Universidad Autónoma de Madrid | Escuela de Doctorado | Facultad de Medicina

Workshop in Health Science and Biomedicine

28 May 2026 School of Medicine UAM

WORKSHOP PROGRAMME

9:00-9.40 **REGISTRATION**

9:45-10:00 **WORKSHOP INAUGURATION (Aula Magna)**

Pilar López Garcia, Dean of the School of Medicine, UAM

Lourdes Ruiz Desviat, Director of EDUAM

Pilar Lopez Larrubia, Director Instituto de Investigaciones Biomédicas Sols-Morreale CSIC-UAM

10:00-11:45 **ORAL COMMUNICATIONS I**

Aula Magna	Oral 1A Moderated by Pilar López Larrubia and Ángela Martínez Valverde
Seminario 1	Oral 1B Moderated by Ignacio Zapardiel and Pilar Serrano Gallardo
Seminario 3	Oral 1C Moderated by Carmen Perez de Nanclares and Susana Guerra

11:45-12:30 **POSTER SESSION AND COFFEE IN DECANATO HALL**

12:30-14:15 **ORAL COMMUNICATIONS II**

Aula Magna	Oral 2A Moderated by Victor Calvo and Ángela Martínez Valverde
Seminario 1	Oral 2B Moderated by Esther Lopez García and Humberto Yevenes Briones
Seminario 3	Oral 2C Moderated by Margarita Diez Guerra y Juan Arredondo

14:15-14:30 **AWARDS AND WORKSHOP CLOSING (Aula Magna)**

Oral Communications 1A Aula Magna (10:00 -11:45)
Moderated by Pilar López Larrubia and Ángela Martínez Valverde

Title: Exploring the Role of Kupffer Cells in Hepatocellular Carcinoma Development
Author: Nauzet Celso Deniz-Eyre

Title: Limited Inflammation Impairs Monocyte-Derived Macrophage Differentiation and Promotes Protumor Tim4^{+} Resident Macrophage Expansion during Peritoneal Colorectal Cancer
Author: Natalia Álvarez-Ladrón

Title: DGKζ-Dependent Immune Remodeling Reflects Antitumor Responses in Bladder Cancer
Author: Ane Ochoa Echeverría

Title: VISIUM HD Spatial Transcriptomics Reveals Tumor–Stroma Reprogramming after RANK–RANKL Inhibition in Luminal B-Like Breast Cancer
Author: Mario Rodríguez-del-Collado

Title: Astrocyte Activation in the Primary Motor Cortex Contributes to the Therapeutic Effects of Subthalamic Nucleus Deep Brain Stimulation
Author: Alejandro Hernandez

Title: Age-Dependent Metabolic Reprogramming of Microglia as a Determinant of Brain Metastasis Progression
Author: Pablo Castillo

Oral Communications 1B Seminario 1 (10:00 -11:45)
Moderated by Ignacio Zapardiel and Pilar Serrano Gallardo

Title: Cardiovascular Health and Circulating Inflammatory Biomarkers in Older Adults
Author: David Gómez Ángel

Title: Prospective Associations between Plasma Amino Acid Concentrations and Objective and Subjective Physical Function in Older Adults
Author: Clara Marcela Durán Arias

Title: Social and Lifestyle Factors Associated with the Risk of Developing Multimorbidity in Middle-Aged and Older Adults
Author: Damián González Beltrán

Title: HDL Lipid Signatures Associated with Cognitive Decline in Older Adults: Evidence from a Longitudinal Cohort Study
Author: Amanda Carolina Padilha Salviatto

Title: Diet Quality and the Progression from Health to Morbidity, Multimorbidity, and Mortality
Author: Aitana Vázquez Fernández

Title: Association of Healthy Dietary Patterns with Frailty Syndrome Progression
Author: Julián Puente Ferreiro

Oral Communications 1C Seminario 3 (10:00 -11:45)
Moderated by Carmen Perez de Nanclares and Susana Guerra

Title: Effects of Coffee Pulp Infusion on Exercise Performance and Systemic Cytokine Responses: A Sex-Specific Analysis
Author: Ricardo Alonso de Celada Granado

Title: Preclinical Therapeutic Potential of Phage FT5P against Vancomycin-Resistant Enterococcus faecium Infections
Author: Laura Ribes Martínez

Title: A Strategic and Collaborative Model to Improve Efficiency, Performance, and Access to Pediatric Hemato-Oncology Clinical Trials
Author: Andrés Gómez Dávila

Title: Inhibition of Serum- and Glucocorticoid-Regulated Kinase 1 as a Novel Therapeutic Strategy for Cardiovascular Diseases
Author: Wilfrido Arrúa

Title: Impact of ISG15 on Monkeypox Virus Infection under Interferon-Stimulated Conditions
Author: Irene Campaña Gómez

Title: Heart Rate Variability and Vascular Stiffness in Preterm-Born Children: Sex Differences and International Cohort Comparisons
Author: Javier García-Rodríguez

Oral Communications 2A Aula Magna (12:30 -14:15)
Moderated by Victor Calvo and Ángela Martínez Valverde

Title: Two Immunometabolic Worlds in High-Grade Gliomas: Interplay between Immune Checkpoints and Tumor Metabolism
Author: Paula Carretero Navarro

Title: TNF-α–Dependent Alterations in Magnetic Resonance Imaging Parameters during High-Fat Diet–Induced Neuroinflammation
Author: Darwin Andrés Córdova Ascurra

Title: Molecular and Structural Mechanisms of mTORC1 Assembly Mediated by the HSP90–R2TP Chaperone System
Author: Álvaro López Codina

Title: In Vivo Intercellular Communication via Extracellular microRNA Carriers and Its Role in Metabolic Disease
Author: Paula Díez Roda

Title: Artificial Intelligence Applications in the Diagnosis and Treatment of Rare Hematological Diseases: A Scoping Review
Author: Greys María Rodelo Olmos

Title: High-Dimensional Spectral Flow Cytometry Reveals Systemic Immune Dysregulation in Pediatric Cystic Fibrosis
Author: Laura Bravo Robles**:**

Oral Communications 2B Seminario 1 (12:30 -14:15)
Moderated by Esther Lopez García and Humberto Yevenes Briones

Title: Benefits, Limitations, and Potential Solutions for Defining Good Practices in Online Counselling Chat Services for Youth
Author: Irati Higuera Lozano

