received exclusive breastfeeding. The average BMIn was 903 ml/day, and no significant differences were observed between countries ($p=0.232$). As expected, BMIn was higher in the exclusive breastfeeding group (931 vs. 728 ml/d, $p0.05$). Isotopic dilution is a valid method for measuring breast milk intake. The results confirm that exclusive breastfeeding is associated with higher volumes of milk consumed and that the nutritional status of the mothers, even with overweight or obesity, does not significantly limit BMIn.

394. P22-20. UNBALANCED MATERNAL DIET DURING PUP'S DEVELOPMENT ALTERS MIRNA EXPRESSION IN ADULT MICE

Carolina Carla Garraza¹, Agustina Castro², María Amanda Rey³, María Guillermina Zubiría⁴, Sabrina Eliana Gambaro⁵, Andrés Giovambattista⁶, Ana Alzamendi⁷

1. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP; Laboratorio de Metabolismo y Tejido Adiposo

2. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP; Laboratorio de Metabolismo y Tejido Adiposo

3. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP; Laboratorio de Metabolismo y Tejido Adiposo

4. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP; Facultad de Ciencias Exactas, UNLP; Laboratorio de Metabolismo y Tejido Adiposo

5. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP; Facultad de Ciencias Exactas, UNLP; Laboratorio de Metabolismo y Tejido Adiposo

6. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP; Facultad de Ciencias Exactas, UNLP; Laboratorio de Metabolismo y Tejido Adiposo

7. Instituto Multidisciplinario de Biología Celular (IMBICE) CONICET-CICPBA-UNLP; Laboratorio de Metabolismo y Tejido Adiposo

caro.garraza9@gmail.com

It is widely accepted that diet quality supply during gestation and lactation programs pup's development. We have previously shown that an unbalanced maternal diet generates permanent alterations in miRNAs regulation, which influence adipose tissue (AT) expansion, in males. Our aim was to evaluate maternal fructose rich diet (FRD) intake impact on AT development in adult female mice. On pregnancy day 1, dams were provided with tap water alone or containing fructose (20% w/v; FRD) and fed ad libitum up to delivery. Six pups were left by mom, and same diet was provided until pups were 21 days old. Females were separated and maintained until 120-days old (experimental day, ED) with normal diet ad libitum. From weaning until ED, body weight and food intake were registered. C and F indicate pups born to control and FRD dams, respectively. On ED, trunk blood was collected, AT depots were dissected and weighed. Parametrial AT (PAT) was used for mRNA expression levels quantification. Our results show that F pups gain more weight despite similar food intake. No differences in AT mass or functional AT gene expression markers such as leptin and adiponectin were observed. When considering miRNA biosynthesis, F pups showed significantly higher expression levels of exportin 5. miR30b expression, a regulator of brown/beige adipogenesis, was found to be significantly

decreased in F offspring, whereas miR-27 tended to be increased. In conclusion, our findings suggest that maternal diet exerts sex-dependent effects on the offspring miRNA regulation pattern, resulting in distinct responses in adulthood.

395. P22-21. CLINICAL CHALLENGES IN VARIEGATE PORPHYRIA WITH HIV INFECTION

Laura Sabina Varela¹, Viviana Alicia Melito², Fabiana Alejandra Caballero³, Marcelo Guolo⁴, Verónica Goñi⁵, Fernando Baccaro⁶, Mariana Agosta⁷, María Pasman⁸, Lucía Tomassi⁹, Ana María Buzaleh¹⁰, Victoria Estela Parera¹¹

1. UBA- CONICET, Hospital de Clínicas José de San Martín;

Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP)

2. UBA- CONICET, Hospital de Clínicas José de San Martín;

Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP)

3. UBA- CONICET, Hospital de Clínicas José de San Martín;

Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP)

4. UBA- CONICET, Hospital de Clínicas José de San Martín;

Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP)

5. UBA- CONICET, Hospital de Clínicas José de San Martín;

Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP)

6. Hospital Fernández; División Terapia Intensiva

7. Hospital Rocca; Terapia Intensiva

8. Hospital Ramos Mejía; Consultorio de Porfirias

9. Hospital Ramos Mejía; Consultorio de Porfirias

10. UBA- CONICET, Hospital de Clínicas José de San Martín;

Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP)

11. UBA- CONICET, Hospital de Clínicas José de San Martín, Argentina.; Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP)

lauravcipy@gmail.com

Variegate Porphyria (VP) is a rare metabolic disorder characterized by deficient activity of protoporphyrinogen oxidase, resulting in the accumulation of neurotoxic porphyrin precursors. We present the case of a 32-year-old woman with HIV who had generalized seizures, psychosis, and polyneuropathy, initially interpreted as secondary to infection. Magnetic resonance imaging suggested vasogenic edema, raising suspicion of autoimmune encephalitis. Despite immunomodulatory therapy, her health worsened, requiring intensive care and extended mechanical ventilation. Biochemical tests confirmed VP: elevated urinary excretion of ALA 44.6 mg/24 h (RV d4), PBG 168.6 mg/24 h (RV d2), and TUP 2246 µg/24 h (RV 20 250). Fecal porphyrins with pattern excretion and plasma porphyrin index (6.8; RV d1.3, I: 625 nm) supported the diagnosis. Genetic testing identified a pathogenic PPOX variant (c.428A>T) consistent with VP. Three Hemin cycles (3 4 mg/kg/day for 4 days) induced biochemical responses: ALA fell to 1.8 mg/24 h and PBG to 2.0 mg/24 h, although relapses occurred with levels up to ALA 14 mg/24 h, PBG 62 mg/24 h, and TUP 2939 µg/24 h. Clinical stabilization was only achieved after Ritonavir withdrawal, emphasizing the role of drug interactions in precipitating crises. This case shows the complex interactions between genetic predisposition, environmental factors, and comorbidities in VP. It emphasizes the importance of genetic and biochemical testing for accurate diagnosis, Hemin administration in crisis management, and the necessity of carefully reviewing prescribed medications. Administering an unsafe or unsuitable drug can greatly affect patients with Porphyria.

396. P22-22. VASCULAR LIPOLYSIS OF REMNANT LIPOPROTEINS AND THE PROTECTIVE ROLE OF HIGH DENSITY LIPOPROTEINS

Gregorio Fariña¹, Luciana Sielecki², Camila Spagnuolo³, Magali Barchuk⁴, Gustavo D. Frechtel⁵, Gabriela Berg⁶, Esteban Martín Repetto⁷, Valeria Zago⁸

1. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires; Departamento de Bioquímica Clínica, Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC).

2. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.; Departamento de Bioquímica Clínica, Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC).

3. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires; Departamento de Bioquímica Clínica, Instituto de

Fisiopatología y Bioquímica Clínica (INFIBIOC).

4. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires; Departamento de Bioquímica Clínica, Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC).

5. UBA-CONICET; Instituto de Inmunología, Genética y Metabolismo (INIGEM)

6. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires; Departamento de Bioquímica Clínica, Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC).

7. Centro de Estudios Farmacológicos y Botánicos (CE-FyBO), UBA-CONICET; Laboratorio de Endocrinología Molecular

8. Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires; Departamento de Bioquímica Clínica, Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC).

goyofari@gmail.com

Introduction: In insulin resistance (IR), remnant lipoproteins (RLP) are elevated and contribute to residual cardiovascular risk. Lipoprotein lipase (LPL), the main enzyme in RLP catabolism, promotes lipolysis that may impair endothelial function. Conversely, high-density lipoproteins (HDL) could exert protective effects. This study evaluated vascular LPL activity in the presence of RLP from patients with and without IR and assessed the modulatory effect of HDL. **Materials and Methods:** Twenty patients were included, ten with IR. Plasma glucose, insulin, and lipid profiles were determined by automated methods. RLP were isolated by ultracentrifugation (density = 1.019 g/mL) and chemically characterized. Aortic rings from Sprague-Dawley rats were incubated with RLP, with or without HDL from a single donor. After 2 h, LPL activity was assessed using radiometric assays. Free fatty acids (FFA), triglycerides, and nitrites were quantified before and after incubation. **Results:** IR patients exhibited an adverse metabolic profile with elevated IR markers. Their RLP contained higher triglyceride and cholesterol levels and induced greater vascular LPL activity than controls. Consequently, FFA production increased, while nitrite levels decreased in the IR group. HDL attenuated these alterations, reducing LPL activity and FFA release and restoring nitrite production. LPL activity correlated positively with IR markers and RLP composition. **Discussion:** RLP from IR patients enhance vascular LPL activity, leading to increased FFA release and impaired nitric oxide production, thus contributing to endothelial dysfunction. HDL partially counteracted these effects. Future studies should examine co-incubation of RLP and HDL from the same patients to better replicate physiological conditions.

POSTERS 23 - REPRODUCCIÓN

DATE & TIME: 20/11/2025 13:00 - 14:30 H

Chairs: Evangelina Capovianco, Fernanda Riera

397. P23-13. PORPHYROMONAS GINGIVALIS POSITIVE GINGIVAL FLUIDS FROM PREGNANT WOMEN IMPAIR TROPHOBLAST AND ENDOTHELIAL FUNCTION IN VITRO

Brenda Lara¹, Luciana D'Eramo², Guillermina Calo³, Ailen Fretes⁴, Luciana Doga⁵, Laura Gliosca⁶, Paula Tribelli⁷, Claudia Perez Leiros⁸, Aldo Squassi⁹, Vanesa Hauk¹⁰

1. Universidad de Buenos Aires - CONICET. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN). Buenos Aires, Argentina; IQUIBICEN

2. Universidad de Buenos Aires - Facultad de Odontología. Cátedra de Odontología Preventiva y Comunitaria. Buenos Aires; Cátedra de Odontología Preventiva y Comunitaria. Buenos Aires.

3. Universidad de Buenos Aires - CONICET. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN). Buenos Aires, Argentina; IQUIBICEN

4. Universidad de Buenos Aires - CONICET. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN). Buenos Aires, Argentina; IQUIBICEN

5. Universidad de Buenos Aires - Facultad de Odontología. Cátedra de Odontología Preventiva y Comunitaria. Buenos Aires; Cátedra de Odontología Preventiva y Comunitaria. Buenos Aires.

