UFV Universidad Francisco de Vitoria

IV CONGRESO SAN ALBERTO MAGNO

SEMILLAS DE CIENCIA, CONSTRUYENDO EL FUTURO

ISBN: 978-84-09-79688-5

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1. INTRODUCCIÓN

La Facultad de Ciencias Experimentales de la Universidad Francisco de Vitoria, tiene el honor de presentar la IV edición del Congreso San Alberto Magno:

“Semillas de Ciencia, Construyendo el Futuro”.

Toda revolución comienza con una semilla. La semilla de una idea, de una pregunta que desafía lo establecido. En los laboratorios donde vosotros, nuestros alumnos, futuros científicos, se forman, y siembran a diario millones de estas semillas. Algunas germinarán en una nueva terapia, otras en un diagnóstico más rápido, otras en un biocombustible que cambiará nuestra energía.

Pero más allá de su potencial concreto, en el corazón de cada una de estas investigaciones, en cada tubo de ensayo, en cada secuencia de ADN descifrada, en cada cultivo celular observado al microscopio, yace una promesa. Una promesa de salud, de sostenibilidad, de vida. Estos no son solo experimentos; son Semillas de Ciencia.

Hoy, son las manos de una nueva generación de biotecnólogos, biomédicos, ingenieros biomédicos, genetistas y farmacéuticos, las que custodian estas semillas.

Sois los arquitectos de un futuro donde las enfermedades tendrán nuevos adversarios, los cultivos agrícolas serán más resilientes, y los tratamientos, más personalizados y eficaces. Este congreso es el campo donde esas semillas comienzan a brotar.

Os damos la bienvenida a este espacio de diálogo, descubrimiento y construcción en comunidad.

El futuro no espera y se construye con el conocimiento que hoy plantamos.

¡Bienvenidos!

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Dr. Cruz Santos Tejedor. Director Escuela Internacional de Doctorado. Vicedecano de Investigación de Facultad Ciencias Experimentales. Profesor de Microbiología, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dra. Lourdes Rufo Nieto. Vicedecana de Gestión Académica y Calidad Facultad Ciencias Experimentales. Profesora de Biología Vegetal y Farmacognosia, Grados de Farmacia y Genética, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dra. Águeda M. Tejera. Directora Grado Genética, Profesora Genética e Ingeniería Genética, Grados en Genética, Biomedicina y Biotecnología, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dr. Ramiro Perezzan Rodríguez. Profesor Química Orgánica, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dra. Esther Grueso Hierro. Profesora Histología, Grado Biomedicina, Facultad Ciencias Experimentales Universidad Francisco de Vitoria.

Dra. Elena Pascual Vega. Vicedecana de Relaciones Externas Facultad Ciencias Experimentales. Profesora de Bioquímica, Grado en Biomedicina, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Estefanía del Valle López. Responsable de Nuevos Proyectos y RRSS, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dra. Noemí García Romero. Profesora Genética, Grado Biomedicina, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dra. Estela Pérez Lago Profesora Microbiología, Grado Biotecnología, Biomedicina y Farmacia, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dra. Teresa de Asúa Corchado. Profesora de Biología Celular. Mentora de alumnos de Facultad Ciencias Experimentales. Universidad Francisco de Vitoria.

Dra. Lucía Montero Montero. Profesora de Cultivos Celulares, Grado Biotecnología, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dra. Maria Tiana Cerrolaza. Profesora de Bioquímica, Grado Genética, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

1.2 Comité Científico

Dra. Esther Grueso Hierro. Profesora Histología, Grado Biomedicina, Facultad Ciencias Experimentales Universidad Francisco de Vitoria.

Dra. Elena Pascual Vega. Vicedecana de Relaciones Externas Facultad Experimentales. Profesora de Bioquímica, Grado en Biomedicina, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dra. Noemí García Romero. Profesora Genética, Grado Biomedicina, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dra. Lourdes Rufo Nieto. Vicedecana de Gestión Académica y Calidad Facultad Ciencias Experimentales. Profesora de Biología Vegetal y Farmacognosia, Grados de Farmacia y Genética, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dr. Ramiro Perezzan Rodríguez. Profesor Química Orgánica, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dra. Águeda M. Tejera. Directora Grado Genética Facultad Ciencias Experimentales. Profesora Genética e Ingeniería Genética, Grados en Genética, Biomedicina y Biotecnología, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dra. Lucía Montero Montero. Profesora de Cultivos Celulares, Grado Biotecnología, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

Dra. Estela Pérez Lago Profesora Microbiología, Grado Biotecnología, Biomedicina y Farmacia, Facultad Ciencias Experimentales, Universidad Francisco de Vitoria.

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3. ABSTRACTS

(1) Neurogenesis analysis in susceptible and resilient fear extinction mice phenotypes

D. Castañer[1]*, M. Ponce-Renilla[1], I. Pereda-Pérez[1], C. Izquierdo-Luengo[1], R.M. Tolón[1], F. Berrendero[1]

[1]Francisco de Vitoria University, Faculty of Experimental Sciences, Madrid, Spain

*Correspondence: diegocastanerperez@gmail.com

Abstract

The ability to extinguish traumatic memories varies significantly across individuals and has importance in the treatment of fear-related psychiatric disorders. Previous research has identified extreme phenotypes—resilient and susceptible—based on extinction performance. However, the neurobiological mechanisms underlying this behavioral variability remain poorly understood, particularly regarding sex-specific differences. This study aims to explore neurogenesis with individual differences in fear extinction performance in male and female mice. Male and C57BL/6J mice underwent Pavlovian fear conditioning followed by a three-day extinction protocol. Based on the trajectory of freezing behavior across sessions, animals were classified into resilient, intermediate, or susceptible groups. Ninety minutes after the final extinction session, mice were perfused, and brains were processed for immunofluorescence. Proliferative activity was assessed using Ki67, while immature neurons were labelled with doublecortin in the subgranular zone of the dentate gyrus and the subventricular zone. Moreover, adult male and female C57BL/6J mice received TMZ (25 mg/kg, i.p.) or VEH for three consecutive days. On day four all groups underwent Pavlovian fear conditioning by a three-day extinction protocol and same perfusion and immunofluorescence procedure used in the previous experiment. Additionally, adult female C57BL/6J mice received TMZ (25 mg/kg, i.p.) or VEH on a 3-on/4-off schedule for three consecutive weeks, following the same fear conditioning, extinction protocols, perfusion and immunofluorescence procedure used in three-day TMZ experiment. No significant differences in Ki67-positive cells were detected across phenotypes or sexes. However, doublecortin expression in the dentate gyrus was significantly increased in susceptible mice compared to both resilient and intermediate groups in males suggesting a possible compensatory neurogenic response to persistent fear. In response to TMZ a significant difference was found in behavior and neurogenesis in male mice after three-day treatment. No significant difference was found in behavior or neurogenesis in neither three-day nor three-week treatment in female mice.

Keywords: *Trauma, animal models, neurogenesis*

(2) Blocking p38 in Kupffer cells prevents Steatosis and Hepatocelullar Carcinoma

Cristina Mencía [1,3,4], María Crespo [2,3], Nauzet Deniz-yre [4], Clara Bonacasa[4], Alfonso Mora [3,4], Elena Rodríguez [4], Luis Leiva-Vega [4], Marta León [4], Alba C. Arcones [4], Guadalupe Sabio[3,4]

[1]Universidad Francisco de Vitoria, Ctra. Pozuelo-Majadahonda KM 1.800, 28223 Majadahonda, Madrid, Spain.

[2]Institute for Clinical Chemistry and Laboratory Medicine, Faculty of Medicine, Technische Universität Dresden, Germany

[3]Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain;
[4]Centro Nacional de Investigaciones Oncológicas (CNIO), Madrid, Spain.

*Correspondence**:** cristinamenciamesonero@gmail.com

Abstract

Hepatocellular carcinoma (HCC) is the most frequent primary liver cancer and often develops in the context of metabolic dysfunction-associated fatty liver disease (MAFLD). Among the key molecular regulators of this progression, stress-activated protein kinases such as p38 MAPK play a central role in hepatic responses to metabolic stress. While p38 activation in hepatocytes promotes lipid accumulation and tumorigenesis, its specific role in Kupffer cells (KCs)the resident macrophages of the liver—remains poorly understood. This study aimed to determine whether the absence of p38 activation in KCs protects against hepatic steatosis and HCC, and to elucidate the molecular mechanisms involved. Mice lacking MKK3 and MKK6 (the upstream kinases responsible for p38 activation) specifically in KCs were used. Animals were fed either a methionine- and choline-deficient (MCD) diet to induce steatosis or subjected to a hydrodynamic tail-vein injection model combining *c-myc* , *β-catenin,* and *sh-p53* plasmids to promote HCC. Hepatic lipid accumulation, fibrosis, and tumor burden were assessed by histology, biochemical analyses, and in vivo bioluminescence imaging. RNA sequencing, proteomics, and flow cytometry were performed to explore the p38–CD36 signaling axis. Loss of p38 activation in Kupffer cells markedly reduced hepatic steatosis, fibrosis, and tumor formation. Mechanistically, these effects were associated with the downregulation of CD36, a lipid scavenger receptor that mediates fatty acid uptake, leading to decreased intracellular lipid accumulation in hepatocytes. Proteomic analyses suggested a possible interaction between p38 and the transcription factor LXR in the regulation of CD36 expression, although this relationship remains to be experimentally validated. In conclusion, the absence of p38 activation in Kupffer cells protects against hepatic steatosis and hepatocellular carcinoma through CD36 downregulation. Targeting the p38–CD36 pathway in Kupffer cells may represent a promising therapeutic strategy to prevent MAFLD progression and liver cancer development. Nevertheless, additional studies are needed to clarify the mechanisms underlying the p38–CD36 axis.

Keywords: *p38 MAPK, Kupffer cells, steatosis*

(3) Food colorants E102 and E129: functional effects on dental pulp mesenchymal stem cells

Jaume Pujadas[1], Laura Botana[1], Marian Mellén[1], Ismael Santa-María[1] and Maite Iglesias[1]*

[1]Faculty of Experimental Sciences, Universidad Francisco de Vitoria, Madrid, Spain

*Correspondence: m.iglesias@ufv.es

Abstract

Tartrazine (E102) and Allura Red (E129) are synthetic dyes widely used in the food industry. Both belong to the azo dye family, compounds capable of crossing the blood–brain barrier and inducing oxidative stress, inflammation, and structural alterations in brain tissue. Although approved by regulatory agencies such as the FDA and EFSA, recent studies have raised concerns about their safety. Specifically, these studies suggest that prolonged exposure to E102 and E129, either individually or in combination, may be linked to the development of hyperactivity and neurobehavioral alterations in children (ages 3 to 9), whose brains are still in the process of development. In this context, stem cells from human exfoliated deciduous teeth (SHED) stand out as a valuable in vitro experimental model for studying neurodevelopment due to their high proliferative capacity, plasticity, and potential to differentiate into neuronal lineages. This work aims to delve deeper into the potential cytotoxic and functional effects of E102 and E129, individually and in combination, on SHED cells. To this end, cell viability was assessed using the MTT assay (concentrations ranging from 0.1 to 2 mg/ml), while cell mobility, proliferation, and wound closure capacity were evaluated through functional in vitro assays. The treatment with 0.5 mg/ml of E102, E129, or their combination significantly increased SHED cell mobility, while proliferation remained unchanged. In contrast, 1 mg/ml of E129 markedly reduced wound closure ability, and no morphological alterations were observed after 24 hours. These findings indicate that E102 and E129 do not induce acute cytotoxicity in SHED under the tested conditions but can alter cellular behavior, particularly mobility and migration, suggesting potentially relevant effects on processes related to cell development and regeneration. Further studies are still required to assess their potential impact on neurodevelopment processes.