Title: Structural Deletions in HTLV-1 Proviruses Correlate with Disease Severity in Adult T-Cell Leukemia
Author: Mikel Blanco Otaegui

Title: Development and Validation of New Chronic Rhinosinusitis Control Tests
Author: Diego M. Conti

Title: Cardiometabolic Risk Factors for Type 2 Diabetes across Early and Late Postmenopausal Stages in Prediabetic Women
Author: Juan Carlos Lizarzaburu Robles

Title: Enlarged Perivascular Spaces Reflect Neuropathological Severity of Cerebral Amyloid Angiopathy in Alzheimer's Disease Dementia
Author: Mario Ricciardi Serra

Title: Childhood Loneliness and Disability in First-Episode Psychosis: Mechanisms and Transdiagnostic Effects
Author: Ana Ortiz-Tallo

Oral Communications 2C Seminario 3 (12:30 -14:15)
Moderated by Margarita Diez Guerra y Alejandro Khalil

Title: Targeting the KRAS–RAF1 Interaction in Lung Cancer Using Intrabodies and BioPROTACs
Author: Lucía Lomba Riego

Title: Transcriptomic Profiling of Human Pulmonary Artery Smooth Muscle Cells Reveals COPD- and Emphysema-Specific Signatures
Author: Rosa Andreu Martínez

Title: Mitochondrial Control of Heart-Resident Macrophage Identity and IGF-1–Mediated Protection against Anthracycline-Induced Cardiotoxicity
Author: Elena Moya Ruiz

Title: RANK-Driven Metabolic Reprogramming in Postmenopausal Breast Cancer
Author: María Aránzazu Gómez Díaz

Title: Functional Role of 3′ NCR Stem-Loops in Foot-and-Mouth Disease Virus Biology: Insights from the ΔSL2 Mutant
Author: Miryam Polo Hernández

Title: CRISPR–Cas9 Gene Editing of Hematopoietic Stem and Progenitor Cells for the Treatment of Congenital Dyserythropoietic Anemia Type II
Author: Laura Fernández Rosa

Poster Communications:

Title: The Relationship between Chronic Diseases, Pain, and Loneliness

Author: Carmen Campa

Title: Childhood Loneliness and Disability in First-Episode Psychosis: Mechanisms and Transdiagnostic Effects
Author: Ana Ortiz-Tallo

Title: Hippocampal Function Alterations in Mouse Models of Lamb-Shaffer Syndrome

Author: Pilar Rodríguez-Martin

Title: Regional Differences in Dendritic Spine Morphology and Innervation in the Trisynaptic Circuit of a GSK-3β Overexpression Mouse Model

Author: Marta Alonso Moreno

Title: Longitudinal Study of the Adult Hippocampal Neurogenic Niche in a Mouse Model of Alzheimer's Disease

Author: Ana Victoria Prádanos-Senén

Title: Reduction of Aβ Pathology and Safety Validation of hE2F4DN-Based Gene Therapy for Alzheimer's Disease

Author: Irene Camacho-Olmos

Title: Analysis of the Effects of a Mutant E2F4 Variant in Oligodendrocytes in an Alzheimer's Disease Mouse Model

Author: Cristina González Bragado

Title: Regulation of Fear Conditioning in Wild-Type and FMR1-Knockout Mice

Author: Violeta Araque

Title: Hippocampal LTP and Astrocyte-Dependent Regulation of Neurogenesis

Author: Sofía Inés Martínez-Centeno

Title: MAFG-Driven Melanomagenesis Is Partially Recapitulated by the ECM Remodeler LOXL2

Author: Sara Ruiz Buceta

Title: Integration of Single-Cell RNA Sequencing and Topological Data Analysis for the Study of Leukemic Niches

Author: Gonzalo Soria Alcaide

Title: Identity Crisis: RANK-Driven Luminal Plasticity Induces a Thymic Epithelial-Like Program in the Mammary Gland

Author: Alejandro Sánchez Juan

Title: Characterization of Pathogenic Mutations and Chromosomal Instability Signatures in High-Risk BRCAX Ovarian Cancer

Author: Clara Gordillo Gayo

Title: Evaluation of Epigenetic Biomarkers of Risk and Progression of NSCLC in COPD Patients

Author: Ana Arauzo Cabrera

Title: Role of BRCA2 in Replication Stress-Induced DNA Damage and Chemotherapy Response

Author: Laura Pérez Gómez

Title: Multi-Feature Machine Learning Models for the Identification of Novel Cancer Predisposition Genes Author: JaeJun Lee

Title: Targeting β3-Adrenergic Receptors as a Therapeutic Strategy for Pulmonary Arterial Hypertension Author: Laura de la Bastida Casero

Title: Generation of a Mouse Model to Study Early Stages of Non-Syndromic Thoracic Aortic Disease

Author: Noelia Martín Bermejo

Title: Diet-Induced Obesity and Sex Differences Shape the Neuroinflammatory Landscape in Glioblastoma Author: Raquel González-Alday

Title: Longitudinal MRI and Spectroscopy Study of Bariatric Surgery-Induced Brain Changes in Obese Mice Author: Adriana Ferreiro de Aguiar

Title: Deciphering the Role of NOTCH2 in Endocrine Pancreas Development

Author: Diego Matas Aguado

Title: Reevaluating KLF11 in Human Endocrine Pancreas Development and Monogenic Diabetes Author: Mario Hernanz

Title: Cardiometabolic Risk Factors for Type 2 Diabetes across Menopausal Stages

Author: Juan Carlos Lizarzaburu Robles

Title: Immune Organ-Targeted microRNA Delivery Systems for Cancer Nanoimmunotherapy

Author: Pooria Mohammadi Arvejeh

Title: Development of Bacteria-Reprogrammed T-Cell Immunotherapies for Cancer

Author: Inés de Cáceres Renovell

Title: Functional Evaluation of Novel NRF2 Activators in Neuroinflammation

Author: Marta Olazabal Chias

Title: Structural Deletions in HTLV-1 Proviruses Correlate with Disease Severity in Adult T-Cell Leukemia Author: Mikel Blanco Otaegui

Title: Identification of Structural Variants in BMPR2 in Pulmonary Arterial Hypertension

Author: Lucía Miranda Alcaraz

Title: BP-Flow: A Novel Method to Quantify DNA Supercoiling by Flow Cytometry

Author: Marina Bejarano Franco

Title: Validation of Plasma Lyophilization as an Alternative to Deep-Freezing in Biobanking