6. Universidad de Buenos Aires - Facultad de Odontología. Cátedra de Microbiología; Cátedra de Microbiología

7. Universidad de Buenos Aires - CONICET. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN). Buenos Aires, Argentina; IQUIBICEN

8. Universidad de Buenos Aires - CONICET. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN).

9. Universidad de Buenos Aires - Facultad de Odontología. Cátedra de Odontología Preventiva y Comunitaria. Buenos Aires; Cátedra de Odontología Preventiva y Comunitaria

10. Universidad de Buenos Aires - CONICET. Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN). Buenos Aires, Argentina; IQUIBICEN
brendalara1308@gmail.com

Periodontal disease has been associated with adverse pregnancy outcomes, yet the underlying mechanisms remain unclear. Porphyromonas gingivalis (Pg), a key pathogen in periodontitis, releases outer membrane vesicles (OMV) that promote host-pathogen interactions and contribute to its pathogenesis. During early placentation, trophoblast cells (Tb) play a crucial role in vascular remodeling through interactions with endothelial cells (En). Since we previously showed that PgOMV alter Tb metabolism and function, this study aimed to evaluate the in vitro effect of gingival crevicular fluid (GCF) from pregnant women (16–20 weeks of gestation) on Tb and En function, focusing on Pg and the potential pathogenic role of its OMV in pregnancy complications. Periodontal parameters, including bacterial content in GCF, were assessed in pregnant women attending routine dental care (n=52). PgOMV were isolated by ultracentrifugation. To evaluate GCF effects on Tb function, the HTR-8 human trophoblast cell line was stimulated with GCF (1:5 dilution). Migratory capacity and ROS production were measured by wound-healing and fluorimetry assays, respectively. To study Tb-En crosstalk, conditioned media (CM) was collected from Tb cells pretreated with GCF or PgOMV (18h) and then used to stimulate EA.hy926 endothelial cells. Pg-positive GCF significantly reduced Tb migration (p<0.001) and showed a trend toward increased ROS compared to Pg-negative samples. Notably, Tb pretreatment with PgOMV counteracted GCF-derived effects by reducing ROS (p<0.05). Pg-positive GCF-derived Tb CM also impaired endothelial migration (p<0.05). These findings reveal a deleterious effect of gingival factors on trophoblast-endothelial interactions, suggesting PgOMV as potential pathogenic mediators of placental dysfunction and pregnancy complications.

398. P23-14. SEXUALLY DIMORPHIC EFFECTS OF LPS-INDUCED MATERNAL INFLAMMATION ON PLACENTAL AND FETAL BRAIN NUTRIENT TRANSPORTERS EXPRESSION IN A MURINE MODEL

Ayelen Mirón Granese¹, Marisol Murillo Murillo², Andrea De Laurentiis³, Julieta Aisemberg⁴, Manuel Luis Wolfson⁵, Fernando Correa⁶

1. Centro de Estudios Farmacológicos y Botánicos, Universidad de Buenos Aires-Consejo Nacional de Investigaciones Científicas y Técnicas, Ciudad Autónoma de Buenos Aires, Argentina; Neuroinmunoendocrinología

2. Centro de Estudios Farmacológicos y Botánicos, Universidad de Buenos Aires-Consejo Nacional de Investigaciones Científicas y Técnicas, Ciudad Autónoma de Buenos Aires, Argentina; Neuroinmunoendocrinología

3. Centro de Estudios Farmacológicos y Botánicos, Universidad de Buenos Aires-Consejo Nacional de Investigaciones Científicas y Técnicas, Ciudad Autónoma de Buenos Aires, Argentina; Universidad de Buenos Aires (UBA), Facultad de Odontología, Cátedra de Fisiología, Ciudad Autónoma de Buenos Aires, Argentina; Neuroinmunoendocrinología

4. Centro de Estudios Farmacológicos y Botánicos, Universidad de Buenos Aires-Consejo Nacional de Investigaciones Científicas y Técnicas, Ciudad Autónoma de Buenos Aires, Argentina; Fisiología de la Preñez y el Parto

5. Centro de Estudios Farmacológicos y Botánicos, Univer-

sidad de Buenos Aires-Consejo Nacional de Investigaciones Científicas y Técnicas, Ciudad Autónoma de Buenos Aires, Argentina.; Fisiopatología de la Preñez y el Parto 6. Centro de Estudios Farmacológicos y Botánicos, Universidad de Buenos Aires-Consejo Nacional de Investigaciones Científicas y Técnicas, Ciudad Autónoma de Buenos Aires, Argentina.; Universidad de Buenos Aires (UBA), Facultad de Odontología, Cátedra de Fisiología, Ciudad Autónoma de Buenos Aires, Argentina.; Neuroinmunoendocrinología amirongranese@fmed.uba.ar

Maternal immune activation (MIA), triggered by infection or inflammation during pregnancy, disrupts fetal neurodevelopment through the transplacental transmission of pro-inflammatory cytokines such as IL-6. This immune response promotes neuroinflammation and impairs neural circuit formation, increasing the risk for neurodevelopmental disorders including schizophrenia, bipolar disorder, and autism spectrum disorder. The placenta, serving as the interface between maternal and fetal environments, plays a critical role in regulating nutrient transport and shielding the fetus from inflammatory insults. However, MIA can impair placental function, particularly nutrient transporter expression, with potentially sex-specific effects that remain underexplored. To investigate this, we administered lipopolysaccharide (LPS) to pregnant CD1 mice on gestational day 15 to induce MIA. Six hours post-injection, we collected maternal blood, amniotic fluid, placentas, and fetal brains for analysis. We found that LPS significantly elevated maternal circulating IL-6 levels ($p < 0.05$), with IL-6 protein in amniotic fluid trending higher in males, while IL-6 mRNA expression in placentas showed a trend toward higher levels in females. Analysis of nutrient transporter mRNA expression revealed sex-dependent alterations: Glut3 was downregulated in female placentas ($p < 0.05$) but upregulated in female fetal brains ($p < 0.05$). Slc38a1 was increased in male placentas ($p < 0.05$); Slc38a2 was reduced in female placentas ($p < 0.05$); and Fatcd36 was downregulated only in male placentas ($p < 0.05$), while no changes were detected in fetal brains. These findings demonstrate sexually dimorphic responses to MIA in both placental and fetal brain nutrient transport systems, underscoring the importance of incorporating fetal sex as a biological variable in studies of maternal-fetal immune dynamics and neurodevelopmental risk.

399. P23-15. THE EXPRESSION OF THE UTERINE 5 α -REDUCTASE ENZYME IS EPIGENETICALLY REGULATED IN THE SHORT AND LONG-TERM IN A RAT MODEL OF POLYCYSTIC OVARY SYNDROME

Gisela Soledad Bracho¹, María Virginia Acosta², Gabriela Anahí Altamirano³, Laura Kass⁴, María Florencia Rossetti⁵, Verónica Lis Bosquiazzo⁶

1. Instituto de Salud y Ambiente del Litoral (ISAL, UNL-CO-NICET), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral.; -

2. Instituto de Salud y Ambiente del Litoral (ISAL, UNL-CO-NICET), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral.; -

3. Instituto de Salud y Ambiente del Litoral (ISAL, UNL-CO-NICET), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral.; -

4. Instituto de Salud y Ambiente del Litoral (ISAL, UNL-CO-NICET), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral.; -

5. Instituto de Salud y Ambiente del Litoral (ISAL, UNL-CO-NICET), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral.; -

6. Instituto de Salud y Ambiente del Litoral (ISAL, UNL-CO-NICET), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral.; -
gsbracho@fcbcb.unl.edu.ar

Uterine expression of steroidogenic enzymes is altered in animal models and women with polycystic ovary syndrome (PCOS). This study investigated the short- and long-term effects of PCOS on the transcriptional regulation of 5 α -reductase type I (Srd5a1) on uterine

tissue. PCOS was induced in female Wistar rats via subcutaneous dehydroepiandrosterone injection (6 mg/100 g BW) from postnatal days (PND) 21 to 40, while Controls received sesame oil. For this, samples were collected from animals euthanized at postnatal day 41 (PND41) and 24 months of age. The methylation status at sites within the promoter was determined using Methylation-Sensitive Restriction Enzyme- Polymerase Chain Reaction (MSRE-PCR). At both ages, PCOS rats exhibited significantly higher Srd5a1 mRNA than Control, expressed in relative units: PND41: Control: 0.0051 ± 0.00060 vs. PCOS: 0.0128 ± 0.0016 ; 24 months: Control: 0.0013 ± 0.0001 vs. PCOS: 0.0026 ± 0.0005 ; $p < 0.05$. Epigenetic analysis revealed that at PND41, animals with PCOS showed hypomethylation and hypermethylation at different sites of the Srd5a1 promoter. At 24 months, some sites remained hypomethylated, while others showed no differences between groups. Reduced methylation correlated with elevated Srd5a1 expression. Notably, sites that were hypomethylated at PND41 remained hypomethylated at 24 months, indicating a stable, long-term epigenetic change. In contrast, the hypermethylation observed at PND41 represented a transient modification that was reversed at 24 months. These findings suggest that PCOS induces specific epigenetic modifications that persist with age and regulate Srd5a1 expression.