Keywords: *Tartrazine (E102), Allura Red (E129), SHED cells*

(4) Efecto de la autofagia sobre la apoptosis neuronal: estudio de retina de pollo en fase embrionaria

Cristina Gorgojo García[1]*, Andrea López Fernández[1], Lucía Martínez Baltasar[1], Paula González García[1]

[1]Grado en Biomedicina, Universidad Francisco de Vitoria, Madrid, España

Correspondence: cristinagorgojo@icloud.com

Abstract

A lo largo del desarrollo embrionario, la apoptosis juega un papel fundamental al eliminar células innecesarias o defectuosas, asegurando la correcta maduración del sistema nervioso central (SNC). Simultáneamente, la autofagia actúa como un mecanismo intracelular esencial para el mantenimiento de la homeostasis, reciclando componentes dañados del citoplasma y orgánulos. Diversos estudios sugieren que ambos procesos están estrechamente relacionados, y que la autofagia podría regular la apoptosis neuronal durante la formación del SNC.
El objetivo de este trabajo fue evaluar el papel de la autofagia en la regulación de la apoptosis neuronal durante el desarrollo embrionario, utilizando como modelo experimental retinas embrionarias de pollo. Se seleccionó este modelo por su similitud estructural y funcional con la retina humana y por la facilidad de manipulación embrionaria sin procedimientos invasivos en la madre al desarrollarse independientemente.
Las retinas fueron cultivadas en condiciones control y tratadas con 3-metiladenina (3-MA), un inhibidor de la autofagia que bloquea la activación de PI3K. Mediante la técnica TUNEL, se detectaron fragmentos de ADN característicos de la apoptosis, empleando citometría de flujo para cuantificar los núcleos apoptóticos. Los resultados revelaron un aumento significativo en el porcentaje de núcleos apoptóticos en las retinas tratadas con 3-MA con respecto a las control, indicando que la inhibición de la autofagia incrementa la muerte celular programada. Estos datos apoyan la hipótesis de que la autofagia ejerce una función protectora en la supervivencia neuronal, regulando la apoptosis durante el desarrollo embrionario.
En conclusión, los resultados sugieren que la autofagia no solo contribuye al mantenimiento de la homeostasis celular, sino que también participa activamente en la maduración del SNC. Este trabajo aporta evidencia experimental de la interdependencia entre ambos procesos y sienta las bases para futuras investigaciones sobre su implicación en el desarrollo y patologías del SNC.

Keywords: *autofagia, apoptosis neuronal, técnica TUNEL*

(5) SHED Cells as a Humanized Model of Attention-Deficit/Hyperactivity Disorder

María Izquierdo[1], Marian Mellén[1], Laura Botana[1], Mattia Biondo[2], Ismael Santa María[1]*, Maite Iglesias[1]*

[1]Facultad de Ciencias Experimentales, Universidad Francisco de Vitoria, Madrid, España

[2]Departamento STEBICEF, Universidad de Palermo, Palermo, Italia

*Correspondence: m.iglesias@ufv.es

Abstract
Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by alterations in the organization and connectivity of the central nervous system. The predominantly inattentive presentation, commonly referred to as attention-deficit disorder (ADD), is characterized by persistent difficulties in sustaining attention, organizing tasks, and maintaining mental effort, in the absence of marked hyperactivity or impulsivity. Despite its high prevalence and functional impact, the underlying cellular and molecular mechanisms remain poorly understood. In this context, stem cells derived from exfoliated deciduous teeth (SHED) represent an optimal experimental model to explore neurodevelopmental processes and dopaminergic dysfunctions associated with ADHD. In this study, the feasibility of establishing a humanized cellular model of ADHD was evaluated through the isolation, culture, and characterization of SHED obtained from control individuals (SHED-NT), subjects with attentional phenotype (SHED-ADD), and patients diagnosed with ADHD (SHED-ADHD), compared with dental pulp stem cells from permanent teeth (DPSC). SHED were obtained using the explant method and characterized by their fibroblast like morphology and the expression of mesenchymal markers through immunofluorescence. Cell proliferation was assessed by population doubling, and cell migration was analyzed in real time using the Cell Watcher videotracking system. All cell lines met the phenotypic criteria of human mesenchymal stem cells (hMSC). SHED exhibited higher proliferation than DPSC, whereas SHED-ADHD displayed reduced proliferative capacity, heterogeneous morphology, and disorganized hypermobile migration, characterized by loss of directionality and absence of coordinated wound closure fronts. In contrast, SHED-NT and SHED-ADD showed organized migratory behavior. Overall, this phenotypic and functional characterization represents the first step toward establishing SHED as a potential cellular model. The next phase will include the differentiation of SHED-ADHD into dopaminergic neurons and the analysis of correlations between gene expression profiles and functional parameters, aiming to assess their suitability for translational studies on gene–environment interaction and epigenetic regulation of dopaminergic signaling. This model may provide a unique opportunity to identify biomarkers, explore new pharmacological targets, and develop personalized therapeutic strategies, offering an unprecedented perspective on a poorly understood disorder that profoundly affects daily life, education, and mental health.
Keywords: *ADHD, SHED, neurodevelopment*

(6) *Vibrio cholerae*

Ainhoa Lázaro[1], Paola Perez[1], Alba María Sánchez [1], Luna Bonilla[1*]

[1]Universidad Francisco de Vitoria, Madrid, España

*Correspondence: lunabonsil@gmail.com

Abstract

Vibrio cholerae es una bacteria Gram negativa de la familia Vibrionaceae conocida por ser el agente etiológico de la enfermedad del cólera. Este microorganismo con morfología de bacilo en forma de coma y un único flagelo polar es una bacteria anaerobia facultativa, y halófila, adaptada a ambientes acuáticos de agua dulce y salada. Entre los más de 200 serogrupos identificados, O1 y O139 son aquellos responsables de los brotes epidémicos de cólera: una enfermedad intestinal aguda que continúa siendo un importante problema de salud pública en países en vías de desarrollo del continente africano. La patogenicidad de V. cholerae se debe a diferentes factores de virulencia entre los que destacan: la toxina colérica (CT), el pilus corregulado por toxina (TCP), las adhesinas (GbpA, OmpU) y las mucinasas (HapA) que facilitan la penetración de la bacteria en la mucosa intestinal. Estos mecanismos permiten la colonización del intestino y facilitan la secreción de la toxina colérica (CT), que produce una intensa pérdida de agua y electrolitos y resulta en la diarrea acuosa típica de la enfermedad. El diagnóstico del cólera se realiza mediante tinciones, siembra en medios de cultivo selectivos (TCBS), pruebas bioquímicas y confirmación por serotipificación o PCR. Su tratamiento se centra en la reposición inmediata de líquidos y electrolitos, y en la administración de antibióticos. Con especial énfasis en el desarrollo a futuro de planes de prevención que limiten la transmisión de la bacteria en países en vías de desarrollo y mejoren sus condiciones sanitarias, y de acceso a agua potable.

Keywords: *Vibrio cholerae, Patogenicidad, Terapias*

(7) Induction of neuroprotective and axonal regeneration by deciduous teeth-derived stem cells in embryonic chicken retinas

Andrea León[1], Marian Mellén[1], Laura Botana[1], Ismael Santa María[1], and Maite Iglesias[1*]

[1]Faculty of Experimental Sciences, Universidad Francisco de Vitoria, Madrid, Spain

* Correspondence: m.iglesias@ufv.es

Abstract

Cell-based therapies represent a cornerstone in the advancement of modern regenerative medicine. In previous studies, our group demonstrated that placenta-derived mesenchymal stem cells (hPMSCs) co-cultured with cells from rodent retinas are capable of improving damage in the central nervous system, by promoting axonal growth and restoring neuronal activity. Among the various sources of mesenchymal stem cells, those derived from exfoliated deciduous teeth (SHEDs) stand out for their remarkable proliferative capacity and their ability to differentiate into multiple cell lineages, including adipocytes, chondrocytes, osteocytes and neurons. In addition, SHEDs possess strong therapeutic potential due to their paracrine secretion of neurotropic and growth factors, which play crucial roles in neuronal survival, axonal extension, and synaptic plasticity. In this study, we have evaluated the effects of SHED cells on the neurodevelopment of chicken embryos at two distinct developmental stages: E5 and E13. Comparing these stages allowed us to distinguish between axonogenesis and axonal repair processes using co-culture assays analyzed by fluorescence microscopy. Co-cultures were performed with embryonic retina cells from chickens and varying concentrations of SHEDs. The results revealed that SHEDs significantly reduced cell death at both developmental stages, demonstrating a potent neuroprotective effect. Furthermore, SHEDs promoted a substantial increase in axonal length in dissected neurons and enhanced axonogenesis in early-developing neurons at both E5 and E13. These findings highlight the potential of SHED-derived secreted factors as a promising basis for developing novel therapies aimed at mitigating neurodegeneration and promoting neural repair in diseases such as Alzheimer, Parkinson and spinal cord injuries.

***Keywords**: SHED, Neurodevelopment, Cell therapy*

(8) Investigating the tumor-promoting role of B7-H4 in human intrahepatic cholangiocarcinoma

C. V. Cardona Tenreiro[1,2], E. Bramel[2], M. Facciuto[2], S. Raus[2], D. Sia[2*]

[1]Universidad Francisco de Vitoria, Pozuelo de Alarcón, Madrid, España

[2]Icahn School of Medicine at Mount Sinai, New York, USA

*Correspondence: daniela.sia@mssm.edu

Abstract

Intrahepatic cholangiocarcinoma (iCCA) is a malignancy originating from the intrahepatic bile ducts with a poor prognosis and median overall survival of about twelve months.

While early-stage resection offers a potential cure, treatment options for advanced iCCA are still limited. B7-H4, an immune checkpoint protein of the B7 family, is frequently overexpressed on iCCA tumor cells and contributes to immune evasion by inhibiting T cell activity, promoting tumor progression. Our lab has observed that B7-H4 knockout mice show significantly prolonged survival accompanied by a decrease in collagen fibers length and density, suggesting the hypothesis of a novel role for B7-H4 in extracellular matrix (ECM) remodeling and tumor growth. This is further supported by the transforming growth factor beta (TGF-ß) enrichment in B7-H4+ cells and the presence of high proliferation and desmoplasia, hallmarks of iCCA. In this study, we first determined B7-H4 expression in human iCCA cell lines to select those with high protein and mRNA levels. These were then transfected with different small interfering RNAs (siRNAs) to silence B7-H4, and after identifying the most efficient siRNA, we established the transfected cell lines for functional assays. To explore ECM remodeling, we analyzed changes in the expression of proteins related to TGF-ß pathway when silencing B7-H4, whereas for tumor growth, we performed proliferation assays in transfected cells. These analyses were motivated by the differences between human and mouse B7-H4. Despite structural conservation, their gene location and expression profiles differ, which may impact biological function and experimental interpretation, highlighting the importance of developing stable human cell lines to assess whether B7-H4 contributes to stromal remodeling in humans as observed in mice.

Our results show that B7-H4 is consistently expressed in various human iCCA tumor cells and their transfection with various siB7-H4 results in a significant reduction in protein levels. Moreover, comparing this model to control iCCA cells, changes in protein expression of TGF-ß pathway molecules and variations in cell proliferation consistently suggest that B7-H4 is indeed involved in stromal remodeling and tumor growth in iCCA.

Thereby, modulating B7-H4 expression in human iCCA cell lines establishes a suitable in vitro model to further investigate its functional role in iCCA. The observation of similarities when compared to previous findings in mouse models support the translational relevance of our results and confirm the potential of B7-H4 as a therapeutic target for iCCA.

Keywords: *B7-H4, iCCA, ECM remodeling*

(9) Expanding therapeutic strategies in brain tumors: from drug repurposing in glioblastoma to development of novel agents for diffuse midline glioma

Raquel De La Flor-Laserna[1], Laura Mateos-Madrigal[1], Lucía Castañeda-González[1], Álvaro Monago-Sánchez[1,2], Carlos Martínez-Riveiro[1,2], Josefa Carrión-Navarro[1,2], Noemí García-Romero[1]*, Ángel Ayuso-Sacido[1,2]

[1]Faculty of Experimental Sciences, Universidad Francisco de Vitoria, 28293-Madrid, Spain

[2]Brain Tumor Laboratory, Fundación Vithas, Grupo Hospitales Vithas, 28043-Madrid, Spain

*Correspondence:noemi.garcia@ufv.es

Abstract

Glioblastoma (GBM) represents the most aggressive and lethal form of adult brain cancer, characterized by high infiltrative capacity, resistance to conventional treatments, and a mean survival rate of approximately 15 months. In the pediatric context, diffuse midline glioma (DMG) affects critical brain regions such as the pons and thalamus, with an average survival of less than a year. Around 80% of DMG cases harbor the H3K27M mutation, leading to profound epigenetic dysregulation and uncontrolled tumor proliferation. Despite current multimodal treatments, effective therapeutic alternatives are urgently needed.

This study explores two complementary strategies aimed at expanding the therapeutic landscape of malignant gliomas. First, a drug repositioning approach was applied to patient-derived GBM stem cells using clinically approved compounds (Gefitinib and PSB). Cell viability assays (MTS) revealed a significant reduction in cell survival, with an additive effect observed when both drugs were combined. Second, novel agents (C1 and C4) were evaluated in DMG models. Western blot analyses demonstrated increased γH2AX and cleaved caspase-3 expression, indicating enhanced DNA damage and apoptosis after treatment with C1, both alone and in combination with irradiation. Additionally, Human Oncology Array profiling showed that treatment with C4 modulated the expression of key tumor progression proteins, increasing transcriptional factor such us p53, p27, and reducing the levels of survivin, consistent with antiproliferative and proapoptotic activity.

These results support the potential of pharmacological repositioning and the development of novel agents as promising strategies to improve therapeutic outcomes in highly aggressive brain tumors such as GBM and DMG.