Author: Daniel Alba Olano

Title: Circadian Rhythm Disruption and Microbiome Alterations in Cabin Crew

Author: Daniel Alba Olano

Title: Surface Functionalization of Multimodal Iron Oxide Nanotracers for Glioblastoma Theranostics

Author: Andrea Rodríguez-San Pedro

Title: Identification of Chromosomal Integration Sites in E. coli Nissle 1917 for Therapeutic Protein Expression
Author: Ana Ferrández Múrtula

Title: In Vivo Communication via Extracellular microRNA Carriers in Metabolic Disease

Author: Paula Díez Roda

Title: A Novel Skeletal Muscle ETFDH Knockout Model Demonstrates Systemic Consequences of FAO Deficiency

Author: Beñat Salegi Ansa

Title: Uncovering the Crucial Role of the 3′ NCR Stem Loops in Foot and Mouth Disease Virus Biology: Insights from the ΔSL2 Mutant

Author: Miryam Polo Hernández

Title: Initial Steps of a Scoping Review on Artificial Intelligence in the Diagnosis and Treatment of Rare Hematological Diseases

Author: Greys María Rodelo Olmos

Oral and Poster Communication Abstracts

PhD Student Name and surname: Nauzet Celso Deniz Eyre
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: ORAL (or poster or any kind)

TITLE: Exploring the role of Kupffer cells in hepatocellular carcinoma development

Authors: Nauzet Celso Deniz-Eyre[1,2], Clara Bonacasa[1,2], Alfonso Mora[1], Marta León[1], Elena Rodríguez[1], Luis Leiva-Vega[1], María Crespo[3], Magdalena Leiva[1,4], Alba Concepción Arcones[1]*, Guadalupe Sabio[1,3]*

AFFILIATIONS:
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ABSTRACT (350 Word limit)

Background:
Hepatocellular carcinoma (HCC) is strongly linked to chronic liver diseases, including metabolic dysfunction-associated fatty liver disease (MAFLD). Stress-activated protein kinases (SAPKs), particularly members of the p38 family, are key regulators of cellular adaptation to stress and have been implicated in HCC progression. Kupffer cells (KCs), the liver's resident macrophages, contribute to tumor development in a context-dependent manner influenced by their origin and activation state. Under stress conditions, resident KCs (resKCs) are replaced by monocyte-derived KCs (moKCs). This study aimed to clarify the role of KC origin and p38 pathway activation in HCC development.

Methodology:
To assess the impact of KC origin on tumor initiation, a Cre-lox system was used to selectively deplete resKCs, promoting their replacement with moKCs through diphtheria toxin administration. Two weeks later, hepatocarcinogenesis was induced via hydrodynamic tail-vein injection of oncogenic and tumor-suppressor-targeting plasmids. To investigate the role of p38 signalling, a second mouse model was generated in which p38 activation was specifically inhibited in KCs by targeting the upstream kinases MKK3 and MKK6 using a Cre-lox approach. Tumor burden and liver regeneration were subsequently evaluated.

Results:
Replacement of resKCs with moKCs led to an increased number of tumors per liver, indicating a protective role for resKCs during HCC initiation. In contrast, inhibition of p38 signalling in KCs significantly reduced tumor incidence, number, and size. Moreover, enhanced hepatocyte proliferation was observed following partial hepatectomy in mice lacking p38 activation in KCs. Mechanistically, p38 inhibition preserved CD8 T-cell functionality, as evidenced by increased interferon gamma (IFNγ) production.

Conclusions:
These findings demonstrate that KC origin and p38 pathway activity critically influence HCC progression. Resident KCs appear to exert protective effects against tumor initiation, whereas p38 activation in KCs promotes tumor development and impairs immune function.

Targeting p38 signaling in KCs not only suppresses tumor growth but also increases healthy liver regeneration. This dual benefit highlights p38 inhibition in KCs as a promising therapeutic strategy for HCC, particularly in patients undergoing liver resection.

Key words: Hepatocellular carcinoma (HCC), Kupffer cells, p38 MAPK pathway, liver regeneration, tumor microenvironment

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PhD Student Name and surname: Natalia Álvarez Ladrón
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: ORAL

TITLE: Limited inflammation impairs monocyte-derived macrophage differentiation and correlates with protumor Tim4^{+} resident macrophage expansion during peritoneal colorectal cancer

Authors: Natalia Álvarez-Ladrón[1,2], Margarita Ferriz[1], Alejandra Gutiérrez-González[1,3], Marta H. Fernández-Sesma[1], Juan Carlos Oliveros[4], Eduard Batlle [5,6,7], Daniele Tauriello[5,6,8] and Carlos Ardavín[1*]

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ABSTRACT (350 Word limit)

Background:
Peritoneal macrophages, including resident (resMØs) and monocyte-derived (moMØs) subsets, are increasingly recognized as drivers of peritoneal tumor progression, yet the mechanisms regulating their expansion and functional specialization during colorectal cancer (CRC) peritoneal metastasis remain unclear.

Methodology:
We used a mouse model of CRC peritoneal metastasis generated by intraperitoneal injection of organoids derived from Apc/Kras/Tgfbr2/Trp53-mutant tumors. Flow cytometry, transcriptomic profiling, and in vivo assays were performed to define the origin, expansion, and protumor functions of peritoneal macrophages during peritoneal tumor growth.

Results:
We found that the low-inflammatory environment of the peritoneal cavity during CRC metastasis limits monocyte recruitment and the generation of Tim4^{-} resMØs and moMØs, while enabling a pronounced proliferation-driven expansion of Tim4^{+} resMØs. Tumor-induced Tim4^{+} resMØs acquired a migratory, protumorigenic transcriptional program characterized by upregulation of key immunoregulatory and

tumor-promoting molecules, including A2A/A2B receptors, ARG1, IDO, IRG1, MMP12, PD-L1/2, SPP1, TREM1, and VEGFα. Consistently, $Tim4^{+}TREM1^{+}$ resMØs migrated to the omentum—the primary site of peritoneal metastasis—where they supported CRC tumor progression.

Conclusion:
These findings identify $Tim4^{+}$ resident macrophages as central orchestrators of CRC peritoneal metastasis and highlight tumor-associated peritoneal macrophages as promising targets for immunotherapeutic intervention.