400. P23-16. IMPACT OF CHRONIC INFLAMMATION ON THE FUNCTIONAL PROPERTIES OF ADULT SERTOLI CELLS: INSIGHTS FROM AN EXPERIMENTAL AUTOIMMUNE ORCHITIS MODEL

Denisse Ferrer Viñals¹, Patricia Verónica Jacobo², Cecilia Lucía Centola³, Ana Clara Romero⁴, Carolina Gabriela Ocampo⁵, Cristian Marcelo Sobarzo⁶, Ivana Sanchez Rojas⁷, María Noel Galardo⁸, María Susana Theas⁹

1. Instituto de Investigaciones Biomédicas (INBIOMED, UBA-CONICET), Facultad de Medicina. Buenos Aires, Argentina; Dinámica de la espermatogénesis en el testículo normal y patológico

2. Instituto de Investigaciones Biomédicas (INBIOMED, UBA-CONICET), Facultad de Medicina. Buenos Aires, Argentina; Dinámica de la espermatogénesis en el testículo normal y patológico

3. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET - FEI - División de Endocrinología, Hospital de Niños "Ricardo Gutiérrez", Buenos Aires, Argentina; Biología celular gonadal

4. Instituto de Investigaciones Biomédicas (INBIOMED, UBA-CONICET), Facultad de Medicina. Buenos Aires, Argentina; Dinámica de la espermatogénesis en el testículo normal y patológico

5. Instituto de Investigaciones Biomédicas (INBIOMED, UBA-CONICET), Facultad de Medicina. Buenos Aires, Argentina; Dinámica de la espermatogénesis en el testículo normal y patológico

6. Instituto de Investigaciones Biomédicas (INBIOMED, UBA-CONICET), Facultad de Medicina. Buenos Aires, Argentina; Inmunología de la Reproducción

7. Instituto de Investigaciones Biomédicas (INBIOMED, UBA-CONICET), Facultad de Medicina. Buenos Aires, Argentina; Dinámica de la espermatogénesis en el testículo normal y patológico

8. Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET - FEI - División de Endocrinología, Hospital de Niños "Ricardo Gutiérrez", Buenos Aires, Argentina; Biología celular gonadal

9. Instituto de Investigaciones Biomédicas (INBIOMED, UBA-CONICET), Facultad de Medicina. Buenos Aires, Argentina; Dinámica de la espermatogénesis en el testículo normal y patológico

lab10inbiomeduba@gmail.com

Sertoli cells (SCs) play a key role in providing metabolic and structural support to the seminiferous epithelium. Under inflammatory conditions such as experimental autoimmune orchitis (EAO), their functionality may be altered affecting processes like lactate production and cell proliferation. This study aimed to evaluate these

parameters in primary cultures of adult SCs obtained from normal (N) and EAO rats under basal conditions and FSH (0.1 $\mu\text{g/mL}$) stimulation. Cells were incubated for 24 and 48 h to assess BrdU incorporation (1.8 $\mu\text{g/mL}$) and lactate production, respectively. Preliminary results show that in testes with severe EAO, lactate production decreased (71.18 $\mu\text{g}/\mu\text{g}$ DNA) compared to N (209.92 $\mu\text{g}/\mu\text{g}$ DNA) and FSH failed to restore lactate output (72.57 $\mu\text{g}/\mu\text{g}$ DNA). No significant differences were found between basal and stimulated conditions within the severe EAO group. In contrast, SCs from the mild EAO group exhibited lactate levels comparable to N (EAO: basal: 227.1, FSH: 296.3; N basal: 209.92, FSH: 297.35) with a trend toward increased lactate production upon FSH stimulation in both groups. BrdU incorporation revealed an increased proliferation in the EAO group (basal: 37.6% vs FSH: 40.85%) compared to N (basal: 13.8% vs FSH: 14.7%). In both groups, FSH stimulation did not significantly modify the proliferative response. Our results suggest that the testicular inflammatory microenvironment compromises Sertoli cell function.

401. P23-17. DEVELOPMENT OF AN OPEN-SOURCE DEEP LEARNING-BASED PLATFORM FOR HUMAN SPERM MOTILITY ANALYSIS

Pilar Ameijeiras¹, Emily Kaplan², Adrian Pacheco Pozo³, Dario Krapf⁴, Ana Romarowski⁵, Diego Krapf⁶, Mariano G Buffone⁷

1. Instituto de Biología y Medicina Experimental, CONICET, Buenos Aires, Argentina.; *Biología Celular y Molecular de la Reproducción*

2. School of Biomedical Engineering, Colorado State University, Fort Collins, CO, USA.; *Department of Electrical and Computer Engineering*

3. Department of Electrical and Computer Engineering, Colorado State University, Fort Collins, CO, USA.; *Biomedical Engineering*

4. Instituto de Biología Molecular y Celular de Rosario, CONICET-UNR, Rosario, Argentina.; *Cascadas de Señalización Celular*

5. Instituto de Biología y Medicina Experimental, CONICET, Buenos Aires, Argentina.; *Biología Celular y Molecular de la Reproducción*

6. Colorado State University, Fort Collins, CO, USA.; *Department of Electrical and Computer Engineering*

7. Instituto de Biología y Medicina Experimental, CONICET, Buenos Aires, Argentina.; *Biología Celular y Molecular de la Reproducción*

pili.ameijeiras98@gmail.com

Sperm motility analysis is essential for assessing sperm quality and predicting fertilization potential. While computer-assisted sperm analysis (CASA) systems are widely used, they are costly, not always implemented in clinics, and provide limited predictive value for treatment outcomes. We propose that single-particle trajectories can provide deeper insights into sperm dynamics than conventional CASA. To this end, we have developed an open-source, user-friendly deep learning-based platform for sperm motility analysis in humans and other species, enabling accurate segmentation, complete trajectory tracking, and novel motility descriptors. By integrating advanced metrics such as power spectral density and orientation autocorrelation with standard motility parameters, we characterize key physiological states, including hyperactivation, a capacitation-associated transition required for fertilization. Dimensionality reduction and unsupervised clustering are applied to define multiparametric motility states. Our main aim is to combine these detailed motility features to enhance the prediction of fertilization potential in patients undergoing assisted reproductive technologies (ART). Through an established partnership with a reproductive medicine clinic, we have applied this framework to samples from both healthy donors and patients undergoing ARTs to understand the population distribution of these parameters. This is the first study to apply random walk analysis to sperm motility. In the future, multivariable regression will identify interpretable predictors, while random forest classifiers will optimize predictive accuracy for ART outcomes, including fertilization, pregnancy, and live birth. We expect this open-source, predictive platform to set a new

standard for sperm function assessment, improving male infertility diagnostics and enhancing ART outcomes.

402. P23-18. FLAGELLAR ABNORMALITIES IN SLO3-DEFICIENT MOUSE SPERM ARE LINKED TO MEMBRANE CHOLESTEROL DYNAMICS AND OSMOREGULATION

Lucila R. Gómez Olivieri¹, Paula A. Balestrini², Pilar Ameijeiras³, Ana Romarowski⁴, Celia Santi⁵, Diego Krapf⁶, Clara I. Marin Briggiler⁷, Guillermina M. Luque⁸, Mariano G. Buffone⁹

1. Instituto de Biología y Medicina Experimental (IBYME-CO-NICET); *Biología Celular y Molecular de la Reproducción*

2. Instituto de Biología y Medicina Experimental (IBYME-CO-NICET); *Biología Celular y Molecular de la Reproducción*

3. Instituto de Biología y Medicina Experimental (IBYME-CO-NICET); *Biología Celular y Molecular de la Reproducción*

4. Instituto de Biología y Medicina Experimental (IBYME-CO-NICET); *Biología Celular y Molecular de la Reproducción*

5. Washington University; *Department of Obstetrics and Gynecology*

6. Colorado State University; *Department of Electrical and Computer Engineering*

7. Instituto de Biología y Medicina Experimental (IBYME-CO-NICET); *Biología Celular y Molecular de la Reproducción*

8. Instituto de Biología y Medicina Experimental (IBYME-CO-NICET); *Biología Celular y Molecular de la Reproducción*

9. Instituto de Biología y Medicina Experimental (IBYME-CO-NICET); *Biología Celular y Molecular de la Reproducción*

lgomezolivieri@gmail.com

Sperm lacking SLO3, a sperm-specific K⁺ channel, cannot hyperpolarize their plasma membrane potential (Em) during capacitation, a critical step for fertilization, leading to infertility. In this work, we found that a fraction of SLO3 KO sperm exhibit a bending of the flagellum known as hairpin. However, no structural abnormalities were noted when the flagellums were analyzed using electron microscopy. This fraction increases when cells are incubated under capacitating conditions containing bovine serum albumin (BSA) and bicarbonate (HCO₃⁻), and the effect appears very rapidly. Consistent with our observations in vitro, the hairpin rise was also observed in sperm obtained from the female uterus after mating with SLO3 KO males. To assess whether Em contributes to this morphological change, SLO3 KO sperm were treated with pharmacological agents that promote hyperpolarization: valinomycin, amiloride and genistein. Only the addition of the K⁺ ionophore valinomycin significantly reduced hairpin. Moreover, we observed that the BSA present in the capacitating medium promoted hairpin formation, an effect reproduced by cholesterol depletion with cyclodextrin, indicating that the morphological change is due to cholesterol removal. Given the essential role of K⁺ efflux in maintaining proper cell volume, sperm were incubated in media of different osmolarities. Exposure to hypo-osmotic media increased hairpin formation in both WT and SLO3 KO sperm, with a significantly higher effect in the KO cells. In conclusion, the absence of SLO3 promotes flagellar bending in mouse sperm during capacitation, driven by membrane cholesterol removal and osmotic changes. This morphological defect likely compromises motility and contributes to infertility.

403. P23-19. IMPACT OF HEAT STRESS DURING INTRAUTERINE DEVELOPMENT ON THE EXPRESSION OF HISTONE-MODIFYING ENZYMES IN THE PREOVULATORY FOLLICLES OF DAIRY COWS

Nadia Ormaechea¹, Silvina Schegel², María Emilia Odriozola³, Matías Molina⁴, Ulises Notaro⁵, Emmanuel Angeli⁶, Hugo Ortega⁷, Florencia Rey⁸, Natalia Salvetti⁹, Fernanda Rodriguez¹⁰

1. ICIVET Litoral; *Laboratorio de Biología Celular y Molecular Aplicada*

2. Facultad de Ciencias Veterinarias - Universidad Nacional del Litoral; *Laboratorio de Biología Celular y Molecular Aplicada*

3. ICIVET Litoral; *Laboratorio de Biología Celular y Molecular Aplicada*

4. ICIVET Litoral; *Laboratorio de Biología Celular y Molecular*

lar Aplicada

5. ICIVET Litoral; Laboratorio de Biología Celular y Molecular Aplicada

6. ICIVET Litoral; Laboratorio de Biología Celular y Molecular Aplicada

7. ICIVET Litoral; Laboratorio de Biología Celular y Molecular Aplicada

8. ICIVET Litoral; Laboratorio de Biología Celular y Molecular Aplicada

9. ICIVET Litoral; Laboratorio de Biología Celular y Molecular Aplicada

10. ICIVET Litoral; Laboratorio de Biología Celular y Molecular Aplicada

nadia.ormaechea@hotmail.com

Epigenetic alterations such as DNA methylation and histone modifications, regulates the expression of proteins involved in process such as ovarian development and folliculogenesis. Specifically, histone modifications modulate transcriptional activity in ovarian cells by altering chromatin structure and accessibility. In mammals, gonadal development begins during intrauterine life, and in cattle, these processes can be disrupted by harmful stimuli during gestation, such as heat stress, leading to long-term impairments in progeny fertility. The aim of the study was to evaluate changes in histone deacetylases expression in preovulatory follicles of Holstein cows gestated under high temperature-humidity conditions. Adult Argentinean Holstein cows (n=24) gestated under different Temperature-Humidity Index (THI) during their in utero development were used. Ovarian samples were collected by ovariectomy and the expression of histone deacetylases (HDACs 1, 2 and 3) in granulosa and theca interna cell layers of preovulatory follicles was determined by immunohistochemistry. Gestation was divided into two periods (P1: 0-150 days; P2: 151 days-birth); and three trimesters (T1: 0-90 days; T2: 91-180 days; T3: 181-birth days) in which the exposure to high THI was considered. Positive associations were detected between HDAC-1 expression in granulosa cells of preovulatory follicles and average THI during gestation. Additionally, positive associations were found between HDAC-2 expression in granulosa cells and exposure index during T2. These findings suggest that exposure of dairy cows to high THI during intrauterine development may alter the expression of histone-modifying enzymes thereby impacting ovarian development and ultimately compromising the fertility of daughters in adulthood.