***Keywords**: Glioma; Glioblastoma (GBM), Diffuse Midline Glioma (DMG)*

(10) Differential microRNAs Expression in DS-AMKL and non DS-AMKL cell lines

Ucha Martínez, Fernando[1], Osuna Marco, Marta[1], Galián Guevara, Eva[1], Tejera, Águeda M[1]*

1Faculty of Experimental Sciences, Universidad Francisco de Vitoria, Madrid, Spain

*Correspondence: agueda.tejera@ufv.es

Abstract

Down syndrome (DS) arises from trisomy 21, causing gene dysregulation on chromosome 21 and across other genomic regions. Beyond cognitive and developmental features, DS is characterized by altered cancer susceptibility, showing reduced incidence of most solid tumors but a markedly increased risk of hematological malignancies, particularly acute megakaryoblastic leukemia (AMKL). AMKL, a subtype of acute myeloblastic leukemia that affects megakaryocytes, is more aggressive in DS patients, and in case of recurrence children are less sensitive to chemotherapy. Some genes located in chromosome 21, like GATA1, are related to the development of AMKL, but much is unknown about the mechanisms regulating its development and progression. MiRNAs are small non-coding RNAs, known to participate in gene expression regulation, capable of targeting multiple genes, which makes them promising candidates in multifactorial diseases. In DS-AMKL, some miRNAs encoded in chromosome 21 have already been proven to play a role in leukemogenesis. In this context, we aimed to experimentally assay the differential expression profiles of small RNAs in DS-AMKL across two different AMKL cell lines, one originated from a pediatric patient with DS (CMK), and the other from a patient without DS (MEGAL) by a commercial panel. After identifying the hits, we validated the results for a selected set of miRNAs of interest using quantitative PCR (qPCR). Using cell line Megal as a reference, results confirmed the expression differences observed in the panel. Additionally, we identified several miRNAs located outside chromosome 21 that exhibited marked expression differences between the two cell lines, which may provide valuable insights for future studies. Some of these miRNAs are associated with key pathways implicated in AMKL, including megakaryopoiesis and tumor suppression.Future studies will aim to analyze the expression of their mRNA targets and to evaluate the functional impact of miRNA modulation in CMK cell tumor-related pathways.

Keywords: *Down syndrome, acute megakaryoblastic leukemia, and miRNA*

(11) Investigating the influence of T cell age on immune responses to Influenza A

Ángela Domínguez Balsa[1]*, Cayman Williams[1], Benedict Seddon[1]

[1]Institute of Immunity and Transplantation, University College London, London, United Kingdom

*Correspondence: angela.dominguezbalsa@gmail.com

Abstract

Is the efficiency of T cell response to viral infections determined by the chronological age (host age) or cellular age? It is well known that the immune response declines as we age (immunosenescence). On the other hand, cell age can be studied by tracking the individual T cells through time. By following these labelled cells, there is evidence that newly generated memory T cells had short-term survival and older memory cells persisted much longer in both young and old mice. Therefore, cell age is the main factor determining cell lifespan, not the chronological age. This project aims to understand how T cell age influences antiviral responses to Influenza A. For this purpose, an inducible CD4-Cre fate-reporter mouse model was used to distinguish and track “old” ($mTOM^+$) and “new” ($mTOM^-$) $CD4^+$ T cells. Mice were infected with Influenza A virus 146 days after tamoxifen induction, when $mTOM^+$ signal is largely lost in naïve cells but retained (~40%) in memory phenotype cells. Tissues (spleen, lymph nodes, lungs and mediastinal lymph nodes) were collected at day 9 (acute phase) and day 30 (memory phase) post-infection to analyse effector memory (EM) and antigen-specific (Tet^+) T cell responses. The $mTOM^+$ fraction was lower in flu-responding EM cells than in bulk EM, indicating recruitment of younger cells. However, after 30 days, $mTOM^+$ cells were enriched in both bulk and flu-specific EM populations, demonstrating that aged T cells persist longer after contraction. While both naïve and memory phenotype cells contribute to the Influenza A response, cellular—not chronological—age determines persistence. Aged T cells exhibit a survival advantage during the contraction phase, suggesting that cell-intrinsic aging enhances memory maintenance and may influence long-term immunity.

***Keywords**: T cell age, memory T cells, naïve T cells*

(12) Therapeutic modulation of the podoplanin–CD44 interaction as a strategy to limit invasion in squamous cell carcinoma

Alba Macipe-Feito[1], Santiago Garcés-Fernández[1], Lucía Montero-Montero[1], Sara Temprano-Carazo[1], Estefanía Moreno[2], María Ortiz[1], Susana Álvarez[1], Esther Grueso[1] y Ester Martín Villar[1]

[1]Universidad Francisco de Vitoria, Ctra. Pozuelo-Majadahonda KM 1800. 28223 Majadahonda (Madrid, España)

[2]Departamento de Bioquímica y Biomedicina Molecular. Instituto de Biomedicina, Universidad de Barcelona 08028, Barcelona, España

*Correspondence: alba.macipe@gmail.com

Abstract

Squamous cell carcinoma (SCC) is a malignant epithelial tumor of high incidence, characterized by its marked invasive capacity and metastatic potential. These properties are largely attributed to the intense proteolytic activity exhibited by tumor cells, an essential process for tissue invasion and metastatic dissemination. It has been proposed that such degradation is mediated, at least in part, by the formation of invadopodia, specialized and dynamic actin-based cytoskeletal structures that concentrate high proteolytic activity through matrix metalloproteinases (MMPs).

In previous research, our group identified podoplanin (PDPN) as a key protein in this process in SCC cells. This transmembrane glycoprotein localizes at the adhesion rings of invadopodia, where it interacts with CD44, an adhesion molecule also attributed with pro-invasive properties. Together, they form a complex that promotes directional migration of squamous carcinoma cells. In SCC cells, while podoplanin contributes to invadopodia stabilization, CD44 plays an essential role in focusing the proteolytic degradation associated with these structures. More recent studies from our group indicate that loss of CD44 leads to a diffuse, non-invadopodia-associated degradation pattern, whereas its interaction with podoplanin is required to maintain focused and efficient extracellular matrix (ECM) degradation.

The objective of this study is to determine whether disrupting the interaction between podoplanin and CD44 could reduce the invasive capacity of SCC cells. To this end, we performed co-immunoprecipitation assays, Proximity Ligation Assay (PLA), and fluorescent gelatin degradation assays (GDAs), applying two experimental treatments (A and B).

The results show that treatment A blocks the interaction between PDPN and CD44, resulting in a more diffuse and less localized ECM degradation pattern, comparable to that observed after CD44 depletion. In contrast, treatment B enhances the PDPN–CD44 interaction, promoting an increase in both invadopodia-associated and non-invadopodia-associated degradation.

In conclusion, this work presents new experimental tools (compounds A and B) capable of modulating the PDPN–CD44 interaction, enabling a more precise analysis of its contribution to the invasive behavior of SCC cells. Our results indicate that altering this interaction does not abolish proteolytic capacity but transforms the ECM degradation pattern, potentially influencing invasive potential.

Altogether, these findings highlight the essential role of the PDPN–CD44 complex in the spatial organization and efficiency of invadopodia-mediated degradative activity.

Keywords: *Squamous cell carcinoma, targeted therapies, podoplanin–CD44 axis*

(13) Assessing the role of ARID1A in the Alkylation-induced Unfolded Protein Response in Ovarian Clear Cell Carcinoma

Laura Balaguer Torrijo[1,2], Rebecca Tate[2], Lisiane B. Meira[2*]

[1]Universidad Francisco de Vitoria, Ctra. Pozuelo a Majadahonda km. 1,800, 28223, Pozuelo de Alarcón (Madrid)

[2]Faculty of Health and Medical Science, University of Surrey, Guildford, Surrey, United Kingdom

*Correspondence: l.meira@surrey.ac.uk

Abstract
Ovarian Clear Cell Carcinoma (OCCC) is a chemoresistant subtype of epithelial ovarian cancer, characterized by loss-of-function mutations in *ARID1A*, the DNA-binding subunit of the SWI/SNF chromatin remodeling complex. ARID1A has recently been shown to repress the IRE1α/XBP1 branch of the Unfolded Protein Response (UPR), a cellular pathway that maintains proteostasis under endoplasmic reticulum (ER) stress. In cancer, the UPR plays a dual role—initially protective by enhancing survival, but potentially cytotoxic when stress is unresolved. Thus, *ARID1A*-mutant cancer cells rely on this axis of the UPR for survival and tumor growth. Moreover, alkylating agents, which are cytotoxic drugs widely used in cancer chemotherapy, have been shown to induce the UPR in other cancer types, but the effect of *ARID1A* loss on alkylation-induced UPR in OCCC remains unknown. This project investigates whether ARID1A modulates alkylation-induced UPR in OCCC, aiming to uncover potential therapeutic vulnerabilities for this highly lethal cancer. In order to detect ER stress and measure changes in UPR-related gene expression, the OCCC cell line RMG-1 was treated for 6 hours with the alkylating agent methyl methanesulfonate (MMS). Results showed that MMS induces ER stress and activates the IRE1α/XBP1 branch of the UPR in *ARID1A*-wildtype RMG-1 cells. Using luciferase reporter assays, RT-PCR and RT-qPCR, we observed dose-dependent splicing of XBP1 and upregulation of UPR target genes following MMS treatment. To investigate the role of ARID1A, we validated *ARID1A*-knockout (KO) RMG-1 cell clones by Western blot and Sanger sequencing. Proliferation assays revealed increased growth in *ARID1A*-KO cells compared to parental, highlighting the tumor suppressor role of ARID1A. We then assessed the impact of *ARID1A* loss on MMS-induced UPR. *ARID1A*-KO cells displayed enhanced XBP1 expression and splicing. This response peaks at 1 mM MMS, but decreases at a higher dose, which could indicate a greater sensitivity of the KO cells to alkylation treatment. Altogether, these findings suggest that *ARID1A* deficiency sensitizes OCCC cells to alkylation- induced ER-stress, and that the IRE1α/XBP1 axis could be exploited therapeutically. This knowledge contributes to a better understanding of cellular responses to alkylation-induced damage, as well as to the development of therapeutic strategies for patients with *ARID1A*- mutant OCCC.

Keywords: *ovarian clear cell carcinoma (OCCC), ARID1A, Unfolded Protein Response (UPR)*

(14) Podoplanin-CD44 axis modulates IQGAP1 dynamics to promote invasive behaviour in squamous cell carcinomas through MT1-MMP

Santiago Garcés-Fernández[1], Lucía Montero-Montero[1], Diego Megías[2], Sara Temprano-Carazo[1], Alba Macipe-Feito[1], María Ortiz[1], Rocío Jarcovsky[1], Susana Álvarez[1], Esther Grueso[1] and Ester Martín-Villar [1*]

[1]Faculty of Experimental Science/Biosanitary Research Institute, Universidad Francisco de Vitoria, Madrid, Spain

[2]Advanced Optical Microscopy Unit, Instituto de Salud Carlos III, Madrid, Spain

*Correspondence: ester.martin@ufv.es

Abstract

Invadopodia are actin-rich membrane protrusions specialised in extracellular matrix (ECM) degradation and are critical for cancer cell invasion. Primary cells derived from squamous cell carcinomas (SCCs), an aggressive form of skin cancer, spontaneously form invadopodia in culture. In previous work, we demonstrated that podoplanin, a type I transmembrane mucin-like glycoprotein, controls invadopodia stability in SCC cells via RhoC/cofilin signalling. Recent findings from our lab now indicate that podoplanin and the hyaluronan receptor CD44 cooperate to regulate the mode of ECM degradation by directing proteolytic activity to invadopodia. However, the underlying molecular mechanisms remain unknown.

In this study, we identify a cooperative mechanism through which podoplanin and CD44 control the spatial organisation of membrane type 1 matrix metalloproteinase (MT1-MMP) by regulating the recruitment of the scaffold protein IQGAP1 to invadopodia. Co-immunoprecipitation assays in SCC cells demonstrated that podoplanin, CD44 and MT1-MMP form a molecular complex. To further explore the functional impact of this interaction, we examined MT1-MMP subcellular distribution upon podoplanin and CD44 silencing. Pre-embedding immunolabelling revealed that CD44 depletion led to a significant reduction in MT1-MMP localisation at the plasma membrane, an effect that persisted under combined knockdown conditions. In contrast, podoplanin loss did not significantly impair membrane localisation of MT1-MMP but instead enhanced the CD44–MT1-MMP interaction, as shown by proximity ligation assays. These findings suggest that podoplanin may act as a regulator of this association. In addition, both podoplanin and CD44 were required for efficient recruitment of IQGAP1, a multifunctional scaffold protein involved in cytoskeletal regulation and membrane trafficking, to invadopodia. Their individual or combined depletion resulted in a progressive loss of IQGAP1 from these structures. Given the previously proposed role of IQGAP1 in targeting MT1-MMP to invadopodia, our findings suggest that podoplanin and CD44 cooperate through IQGAP1 to position and regulate MT1-MMP at invadopodia, thereby confining ECM proteolysis to sites of invasion in SCC cells.