Key words: tissue resident macrophages; resident peritoneal macrophages; protumor macrophages; tumor-associated macrophages; monocytes; monocyte-derived macrophages; colorectal cancer; colorectal tumor metastasis, peritoneal metastasis; mouse tumor organoids.

PhD Student Name and surname: Ane Ochoa Echeverría
UAM PhD program: Molecular Biosciencies
COMMUNICATION TYPE: ORAL

TITLE: DGKζ-Dependent Immune Remodeling Reflects Antitumor Responses in Bladder Cancer

Authors: Ane Ochoa Echeverría[1], Elena Andrada[1], Rosa Liébana[1], Isabel Mérida[1]

AFFILIATIONS:
[1] *Centro Nacional de Biotecnología (CNB-CSIC), Madrid, España*

ABSTRACT (350 Word limit)

Background:
Immunotherapy has transformed cancer treatment by harnessing the immune system to control tumor growth. Diacylglycerol kinases (DGKs) are intracellular enzymes that negatively regulate immune activation by converting diacylglycerol into phosphatidic acid, thus limiting DAG-dependent signaling. Among them, DGKζ plays a key immunomodulatory role across immune subsets, including T cells, NK cells, and macrophages, emerging as a brake on effective antitumor immunity. Muscle-invasive bladder cancer (MIBC) is an immunogenic tumor type in which immune checkpoint blockade has shown clinical benefit, yet many patients fail to respond or develop resistance. In this context, DGKζ represents an attractive candidate to potentiate immunotherapies in bladder cancer (BCa).

Methodology:
To explore this, we investigated the role of DGKζ in bladder cancer progression and immunity using a chemically induced preclinical MIBC model (BBN). Wild-type and DGKζ-deficient C57BL/6 mice received BBN in drinking water and were analyzed after 2 and 20 weeks of treatment. Tumor progression was assessed histopathologically, while the tumor immune landscape was characterized by spectral flow cytometry. Peripheral blood was also evaluated to identify circulating immune biomarkers linked to tumor development.

Results:
DGKζ deficiency led to reduced tumor progression and a shift toward a less immunosuppressive, more effector-prone tumor microenvironment. DGKζ-deficient mice displayed distinct $CD4^+$ and $CD8^+$ T-cell populations marked by CD38 expression at baseline, which underwent quantitative and phenotypic remodeling during tumor development. Specifically, an expansion of $CD8^+$ $CD38^+$ $CD103^+$ T cells and a reduction of $CD4^+$ $CD38^+$ $CD103^+$ T cells were observed in blood, with a reciprocal increase of this CD4 subset in tumors. Remarkably, in contrast to wild-type mice, DGKζ-deficient animals exhibited changes in innate and adaptive circulating immune compartments as early as two weeks of BBN exposure.

Conclusion:
Overall, these findings identify DGKζ as a regulator of antitumor immunity in BCa, supporting its targeting and suggesting DGKζ-associated immune populations as biomarkers in MIBC.

Key words: DGKζ; BBN; bladder cancer (MIBC); antitumor immunity; tumor microenvironment; T cells ($CD4^+$, $CD8^+$)

Note: Please send this fully completed abstract as a PDF file, including your surname in the filename, to vicedecanato.medicina.investigacion@uam.es, using "Abstract Workshop 2026" as the email subject.

PhD Student Name and surname: Mario Rodríguez del Collado
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: ORAL COMMUNICATION

TITLE: VISIUM HD Spatial Transcriptomics for mapping tumor-stroma reprogramming after RANK-RANKL inhibition in luminal B-like breast cancer

Authors: M. Rodriguez-del-Collado[1, #], J. Martinez-de-Villarreal[1, #], D. Valcárcel[1, #], A. Barranco[1], A. Vethencourt[2,3,4], E.M. Trinidad[2], G. Soria Alcaide[1], E. Piñeiro[1], G. Gomez[1], M. Jimenez[1], E. J. Caleiras[1], M. Gomez[1], C. Garrido[1], M. Ciscar[1], E. Purqueras[5], E. Hernández[2], A. Urruticoechea[6], I. Cachinero[7], J. Noorbakhsh[8], J.H. Chuang[8], M.J. Gil[2,4], S. Pernas Simon[2,3,4], E. Dorca Duch[5], A. Petit[5], M.T. Soler-Monsó[5], C. Falo[2,3,4], E. Gonzalez-Suarez[1,2*]

AFFILIATIONS: 1: Centro Nacional de Investigaciones Oncológicas (CNIO), Madrid, Spain; 2: IDIBELL, Institut d'Investigacio Biomédica de Bellvitge, Barcelona, Spain; 3: Univertitat de Barcelona. 4: Institut Català d'Oncologia, Medical Oncology Department, Barcelona, Spain; 5: University Hospital of Bellvitge and Institut Català d'Oncologia, Pathology Department, Barcelona, Spain; 6: Onkologikoa, Medical Oncology Department, Donostia, Spain. 7. Statistician department, Researchmar, Barcelona, Spain; 8 The Jackson Laboratory for Genomic Medicine, Farmington, Connecticut; *senior author, #equal contribution

ABSTRACT (350 Word limit)

Background:
Luminal tumors are the most common subtype of breast cancer (BC). Within this category, luminal B-like tumors exhibit low immune infiltration, poor responses to immunotherapy, and high proliferation rates, revealing the need for novel therapies. RANK signalling pathway has emerged as a promising target in BC, as its expression in tumor cells enhances stemness and induces immunosuppression. RANK is also highly expressed in the tumor microenvironment (TME), particularly in tumor-associated macrophages, but its functionality remains underexplored.

Methodology:
In the window-of-opportunity D-BIOMARK trial (NCT03691311), patients with early-stage BC were randomized preoperatively to either denosumab—a monoclonal antibody blocking RANK–RANKL—or a control arm. Bulk tumor transcriptomics, gene set enrichment analysis, and immune deconvolution were used to assess treatment-associated changes. Paired pre- and post-treatment samples from six luminal B-like tumors were analyzed by 10x VisiumHD spatial transcriptomics, with pathologist-guided annotation of tumour and non-invasive tissue, and TME populations inferred using BC single-cell RNA-seq references. Tumor-immune proximity, ligand-receptor interactions, and malignant clonal architecture were evaluated using CellChat and SCEVAN-based copy-number inference. Peripheral blood analyses included T-cell proliferation and circulating cytokine profiling.