404. P23-20. PROXIMAL GONADAL FAT SUPPORTS MALE FERTILITY IN A MURINE MODEL

Jael Dafne Herzfeld¹, Lucía Cuniolo², Lucas Nicolás González³, Patricia Sara Cuasnicú⁴, Mariana Weigel-Muñoz⁵, Vanina Gabriela Da Ros⁶, Débora Juana Cohen⁷

1. IBYME; Laboratorio de Biología de las Gametas

2. IBYME; Laboratorio de Biología de las Gametas

3. IBYME; Laboratorio de Biología de las Gametas

4. IBYME; Laboratorio de Mecanismos Moleculares de la Fertilización

5. IBYME; Laboratorio de Mecanismos Moleculares de la Fertilización

6. IBYME; Laboratorio de Biología de las Gametas

7. IBYME; Laboratorio de Biología de las Gametas

jaael.h@gmail.com

Adipose tissue is currently recognized as an organ with endocrine, metabolic, and immunological functions, capable of directly influencing various physiological processes, including reproduction. Our group was the first to identify two distinct adipose tissue depots surrounding the murine gonads, distinguished by their proximity to the cauda epididymis, where mature sperm are stored: distal gonadal fat and proximal gonadal fat. In a previous study, we characterized both gonadal fat regions under metabolic injury and demonstrated that they possess distinct features, with the proximal gonadal fat suggesting a potential protective role for the cauda epididymis and sperm. Here, we aimed to evaluate the contribution of proximal gonadal fat to male fertility. Ten-week-old C57BL/6 males underwent surgery, either involving the removal of the proximal gonadal fat or a sham procedure. Two weeks post-surgery, no differences were ob-

served in litter size or pup weight between the two groups. However, at 6 weeks, males lacking proximal gonadal fat produced fewer offspring, exhibited increased pup weight, and showed reduced sperm fertilization capacity in vivo assays. At 8 weeks, in vitro epididymal sperm analysis revealed a decrease in concentration and viability, with no changes in their motility and DNA fragmentation. The organ weight and the daily sperm production in the testis remained unaffected. Altogether, these findings identify proximal gonadal fat as a functionally relevant adipose depot and suggest a novel role for this tissue in supporting male reproductive performance.

405. P23-21. PEDF ACT AS A DECAPACITATION FACTOR IN MOUSE EPIDIDYMAL SPERM

María Inés Conte¹, Rocio Agüero², Jorge Leporatti³, Jorge Ibañez⁴, Claudia Aguilera Merlo⁵, María Angeles Monclus⁶

1. IHEM - FCM - UNCuyo - CONICET; LIAM - IHEM

2. IHEM - CONICET - CCT Mendoza; LIAM - IHEM

3. Univ. San Luis; Matemáticas

4. IHEM - CCT Conicet Mendoza; Microscopia

5. FFB - UNSL; Histología

6. IHEM - FCM - CCT Conicet Mendoza; LIAM

miconte@fcm.uncu.edu.ar

PEDF act as a decapacitation factor in mouse epididymal sperm Conte MI2, Agüero R1, Leporatti J3, Ibañez J 1,2, Funes AK 1,4, Aguilera Merlo C3, Monclus MA1,2, Fornes MW1 1 Instituto de Histología y Embriología de Mendoza (IHEM) – CCT Conicet Mendoza – UNCuyo. 2 Facultad de Medicina – Universidad Nacional de Cuyo 3 Facultad de Química, Bioquímica y Farmacia UNSL 4 Facultad de Farmacia y Bioquímica, Universidad Juan Agustín Maza Capacitation is a complex process with changes in sperm head's biochemistry and composition. Because of it, the sperm is capable of face capacitation, hyperactivation, acrosome reaction and finally achieve the fertilization of the egg. However, there are proteins known as decapacitating factors inside the epididymal lumen that are essential to prevent early capacitation. Most of them belong to the serpin family like serpin a 2. PEDF (Pigment Epithelium Derived Factor) is a type of serine protease described by our group in rat male reproductive organs and regulated by androgens. In other tissues, PEDF plays a protective role, but in male reproductive tract, remains unknown. In this study we evaluate PEDF in capacitation and acrosome reaction in mouse epididymal sperm. We analyzed the suppression of PEDF endogen activity by blocking with the specific antibody and then, the function was recovered by adding recombinant PEDF to sperm in capacitating media. Capacitation was evaluated by CTC stain, acrosome reaction was induced with progesterone or calcium ionophore and analyzed with Coomassie blue. Our data shows that the addition of recombinant PEDF is related

POSTERS 24- SAIC - ONCOLOGÍA 4

DATE & TIME: 20/11/2025 13:00 - 14:30 H

Chairs: Andrea Lloaiza Perez, Florencia Gottardo, Juan Miguel Bayo

406. P24-17. EFFECT OF THE PSYCHEDELIC DRUG NORIBOGAINE ON VIABILITY AND INFLAMMATORY GENE EXPRESSION OF HUMAN GLIOBLASTOMA CELLS

Matías Luis Senovieski ^{*1}, Sofía Villalba ^{*2}, Ayelen Martín³, Verónica Bisagno^{*4}, Patricia Pennisi^{*5}

1. Centro de investigaciones endocrinológicas "Dr. Cesar Bergada", Hospital de Niños "Dr. Ricardo Gutierrez", CONICET, Ciudad Autónoma de Buenos Aires, Argentina.; Factores de crecimiento y biología tumoral

2. Instituto de Investigaciones en Medicina Traslacional, Facultad de Ciencias Biomédicas, CONICET-Universidad Austral, Buenos Aires, Argentina.; Neurofarmacología y Sustancias Psicoactivas

3. Centro de investigaciones endocrinológicas "Dr. Cesar Bergada", CEDIE, CONICET, FEI, Div. Endocrinología Hospital de Niños "Dr. Ricardo Gutierrez", Ciudad Autónoma de Buenos Aires, Argentina.; Factores de Crecimiento y Biología Tumoral

4. Instituto de Investigaciones en Medicina Traslacional,

Facultad de Ciencias Biomédicas, CONICET-Universidad Austral, Buenos Aires, Argentina.; Neurofarmacología y Sustancias Psicoactivas

5. Centro de investigaciones endocrinológicas "Dr. Cesar Bergada", CEDIE, CONICET, FEI, Div. Endocrinología Hospital de Niños "Dr. Ricardo Gutierrez", Ciudad Autónoma de Buenos Aires, Argentina.; Factores de Crecimiento y Biología Tumoral

msenovieski@cedie.org.ar

Noribogaine is the main active metabolite of ibogaine, a psychedelic drug that targets the serotonin 2A receptor (5-HT_{2A}). This receptor has been linked to the pro-inflammatory effects of serotonin, and its expression has been particularly detected in astrocytes and microglia. The human glioblastoma cell line U87MG expresses receptors for various neurotransmitters, including the serotonin receptor, which is associated with cell proliferation, migration, and survival. The aim of this study was to investigate the effect of noribogaine as an inhibitor of U87MG cell viability and its potential role in modulating the immune response of glioma cells. U87MG cell viability was analyzed in the presence of different concentrations of noribogaine (0.1 to 100 μ M), with cell counts performed at 24 and 72 hours. A decrease in U87MG cell viability was observed at noribogaine concentrations of 50 and 100 μ M (Kruskal-Wallis test, $p < 0.05$). To evaluate changes in the expression of pro- and anti-inflammatory genes (IL1 β , TNF α , and TGF β) by qPCR, concentrations of 10 μ M (no effect on cell viability) and 50 μ M (lowest concentration with a significant effect) were selected for 1- and 72-hour cultures. Results showed changes in the expression profiles of pro- and anti-inflammatory genes under both acute and chronic noribogaine stimulation. In conclusion, the presence of noribogaine decreases the viability of U87MG cells and may modulate their immune response profile.

407. P24-18. FERROPTOSIS DETECTION IN OSTEOSARCOMA SAMPLES TREATED WITH STANDARD NEOADJUVANT CHEMOTHERAPY

Alejo De Luca¹, Matías Valenzuela Alvarez², Jerónimo Auzmendi³, Gastón Angelini Marquiani⁴, Maximiliano D'adamo⁵, Mónica Loresi⁶, Germán Farfalli⁷, José Ignacio Albergo⁸, Luis Aponte⁹, Pablo Roitman¹⁰, Malena Mazza¹¹, Marcela F. Bontrade¹²

1. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano Buenos Aires (HIBA)- Universidad del Hospital Italiano (IUHI), Buenos Aires, Argentina.; Laboratorio de Procesos Remodelativos y Nichos Celulares
2. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano Buenos Aires (HIBA)- Universidad del Hospital Italiano (IUHI), Buenos Aires, Argentina.; Laboratorio de Procesos Remodelativos y Nichos Celulares
3. Instituto de Investigaciones Farmacológicas, UBA - CONICET; Laboratorio de Epilepsia

4. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano Buenos Aires (HIBA)- Universidad del Hospital Italiano (IUHI), Buenos Aires, Argentina.; Laboratorio de Procesos Remodelativos y Nichos Celulares
5. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano Buenos Aires (HIBA)- Universidad del Hospital Italiano (IUHI), Buenos Aires, Argentina.; Laboratorio de Histología y Microscopía

6. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano Buenos Aires (HIBA)- Universidad del Hospital Italiano (IUHI), Buenos Aires, Argentina.; Laboratorio de Histología y Microscopía