Keywords: *Squamous Cell Carcinoma (SCC), invadopodia, podoplanin/CD44/MT1-MMP*

(15) Simulating Non-Equilibrium Active Matter: A Mobile Automata-Inspired MALA Approach

Jorge Barcenilla[1], Lucia Benito[1], Diego Herráez[1]

[1] Faculty of Experimental Sciences, Universidad Francisco de Vitoria, Madrid, Spain

*Correspondence: jorge.barcenilla@ufv.es

Abstract

Cellular biophysics is a specialized field focused on the study of the physical principles governing biological processes at a fundamental level. At these scales, the dynamics of biological matter result from a complex network of interactions far from thermodynamic equilibrium, embedded in overdamped media dominated by stochastic noise inherent to temperature. The identification of patterns of active behavior, as well as dynamic control mechanisms, involves significant multidisciplinary efforts in which experimental observations must be explained and simulated in terms of fundamental physical models. In this work, an approach to simulating the active dynamics of matter at the mesoscale is presented. Starting from the stochastic Langevin equations and inspired by the concepts of mobile cellular automata, a generalizable scheme is proposed in which the active dynamics of complex stochastic networks are described in terms of a discrete system that explores an n-dimensional probabilistic space, determined by the interaction potential, following the evolution rules imposed by the Metropolis Adjusted Langevin Algorithm (MALA). Comparison of this approach with a standard simulation model shows how this method can reproduce the out-of-equilibrium active dynamics characteristic of active matter, such as softening, entropic reduction, or the breaking of detailed balance.

Keywords: *Cellular biophysics, Active matter, MALA*

(16) *Cannabis sativa:* el interés clínico de los cannabinoides en terapias farmacológicas para el tratamiento de trastornos y enfermedades neurológicas y psiquiátricas

Jimena López Sáenz de Pipaón[1*]

[1]Universidad Francisco de Vitoria, Madrid, España

*Correspondence: jmlsp95@gmail.com

Abstract

La especie vegetal Cannabis sativa presenta unos metabolitos secundarios de alto interés clínico: los cannabinoides. Dadas sus propiedades moleculares, son capaces de interaccionar con el sistema endocannabinoide del encéfalo, lo cual ha permitido el tratamiento de numerosos trastornos y enfermedades del sistema nervioso y psiquiátricas.

El Sistema endocannabinoide está compuesto por los receptores CB1 y CB2, cuyas funciones el control cognitivo, memoria, regulación de los sistemas simpático y parasimpático; y la respuesta inmune y neuro protectora respectivamente.

Estos pueden ser alterados por el THC y el CBD, moléculas encontradas en Cannabis sativa, siendo el THC un psicoactivo y el CBD ansiolítico y antiinflamatorio.

Existen fármacos como el Epidiolex o el Sativex cuya fórmula está basada en el CBD y el THC. Estos fármacos se utilizan para tratar enfermedades neurológicas como la Epilepsia refractaria o la Esclerosis Múltiple.

Por otro lado, existen tratamientos menos establecidos como el consumo regulado medicamente de CBD para paliar los síntomas de trastornos como la ansiedad, el síndrome de estrés postraumático o la esquizofrenia.

Además, existen muchos prejuicios acerca del uso de estas terapias, tales como la posibilidad de adicción o el empeoramiento de otros síntomas. Sin embargo, existen numerosos estudios que demuestran que, consumiendo una dosis establecida y controlada de estos fármacos, no solo son se ve mucha eficacia, sino que se reducen los efectos secundarios.

En cuanto al futuro de estos tratamientos, ya se están investigando nuevas moléculas también halladas en Cannabis sativa como el CBG, CBC o el THCV, que están mostrando prometedores potenciales antiinflamatorios, neuroprotectores y hasta propiedades de mejoras metabólicas.

***Keywords**: receptores, CBD, endocannabinoide*

(17) La neurogénesis adulta y el imprinting

Juan Toledano[1*]

[1]Universidad Francisco de Vitoria, Madrid, España

*Correspondence: jtolegar@gmail.com

Abstract

La neurogénesis adulta consiste en la generación de nuevas neuronas a partir de células madre neurales (NSC) en el cerebro adulto. Este proceso es vital para la plasticidad estructural y funcional del sistema nervioso, siendo esencial para funciones cognitivas como la memoria y el aprendizaje espacial. Las NSC son células multipotentes capaces de autorrenovarse y diferenciarse en neuronas, astrocitos y oligodendrocitos.

La neurogénesis ocurre principalmente en dos nichos neurogénicos: la Zona Subventricular (SVZ) del ventrículo lateral y la Zona Subgranular (SGZ) del giro dentado en el hipocampo. Mientras la SVZ produce neuroblastos que migran al bulbo olfatorio, la SGZ integra las nuevas neuronas en circuitos locales que contribuyen a la memoria y el aprendizaje. La regulación de este proceso involucra neurotrofinas, especialmente el BDNF, que promueve la maduración y diferenciación neuronal.

Un mecanismo epigenético crucial que interviene es el imprinting genómico. Este proceso causa que un pequeño grupo de genes se exprese de forma monoalélica, activándose solo la copia heredada de uno de los progenitores, mientras la otra se silencia. Este fenómeno, que exceptúa las leyes de Mendel, se controla mediante la metilación del ADN en las Regiones de Control de Impronta (ICRs).

La desregulación del imprinting genómico en los nichos neurogénicos se relaciona con diversas afectaciones cerebrales. Por ejemplo, la sobreexpresión de EZH2 en la SVZ se asocia con el desarrollo de glioblastomas. Además, la disfunción de factores como TET2 y DNMT1 en el hipocampo se vincula con el deterioro cognitivo, fallos en la sinaptogénesis y la Enfermedad de Alzheimer, así como con el agotamiento de las NSC y el envejecimiento.

***Keywords**: neurogénesis adulta, imprinting, células madre neurales*

(18) Study of IDH1/IDH2: Neomorphic Enzyme and Pharmacogenomic Eligibility

Laura Gimeno Tello[1]*, Sara González Sánchez[1], Íñigo Mancho Calleja[1], Alexia Maria Maté Galaup[1]

[1]Facultad de ciencias experimentales, Universidad Francisco de Vitoria, Madrid

*Correspondence: lgimenotello@gmail.com

Abstract

The study of IDH1 (isocitrate dehydrogenase (NADP(+)) 1) and IDH2 (isocitrate dehydrogenase (NADP(+)) 2) genes is essential due to the critical oncological and pharmacogenomic relevance acquired by their mutations, as they define specific patient subgroups and determine therapeutic eligibility. These genes encode crucial NADP+-dependent enzymes that participate in intermediate metabolism and redox balance. Their canonical function is to catalyse the oxidative decarboxylation of isocitrate to produce a-ketoglutarate and NADPH.

However, when these genes are altered, mutations transform their normal enzymatic function, resulting in the generation of a neoform enzyme that produces the oncometabolite 2-hydroxyglutarate (2-HG). The accumulation of 2-HG is highly pathogenic because it inhibits a-ketoglutarate-dependent enzymes, which leads to epigenetic blockade via epigenetic hypermethylation and stops cellular differentiation, a mechanism that decisively favors tumorigenesis.

These severe pathological consequences are associated with a wide range of neoplasms, including central nervous system tumors like Grade II-III gliomas and glioblastoma multiforme, hematological neoplasms such as acute myeloid leukemia, and skeletal tumors like central chondrosarcoma, Ollier disease, and Maffucci syndrome. IDH dysfunction is also linked to metabolic disorders (Aciduria 2-HG type II) and neurodegenerative diseases (Parkinson, Alzheimer, ALS, Huntington)

Given the nature of these genetic alterations as an oncogenic driver, the pharmacogenomic implication is direct and linked to pharmacodynamics: IDH1 and IDH2 mutations define specific patient subgroups where the therapeutic efficacy of targeted therapies depends directly on the confirmed presence of these alterations. For this reason, personalized intervention is mandatory, and some drugs require prior genetic testing before administration to ensure they are administered only to patients with a confirmed mutation. Furthermore, these mutations have been observed to potentially increase sensitivity to the chemotherapeutic agent venetoclax, broadening the pharmacological relevance of IDH.

Keywords: *IDH1, IDH2, pharmacogenomics, mutation, neoform enzyme, 2-Hydroxyglutarate (2-HG), oncometabolite, epigenetic blockade, patients subgroups*

(19) *Mycobacterium tuberculosis*: un viejo enemigo con nuevas lecciones

Irene López[1], Laura Valenciano[1*], Ana González[1], Daniela Rubinos[1], Sofía España[1]

[1]Universidad Francisco de Vitoria, Madrid, España

*Correspondence: lauravalencianosastre@gmail.com

Abstract

Mycobacterium tuberculosis es una bacteria que se caracteriza por no pertenecer a la clasificación común de gramnegativas/grampositivas. Es una micobacteria que causa brotes de tuberculosis, transmitiéndose por gotas respiratorias y afectando principalmente a los pulmones, aunque puede diseminarse a otros órganos en fases avanzadas. Su compleja pared celular hace que sea muy difícil de tratar y de eliminar, ya que son capaces de escapar de los mecanismos de defensa del sistema inmune y crecer en el interior de los macrófagos tras ser fagocitados. Esta enfermedad puede cursarse de forma asintomática o sintomática, cuando se producen cavitaciones pulmonares, necrosis e inflamación. El tratamiento actual consiste en antibióticos, en función de si es una M. tuberculosis sensible o multirresistente. Actualmente, se están estudiando numerosos tratamientos innovadores para esta bacteria (vacunas, inmunoterapia, terapia con bacteriófagos…), debido a la creciente resistencia a antibióticos que se está dando de forma generalizada.Búsqueda exhaustiva de información, recopilación y metaanálisis de artículos en National Institutes of Health (NIH), Pubmed.Póster divulgativo que recopila información esencial sobre M. tuberculosis, sus factores de virulencia, tratamientos actuales, dianas terapéuticas para futuras terapias y características morfológicas. Mycobacterium tuberculosis es una bacteria muy peligrosa, de fácil transmisión y diseminación rápida. Causa tuberculosis, una enfermedad grave que afecta a los pulmones, y es capaz de evadir el sistema inmune y sacar provecho de él para dividirse y diseminar por el tejido pulmonar. Es de suma importancia invertir en investigación para futuras terapias alternativas, pues las bacterias cada vez desarrollan más resistencias a antibióticos, lo cual puede suponer un problema de salud pública a nivel global.

Keywords: *Mycobacterium, tuberculosis, patogenia*

(20) Alphaviruses vs IFN: A Host-Viral Conflict Across the Old World and New World

Marcos Múñez García[1]*, Georgios Moschonas[2, 3], Santiago Vidal Freire[2, 3], Anastasija Čupić[2, 4], Gustavo Palacios[2, 3], Lisa Miorin[2, 3] and Adolfo García-Sastre[2, 3, 5]

[1]Experimental Sciences Faculty, Universidad Francisco de Vitoria, Madrid, Spain

[2]Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, New York, USA

[3]Global Health and Emerging Pathogens Institute, Icahn School of Medicine at Mount Sinai, New York, New York, USA

[4]Graduate School of Biomedical Sciences, Icahn School of Medicine at Mount Sinai, New York, New York, USA

[5]Department of Medicine, Division of Infectious Diseases, Icahn School of Medicine at Mount Sinai, New York, New York, USA

*Correspondence: marc.munez@gmail.com

Abstract

Alphaviruses are globally widespread arboviruses that differ not only in geographic distribution but also in clinical manifestations. While many exhibit neurotropism, Old World alphaviruses such as Sindbis virus (SINV) are primarily associated with fever, rash, and arthralgia, whereas New World alphaviruses such as Venezuelan equine encephalitis virus (VEEV) tend to cause severe neurovirulence and encephalitis outbreaks. These enveloped, single-stranded positive-sense RNA viruses generate double-stranded RNA intermediates during replication, which activate pattern recognition receptors such as RIG-I and MDA5. This triggers MAVS-mediated signaling and IRF3 nuclear translocation, leading to type I interferon (IFN-I) production and subsequent induction of interferon- stimulated genes (ISGs). It is well known that viruses have developed mechanisms to antagonize key steps of the IFN pathway to evade innate immunity. This study aimed to evaluate the ability of SINV and VEEV to antagonize IFN-I responses and to identify the specific viral proteins responsible. We performed reporter assays in HEK293T cell lines expressing firefly luciferase under the control of IFN-β or ISRE promoters, to assess viral impact on both IFN production and ISG induction. Reporter cells were first infected with SINV or VEEV and then stimulated with poly(I:C) or IFN-I, respectively, observing that both viruses significantly reduced luciferase signal in a viral load-dependent manner, indicating suppression of both IFN production and ISG induction. Functional studies further revealed that this antagonism is mediated by specific and conserved mechanisms acting at multiple levels of the pathway, although the magnitude and pattern of inhibition differ between SINV and VEEV. In conclusion, SINV and VEEV antagonize the IFN-I pathway at multiple levels. This work contributes to a better understanding of how distinct evolutionary pressures shape immune evasion strategies, providing a basis for further research on alphavirus-host interactions and potential antiviral interventions.