Results:
Denosumab treatment was associated with increased immune infiltration, particularly in luminal B-like tumors. Bulk transcriptomic analyses showed enrichment of inflammatory and interferon-related programs after treatment. Immune deconvolution indicated increased monocyte-related signals and reduced immunosuppressive macrophage and regulatory T-cell signals in treated tumors. Spatial transcriptomics identified treatment-associated transcriptional changes across tumor, myeloid, endothelial, and stromal compartments, with immune-related signatures enriched post-treatment. Spatial analyses showed increased localization of immune cells near tumor regions after treatment. Ligand-receptor analysis suggested reduced tumor-stroma and extracellular matrix-related interactions together with increased immune-associated signaling. Copy-number analyses supported the presence of treatment-associated changes in malignant cell states. Peripheral analyses showed increased T-cell proliferation and changes in circulating cytokines following denosumab. Baseline enrichment of immunosuppressive macrophages and low circulating MCP-2 were associated with greater immunologic response to treatment.

Conclusion:
Short-term preoperative denosumab was associated with local and systemic changes in early-stage luminal BC, with the strongest effects observed in luminal B-like tumors. These findings support further evaluation of RANKL blockade as a TME-modulating strategy and suggest candidate biomarkers associated with treatment-related immune remodeling.

Key words: Denosumab; RANK/RANKL; Luminal breast cancer; Tumor microenvironment; Spatial transcriptomics; VISIUMHD

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Alejandro Hernandez
UAM PhD program: Biociencias moleculares
COMMUNICATION TYPE: Oral

TITLE: Astrocytes activation in the primary motor cortex contributes to the therapeutic effects of subthalamic nucleus deep brain stimulation

Authors: Alejandro Hernandez[1] and Eduardo D. Martín[1]

AFFILIATIONS:
[1] *Centro de Neurociencias Cajal, CSIC, Madrid, Spain.*

ABSTRACT (350 Word limit)

Background:
Parkinson's disease (PD) is a neurodegenerative disease characterized by the loss of nigro-striatal dopaminergic neurons which results in motor deficits. When pharmacological treatment develops motor complications the most effective treatment is the implantation of an electrode in basal ganglia nuclei for chronic stimulation. Deep brain stimulation at of the subthalamic nucleus (STN DBS) remains the most efficient strategy.

Accumulating evidence shows that STN DBS modifies cortical activity. Astrocytes are key elements in brain physiology, sensing synaptic activity and triggering in response the release of gliotransmitters that regulate synaptic transmission and plasticity. However, the effects of STN DBS on astrocytic activity and their possible role modifying synaptic transmission and plasticity remains unknow.

Methodology:

Fiber photometry recordings were used to measure in vivo astrocytes Ca^{2+} activity in the primary motor cortex (M1). Slices were used to study ex vivo the effects of DBS to L2/3 to L5 synaptic plasticity of M1 using whole-cell patch-clamp recordings of L5 neurons. Synaptic plasticity was induced by a protocol of spike-timing dependent plasticity consisting of pairing a presynaptic stimulus with a postsynaptic action potential. Astrocytic involvement was evaluated using selective reduction of Ca^{2+} activity. Motor behavioral tests were used to evaluate DBS and selective activation of astrocytes using chemogenetics in 6-hydroxydopamine (6-OHDA) mice.

Results:
Results showed that astrocytes Ca^{2+} activity correlated with DBS current intensity. We observed that DBS was able to switch the synaptic plasticity from an LTD to an LTP. This switch depends on astrocytes activity, given that reducing Ca^{2+} activity produces an LTD. The astrocytes activation during DBS also occurs in the 6-OHDA PD mice model and correlates with a motor improvement in the distance travelled in an open field. Selective activation of M1 astrocytes using DREADDs in 6-OHDA mice improves motor performance during the rotarod test.

Conclusion:

Their study reveals astrocytes as active components of motor cortex synaptic plasticity induced by DBS. In addition, M1 astrocytes activation by chemogenetics reproduced the therapeutics effects of DBS in Parkinsonian model mice.

Key words: DBS; Motor cortex; Synaptic plasticity; Astrocytes.

This research was supported by grant PID2023–149021NB-I00 (MCIU), AEI/10.13039/501100011033, Spain to E.D.M. and predoctoral fellow from Fundación Tatiana Pérez de Guzmán el Bueno to A.H.

Aged-dependent metabolic reprogramming of microglia as a determinant factor in the development and progression of brain metastases

Introduction

Brain metastasis occurs when cancer cells spread to the brain, where the immunosuppressive environment and unique metabolic demands complicate treatment. Aging exacerbates these challenges by altering the tumor microenvironment, affecting nutrient availability, inflammation, and immune function. These age-related changes can influence metastatic progression, highlighting aging as a critical but often overlooked factor in brain metastasis. A fundamental question to address is how aging impacts the metabolic fitness of immune cells and how these changes negatively affect the progression of brain metastasis. We hypothesize that the decline in immune activity during aging is caused by dysregulated metabolism. Therefore, restoring the metabolic fitness of immune cells would be highly beneficial in enhancing their ability to suppress brain metastasis.

Materials and methods

To further investigate this, we developed a model featuring specific ablation of mitochondrial complex III in microglia by crossing Uqcrq floxed and Tmem119-cre/ERT2 mice (referred to as QPC KO). This model demonstrated that mice with ETC-deficient microglia developed larger brain metastases. We propose to utilize this newly generated mouse model, which mimics the effects of aging through deficient mitochondrial metabolism in microglia, to examine the role of mitochondrial metabolism in the anti-tumor function of microglia. Our aim is to elucidate how and why these processes are impaired with age.

Results and discussion

Our preliminary data, obtained from RNA-seq analysis of tumor-associated and resting microglia in young and old mice, revealed significant differences in microglial activation between the two age groups. Notably, pathways related to mitochondrial oxidative metabolism were particularly impaired with age.

Conclusion

These findings suggest that mitochondrial metabolism is crucial for microglial activation and anti-tumor function, while aging hinders these adaptive mechanisms.