7. Ortopedia oncológica, Hospital Italiano Buenos Aires (HIBA);

8. Ortopedia oncológica, Hospital Italiano Buenos Aires (HIBA);

9. Ortopedia oncológica, Hospital Italiano Buenos Aires (HIBA);

10. Anatomía patológica, Hospital Italiano Buenos Aires (HIBA);

11. Anatomía patológica, Hospital Italiano Buenos Aires (HIBA);

12. Instituto de Medicina Traslacional e Ingeniería Biomédica (IMTIB) / CONICET-Hospital Italiano Buenos Aires (HIBA)- Universidad del Hospital Italiano (IUHI), Buenos Aires, Argentina.; Laboratorio de Procesos Remodelativos y Nichos Celulares
alejo.de@comunidad.ub.edu.ar

Osteosarcoma (OS), the most frequent primary malignant bone tumor in children and adolescents, is characterized by its high metastatic potential, with pulmonary dissemination remaining the leading cause of therapeutic failure. Standard neoadjuvant chemotherapy typically involves doxorubicin, cisplatin, and methotrexate. However, resistance and relapse remain common. Ferroptosis, an iron-dependent form of regulated cell death, has been associated with enhanced cisplatin sensitivity, suggesting its potential relevance in OS. In this study, we investigated the presence of ferroptosis in primary OS tumors and lung metastases from patients treated with standard chemotherapy. Tissue sections were stained with Perl's Prussian blue, a histochemical method to detect iron accumulation, and examined for ferroptotic features. Ferroptosis was identified in 82.35% of primary tumor samples, although the extent of staining varied across cases, indicating heterogeneity in ferroptotic activity. Similarly, 83.33% of pulmonary metastases displayed ferroptosis, demonstrating that this process occurs not only in primary tumors but also in metastatic lesions. To our knowledge, this is the first report providing histological evidence of ferroptosis in OS using Perl's staining, representing a novel approach to visualize this cell death pathway in human samples. The underlying causes responsible for ferroptosis induction under chemotherapy remain unclear and will require further investigation, particularly regarding the interaction with cisplatin and other cytotoxic agents. These findings underscore the biological importance of ferroptosis in OS and highlight its potential as a prognostic marker and therapeutic target. Future studies with larger cohorts are needed to validate these observations and explore their translational impact.

408. P24-19. GAMMA-SYNUCLEIN AS A KEY MODULATOR OF MELANOMA CELL MIGRATION AND SIGNALING

Pablo Martínez¹, Leonardo Juan de Paz², Mauricio Menacho Márquez³

1. Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).

2. Facultad de Ciencias Médicas. Universidad Nacional de Rosario.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB).

3. Facultad de Ciencias Médicas. Universidad Nacional de Rosario. CONICET.; Centro de Investigación del Cáncer de Rosario (CIC-R) y Centro de Investigación y Producción de Reactivos Biológicos (CIPReB). IDICER.

pablmartinezponce2001@gmail.com

Gamma-synuclein (γ S) has been implicated in tumor progression in several cancers by promoting proliferation, apoptosis resistance, migration, and invasion. This study aimed to elucidate γ S's role in melanoma, a highly aggressive skin cancer. Modulation of γ S levels in B16-F0 melanoma cells revealed its significant influence on key processes as proliferation, migration, and adhesion. Immunostaining showed that γ S overexpression enhanced organization and stability of microtubules and actin stress fibers, along with the formation of filopodia and lamellipodia, indicative of an invasive phenotype. In contrast, γ S knockdown decreased microtubule visibility and preserved actin structures similar to control cells. Quantitative analysis indicated that γ S overexpression increased cell size, while both overexpression and silencing reduced nuclear size. Morphological assessment revealed a predominance of elongated and kidney-shaped nuclei in γ S-overexpressing cells, potentially facilitating migration. Functional assays demonstrated that γ S silencing reduced phosphorylation of AKT and ERK, crucial components of PI3K/AKT and MAPK signaling pathways. While γ S overexpression diminished active AKT levels, ERK activation remained unchanged. Additionally, γ S positively regulated MAP2K1 transcript levels. Western blot and immunocytochemistry confirmed that decreased γ S expression upregulated epithelial markers E-cadherin and β -catenin, suggesting reduced invasiveness. Moreover, focal adhesion kinase (FAK) activation, detected by phosphorylated FAK(pY397), was elevated in γ S-overexpressing cells, correlating with heightened migra-

tory capacity. Adhesion assays revealed enhanced binding to collagen and lysine substrates regardless of γ S modulation, highlighting its complex role in cell-matrix interactions. These findings position γ S as a critical regulator of cytoskeletal dynamics, signaling, and adhesion in melanoma, supporting its potential as a therapeutic target.

409. P24-20. iNOS DERIVED NO PROMOTE GBM-BRAIN CONNECTIVITY

Elsa Lourdes Hincapié Arias¹, Lorena Rela², Denise Belgorosky #³, Ana María Eiján #⁴

1. Instituto de Oncología Ángel H. Roffo; Área Investigación
2. Universidad de Buenos Aires. Facultad de Ciencias Médicas.; Departamento de Ciencias Fisiológicas.
3. Instituto de Oncología Ángel H. Roffo; Área Investigación
4. Instituto de Oncología Ángel H. Roffo; Área Investigación elshincapie@gmail.com

Introduction: Glioblastoma (GBM, grade IV) has a poor survival rate despite current therapies, highlighting the need for novel approaches. Recent evidence suggests that synaptic activity may drive GBM growth. Nitric oxide (NO), produced by inducible NO synthase (iNOS), not only sustains the glioma stem cell niche, but also may facilitate tumor-brain interactions through gap junctions synapse association. **Objective:** To analyze the iNOS/NO role in the GBM-brain cells interaction. **Methods:** GL26 (GBM murine cell line) spheroid growth (50x10³cells/ml) was assessed after brain conditioned medium (BCM) exposure. GL26-brain cells (C57BL/6) co-cultures cell ratio and junctions (%) were analyzed under iNOS inhibitor (S-methylisothiourea SMT, 200 μ M) and Gabapentin (Gp, 250 μ M), a GABA analogue. Immunofluorescence (IF): connexin-43 (Cx), vimentin (Vim). Pluripotent-enriched GL26 spheres migration (%), speed (μ m/h) and Vim expression (qPCR) were measured. **Results:** GL26 spheroids diameter increased when exposed to BCM (100%, $p < 0.01$). In co-cultures, SMT reduced GL26/brain cell proportion and cell junctions (80%, $p < 0.05$), whereas Gp increased them (50%, $p < 0.5$). SMT+Gp decreased co-cultures cell ratio (55%, $p < 0.01$) and junctions (90%, $p < 0.001$) compared to Gp alone. Cx and Vim expression was observed by IF. In 3D assays, SMT enhanced GL26 sphere migration and speed (50%, $p < 0.01$), and decreased Vim expression (50% $p < 0.05$). **Conclusion:** iNOS-derived NO plays a key role supporting GBM spheroids growth and tumor-brain association. Inhibition of iNOS (SMT) reduces these connections but unexpectedly increases tumor cell migration, possibly reflecting a failed attempt to establish interactions with the brain.

410. P24-21. PRELIMINARY EVALUATION OF BORON NEUTRON CAPTURE THERAPY (BNCT) IN COLON CANCER CELLS

María A. Palermo Rodríguez¹, Carla Rodríguez², Debora N. Frydryk Benítez³, Lya N.I. Brito Guerrero⁴, Paula Curotto⁵, Silvia I. Thorp⁶, Mónica A. Palmieri⁷, María Silvina Olivera⁸, Marcela A. Garabalino⁹, Emiliano C.C. Pozz¹⁰, Andrea Monti Hughes¹¹, Yanina V. Langle¹², VERONICA ANDREA TRIVILLIN¹³

1. Comisión Nacional de Energía Atómica (CNEA), Av. Gral. Paz 1499, Buenos Aires, Argentina; Departamento de Radiobiología
2. Comisión Nacional de Energía Atómica (CNEA), Av. Gral. Paz 1499, Buenos Aires, Argentina; Departamento de Radiobiología
3. Comisión Nacional de Energía Atómica (CNEA), Av. Gral. Paz 1499, Buenos Aires, Argentina; Departamento de Radiobiología
4. Comisión Nacional de Energía Atómica (CNEA), Av. Gral. Paz 1499, Buenos Aires, Argentina; Departamento de Radiobiología
5. Comisión Nacional de Energía Atómica (CNEA), Av. Gral. Paz 1499, Buenos Aires, Argentina; Reactor RA-3
6. Comisión Nacional de Energía Atómica (CNEA), Av. Gral. Paz 1499, Buenos Aires, Argentina; Dosimetría
7. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (UBA), CABA, Argentina; Departamento de Biodiversidad y Biología Experimental (DBBE).
8. Comisión Nacional de Energía Atómica (CNEA), Av. Gral. Paz 1499, Buenos Aires, Argentina; Química
9. Comisión Nacional de Energía Atómica (CNEA), Av. Gral. Paz 1499, Buenos Aires, Argentina; Departamento de Radiobiología

10. Comisión Nacional de Energía Atómica (CNEA), Av. Gral. Paz 1499, Buenos Aires, Argentina; Reactor RA-3

11. Comisión Nacional de Energía Atómica (CNEA), Av. Gral. Paz 1499, Buenos Aires, Argentina / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; Departamento de Radiobiología

12. Universidad de Buenos Aires, Instituto de Oncología Ángel H. Roffo, Av. S. Martín 5481, Buenos Aires, Argentina.; Investigación y Bioterío

13. Comisión Nacional de Energía Atómica (CNEA), Av. Gral. Paz 1499, Buenos Aires, Argentina / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; Departamento de Radiobiología maryalepalermo@gmail.com

Boron Neutron Capture Therapy (BNCT) is a radiotherapeutic modality based on the selective administration of boron-10 (¹⁰B) to tumor cells, followed by the irradiation with thermal neutrons from a nuclear reactor or accelerator, generating alpha particles and ⁷Li nuclei with highly localized effects at the cellular level. High-LET radiation is a potent inducer of DNA damage, particularly DNA double-strand breaks. Boronophenylalanine (BPA) and sodium borocaptate (BSH) are compounds approved for clinical use. However, sodium decahydrodecaborate (GB-10) has also been approved by the FDA for biodistribution studies. The objective of this study was to analyze the sensitivity of DHD/K12/TRb colon cancer cells to irradiation with neutrons in the presence or absence of BPA or GB-10, evaluating the clonogenic survival. DHD/K12/TRb colon cells were cultured in DMEM/F-10 (1:1) supplemented with 10% FBS. BPA-BNCT and GB-10-BNCT were administered at a concentration of 50 mg 10B/L. The absorbed doses for survival curve generation were 1, 3, and 5 Gy. Controls included non-treated cells and cells exposed to the respective boron-containing compounds. The data were fitted to the linear-quadratic model, showing that BPA induced a significant decrease in survival at 3 Gy ($\alpha = 1.9386$; $\beta = -0.2387$; SF = 0.026), while GB-10 produced a more gradual effect ($\alpha = 0.1916$; $\beta = 0.0593$; SF = 0.08952), both statistically significant ($p < 0.05$). A feasibility study is currently underway. Preliminary data demonstrate dose-dependent cytotoxic effects of BNCT in colon cancer cells, particularly with BPA, supporting continued evaluation of BNCT as a potential therapeutic approach for colorectal cancer.