Keywords: *alphaviruses, IFN, innate immune evasion*

(21) Encapsulins as drug delivery systems: do they activate immune response?

Marta Paniagua Ros[1*], Jeroen J.L.M. Cornelissen[2], Sandra Michel – Souzy[2]

[1]Universidad Francisco de Vitoria, Madrid, España

[2]University of Twente, Enschede, Netherlands

* Correspondence: marta.paniros@gmail.com

Abstract

Encapsulins are bacterial protein nanocages that form nanocompartments capable of encapsulating diverse molecules. This confers spatial control over biological processes, increases molecular stability, and reduces toxicity. Their surface can be functionalized by inserting peptide sequences for targeting or purification, and cargo molecules can be modified to allow efficient loading within the cage. Moreover, encapsulins can be heterologously produced in organisms such as Escherichia coli, positioning them as promising candidates for drug delivery applications.

A crucial feature for any nanocarrier intended for drug delivery is its ability to evade immune detection. Therefore, this study evaluated the immunogenic potential of eight Thermotoga maritima encapsulin variants. These variants were selected based on previous studies considering their stability and capacity to reach target cells and were expressed in two E. coli strains: BL21 (wild type) and ClearColi (lipopolysaccharide-free). The adaptive response was evaluated by measuring activation of T-helper lymphocytes via CD4 expression.

Preliminary results indicated that the immunogenicity of these encapsulin variants depends not on the nanocage itself but on its surface functionalization. Additionally, the use of ClearColi as an expression system reduced immune response. Variants carrying a His purification tag at the C-terminus exhibited higher immunogenicity compared to those with a Strep tag. These findings highlight the importance of functionalization and expression system in modulating immune recognition. Consequently, future encapsulin engineering for drug delivery should include systematic immunogenicity assessments to ensure biocompatibility and safety.

Keywords: *Encapsulins, Immunogenicity, Drug delivery*

(22) pAIper check

Patricia Escribano[1], María de las Mercedes Molina[1], Alba Montáñez[1], Mónica Sánchez[1] and Roberto Ávila[1]*

[1]Faculty of Experimental Sciences, Universidad Francisco de Vitoria, Madrid, Spain

*Correspondence: robertoavilagarcia@gmail.com

Abstract

The pAIper check system is a modular software tool based on Artificial Intelligence (AI) designed to address the growing need for objective and efficient evaluation in academic communication. Its development arises from the necessity to provide students and new researchers with a reliable mechanism for self-assessing and enhancing the quality, rigor, and transparency of their manuscripts. The main objective of this work is to present a robust, scalable, and user-friendly system that supports the initial phases of peer review, promoting methodological and ethical excellence from the outset.

The pAIper check architecture implements a set of interconnected modules, each focused on a critical pillar of scientific quality. These modules perform a rigorous analysis that includes the formal Structure and Completeness of the document, Linguistic Quality Control specialized in scientific terminology, and the narrative Coherence and Cohesion of the argument to ensure a logical flow of ideas. Furthermore, Methodological Reproducibility is addressed by verifying the clarity of the methods and the accessibility of data and/or code. Finally, References and Citation validation guarantees bibliographical support, and the Scientific Quality Evaluation focuses on the rigor, novelty, and significance of the work's contribution. After processing, the system compiles the results and generates a Detailed Evaluation Report, providing scores by category and constructive feedback. pAIper check offers an automated solution to raise academic and ethical standards, optimizing review time and improving the quality of academic works.

Keywords: *Artificial Intelligence, Academic Evaluation, Scientific Rigor*

(23) Characterization of a novel hmxa knock-in mouse model

Fabiola Carretero Bellver[1], Anastasija Cupic[2,3], Daniel Flores[2], Adolfo García-Sastre[2,4,5,6] , Lisa Miorin[2,4]

[1]Experimental Sciences department, Universidad Francisco de Vitoria, Madrid, Spain

[2] Microbiology, Icahn School of Medicine at Mount Sinai, New York, NY

[3]Graduate School of Biomedical Sciences, Icahn School of Medicine at Mount Sinai, New York, New York, USA

[4]Global Health Emerging Pathogens Institute, Icahn School of Medicine at Mount Sinai, New York, New York, USA

[5]Department of Medicine, Division of Infectious Diseases, Icahn School of Medicine at Mount Sinai, New York, New York, USA

[6]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, New York, USA

Abstract

The myxovirus resistance protein A (MxA), encoded by the interferon-inducible MX1gene, plays a crucial role in the human innate immune response against viral pathogens, including influenza viruses, being able to restrict viral replication and modulate cross species transmission. Therefore, it is a critical factor in understanding influenza pathogenesis and pandemic potential.

Traditional laboratory mouse strains experience some limitations when used as models for studying MxA function because most of them carry non-functional Mx1 alleles due to genetic deletions. Alternative models that cover this problem are: A2G congenic mice possess a functional murine Mx1 gene but differ in protein function and specificity compared to human MxA. Also, transgenic mice expressing human MX1 under IFN inducible promoters have been developed but they often exhibit non-physiological expression and variable transgene integration. These limitations highlight the need for a novel murine model that allows controlled and physiological expression of human MxA.

Here we characterize a novel mouse model and two mutant lines providing a valuable tool for pandemic preparedness and therapeutic development against viral infections.

(24) Estudio de la senescencia en células de fibroblasto humano

Navarro-Valcárcel N[1*], Lobo-Aldezabal A[1], Escobar-Gómez-Rodulfo M[1], Fernández-Martos S[1,2], Espada J[2,3]

[1]Universidad Francisco de Vitoria, Madrid, España

[2]Skin Target, Madrid, España

[3]Gregorio Marañón, Madrid, España

*Correspondence: nerenavarro@hotmail.com

Abstract

La piel, el órgano más extenso del cuerpo humano, desempeña funciones esenciales de protección, regulación térmica y reparación tisular. En la dermis, los fibroblastos son responsables principalmente de la síntesis de colágeno y de los componentes de la matriz extracelular, siendo fundamentales en la cicatrización. Sin embargo, con la edad o la exposición a agentes como la bleomicina, estas células pueden entrar en senescencia, caracterizada por la pérdida de proliferación, cambios morfológicos y aumento de la actividad β-galactosidasa asociada a senescencia (SA-β-Gal). Este proceso contribuye a la inflamación crónica y al deterioro de la regeneración cutánea.

Se buscó establecer un modelo in vitro de senescencia en fibroblastos humanos y evaluar el posible efecto senolítico de un compuesto experimental (tratamiento X). Las células se sembraron y, tras 24 h, se trataron con bleomicina (10–30 µM). Posteriormente, el medio se reemplazó y se añadió el tratamiento X. Los cultivos se mantuvieron durante 6 días antes de los análisis morfológicos, de viabilidad y de tinción SA-β-Gal para evaluar los cambios asociados a la senescencia y la respuesta al tratamiento.

La exposición a bleomicina provocó alteraciones morfológicas, como agrandamiento celular y una marcada disminución de la tasa proliferativa, confirmando la inducción de senescencia, especialmente a 10 µM. La tinción SA-β-Gal evidenció un incremento significativo de la actividad en células tratadas con bleomicina, mientras que la presencia del compuesto X redujo notablemente la proporción de células positivas, indicando una posible acción senolítica. Finalmente, el tratamiento con el compuesto X tras la exposición a 10 µM de bleomicina mostró una ligera mejora en el número de células y en la viabilidad, apoyando su posible potencial para contrarrestar los efectos senescentes.

En conjunto, se estableció un modelo reproducible de senescencia en fibroblastos humanos inducida por bleomicina, identificándose 10 µM como la concentración óptima. El tratamiento con el compuesto X redujo la actividad β-galactosidasa y mejoró la viabilidad celular tras la exposición a bleomicina, lo que sugiere un potencial efecto senolítico capaz de atenuar la senescencia inducida y favorecer

la regeneración cutánea, constituyendo una base prometedora para futuras investigaciones.

Keywords: *Senescencia, fibroblastos y bleomicina*

(25) Patient-derived glioma organoids identify alectinib and ruxolitinib as potential therapies

Alvaro Monago-Sánchez [1,2] *, Laura Mateos-Madrigal [1,2], Ana Hernández-Martínez [1,2], Josefa Carrión-Navarro [1,2], Carlos Martínez-Ribeiro [1,2], Raquel Gutiérrez-González [3], Santiago Gil-Robles Mathieu [4], Cristina Aracil González [4], Francisco Pérez-Rodríguez [5], Beatríz Martín-Jouve [6], Antonio J Sánchez-López [8,9,10], Noemi García-Romero [1,2], Ángel Ayuso Sacido [1,2,7]

[1]Faculty of Experimental Sciences, Universidad Francisco de Vitoria, Madrid, Spain

[2]Brain Tumour Laboratory, Fundación Vithas, Grupo Hospitales Vithas

[3]Hospital Universitario Puerta de Hierro, Madrid, Spain

[4]Hospital Universitario Quironsalud, Madrid, Spain

[5]Fundación de Investigación HM Hospitales, HM Hospitales, Madrid, Spain

[6]Electron Microscopy Unit, Centro Nacional de Biotecnología-CSIC, Campus Universidad Autónoma de Madrid, Madrid, Spain

[7]Faculty of Medicine, Universidad Francisco de Vitoria, Madrid, Spain

[8]Neuroimmunology Unit, Instituto de Investigación Sanitaria Puerta de Hierro-Segovia de Arana, 28222, Madrid, Spain

[9]Red Española de Esclerosis Múltiple (REEM), 08028, Barcelona, Spain

[10]Biobank, Instituto de Investigación Sanitaria Puerta de Hierro-Segovia de Arana, 28222, Madrid, Spain

*Correspondence: alvaro.monago@ufv.es

Abstract

Gliomas are the most common primary brain malignancies in adults, classified by aggressiveness into low-grade gliomas (LGG, grades II–III) and high-grade gliomas (HGG, grade IV). Glioblastoma (GBM), a grade IV IDH1 wild-type astrocytoma, is the most prevalent and aggressive form, with an incidence of 3.22 cases per 100,000 people. GBM's high inter- and intra-tumoral heterogeneity contributes to its poor prognosis, with a median overall survival of 15 months and a 5-year survival rate of ~5%. Despite this, the standard of care—maximal surgical resection, radiotherapy, and temozolomide (TMZ) chemotherapy—has seen little advancement. LGG research faces challenges due to low proliferation rates and tumor heterogeneity, limiting conventional preclinical models. In this context,

patient-derived in vitro models like organoids provide a promising platform for personalized medicine.

In this study, we generated patient-derived organoids from over 50 glioma patients, characterized them based on histology, microstructure, expression patterns, and growth, and evaluated their response to SOC therapies. Subsequently, RNA-seq data was used for *de novo* drug Discovery via the DiSCoVER platform, with candidate compounds validated *in vitro*.

Organoid establishment was successful in most cases, with a higher success rate for GBM-derived organoids compared to LGG. Organoids proliferated and mimicked parental tissue in histology, microstructure, and expression patterns. However, biobanking proved unsatisfactory. Screening of common chemotherapeutic compounds revealed that SOC TMZ and other commonly used treatments had little effect on viability, whereas gefitinib showed a notable impact. Our *de novo in silico* approach identified alectinib, ruxolitinib, and dabrafenib as promising candidates, which were confirmed to significantly reduce viability, impair migration, and alter key molecular pathways.

In conclusion, while patient-derived glioma organoids present limitations in proliferative capacities and biobanking efficiency that must be addressed for clinical implementation, they remain an invaluable preclinical tool. As demonstrated in this work, the combination of organoids with bioinformatics tools like DiSCoVER establishes a potent platform for testing novel therapeutic strategies in the context of untreatable cancers such as gliomas.