PhD Student Name and surname: David Gómez Ángel
UAM PhD program: Epidemiología y Salud Pública
COMMUNICATION TYPE: ORAL

TITLE: Cardiovascular health and circulating inflammatory biomarkers in older adults

Authors: D. Gómez Ángel[1], M. Sotos-Prieto[1,3,4,5], E. García-Esquinas[1,2,3], B. Fabre Estremera[6], A. Buño Soto, F. Rodríguez Artalejo[1,3,5], R. Ortolá[1,3]

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ABSTRACT (350 Word limit)

Background:
Inflammation is a central pathway linking poor cardiovascular health to aging-related disease. However, whether cardiovascular health, assessed using the American Heart Association's Life's Essential 8 (LE8), and its individual components are associated with multiple circulating inflammatory biomarkers in older adults remains unclear.

Methodology:
We conducted a cross-sectional analysis of 2,458 community-dwelling older adults from the Seniors-ENRICA-2 cohort (mean age 71.5 years, 52.6% women). Cardiovascular health was assessed using the American Heart Association's LE8, categorized as low (<50), moderate (50-79), and high (≥80). Circulating growth differentiation factor-15 (GDF-15), interleukin-6 (IL-6), neutrophil-to-lymphocyte ratio (NLR), and C-reactive protein (CRP) concentrations were measured and log-transformed for analysis. Linear regression models were used to estimate mean percentage differences (95% CI) in biomarker concentrations across LE8 categories and per 10-point increment in LE8. Models were sequentially adjusted for sociodemographic factors, lifestyle variables, clinical morbidities and estimated glomerular filtration rate. Analyses included 2,458 participants for GDF-15, IL-6, and NLR, and 1,085 for CRP.

Results:
In the fully adjusted model, higher LE8 scores were consistently associated with lower concentrations of all four biomarkers. Specifically, each 10-point increase in LE8 was associated with 7.98% lower GDF-15 concentrations (95% CI -9.34; -6.62), 6.47% lower IL-6 (-8.28; -4.67), 2.76% lower NLR (-4.08; -1.44), and 18.86% lower CRP (-25.57; -12.15). Component analyses suggested that not all LE8 metrics contributed equally and that their associations varied across biomarkers. Overall, healthier diet, lower nicotine exposure, adequate BMI, and better glycemic control showed the most consistent inverse associations.

Conclusion:
Higher LE8 scores were consistently associated with a more favorable inflammatory profile in older adults. Promoting optimal cardiovascular health may therefore contribute to lower systemic inflammation and healthier aging.

Key words: Cardiovascular health; Life's Essential 8; inflammation; GDF-15; interleukin-6; C-reactive protein; neutrophil-to-lymphocyte ratio; older adults

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PhD Student Name and surname: Clara Marcela Durán Arias
UAM PhD program: Epidemiology and public health
COMMUNICATION TYPE: ORAL

TITLE: PROSPECTIVE ASSOCIATION BETWEEN PLASMA CONCENTRATIONS OF AMINO ACIDS AND OBJECTIVE AND SUBJECTIVE PHYSICAL FUNCTION IN OLDER ADULTS

Authors: Marcela Durán Arias[1] and Francisco Félix Caballero[1,2]

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ABSTRACT (350 Word limit)

Background:
Physical function is a key component of health status among older people and reflects an individual's ability to perform daily activities with certain or full autonomy. Different plasma amino acids have been identified as biomarkers for the aging process as well as for the skeletal muscle function. Since older adults tend to evaluate their own health status more positively when compared with objective assessments, this study considers both objective and subjective measures of physical function to evaluate the differential prospective association between plasma concentrations of amino acid and the objective and subjective physical function.

Methodology:
This study uses data from 822 community-dwelling individuals older than 65 years participating in the Seniors-ENRICA 2 cohort. Data was gathered through a telephone interview, and home visits to perform a physical examination and take blood samples. Plasma amino acid concentrations were measured by means of high-throughput proton nuclear magnetic resonance spectroscopy. Objective physical function was assessed with the Short Physical Performance Battery, while subjective physical function was measured using the physical component of the 12 item Short Form Health Survey. Multilevel mixed-effects linear regression models were used to assess the prospective association between plasma concentrations of amino acids and objective and subjective physical function, after adjusting for sociodemographic, socioeconomic status, and lifestyle behaviors.

Results:
The baseline mean age was 70.8 years (SD = 4.0), and 52.6% of the participants were men. In the fully adjusted model, a significant association was found between plasma concentrations of alanine [Coef. = 0.14, 95% CI = (0.08, 0.20), p<0.001], phenylalanine [0.13 (0.06, 0.19), p<0.001], and tyrosine [0.09 (0.02, 0.15), p=0.010], and objective physical function. No significant associations were found for subjective physical functioning in the fully adjusted models for any of the amino acids considered.

Conclusion:
Higher plasma concentrations of alanine, phenylalanine and tyrosine are prospectively associated with objective physical function in older adults. Objective and subjective physical function measures can reflect complementary but distinct dimensions of health.

Key words: Amino acids, objective physical function, subjective physical function, older adults, aging process.

PhD Student Name and surname: Damián González Beltrán
UAM PhD program: Epidemiology and Public Health
COMMUNICATION TYPE: ORAL

TITLE: Social and lifestyle factors associated with the risk of developing multimorbidity in middle-aged and older adults

Authors: Damián González-Beltrán[1], Esther Lopez-Garcia[1,2], Francisco Félix Caballero[1].

AFFILIATIONS:

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[2] *IMDEA-Nutrition Institute, CEI UAM+CSIC, Madrid, Spain.*

ABSTRACT (350 Word limit)

Background:
Previous studies have identified several determinants of multimorbidity, but social factors remain unclear. Therefore, we aimed to explore the association between social and lifestyle factors and the risk of developing multimorbidity in middle-aged and older population from the United Kingdom.

Methodology:
This prospective study uses data from the UK Biobank cohort, comprising 407,115 participants with multimorbidity free at baseline, recruited from 2006 to 2010 and followed up until May 31, 2022. Multimorbidity was defined as having two or more chronic diseases. Cox proportional hazards models were conducted to analyse the association between social and lifestyle factors and the risk of developing multimorbidity, adjusting for sociodemographic and anthropometric characteristics.

Results:
A total of 33,794 participants developed multimorbidity during a median follow-up of 13.2 years. The baseline mean age was 56.2 years (SD = 8.08), and 54.6 % of participants were women. In the fully adjusted models, loneliness (HR = 1.30; 95 % CI = 1.25–1.36), social isolation (HR = 1.15; 95 % CI = 1.11–1.19), previous (HR = 1.25; 95 % CI = 1.22–1.28) and current smokers (HR = 2.10; 95 % CI = 2.04–2.17), non-optimal sleep duration (HR = 1.23; 95 % CI = 1.20–1.26), high sedentary lifestyle (HR = 1.22; 95 % CI = 1.19–1.25), and high meat intake (HR = 1.09; 95 % CI = 1.06–1.11) were associated with an increased risk of incident multimorbidity.