411. P24-22. STUDY OF CROSS-RESISTANCE BETWEEN PHOTODYNAMIC THERAPY AND CHEMOTHERAPY IN THE TREATMENT OF OVARIAN CANCER

Julietta Batista¹, Daniel Sáenz², Mariela Céspedes³, Leandro Mamone⁴, Adriana Casas⁵, Gabriela Di Venosa⁶

1. Centro de Investigaciones sobre Porfirinas y Porfirias (CI-PYP)- Hospital de Clínicas "José de San Martín"-UBA-CO-NICET.; Laboratorio de Terapias Fotoasistidas.
2. Centro de Investigaciones sobre Porfirinas y Porfirias (CI-PYP)- Hospital de Clínicas "José de San Martín"-UBA-CO-NICET.; Laboratorio de Terapias Fotoasistidas.
3. Centro de Investigaciones sobre Porfirinas y Porfirias (CI-PYP)- Hospital de Clínicas "José de San Martín"-UBA-CO-NICET.; Laboratorio de Terapias Fotoasistidas.
4. Centro de Investigaciones sobre Porfirinas y Porfirias (CI-PYP)- Hospital de Clínicas "José de San Martín"-UBA-CO-NICET.; Laboratorio de Terapias Fotoasistidas.
5. Centro de Investigaciones sobre Porfirinas y Porfirias (CI-PYP)- Hospital de Clínicas "José de San Martín"-UBA-CO-NICET.; Laboratorio de Terapias Fotoasistidas.
6. Centro de Investigaciones sobre Porfirinas y Porfirias (CI-PYP)- Hospital de Clínicas "José de San Martín"-UBA-CO-NICET.; Laboratorio de Terapias Fotoasistidas. batista.julietta.alejandra@gmail.com

Ovarian cancer is one of the leading causes of death from gynecological cancer due to the presence of intraperitoneal metastasis at the time of diagnosis, which limits the effectiveness of chemotherapy. The urgency for new therapeutic strategies is evident, and photodynamic therapy (PDT) with 5-aminolevulinic acid (ALA-PDT) emerges as a promising alternative. PDT is based on the use of

photosensitizers that accumulate in tumor cells, and after light activation, photochemical reactions are triggered, destroying the tumor. Protoporphyrin IX is the photosensitizer synthesized within the cells after ALA exposure. Resistance in oncological treatments is a challenge, as it varies depending on the cellular origin and the therapy used. Therefore, the objective of this work was to study cross-resistance to PDT and Cisplatin (Cis) in cell populations derived from the IGROV-1 cell line, considering the DL50 (light dose that produces 50% cell death) and the 50% Inhibitory concentration (IC50). LD50s were 0.24 ± 0.03 J/cm² for IGROV1 and more than 2.5 J/cm² for the ALA-PDT-resistant cells IGROV-RZ. IC50s were 5.89 ± 0.76 μ M for the resistant cells to cisplatin IGROV-Rcis and 3.0 ± 0.4 μ M for IGROV-1. Differences among the cells were studied in terms of morphological and metabolic characteristics, pointing out the disorganization of F-actin as a possible mechanism of resistance to ALA-PDT. No differences were observed regarding porphyrin production and cell migration among the studied cell populations. No cross-resistance was found between treatments, suggesting that ALA-PDT could be used in combination with cisplatin to optimize therapeutic strategies in ovarian cancer.

412. P24-23. SEQUENTIAL BORON NEUTRON CAPTURE THERAPY (BNCT) WITH BPA AND GB-10 IN DIFFUSE LUNG METASTASES IN BDIX RATS: BLOOD BORON CONCENTRATION, TUMOUR CONTROL AND ACTIVATION OF THE IMMUNE RESPONSE

Debora N. Frydryk Benitez¹, Mónica A. Palmieri², Carolina B. Iglesias³, Paula Curotto⁴, Silvia I. Thorp⁵, Marcela A. Garabalino⁶, Emiliano C.C. Pozzi⁷, Paula S. Ramos⁸, Miguel A. Pérez⁹, Agustina M. Portu¹⁰, María A. Palermo¹¹, Lya N. I. Brito Guerrero¹², Martín V. Viale¹³, Andrea Monti Hughes¹⁴, Yanina V. Langle¹⁵, Verónica A. Trivillin¹⁶

1. Comisión Nacional de Energía Atómica (CNEA) / Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (UBA), Argentina.; Departamento de Radiobiología / Departamento de Química Biológica
2. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (UBA), Argentina.; Departamento de Biodiversidad y Biología Experimental (DBBE)
3. Instituto de Oncología Ángel H. Roffo, UBA, Argentina.; Área de investigación
4. Comisión Nacional de Energía Atómica (CNEA), Argentina.; Reactor RA-3
5. Comisión Nacional de Energía Atómica (CNEA), Argentina.; Reactor RA-3
6. Comisión Nacional de Energía Atómica (CNEA), Argentina.; Departamento de Radiobiología
7. Comisión Nacional de Energía Atómica (CNEA), Argentina.; Reactor RA-3
8. Comisión Nacional de Energía Atómica (CNEA), Argentina.; Reactor RA-3
9. Facultad de Odontología, UBA, Argentina.; Histología
10. Comisión Nacional de Energía Atómica (CNEA) / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina.; Departamento de Radiobiología
11. Comisión Nacional de Energía Atómica (CNEA), Argentina.; Departamento de Radiobiología
12. Comisión Nacional de Energía Atómica (CNEA), Argentina.; Departamento de Radiobiología
13. Instituto de Nanociencia y Nanotecnología, (CNEA-CONICET), Nodo Constituyentes, Buenos Aires, Argentina.; Bioterio y cultivo celular.
14. Comisión Nacional de Energía Atómica (CNEA) / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina.; Departamento de Radiobiología
15. Instituto de Oncología Ángel H. Roffo, UBA, Argentina.; Área de investigación y Bioterio
16. Comisión Nacional de Energía Atómica (CNEA) / Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina.; Departamento de Radiobiología

debora_nbh@hotmail.com

The lung, frequently affected by colorectal metastases, is a sensitive organ with limited options under conventional treatments. Boron Neutron Capture Therapy (BNCT) offers a promising alternative. Boronophenylalanine (BPA) accumulates in tumor parenchyma and skin, while sodium decahydrodecaborate (GB-10) diffuses into the tumor stroma. Their combination in sequential BNCT (BNCT-Seq7) targets distinct tumor cell populations. This study assessed BNCT-Seq7 in BDIX rats with diffuse lung metastases using a two-application protocol, 7 days apart: BPA-BNCT (46.5 mg 10B/kg) followed by GB-10-BNCT (50 mg 10B/kg). Oligo-fucoidan was administered to mitigate dermatitis. Colon cancer cells were inoculated after the second irradiation to evaluate the abscopal effect. Clinical parameters, blood boron concentration, lung metastatic response, tumor volume, radiotoxicity in skin and immune profiles in lung, tumor, and lymph nodes were analyzed. An inverse relationship was observed between blood BPA concentration and metastasis: boron values near the reference range (13.7 ± 2.3 ppm) correlated with <1% metastases incidence, whereas levels <7 ppm correlated with 3%–28.7% metastases incidence. BNCT-Seq7 significantly reduced pulmonary metastases versus SHAM ($p \leq 0.05$), confirmed macroscopically and by H&E histology. BNCT-Seq7 induced moderate–severe dermatitis, partially mitigated by Oligo-fucoidan. Preliminary flow cytometry analysis revealed a cytotoxic immune profile: in metastatic lungs, BNCT increased NK and NKT cells, reduced Tregs, and elevated the CD8/Treg ratio compared with SHAM. In secondary tumors, only CD8/Treg ratio increased. BNCT-Seq7 results a promising therapy for diffuse lung metastases, inducing local and systemic immune responses that support distant tumor control via the abscopal effect, with efficacy strongly influenced by blood boron levels.