Keywords: *Glioma, Organoids, Personalised therapies*

(26) Hydrogel formation from sugar production by product

Malena Carbonero[1,2], James Carlsson[2], Niklas Wahlström[2] and Francisco Vilaplana[2*]

[1]Universidad Francisco de Vitoria, Madrid, Spain

[2]Kungliga Tekniska Högskolan, Stockholm, Sweden

*Correspondence: franvila@kth.se

Abstract

Sugar beet is a vegetable used for half of the sugar production due to its high sucrose content. During sugar processing, a fibrous byproduct rich in pectin (15–30%) is produced. Pectins are polysaccharides widely used as thickening agents in the food industry, in cosmetics for their viscous properties, and as prebiotics. Current research also explores their use in textile fiber production and biomedical applications as scaffolds. Structurally, pectins consist of three main domains: homogalacturonan (HG), rhamnogalacturonan I (RGI), and rhamnogalacturonan II (RGII). HG is a linear chain composed solely of galacturonic acid. The RGI linear backbone is made up of galacturonic acid and rhamnose, with rhamnose residues branching into arabinan or galactan side chains. Within these chains, ferulic acid (FA) may be attached. In the presence of oxidative enzymes such as laccase, FA can form dimers that act as cross-linking agents, enabling the formation of hydrogels. This study aimed to evaluate the ability to extract pectins (SBP) from the byproduct of sugar production and its ability to form hydrogels. The SBP extraction was done via subcritical water extraction under acidic and neutral conditions for 20 and 40 minutes. It was done under different conditions to assess whether they influence SBP properties. Chemical analysis revealed that galacturonic acid is the main monosaccharide in all samples, which could be the HG domain of the pectins. There is also a high presence of arabinose, galactose and rhamnose which could suggest that the RGI domain has also been extracted. The starch content was below 2%, meaning it could not contribute to gel formation. It was expected that higher FA content would produce stronger gels due to increased crosslinking, but rheological analysis showed this was not the case. All SBP samples were able to form hydrogels; however, those extracted under neutral pH conditions produced much weaker gels compared to those obtained under acidic conditions. This correlates with the higher FA concentration after gelation in neutral extractions. These findings suggest that the extraction conditions influence the composition, structure and properties of SBP.

***Keywords**: pectin, extraction, hydrogels*

(27) Translational Insights into New Treatments for Diffuse Gliomas

Laura Mateos Madrigal[1,2*], Carlos Martínez Riveiro[1,2], Álvaro Monago Sánchez[1,2], Josefa Carrión Navarro[1,2], Noemí García Romero[1,2], Ángel Ayuso Sacido[1,2,3]

[1]Faculty of Experimental Sciences, Universidad Francisco de Vitoria, 28223-Madrid, Spain

[2]Brain Tumor Laboratory, Fundación Vithas, Grupo Hospitales Vithas, 28043-Madrid, Spain

[3]Faculty of Medicine, Universidad Francisco de Vitoria, 28223-Madrid, Spain

*Correspondence: lauramateos2002@gmail.com

Abstract

Gliomas are the most common malignant brain tumors in adults, accounting for over 80% of primary Central Nervous System (CNS) malignancies. Their incidence ranges from 4.7 to 5.7 cases per 100,000 people annually. Among them, glioblastoma (GBM) represents the most aggressive subtype. It is characterized by rapid growth, infiltration, and resistance to conventional therapies. GBM is typically treated with maximal surgical resection followed by radiotherapy and temozolomide. In contrast, diffuse intrinsic pontine glioma (DIPG) affects children and arises in the pons, with a median survival of less than one year. DIPG remains largely inoperable and refractory to chemotherapy. Despite advances, both tumors show poor prognosis due to molecular heterogeneity, resistance mechanisms, and the limited efficacy of standard treatments. Therefore, novel therapeutic strategies, including drug repurposing and targeted therapies, are urgently needed.

This project aims to test novel and repurposed compounds against gliomas: transcription and topoisomerase II inhibitors (Compound 1 series and Compound 4) in DIPG wild-type and H3 K27M-mutant cells, and DisCover-identified kinase inhibitors (ruxolitinib, alectinib, dabrafenib) in GBM38, U87, and U373 cells to evaluate antiproliferative and pro-apoptotic effects.

We screened both novel and repurposed compounds in paediatric DIPG and adult GBM models and found that transcriptional inhibitor Compound 1 and topoisomerase II poison Compound 4 selectively kill DIPG cells while sparing normal mesenchymal cells; Compound 1 potentially induces DNA damage and apoptosis, especially when combines with radiotherapy, and Compound 4 remodels the tumour proteome by suppressing survival pathways and activating damage and inflammatory signals. In GBM38, U87 and U373 lines, DisCover predicted kinase inhibitors (alectinib, ruxolitinib, dabrafenib) each reduced viability in a dose-dependent manner, with alectinib the most potent, and all

three impaired U373 cell migration, highlighting their promise as targeted, tumor-selective therapies for diffuse gliomas.

We identified four experimental agents (Compounds 1, 1A/1B, and 4) that selectively kill DIPG cells while sparing normal mesenchymal cells. Compound 1 induces potent DNA damage and apoptosis—synergizing with radiotherapy—whereas Compound 4 downregulates survival pathways and activates damage and inflammatory signals. In GBM models, repurposed kinase inhibitors (alectinib, ruxolitinib, dabrafenib) showed strong, dose-dependent cytotoxicity, with alectinib most potent. All three kinase inhibitors also impaired GBM cell migration, highlighting their anti-invasive potential.

Keywords: *gliomas, drug repurposing, targeted therapies*

(28) CRISPR- and dTAG-Mediated Specific Targeting of LMNA^{R249W} in Human Myoblasts

Adrián Martínez Fernández[1,2,3], Iván Hernández[1,2], María Luisa Martínez[1,2], Sonia Mekolaris[1,4], Mario Santafé[1,2], Anna Cereseto[5], Déborah Gómez-Domínguez[1,2], Ignacio Pérez de Castro[1,2,*]

[1]Rare Diseases Institute, Carlos III Health Institute, Madrid, Spain

[2]Advanced Therapies Department, Carlos III Health Institute, Madrid, Spain

[3]Molecular Biomedicine MSc Program, Autonomous University of Madrid, Madrid, Spain

[4]West Attica University, Athens, Greece

[5]Department of Computational, Cellular and Integrative Biology (CIBIO), University of Trento, Trento, Italy

*Correspondence: iperez@isciii.es

Abstract

Lamin A/C p.R249W is a dominant-negative variant that disrupts nuclear envelope architecture and impairs myogenic differentiation in congenital muscular dystrophy (L-CMD), causing the most severe phenotype. To reverse its negative effects, we evaluated two complementary strategies in human myoblasts: (1) allele-specific DNA disruption using CoCas9, a compact CRISPR nuclease from the human microbiome, and (2) post-translational depletion via the dTAG system. CoCas9 and a guide RNA targeting the c.745C>T variant were delivered by plasmid electroporation. Deep sequencing of fluorescence-enriched cells showed selective editing of the pathogenic allele, yielding two consistent frameshift indels, no wild-type modifications, and an average efficiency of 1.39 ± 1.2%. For protein depletion, LMNA^{R249W} was fused to an FKBP12^{F36V} degron and expressed after lentiviral transduction. Treatment with 0.5 µM dTAG-13 for seven days reduced pathogenic protein levels by up to 73%, though residual protein persisted. Responsive clones exhibited partial restoration of nuclear roundness within 24 hours, while differentiation impairment was not reverted, observing clone-specific variable changes. These preliminary findings demonstrate that CoCas9-sgRNA2 enables precise, allele-selective genome editing with predictable outcomes, while dTAG provides selective and tunable reduction of LMNA^{R249W}, partially restoring nuclear roundness.

Keywords: *CRISPR, dTAG, LMNA^{R249W}*

(29) Evaluation of the antimicrobial activity among peptides of the black soldier fly

Ana Martín Secades[1], Paz Núñez Valiente[1], Olga Zafra[1], Cruz Santos[1*]

[1]Faculty of Experimental Sciences, Universidad Francisco de Vitoria, Madrid, Spain

*Correspondence: c.santos@ufv.es

Abstract

Antibiotic resistance represents a major global health challenge, limiting the effectiveness of conventional treatments and highlighting the urgent need for alternative antimicrobial strategies. Antimicrobial peptides (AMPs) are short amino acid sequences that play a key role in innate immunity of many organisms. They exhibit broad-spectrum activity and unique mechanisms of action distinct from those of conventional antibiotics, making them promising candidates against multidrug-resistant pathogens. The black soldier fly (*Hermetia illucens*), a saprophagous insect constantly exposed to a rich microbial environment, is a potential source of novel AMPs. In a collaborative project done with the biotech company DAPIBUS, thirteen peptides from *H. illucens* were evaluated for their antimicrobial activity against *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*. While individual peptides showed no activity, the combination of peptides DPB3 and DPB9 demonstrated a clear inhibitory effect on Gram-negative bacteria, comparable to that observed with the complete peptide mixture, suggesting a synergistic interaction between these two components. No activity was detected against *S. aureus*, the only Gram-positive species tested so far. Future work will focus on determining the minimum inhibitory concentration (MIC) of the DPB3+DPB9 combination, elucidating their mechanism of action through time-kill and membrane permeabilization assays, and evaluating potential synergistic effects with conventional antibiotics such as ampicillin, chloramphenicol, and cefazolin. Additionally, cytotoxicity assays using mammalian cell lines will assess their biocompatibility. These results highlight the potential of *H. illucens*-derived AMPs as safe and effective agents to enhance antibiotic efficacy against Gram-negative multidrug-resistant infections, opening new strategies for peptide-based therapeutic development.

Keywords: *antimicrobial peptides, Hermetia illucens, Gram-negative bacteria, antibiotic resistance*

(30) Análisis del efecto de inhibidores de la chaperonina CCT en la organización del citoesqueleto y la migración en células tumorales

Beatriz García López[1], Ana Andrade[1], Ana Bonnin[1], Jorge Cuéllar[2], Elena Pascual[1*]

[1]Facultad de Ciencias Experimentales, Universidad Francisco de Vitoria, Madrid, España

[2]Departamento Estructura de Macromoléculas, Centro Nacional de Biotecnología (CNB-CSIC), Madrid, España

* Correspondence: elena.pascual@ufv.es

Abstract

Las chaperonas moleculares ayudan en el mantenimiento de la proteostasis, salvaguardando la integridad y plegamiento de numerosas proteínas celulares. Una de ellas es la chaperonina eucariota CCT (Chaperonin-containing TCP 1), cuyos sustratos principales son las proteínas citoesqueléticas actina y tubulina. La relación de estas proteínas con procesos fundamentales como la progresión del ciclo celular o la capacidad migratoria permiten hipotetizar que la modulación de la actividad de CCT puede afectar a la supervivencia celular. Además, numerosos estudios relacionan directamente la sobreexpresión de CCT con cáncer y una peor prognosis de la patología. Por todo ello, CCT se presenta como una interesante diana terapéutica. En nuestro laboratorio se han descrito recientemente dos moléculas con actividad moduladora de CCT in vitro. Ensayos realizados en un modelo celular de cáncer de mama demostraron una toxicidad selectiva de estas moléculas en líneas tumorales frente a células sanas. Este proyecto trata de caracterizar en detalle el efecto de estos moduladores a nivel celular, evaluando el efecto sobre la integridad estructural del citoesqueleto y la capacidad migratoria de la línea celular de cáncer de mama triple negativo MDA-MB-231. Ensayos de inmunofluorescencia permitieron cuantificar la intensidad de fluorescencia de actina y tubulina tras el tratamiento con los moduladores. Las células tratadas con Modulador 1 mostraron una reducción significativa en la intensidad de para ambas proteínas, efecto que no se apreció con el Modulador 2. Mediante microscopía de superresolución STED se analizó en detalle la desaparición de filamentos de actina después de 24 h de tratamiento, en células MDA-MB-231, y no en células sanas, en línea con la selectividad descrita en estudios previos del grupo. La capacidad migratoria de las células tumorales tras los tratamientos se evaluó mediante ensayos de herida. Se observó una reducción significativa en la capacidad migratoria en las células tratadas con ambos moduladores en comparación con el control sin tratar. Estos hallazgos sugieren que la inhibición farmacológica de CCT puede ejercer un efecto sobre la organización del citoesqueleto que resulta en una menor capacidad migratoria de células tumorales tratadas con estas moléculas.

***Keywords**: Chaperonina CCT, citoesqueleto, migración celular*

(31) Impact of autophagy inhibition on cell apoptosis in the neurodevelopment of embryonic chick retina: a Flow Cytometry and TUNEL analysis study

Candelas Bezares López[1*], Raquel de la Flor Laserna[1]

[1]Faculty of Experimental Sciences, Universidad Francisco de Vitoria, 28293-Madrid, Spain

*Correspondence: candesbezares@gmail.com

Abstract

During central nervous system development, apoptosis and autophagy operate as interconnected mechanisms that govern cellular remodeling and survival; apoptosis removes unnecessary or damaged cells, whereas autophagy maintains metabolic balance by recycling cytoplasmic components and organelles. Their interplay remains complex and context-dependent, particularly in early neurogenesis. In this study, we investigated how autophagy inhibition influences apoptosis in the embryonic chick retina (E6). Retinal explants were cultured either in control medium or treated with 3-methyladenine (3-MA), a classical inhibitor of autophagy; apoptotic cell death was then assessed by flow cytometry using Annexin V/PI staining and by quantitative and qualitative TUNEL assays. The TUNEL analyses (both flow-based and microscopic) revealed an increased number of apoptotic nuclei upon 3-MA treatment, suggesting that autophagy suppression promotes cell death; however, Annexin V labeling indicated higher phosphatidylserine exposure in control retinas, revealing an apparent discrepancy between assays. Morphological examination showed larger, TUNEL-positive cells in treated samples, consistent with impaired phagocytosis and defective clearance of apoptotic bodies. Taken together, these results suggest that autophagy inhibition disrupts ATP-dependent phosphatidylserine externalization, altering the recognition and removal of apoptotic cells. This study highlights the methodological and metabolic nuances underlying the balance between autophagy and apoptosis, during neurodevelopment and supports further exploration of how energy homeostasis and phagocytosis contribute to cell fate regulation in the developing retina.