Conclusion:
Loneliness, social isolation and lifestyle factors contribute to the risk of developing multimorbidity. This study emphasizes the importance of adopting a comprehensive approach that considers social and lifestyle factors as a primary predictor of multimorbidity.

Key words: Multimorbidity; Social factors; Lifestyle behaviours; Middle-aged; Older adults.

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Amanda Carolina Padilha Salviatto

UAM PhD program: Epidemiología y Salud Publica

COMMUNICATION TYPE: ORAL

TITLE: Lipid signature for cognitive decline emerges from HDL particles: A longitudinal study of older adults from the Seniors ENRICA-2 Cohort.

Authors: Amanda Carolina Padilha Salviatto[1], Esther Lopez-Garcia [1,2,3] & Francisco Félix Caballero [1,2]

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ABSTRACT (350 Word limit)

Background:
Lipid metabolism plays a crucial role in brain function, and the relationship between lipidomic profiles and cognitive decline remains poorly understood. High-density lipoprotein (HDL) particles are increasingly recognized as functionally heterogeneous, and their composition may be more relevant than total HDL cholesterol levels in neurological processes.

Objective

To investigate the association between lipidomic profiles' composition and longitudinal trajectories of cognitive decline in older adults

Methodology:
We analyzed data from 1488 participants aged ≥65 years from the Seniors ENRICA-2 cohort. Lipidomic profiling was performed using nuclear magnetic resonance spectroscopy (NMR). Principal components analysis (PCA) was applied to lipid subclasses (VLDL, LDL, HDL) to reduce dimensionality and capture underlying lipid structure. Cognitive function was assessed across three waves, and a standardized global cognition z-score was derived from multiple tests (DSFT, Luria,

Go/No-Go, FCSRT, verbal fluency, clock drawing, MMSE, SCD). Linear mixed-effects models with random intercepts and slopes were used to evaluate associations between HDL components and cognitive trajectories, adjusting for sociodemographic, lifestyle, and clinical factors**.**

Results:
Among HDL components, PC3 was consistently associated with steeper cognitive decline over time (β_interaction ≈ −0.034, p = 0.003), independent of confounders. This association was most pronounced in executive function and motor sequencing domains. Decomposition of HDL PC3 revealed a coherent pattern: cholesterol esters (CE) and free cholesterol (C) were associated with more favorable cognitive trajectories (XL HDL CE % β ≈ 0.028, p ≈ 0.05), whereas triglyceride in medium-sized HDL particles was associated with worse outcomes (M HDL TG %, β ≈ −0.027, p ≈ 0.02). Additionally, phospholipides in extra-large HDL particles emerged as an independent adverse marker (XL HDL PL %, β ≈ −0.041, p = 0.008), suggesting a role for HDL structural remodeling. Participants in the highest tertile of HDL PC3 exhibited significantly greater cognitive decline than those in the lowest tertile.

Conclusion:
HDL composition, rather than total HDL levels, is associated with cognitive decline in older adults. A lipid pattern characterized by reduced cholesterol content in triglycerides and phospholipids reflects a potentially dysfunctional HDL profile linked to neurocognitive deterioration.

Key words: cognition, lipids, HDL, metabolomic, Enrica-2

PhD Student Name and surname: Aitana Vázquez Fernández
UAM PhD program: Epidemiology and Public Health
COMMUNICATION TYPE: ORAL

TITLE: Diet quality in the progression from healthy status to morbidity, multimorbidity and mortality

Authors: Aitana Vázquez-Fernández[1], Francisco Félix Caballero[1], Esther Lopez-Garcia[1,4]

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ABSTRACT (350 Word limit)

Background:
Diet quality may influence the progression from health to chronic disease, multimorbidity, and death, but current evidence is limited. We aimed to assess the association between diet quality and the risk of transitioning between these four health states.

Methodology: A total of 84,293 healthy individuals (40-70 years) from the UK Biobank were included and diet quality was assessed through four separate exposures using well-established scores: the Alternate Mediterranean Diet Index (aMED), the Dietary Approaches to Stop Hypertension (DASH), the Alternative Healthy Eating Index 2010 (AHEI-2010), and the healthful Plant-based Diet Index (hPDI). Using multi-state models, we assessed the relationship between diet quality and progression from a healthy status to developing one predefined chronic disease, to multimorbidity and lastly, to death.

Results:
Over 11.2 years follow-up, 22,723 participants developed one predefined chronic disease and 4368 progressed to multimorbidity. A total of 2886 deaths occurred: 770 after multimorbidity, 1512 after one chronic condition, and 604 among participants who did not develop any of the diseases under study. Higher adherence to aMED, DASH, and AHEI-2010 was associated with a reduced risk of developing one chronic disease [HR (95% CI) for highest vs. lowest tertile: 0.92 (0.89, 0.95), 0.94 (0.91, 0.98), and 0.92 (0.89, 0.95)]. aMED was also associated with lower risk of death without any disease [HR: 0.72 (0.56, 0.92)]. aMED and DASH were associated with lower risk of progression to multimorbidity [HRs: 0.92 (0.86, 0.98) and 0.90 (0.83, 0.98)]. aMED and hPDI were associated with lower risk of death after one disease [HRs: 0.89 (0.79, 1.00) and 0.87 (0.77, 0.98)]. All scores except hPDI were associated with a reduced risk of death after multimorbidity [0.76 (0.61, 0.95) for aMED, 0.71 (0.59, 0.86) for DASH, and 0.80 (0.65, 0.97) for AHEI-2010].

Conclusion:
Our findings indicate that greater adherence to healthy dietary patterns is associated with a reduced risk of progression towards one predefined chronic condition, multimorbidity and death, highlighting their protective role in long-term health.

Key words: multimorbidity; chronic disease; mortality; dietary patterns; transitions; multi-state models.

PhD Student Name and Surname: Julián Puente Ferreiro
UAM PhD program: Epidemiology and Public Health
COMMUNICATION TYPE: ORAL

TITLE: Association of healthy dietary patterns with frailty syndrome progression

Puente-Ferreiro Julián [1], Yévenes-Briones Humberto [1], López-García Esther [1,2]

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ABSTRACT (350-word limit)
Background: Understanding how diet patterns influence the development and progression of frailty is crucial for planning healthcare and prevention, but evidence is rather limited. Our aim was to assess the association between diet quality across different states of frailty.