413. P24-24. ORTHOTOPIC PANCREATIC TUMOR MODEL IN HAMSTERS: IN VIVO AND EX VIVO MICRO PET/CT IMAGES AT LANAIP-CNEA

Yago Dores Dores¹, Lucila Rogulich², Agustina M. Portu³, Ivan Peñuelas⁴, María Collantes⁵, Debora Frydryk Benitez⁶, Verónica A. Trivillin⁷, Mónica A. Palmieri⁸, Carla B. Rodríguez⁹, Daniela Speisky¹⁰, Miguel A. Perez¹¹, Mirta Kujaruk¹², Eduardo Cafferata¹³, Emiliano C.C. Pozzi¹⁴, Andrea Monti Hughes¹⁵

1. Comisión Nacional de Energía Atómica (CNEA), Argentina; LANAIP
2. Comisión Nacional de Energía Atómica (CNEA), Argentina; LANAIP
3. Comisión Nacional de Energía Atómica (CNEA), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; Div. Radiomicrobiología, Depto Radiobiología
4. Clínica Universidad Navarra, Pamplona, España; Translational Molecular Imaging Unit
5. Clínica Universidad Navarra, Pamplona, España; Translational Molecular Imaging Unit
6. Comisión Nacional de Energía Atómica (CNEA); Departamento de Biodiversidad y Biología Experimental (DBBE), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (UBA), CABA, Argentina; Div. Patología de la Radiación, Depto Radiobiología
7. Comisión Nacional de Energía Atómica (CNEA), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; Div. Patología de la Radiación, Depto Radiobiología
8. Departamento de Biodiversidad y Biología Experimental (DBBE), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires (UBA), CABA, Argentina; Departamento de Biodiversidad y Biología Experimental (DBBE)
9. Comisión Nacional de Energía Atómica (CNEA), Argentina; Div. Bioquímica Nuclear, Depto Radiobiología
10. Hospital de Gastroenterología Dr. Carlos Bonorino Udaondo, Buenos Aires, Argentina; Unidad de Anatomía Patológica
11. Facultad de Odontología, UBA, Argentina; Cátedra Anatomía Patológica
12. Hospital de Gastroenterología Dr. Carlos Bonorino Udaondo, Buenos Aires, Argentina; Unidad de Anatomía Patológica

13. Fundación Instituto Leloir, CONICET, Argentina; Laboratorio de terapia molecular y celular
 14. Comisión Nacional de Energía Atómica (CNEA), Argentina; División Haces y Nuevos Usos
 15. Comisión Nacional de Energía Atómica (CNEA), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; Div Patología de la Radiación, Depto Radiobiología
 yagodores@gmail.com

Pancreatic ductal adenocarcinoma is an aggressive type of cancer. We have established an orthotopic pancreatic tumor model in Syrian hamsters. As these are intra-abdominal tumors, a preclinical imaging technique would reduce the number of animals needed to evaluate tumor progression and therapies. In this study, we evaluated hamster pancreatic tumor detection with microPET/CT at the National Laboratory of Preclinical Imaging (LANAIP-CNEA). Hamster pancreatic tumor cells (HapT1, 5x10⁵ cells) were injected beneath the capsule of the pancreas (splenic lobe). Based on previous observations, we performed microPET/CT studies at 14 days post-inoculation. Images were taken at 1h, 2h, 3h after [18F]FDG administration (350-420 uCi, 10 min duration / CT at 35kV, 200uA, 15 min duration) in 3 animals: 2 injected intrajugularly and 1 in the gingival vein. After 3h, animals were euthanized, and organs extracted were placed in a 24-well culture plate and imaged ex vivo by microPET/CT studies to correlate [18F]FDG accumulation observed in vivo. Histological evaluation of the tumors and surrounded organs was performed. Qualitative observations demonstrated strong [18F]FDG accumulation in the tumor with both administration routes. In the intrajugular images, [18F]FDG accumulated also in the injection site, while gingival injection avoided this effect, improving microPET/CT images for hamsters. Ex vivo studies have confirmed substantial [18F]FDG accumulation in the tumor: tumor-to-muscle ratio uptake was 22.1. We were able to detect the orthotopic pancreatic tumor model in hamsters by in vivo and ex vivo microPET/CT imaging. Being gingival administration possible, better images will be obtained while increasing animal welfare.

414. P24-25. PCNA-BINDING PEPTIDES DISRUPT TLS POLYMERASE RECRUITMENT AND POTENTIATE CANCER CELL SENSITIVITY TO THERAPEUTICS

Yiovana Verónica Okraine¹, María Belén de la Vega², Sofía Venerus Arbilla³, Ginette Moyano⁴, María Candelaria Mares Ahlers⁵, Ariel Abramovici Blasco⁶, Lilen Ivonne Caimi⁷, Sabrina Florencia Mansilla⁸, Vanesa Gottfredi⁹

1. Fundación Instituto Leloir, Consejo Nacional de Investigaciones Científicas y Técnicas (IIBBA), Buenos Aires 1405, CABA, Argentina; Ciclo Celular y Estabilidad Genómica
2. Fundación Instituto Leloir, Consejo Nacional de Investigaciones Científicas y Técnicas (IIBBA), Buenos Aires 1405, CABA, Argentina; Ciclo Celular y Estabilidad Genómica
3. Fundación Instituto Leloir, Consejo Nacional de Investigaciones Científicas y Técnicas (IIBBA), Buenos Aires 1405, CABA, Argentina; Ciclo Celular y Estabilidad Genómica
4. Fundación Instituto Leloir, Consejo Nacional de Investigaciones Científicas y Técnicas (IIBBA), Buenos Aires 1405, CABA, Argentina; Ciclo Celular y Estabilidad Genómica
5. Fundación Instituto Leloir, Consejo Nacional de Investigaciones Científicas y Técnicas (IIBBA), Buenos Aires 1405, CABA, Argentina; Ciclo Celular y Estabilidad Genómica
6. Fundación Instituto Leloir, Consejo Nacional de Investigaciones Científicas y Técnicas (IIBBA), Buenos Aires 1405, CABA, Argentina; Ciclo Celular y Estabilidad Genómica
7. Fundación Instituto Leloir, Consejo Nacional de Investigaciones Científicas y Técnicas (IIBBA), Buenos Aires 1405, CABA, Argentina; Ciclo Celular y Estabilidad Genómica
8. Fundación Instituto Leloir, Consejo Nacional de Investigaciones Científicas y Técnicas (IIBBA), Buenos Aires 1405, CABA, Argentina; Ciclo Celular y Estabilidad Genómica
9. Fundación Instituto Leloir, Consejo Nacional de Investigaciones Científicas y Técnicas (IIBBA), Buenos Aires 1405, CABA, Argentina; Ciclo Celular y Estabilidad Genómica
 vero_okraine@yahoo.com

Cancer cells that survive chemotherapy complete DNA replication despite chemotherapy-induced DNA damage. This occurs due to tolerance mechanisms such as translesion DNA synthesis (TLS), which involves specialized DNA polymerases (S-Pols). Given their role in replicating damaged DNA, we evaluated the effects of inhibiting individual S-Pols. However, due to redundancy among S-Pols, a strategy for their global inhibition is required. Since S-Pols are recruited to the replisome via their PCNA-binding domains, we hypothesized that delivering a peptide with a strong PCNA-binding motif would displace S-Pols globally. The cyclin kinase inhibitor p21 contains one of the strongest PCNA-binding motifs. We designed a peptide representing the C-terminal PCNA-interacting region (PIR) of p21. As expected, the PIR peptide displaced S-Pols from PCNA-associated replication factories and enhanced cancer cell killing by DNA-damaging agents such as cisplatin, hydroxyurea, olaparib, and UV light. Notably, the peptide also increased cytotoxicity induced by non-DNA-damaging agents, including Chk1, ATR, and Wee1 inhibitors. Mutation of the PCNA-binding site within the PIR peptide abolished its cytotoxic effect. Supporting this approach, a less potent PIR from S-Pol eta also displaced S-Pols and enhanced cell killing by all agents tested. These findings indicate that global displacement of S-Pols from PCNA can be achieved via PIR peptides and represents a promising strategy to boost the efficacy of cancer therapies involving both DNA-damaging and non-DNA-damaging agents.

415. P24-26. RADIOBIOLOGICAL CHARACTERIZATION OF ADULT AND PEDIATRIC GLIOBLASTOMA CELL LINES WITH A VERTICAL PROTON BEAM AT THE TANDAR ACCELERATOR

Julia Milena Gallino Fernández¹, Jesús Dasyam Figari Yegros², Ezequiel Ignacio Canay³, Luciano Fiore⁴, Greta Abril Bolzi⁵, Martín Alejo Alurralde⁶, Andres Arazí⁷, Sara Josefina Gonzalez⁸, Agustina Mariana Portu⁹, Lucia Laura Policastro¹⁰

1. CNEA; Instituto de Nanociencias y Nanotecnología (CNEA-CONICET); Departamento de Nanomedicina y Medicina de Precisión, Gerencia de Desarrollo Tecnológico
2. CNEA; Gerencia de Investigaciones y Aplicaciones
3. CNEA; Gerencia de Área Aplicaciones Nucleares a la Salud
4. CNEA; Instituto de Nanociencias y Nanotecnología (CNEA-CONICET); Departamento de Nanomedicina y Medicina de Precisión, Gerencia de Desarrollo Tecnológico
5. CNEA; Departamento de Nanomedicina y Medicina de Precisión, Gerencia de Desarrollo Tecnológico
6. CNEA; Gerencia de Investigaciones y Aplicaciones
7. CNEA; CONICET; Gerencia de Investigaciones y Aplicaciones
8. CNEA; CONICET; Gerencia de Área Aplicaciones Nucleares a la Salud
9. CNEA; CONICET; Gerencia de Área Aplicaciones Nucleares a la Salud
10. CNEA; CONICET; Instituto de Nanociencias y Nanotecnología (CNEA-CONICET); Departamento de Nanomedicina y Medicina de Precisión, Gerencia de Desarrollo Tecnológico
 juliagallino@gmail.com

Proton therapy is an advanced radiotherapy modality that employs charged particles to deliver highly conformal doses to tumors while sparing surrounding healthy tissues. Its unique physical properties offer superior dose distribution compared to conventional photon-based treatments, making it especially advantageous for tumors located in sensitive regions such as the brain. Glioblastoma, the most aggressive primary brain tumor in adults, and high-grade pediatric gliomas remain major therapeutic challenges that demand more effective treatment strategies. In this context, the upcoming Argentine Center of Proton Therapy (CeArP), the first facility in South America, represents a milestone for patient care and translational research. As part of national research efforts, a vertical external proton beam with energies up to 20 MeV has been developed and characterized at the TANDAR Accelerator located at the Constituyentes Atomic Center. The present study investigates proton-based

therapies and potential radiosensitizers for adult and pediatric gliomas in vitro, in organoid models, and in vivo. At this stage, we established the radiobiological characterization of adult (U251) and pediatric (SF8628) glioblastoma cell lines. Clonogenic survival assays were performed following proton irradiation at doses ranging from 0.5 to 6 Gy, with crystal violet staining 15 days post-irradiation. Survival curves were fitted to the linear-quadratic model, yielding the following radiobiological parameters: U251, $\alpha = 0.12$ and $\beta = 0.17$; SF8628, $\alpha = 0.19$ and $\beta = 0.86$. These findings provide a foundation for the development of novel proton-based therapeutic strategies to improve outcomes in glioblastoma.