Keywords: *neurodevelopment, autophagy, apoptosis*

(32) Production of anti-BCMA CAR T cells for multiple myeloma treatment. Phenotypic and functional characterization

María de las Candelas Bezares López[1*], Juan Roberto Rodríguez Madoz[1]

[1]Hemato-Oncology Program, CIMA - University of Navarra, Spain

*Correspondence: candesbezares@gmail.com

Abstract

Multiple myeloma or MM, remains an incurable plasma cell malignancy; even with the advent of proteasome inhibitors and monoclonal antibodies, most patients eventually relapse and refractory disease. In this context, chimeric antigen receptor T-cell (CAR-T) therapy has transformed the therapeutic landscape by redirecting T lymphocytes to recognize and eliminate tumor cells in an MHC-independent manner. Here, we established an in vitro model of allogeneic anti-BCMA CAR-T cells, generated from healthy donor T lymphocytes, to evaluate their transduction efficiency, phenotypic evolution, and cytotoxic function against MM.1S myeloma cells. T cells were isolated, activated, and lentivirally transduced with an EF1α-driven construct encoding an anti-BCMA scFv linked to 4-1BB and CD3ζ signaling domains; after expansion, flow cytometry revealed efficient CAR expression (BFP^+) and a phenotypic shift from naïve/central-memory to effector subsets. Functionally, CAR-T cells displayed potent antigen-specific cytotoxicity, leading to a marked reduction of GFP^+ MM.1S targets when compared to untransduced controls. Together, these findings confirm the successful generation of functional anti-BCMA CAR-T cells and support this system as a reproducible in vitro platform for dissecting the phenotypic and functional maturation of CAR-T cells during tumor interaction.

Keywords: *CAR-T generation, BCMA-Targeting, cytotoxicity*

(33) Catalizadores mesoporosos integrados en PLA para la síntesis eco-eficiente de esqueletos de fármacos

E. Margüello Molina[1]*, A.J. Arias San Román[1], I. Álvarez García[1], M. Wojtusik Wojtusik[1], D. González Rodal[1]

[1]Facultad de Ciencias Experimentales, Universidad Francisco de Vitoria, Ctra. Pozuelo-Majadahonda 1800, 28223, Pozuelo de Alarcón, Madrid, España

*Correspondence: e.marguello.molina@gmail.com

Abstract

La creciente demanda de procesos químicos sostenibles ha situado a la química verde en el centro de la investigación actual. Sus principios buscan rediseñar rutas sintéticas para minimizar residuos, reducir el consumo energético y sustituir reactivos peligrosos por alternativas renovables y respetuosas con el medio ambiente. Entre estas estrategias, la catálisis heterogénea destaca como herramienta esencial para lograr transformaciones más limpias y eficientes, permitiendo la recuperación del catalizador y manteniendo una elevada actividad y selectividad. En este contexto, los materiales catalíticos mesoporosos ofrecen ventajas notables gracias a su alta área superficial, estructura porosa ordenada y estabilidad, facilitando la difusión de reactivos y aumentando la accesibilidad a los sitios activos. En este trabajo se emplearon materiales mesoporosos funcionalizados con líquidos iónicos y aminoácidos, especies que crean entornos activos capaces de favorecer interacciones moleculares y acelerar la reacción en condiciones suaves. La actividad catalítica se evaluó en la formación de 2-amino-4H-cromenos empleando condiciones suaves y reactivos simples, demostrando un comportamiento eficiente alineado con los principios de la química verde. Los resultados muestran elevadas conversiones incluso con baja carga catalítica y escasa dependencia de la temperatura, lo que evidencia la eficacia del sistema y su potencial para operaciones de bajo consumo energético. Además, de forma preliminar, se incorporaron los catalizadores a una matriz de ácido poliláctico (PLA) mediante impresión 3D, manteniendo la integridad del material y abriendo una vía prometedora para el diseño de estructuras catalíticas biodegradables y reutilizables orientadas a procesos sostenibles.

En conjunto, este estudio demuestra que la combinación de estructuras mesoporosas funcionalizadas y soportes renovables constituye una estrategia eficaz y versátil para desarrollar plataformas catalíticas alineadas con los objetivos de la química verde y la síntesis ecoeficiente de compuestos bioactivos.

***Keywords**: catálisis heterogénea, síntesis eco-eficiente, 2-amino-4H-cromenos*

(34) From flickering to networks: mapping red blood cell membrane dynamics using horizontal visibility graphs

Lucía Benito-Barca[1,2], Diego Herráez-Aguilar[1*]

[1]Faculty of Experimental Sciences, Francisco de Vitoria University (UFV), Pozuelo de Alarcón, Madrid, Spain

[2]Higher Technical School of Engineering, Francisco de Vitoria University (UFV), Pozuelo de Alarcón, Madrid, Spain

*Correspondence: diego.herraez@ufv.es

Abstract

Red blood cells (RBCs) are the most abundant cells in the human body and play a crucial role in maintaining gas homeostasis. Their membrane and internal composition are finely adapted for efficient gas transport. Pathological alterations in membrane mechanics, cytoskeletal organization, or metabolic activity can impair these functions, leading to deficient oxygen delivery and potentially severe systemic consequences. The flickering of red blood cells (RBCs) reflects the complex thermal and active fluctuations of their membranes, which are closely related to the cell's mechanical properties and physiological state. Traditional analyses of flickering dynamics often rely on spectral or correlation methods, which may overlook nonlinear and non-stationary features. In this work, we apply the Horizontal Visibility Graph (HVG) framework to transform RBC membrane fluctuations into complex networks, enabling the quantification of temporal correlations and dynamical patterns through network topology. The topological properties of the resulting HVGs successfully capture the main features of the flickering phenomenon: (i) metabolic dependence, as they discriminate among healthy, inactive, and fixed cells; (ii) spatial heterogeneity, reflected by local variations of HVG features along the membrane; and (iii) non-equilibrium behavior and entropy production, consistent with the thermodynamic uncertainty principle, whereby increased process precision entails reduced efficiency and higher entropy production. This network-based approach provides a novel and sensitive framework to characterize membrane mechanics and to detect alterations in RBC biophysics under diverse physiological or pathological conditions.

***Keywords**: Red Blood Cells, Horizontal Visibility Graphs, Entropy Production*

(35) Characterization of mitochondrial and phenotypic changes in vascular smooth muscle cells associated with systemic lupus erythematosus

Lorena Andrade-Martín[1,2,*], Sofía Miñano[2], Néstor de la Visitación[2], Diego Salagre[2], Ahmad Agil[2], Marta Toral[2,3,4] and Juan Duarte[2,3,4].

[1]Faculty of Experimental Sciences, Universidad Francisco de Vitoria, Madrid, Spain

[2]Department of Pharmacology, Universidad de Granada, Granada, Spain

[3]Instituto de Investigación Biosanitaria de Granada (ibs.GRANADA), Granada, Spain

[4]CIBER of Cardiovascular Diseases (CIBERCV), Spain

* Correspondence: lorena.andrade.madrid@gmail.com

Abstract

Systemic lupus erythematosus (SLE) is associated with a high risk of cardiovascular complications, in which vascular smooth muscle cells (VSMCs) play a central role in vascular remodelling and dysfunction. The aim of this study was to evaluate how different inflammatory stimuli modulate mitochondrial function, phenotypic plasticity, and vascular contractility in VSMCs.

For its development, primary cultures of murine aortic VSMCs were isolated and incubated with IFN-γ or with human plasma from healthy donors (SN) and from normotensive (LN) and hypertensive (LH) lupus patients. Parameters of mitochondrial dynamics (fusion and fission proteins), energy metabolism, cellular respiration by high-resolution respirometry, and expression of contractile and extracellular matrix remodelling genes were analysed. In addition, vascular function was assessed in mouse thoracic aortic rings incubated with plasma from the different groups.

IFN-γ induced mild changes in VSMCs, with slight downregulation of contractile genes and a non-significant increase in fusion/fission proteins. In contrast, lupus plasma triggered profound alterations: cells incubated with LH plasma showed overexpression of MFN2, OPA1 and UCP2, together with a selective increase in FIS1. These changes were accompanied by a marked reduction in respiratory capacity and respiratory control ratio, indicating mitochondrial dysfunction. At the phenotypic level, both LN and LH significantly reduced the expression of contractile genes (*MYH11*, *ACTA2*, and *TAGLN2*), with this effect being more pronounced in the LH group, where increased expression of synthetic markers (*MMP2*, *MMP9*, and *COL1A1*) was also observed. Finally, aortic rings treated with LH plasma exhibited reduced contractility.

Considering the obtained results, lupus plasma, particularly from hypertensive patients, induces in VSMCs a synthetic, inflammatory, and fibrotic phenotype, accompanied by mitochondrial dysfunction and reduced vascular contractility.

Keywords: *Systemic lupus erythematosus; vascular smooth muscle cells; mitochondrial dysfunction; vascular remodelling; hypertension*

(36) Investigating the immunomodulatory role of podoplanin in skin inflammation

María Ortiz[1], Sara Temprano-Carazo[1], Santiago Garcés-Fernández[1], Lucía Montero-Montero[1], Rocío Jarcovsky[1], Esther Grueso[1], Diego Megías[2], Susana Álvarez[1] and Ester Martín-Villar[1*].

[1]Faculty of Experimental Sciences, Universidad Francisco de Vitoria, Madrid, Spain

[2]Advanced Optical Microscopy Unit, Instituto de Salud Carlos III, Madrid, Spain

*Correspondence: ester.martin@ufv.es

Abstract

The skin constitutes the first physical and immunological barrier against the external environment, and chronic inflammation plays a key role in the development of skin pathologies such as squamous cell carcinoma (SCC). Podoplanin (PDPN) is a transmembrane glycoprotein essential for lymphatic, cardiac, and pulmonary development, with immunomodulatory functions that remain poorly defined, particularly in the skin. Under physiological conditions, its expression is restricted to lymphatic vessels, hair follicles, and sebaceous glands; however, it is induced in basal keratinocytes and dermal fibroblasts under inflammatory or hyperproliferative stimuli, and its upregulation has been associated with SCC progression. This study aims to characterize the immunomodulatory effects of podoplanin in skin inflammation using two complementary murine models with altered PDPN expression or functionality, combined with topical application of the proinflammatory agent 12-O-tetradecanoylphorbol-13-acetate (TPA). Histological analysis revealed that systemic blockade of podoplanin disrupts epidermal and dermal architecture, causing tissue disorganization and reduced cohesion in the basal layer. Immunofluorescence staining for the pan-leukocyte marker CD45 showed an increased recruitment of $CD45^+$ immune cells both under basal conditions and following TPA stimulation. Similarly, epidermal deletion of podoplanin altered the hyperplastic response to TPA and decreased basal layer cohesion, accompanied by greater leukocyte infiltration. Cytokine profiling confirmed an exacerbated response to mild stimuli and a deregulated response to TPA, indicating loss of epithelial and immune homeostasis in knockout mice. Altogether, these findings suggest that podoplanin acts as a regulator of cutaneous immune microenvironment, modulating tissue organization, cell recruitment, and inflammatory response, although further studies are required to precisely define its immunomodulatory role.