416. P24-27. PROTON THERAPY: RADIOBIOLOGICAL CHARACTERIZATION OF AN EXTERNAL VERTICAL BEAM AT THE TANDAR ACCELERATOR WITH HT29 CANCER CELLS

Justine Frison Lovera¹, Jesús Figari², Ezequiel Canay³, Marina Perona⁴, Martín Alurralde⁵, Matías Valero⁶, Marina Carpano⁷, Romina Oglio⁸, Agustina Portu⁹, Andrés Arazí¹⁰, Carla Rodríguez¹¹, Lisa Thomasz¹²

1. National Commission of Atomic Energy; Nuclear Biochemistry Division, Radiobiology Department
 2. National Commission of Atomic Energy; Scientific and Technical Research National Council (CONICET); Tandar Laboratory
 3. National Commission of Atomic Energy; Laboratory of Nuclear Tracks and Neutron Autoradiography
 4. National Commission of Atomic Energy; Scientific and Technical Research National Council (CONICET); Nuclear Biochemistry Division
 5. National Commission of Atomic Energy; Tandar Laboratory
 6. National Commission of Atomic Energy; BNCT Coordination Department
 7. National Commission of Atomic Energy; Nuclear Biochemistry Division
 8. National Commission of Atomic Energy; Nuclear Biochemistry Division
 9. National Commission of Atomic Energy; Scientific and Technical Research National Council (CONICET); Laboratory of Nuclear Tracks and Neutron Autoradiography
 10. National Commission of Atomic Energy; Scientific and Technical Research National Council (CONICET); Tandar Laboratory
 11. National Commission of Atomic Energy; Nuclear Biochemistry Division
 12. National Commission of Atomic Energy; Scientific and Technical Research National Council (CONICET); Nuclear Biochemistry Division
- jus.frison@hotmail.com

Proton therapy is the most precise and non-invasive treatment for cancer and will soon be implemented at the Argentine Center of Protontherapy (CeArP). To support this development, an external vertical proton beam with energies up to 20 MeV, has been implemented at the TANDAR accelerator. This beam is suitable for in vitro and small animal s irradiations. This is the only active external beam in Argentina prior to the commissioning of the clinical proton beam at the CeArP. Aim: To determine the radiosensitivity of HT29 cell line irradiated with the vertical proton beam of the TANDAR accelerator. Methodology: HT29 colorectal cancer cells were irradiated with protons at doses between 1 and 8 Gy. Survival curves were obtained by clonogenic assays immediately after the irradiation. Results: The survival fraction at 2 Gy (SF2) for HT29 cells after proton irradiation was 0.53 ± 0.05 . Reported SF2 for HT29 cells is 0.55 ± 0.03 and 0.33 ± 0.05 after α - and neutron irradiation, respectively. The analysis of the fitted survival curve determined the parameters: $a = 0.10 \pm 0.06$ and $b = 0.08 \pm 0.01$, yielding an α/β ratio of 1.25 Gy. Conclusion: HT29 cells displayed a pronounced radiosensitivity with an $\alpha/\beta = 1.25$ Gy, consistent with the radiosensitivity reported for plateau proton irradiation and g photons ($\alpha/\beta \approx 6$ Gy). The SF2 for HT29 obtained are consistent for low-LET radiation. The shoulder in the survival curve supports the predominance of sublethal damage. In contrast, lower SF2 values, reflects higher cytotoxicity of high-LET

radiation. These results validates TANDAR vertical proton beam for investigating mechanisms of radioresistance and potential radiosensitizing strategies.

417. P24-28. EXPERIMENTAL STUDIES ON THE APPLICATION OF BORON NEUTRON CAPTURE THERAPY FOR THE TREATMENT OF TRIPLE-NEGATIVE BREAST CANCER

Antonella Pastini¹, Diego Javier Brites Neira², Andrés Bechis³, María Silvina Olivera⁴, , Martín Krasnapolski⁵, Hugo Cerecetto⁶, Marcos Couto Sire⁷, Pablo Menéndez⁸, Laura Todaro⁹, Alejandro Urtreger¹⁰, María Alejandra Dagrosa¹¹

1. Instituto de Oncología "Ángel Roffo. Universidad de Buenos Aires; Centro Oncológico de Medicina Nuclear Instituto de Oncología "Ángel Roffo. Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina
2. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Área Investigación
3. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina.; Área Investigación
4. Comisión Nacional de Energía Atómica; Departamento Boro
5. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Área Diagnóstica. Departamento de Patología
6. Facultad de Ciencias. Universidad de la República. Montevideo, Uruguay; Grupo de Química Orgánica Medicinal
7. Facultad de Ciencias. Universidad de la República. Montevideo, Uruguay; Grupo de Química Orgánica Medicinal
8. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Dirección de Terapia Radiante y Medicina Nuclear
9. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Área Investigación
10. Instituto de Oncología "Ángel Roffo". Facultad de Medicina. Universidad de Buenos Aires. Ciudad Autónoma de Buenos Aires, Argentina; Área Investigación
11. Instituto de Oncología "Ángel Roffo. Universidad de Buenos Aires-Comisión Nacional de Energía Atómica. Buenos Aires, Argentina.; Centro Oncológico de Medicina Nuclear antonellapastini@gmail.com

Introduction: Triple-Negative Breast Cancer (TNBC) is a highly aggressive subtype, characterized by marked heterogeneity, metastatic potential and poor prognosis. Boron Neutron Capture Therapy (BNCT) emerges as an alternative strategy, based on the nuclear reaction $^{10}\text{B} (n, \alpha)^7\text{Li}$, which locally generates high linear energy transfer (LET) particles. To improve BNCT efficacy, bimodal compounds derived from lapatinib and erlotinib enriched with boron (Cmpd.1 and Cmpd.4, respectively) were developed. These molecules combine tyrosine kinase inhibition with boron delivery into tumor cells. Objective: Evaluate the effect of BNCT using boron-containing chemotherapeutic compounds in the treatment of TNBC. Materials and Methods: Human TNBC cells (Hs578T) were incubated with boronophenylalanine (BPA), Cmpd.1, or Cmpd.4 at concentrations below their IC50 during 2, 4 and 24 h. Boron content was determined by ICP-AES spectroscopy. Subsequently, cells were incubated with 1 ppm boron-10 and irradiated in the RA-3 nuclear reactor (neutron flux = 3.3×10^{11} n/cm²·min). Cell survival was assessed by MTS assay, and cell death was analyzed by flow cytometry (Annexin V-FITC/PI). Results: Hs578T cells showed significant uptake of compound Cmpd.4 at 24 h, seven-fold higher than BPA. Irradiation studies showed a decrease in cell survival after treatment with the new boron compounds. Moreover, Cmpd.1 and Cmpd.4 increased the proportion of late apoptotic cells. Conclusion: Both bifunctional compounds (erlotinib and lapatinib borated) emerge as promising boron carriers for BNCT treatment of TNBC, as they exhibited higher cellular uptake, increased cell death and enhanced late apoptosis.

418. P24-29. MODULATION OF OXIDATIVE STRESS BY THE

COMBINATION OF MENADIONE AND CALCITRIOL AS AN ANTIPROLIFERATIVE STRATEGY IN COLON CANCER CELLS

Romina Kohan¹, Alejandro Collin², Francisco Beltramo³, Jeremías Brochero Félix⁴, Victoria Scalerandi⁵, Gabriela Picotto⁶

1. Chair of Biochemistry and Molecular Biology, Faculty of Medical Sciences, National University of Córdoba (UNC); Institute of Health Sciences Research (INICSA), CONICET-UNC. Córdoba, Argentina; Chair of Cellular and Molecular Biology A, Faculty of Dentistry, UNC, Córdoba, Argentina.; Laboratorio de Metabolismo Fosfocálcico y Vitamina D "Dr. Fernando Cañas", INICSA-CONICET

2. Chair of Biochemistry and Molecular Biology, Faculty of Medical Sciences, National University of Córdoba (UNC); Institute of Health Sciences Research (INICSA), CONICET-UNC. Córdoba, Argentina; Laboratorio de Metabolismo Fosfocálcico y Vitamina D "Dr. Fernando Cañas", INICSA-CONICET

3. Chair of Biochemistry and Molecular Biology, Faculty of Medical Sciences, National University of Córdoba (UNC); Laboratorio de Metabolismo Fosfocálcico y Vitamina D "Dr. Fernando Cañas", INICSA-CONICET

4. Chair of Biochemistry and Molecular Biology, Faculty of Medical Sciences, National University of Córdoba (UNC); Laboratorio de Metabolismo Fosfocálcico y Vitamina D "Dr. Fernando Cañas", INICSA-CONICET

5. Chair of Biochemistry and Molecular Biology, Faculty of Medical Sciences, National University of Córdoba (UNC); Laboratorio de Metabolismo Fosfocálcico y Vitamina D "Dr. Fernando Cañas", INICSA-CONICET

6. Chair of Biochemistry and Molecular Biology, Faculty of Medical Sciences, National University of Córdoba (UNC);

Institute of Health Sciences Research (INICSA), CONICET-UNC. Córdoba, Argentina; Laboratorio de Metabolismo Fosfocálcico y Vitamina D "Dr. Fernando Cañas", INICSA-CONICET

romina.kohan@unc.edu.ar

Colorectal cancer is the second leading cause of cancer mortality worldwide, prompting the search for new therapies, especially for resistant variants. Based on the literature and our previous findings, menadione (MEN) and calcitriol (D) were shown to modulate oxidative status (OS) in breast and colon cancer cell lines. We aimed to elucidate the molecular mechanisms of the antiproliferative action of their combination in Caco-2 colon adenocarcinoma cells. Cells were treated with MEN (20 μ M), D (200 nM), or their combination for 48 hours. Cell proliferation and migration were assessed by crystal violet staining and the wound assay, respectively. Apoptosis, cell cycle, and reactive oxygen species (ROS) levels were quantified by flow cytometry, while superoxide anion (SA) levels and catalase (CAT) activity were measured spectrophotometrically. Autophagy inhibitors and antioxidants were used to identify possible mechanisms of cell death. Our results demonstrate that the MEN+D combination exhibited a dose- and time-dependent antiproliferative effect, reducing proliferation by 50% and delaying cell migration. This cytotoxic effect was associated with a significant increase in ROS (60%), SA (80%), and CAT activity (150%), suggesting a profound alteration of the redox balance. The combination induced cell cycle arrest in G2/M phase and an increase in apoptosis and necrosis. In conclusion, this study suggests that the MEN+D antiproliferative effect in Caco-2 cells operates through the induction of OS and the consequent disruption of the cell cycle, leading to increased apoptosis. These findings position this combination as a potential complementary therapeutic strategy for the treatment of colon cancer.