Keywords: podoplanin, skin inflammation, immunomodulation

(37) Analysis of endocytic trafficking and vesicular secretion defects in Epstein-Barr virus (EBV)-immortalized B lymphocytes carrying a Rab27a mutation: a clinical case study of Griscelli syndrome type 2 (GS2)

Paula Boza Martín[1], Hugh Thomson Reyburn[2], Mar Valés Gómez[2]

[1]Universidad Francisco de Vitoria, Madrid, Spain

[2]Centro Nacional de Biotecnología (CNB-CSIC), Madrid, Spain

Correspondence: Paulabozamartin4@gmail.com

Abstract

Griscelli syndrome type 2 (GS2) is a primary autosomal recessive immunodeficiency caused by mutations in the RAB27A gene, which encodes a small GTPase essential for vesicular trafficking in pigmentary and immune cells. Rab27a regulates the fusion of multivesicular bodies (MVBs) with the plasma membrane and the secretion of cytotoxic granules in T and NK cells. Loss of Rab27a function leads to partial albinism and severe immunodeficiency, often associated with hemophagocytic lymphohistiocytosis (HLH). While its role in T and NK cells has been extensively characterized, its function in B lymphocytes and extracellular vesicle (EV) secretion remains poorly understood.
We investigated a GS2 patient carrying a homozygous RAB27A (c.209T>C; p.Leu70Pro) mutation, classified as a variant of uncertain significance. Although the patient presented no severe clinical manifestations, functional assays revealed defective NK cell degranulation and cytotoxicity. The aim of this study was to analyze vesicular secretion and endolysosomal organization in EBV-immortalized B lymphocytes from the patient (LB MUT) compared to a healthy donor (LB WT). Vesicular fractions were isolated by differential centrifugation; nanoparticle tracking analysis (NTA) was used to assess size and concentration, while western blotting and sandwich ELISA were employed to evaluate protein markers (CD9, CD81, Rab27a). Transmission electron microscopy (TEM) was used for subcellular morphology assessment.
LB MUT cells showed a complete loss of Rab27a expression, a reduction in small EV secretion, altered tetraspanin profiles (decreased CD9 and abnormally increased CD81), and β-actin accumulation in medium-sized EVs. Ultrastructural analysis revealed enlarged MVBs, increased lysosomes, and altered mitochondria, consistent with exocytic blockage and cellular stress.
In summary, the RAB27A (Leu70Pro) mutation markedly disrupts vesicular and endolysosomal homeostasis in B lymphocytes, potentially contributing to the immunological dysfunction observed in GS2.

Keywords: *Rab27a, Griscelli syndrome type 2 (GS2), Extracellular vesicles (EVs), B lymphocytes*

(38) Suplementación con Creatina Más Allá del Deporte: Beneficios de los Diferentes Tipos de Creatina para Mujeres, Veganos y Poblaciones Clínicas

Samuel Bermejo[1]

[1]Universidad Francisco de Vitoria, Madrid, España

*Correspondence: samuelbermejo.nunez@gmail.com

Abstract

La creatina monohidratada es un suplemento nutricional ampliamente reconocido por su capacidad para mejorar el rendimiento en ejercicios de alta intensidad mediante el aumento de las reservas intramusculares de fosfocreatina y contribuye a que la producción de ATP se acelere. Sin embargo, su utilidad trasciende el ámbito deportivo. Este poster resume la evidencia científica actual sobre los beneficios de la suplementación con creatina en poblaciones específicas: mujeres, veganos y diversas condiciones clínicas.

En mujeres, puede ayudar a mitigar la fatiga asociada a las fluctuaciones hormonales del ciclo menstrual. Los veganos, al tener niveles bajos de creatina, experimentan mejoras más marcadas en el rendimiento físico y cognitivo. En el ámbito clínico, la creatina muestra potencial como contribuyente en el manejo de enfermedades neuromusculares, neurodegenerativas (como Parkinson y Huntington) y en la recuperación de traumatismos craneoencefálicos, gracias a su papel en el metabolismo energético cerebral y muscular.

Este póster también aborda y desmiente mitos comunes basándose en hallazgos científicos, concluyendo que la creatina no causa daño renal o hepático, ni alopecia, en individuos sanos con una suplementación adecuada. Se destaca la seguridad y eficacia de la creatina monohidratada, recomendando un protocolo de mantenimiento de 3-5 g/día como la estrategia más práctica y bien tolerada. La suplementación con creatina monohidratada se presenta, así como una intervención segura y versátil, respaldada por un sólido cuerpo de evidencia, para mejorar la salud y el rendimiento en diversos contextos y poblaciones.

***Keywords**: Creatina, salud, evidencia científica*

(39) Effects of dental pulp mesenchymal stromal cells on neuronal regeneration and axonal outgrowth: an in vitro co-culture model

Sención Ávila, Yariliz Aimée[1]*, Mellén Rodríguez, Marian[1], Botana Veguillas, Laura[1], Santa María Pérez, Ismael[1], Iglesias Badiola, Maite[1]

[1]Francisco de Vitoria Biosanitary Research Institute (IIB-1 UFV), Madrid, Spain

*Correspondence: drayarilizsencion@gmail.com

Abstract

Mesenchymal stromal cells (MSC) derived from dental pulp are promising candidates for neuroregenerative therapies due to their accessibility, multipotency, and paracrine signaling. Among them, stem cells from exfoliated deciduous teeth (SHED) and adult dental pulp stem cells (DPSC) represent developmentally distinct populations with potential effects on neural repair. This study compares the influence of SHED and DPSC on retinal neurogenesis, axogenesis, and axonal regeneration using an in vitro co-culture model with retinal neurons from Gallus gallus domesticus embryos. Retinas were isolated from 5-day-old embryos, a stage selected for its high neurogenic activity and sensitivity to external cues, allowing optimal assessment of stem cell effects on early neuronal development. Retinal cells were enzymatically dissociated with papain and plated at 3×10^4 cells/cm². Cocultures were maintained for 72 hours with SHED, DPSC, HaCaT keratinocytes (non-neuronal control), or poly-L-lysine (PLL)–coated substrates (cell-free substrate control). Cultures were immunostained for proliferation (EdU), neuronal differentiation (TUJ1/βIII-tubulin), and nuclear labeling (DAPI). Imaging and quantitative analysis were performed using a custom ImageJ macro. Statistical analysis was conducted with GraphPad Prism. DPSC favored proliferation and neuronal differentiation of retinal ganglion cells more effectively than SHED. SHED did not significantly enhance proliferation but showed a modest increase in neurodifferentiation compared to controls. SHED supported axogenesis in newly generated (EdU^+) retinal neurons and stimulated axonal regeneration in 21 ± 2% of pre-existing (EdU^-) neurons, with a mean axon length of 36.72 µm. These findings suggest distinct tendencies: DPSC promote mitogenic and differentiative responses, while SHED exhibit targeted neuroregenerative effects. This co-culture model offers a sensitive platform to evaluate stem cell–derived secretomes and may be applicable to the study of neurodevelopmental disorders such as attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and Rett syndrome.

Keywords: *SHED, neuronal regeneration, stem cell therapy*

(40) Leukodomics – Dinámica del núcleo celular en la investigación de la Leucemia Linfoblástica Aguda

Carlos del Pozo-Rojas[1], Lucía Benito-Barca[1], Diego Herráez-Aguilar[1*], Judith Ortega[2], Macarena Calero[2], Francisco Monroy[2], Elena Sánchez[3], Manuel Ramírez[3]

[1]Universidad Francisco de Vitoria, Pozuelo de Alarcón, España

[2]BIOPHYS-HUB. Dpto. Química Física. Universidad Complutense de Madrid, España

[3]Servicio de Oncohematología. Hospital Niño Jesús, Madrid, España

*Correspondence: diego.herraez@ufv.es

Abstract

La Leucemia Linfoblástica Aguda infantil (LLA) es el cáncer pediátrico más frecuente, caracterizado por la proliferación incontrolada de linfoblastos y una marcada heterogeneidad genética y molecular que dificulta la estratificación del riesgo y la medicina personalizada. En este contexto, las propiedades mecánicas celulares emergen como nuevos biomarcadores complementarios a la genómica y la proteómica. Este estudio, enmarcado en el proyecto LEUKODOMICS, propone un enfoque biofísico para caracterizar el mecanoma nuclear (el conjunto de propiedades mecánicas del núcleo celular), en muestras primarias de médula ósea de 25 pacientes pediátricos con LLA diagnosticada. Las células se marcaron con sondas fluorescentes (Hoechst, CD34, CD7/19 y ZOMBIE-NIR) y se analizaron mediante microscopía confocal (NIKON AX) y algoritmos de Multiple Particle Tracking (250 fps, 20 s) para registrar trayectorias estocásticas nucleares. A partir de estas trayectorias se estimaron parámetros viscoelásticos bajo condiciones de estado estacionario no equilibrado (NESS), incluyendo rigidez, coherencia dinámica y disipación energética. Los mapas espaciales obtenidos muestran una heterogeneidad mecánica submicrométrica, con una tendencia a mayor rigidez en la periferia nuclear, posiblemente asociada a la red de láminas nucleares. Los análisis correlativos indican que la rigidez media se relaciona positivamente con el contenido de ADN y negativamente con la expresión de CD34 y CD19/7, sin diferencias significativas entre fenotipos B y T. Asimismo, las propiedades mecánicas siguen leyes de escala universales que sugieren un comportamiento de materia activa modulado por la actividad metabólica. En conclusión, el mecanoma nuclear ofrece una nueva dimensión para la caracterización funcional de las células leucémicas, con potencial para integrarse en modelos predictivos de riesgo clínico y respuesta terapéutica en LLA infantil.

***Keywords**: leucemia linfoblástica aguda, biofísica, mecanoma nuclear*

(41) High-Intensity Interval Exercise–Conditioned Human Serum Differentially Modulates Signaling and Transcriptional Programs in Luminal A and Triple-Negative Breast Cancer Cell Lines

Pablo Ledesma-Roncero[1], Jorge Gutiérrez-Hellin[2], Miguel López-Moreno[2], Álvaro Mónago-Sánchez[1,3], Yonina Bykov[4], Sara Cuadrado-Castaño[4,5,6], Nuria Mendoza-Laiz[2], Maite Iglesias[1], Cruz Santos-Tejedor[1], and Mayalen Valero-Breton[2]*

[1]Faculty of Experimental Sciences, Universidad Francisco de Vitoria, Madrid, Spain

[2]Faculty of Health Sciences, Universidad Francisco de Vitoria, Madrid, Spain

[3]Brain Tumor Laboratory, Fundación Vithas, Grupo Hospitales Vithas

[4]Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, USA

[5]Icahn Genomics Institute, Icahn School of Medicine at Mount Sinai, New York, USA

[6]Marc and Jennifer Lipschultz Precision Immunology Institute, Icahn School of Medicine at Mount Sinai, New York, USA

*Correspondence: mayalen.valero@ufv.es

Abstract

Exercise is a promising non-pharmacological strategy within integrative oncology, acting through acute systemic responses and chronic adaptations. High-intensity interval exercise (HIIE) induces transient elevations in circulating exerkines, signaling molecules released from multiple organs, including myokines, cytokines, and metabolites, which may influence tumor cell behavior. Although post-HIIE serum has been shown to reduce breast cancer cell viability, the underlying mechanisms and time-dependent effects remain unclear. Four physically inactive women (18–30 years) completed a single HIIE session following a maximal aerobic power test. Blood samples collected before and immediately after exercise were used to generate pre- and post-HIIE serum. MCF-7 and MDA-MB-231 breast cancer cells were treated with 10% human serum under two paradigms: (1) continuous exposure for 24, 48 and 72 h and

(2) 3 h daily pulses of post-HIIE serum to mimic transient physiological fluctuations. Assays included viability, apoptosis/necrosis, protein levels, and transcriptomic profiling. HIIE produced a strong physiological response, increasing blood lactate and decreasing serum 17β-estradiol. Continuous exposure to post-HIIE serum for 48 h did not alter viability or apoptosis but reduced pro-growth and inflammatory signaling (lower 4E-BP1 phosphorylation in MDA-MB-231 and reduced MyD88 and p-NF-κB in both lines). Transcriptomic

and mitochondrial analyses showed subtype-specific profiles: MCF-7 exhibited enrichment of estrogen response, oxidative phosphorylation, and DNA repair pathways, whereas MDA-MB-231 upregulated cell-cycle programs with negative enrichment of oxidative phosphorylation, consistent with differential mitochondrial stress. In line with these signatures, MCF-7 repressed angiogenic and inflammatory programs, whereas MDA-MB-231 upregulated E2F/G2M cell-cycle pathways, yet both subtypes converged on MyD88/p-NF-κB downregulation as a shared anti-inflammatory response. Importantly, short 3 h daily pulses of post-HIIE serum significantly reduced viability at 48 h and 72 h in both lines, particularly in MCF-7, indicating that transient exposure intensifies antiproliferative effects. In conclusion, under 48 h continuous exposure, post-HIIE serum modulates inflammatory and mitochondrial pathways in breast cancer cells, eliciting shared anti-inflammatory effects but divergent metabolic adaptations. These findings reveal that mitochondrial activity and inflammatory signaling are early responders to exercise-conditioned serum, extending its influence beyond short-term viability. Transient 3 h pulses, which better reflect physiological exerkine kinetics, produce stronger reductions in cell viability, underscoring the importance of temporal dynamics when modeling exercise-induced antitumor effects.

Keywords: High-intensity interval exercise; Exercise-conditioned human serum; Breast cancer

ISBN: 978-84-09-79688-5