Methods: Data from the Nurses' Health Study and multistate modelling were used to define four states, considering competitive risks: from a healthy status to developing prefrailty, to frailty and lastly, to death. These states were defined using FRAIL criteria. A total of 56,628 healthy women (>60 years) from the Nurses' Health Study were included. Diet quality was assessed as five different cumulatively averaged time-varying exposures using well-established scores: Alternative Healthy Eating Index 2010 (AHEI-2010), Dietary Approaches to Stop Hypertension (DASH), Alternative Mediterranean Diet Index (aMED), healthful Plant-based Diet Index (hPDI) and Planetary Health Diet Index (PHDI); while also accommodating relevant time-varying covariates for adjustment.

Results: Over 30 years follow-up, 41,869 participants developed prefrailty and 11,664 progressed to frailty. A total of 15,493 deaths occurred: 4374 after frailty, 7600 after prefrailty, and 3519 among participants who did not attain any FRAIL criterion. Higher adherence to all dietary patterns was associated with reduced risk in progressions from a healthy status to prefrailty and prefrailty to frailty. AHEI-2010 was also associated with lower risk of progression from healthy to mortality [HR (95%CI) for highest vs. lowest quintile: 0.84 (0.75, 0.94)]. aMED and PHDI were more strongly associated with a decreased risk of progression from healthy to prefrail, and prefrail to frail [HRs for highest vs. lowest quintile: 0.74 (0.71, 0.76), and 0.68 (0.63, 0.73) for aMED; 0.77 (0.74, 0.79), and 0.72 (0.67, 0.77) for PHDI]. DASH and hPDI were more strongly associated with a decreased risk of progression from prefrail to mortality [HRs for highest vs. lowest quintile: 0.89 (0.82, 0.96) for DASH; 0.88 (0.81, 0.95) for hPDI].

Conclusions: Greater adherence to healthy diet patterns was associated with a reduced risk of progression towards frailty syndrome and mortality, with specific diet patterns showing stronger associations depending on the transition. These results highlight their protective role in long-term health.

Keywords: frailty, diet quality, aging, multistate modelling.

PhD Student Name and surname: Ricardo Alonso de Celada Granado
UAM PhD program: Pharmacology & Physiology
COMMUNICATION TYPE: ORAL

TITLE: **Effects of coffee pulp infusion on exercise performance and systemic cytokine response: a sex-specific analysis in a healthy young population**

Authors: Ricardo Alonso de Celada[1], Javier García-Rodríguez[1], Pilar Rodríguez-Rodríguez[1], Silvia M. Arribas[1], Vanesa Benítez[2,3], David Ramiro-Cortijo[1].

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ABSTRACT

Background: Exercise-induced muscle damage is associated with increased pain and changes in pro- and anti-inflammatory cytokines. Bioactive compounds have gained attention as potential modulators of these responses. Coffee by-products, such as coffee pulp, are rich in polyphenols and antioxidant compounds, which exert anti-inflammatory and analgesic effects. However, evidence on their role in post-exercise recovery, particularly in untrained populations, remains limited. The aim was to evaluate the effect of a coffee pulp infusion on perceived pain and systemic inflammation cytokines following physical activity.

Methodology: 59 healthy untrained young adults (34 female and 25 male) were recruited; their body composition was determined, and capillary blood samples were collected. The participants performed a step test at 15 cpm until exhaustion and were asked to survey perceived pain. After 2h, other blood sample was collected. At 48h, participants completed the pain survey, and a third blood sample was collected. At that point, participants were randomized to intake 2 daily infusions for 45 days: 1) wheat (placebo, A) or 2) coffee pulp (B). Then, the procedures described above were repeated. In the blood IL-1β, IL-6, IL-1α, IL-1ra and IL-10 cytokines were quantified.

Results: In both interventional groups and genders, the repetitions of the test were higher post-infusions. In male, lower body pain scores were lower following the group B. Regarding inflammation, 2h after the test, female in the group B showed a trend toward increased IL-6 (P=0.079) and IL-10 (P=0.056). At 48h in B-male, a trend toward a decrease in IL-10 (P=0.068) and IL-1α (P=0.097) was observed. However, at 2h in A, a trend towards a decrease in IL-1β (P=0.085) was observed.

Conclusion: Prior experience with the test might improve the performance in the physical activity. In male, coffee pulp infusion could reduce lower body pain, potentially an analgesic effect after physical activity. In addition, this infusion might influence exercise-induced inflammation in both sexes. These results show that coffee pulp can be a potential recovery agent for non-trained individuals.

Keywords: Polyphenols, Pain, Recovery, Coffee Pulp, Systemic inflammation, Cytokines, Sex differences.

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Laura Ribes Martínez
UAM PhD program: Microbiology
COMMUNICATION TYPE: ORAL

TITLE: Preclinical Therapeutic Potential of Phage FT5P against Vancomycin-Resistant *Enterococcus Faecium* Infections

Authors: Laura Ribes-Martínez[1,2], Mark J Van Raaij[3], María Pérez-Vázquez[4], Javier E Cañada-García[2,4], Jaime Esteban[1,2], John Jairo Aguilera-Correa[1,2] and Meritxell García-Quintanilla[1,2]

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ABSTRACT (350 Word limit)

Background:
Enterococcus faecium, classified by the World Health Organization as a high-priority ESKAPE pathogen, exhibits intrinsic multidrug resistance, environmental persistence, and strong biofilm formation, facilitating adaptation to hospital settings. Vancomycin-resistant *E. faecium* (VRE) is an increasing global nosocomial threat, particularly in immunocompromised and critically ill patients. Given limited therapeutic options, alternative strategies such as phage therapy are potentialized. We aimed to characterize phage FT5P and evaluate its preclinical therapeutic potential against VRE.

Methodology:
Phage FT5P was isolated from hospital wastewater. Morphology was assessed by electron microscopy and genome sequencing. Stability was evaluated across pH 1-10.5, temperatures -80°C to 60°C, and in active and heat-inactivated human serum. Host range was tested against 86 multidrug-resistant clinical isolates. Lytic activity was analyzed through growth curves (MOI 0.1-10). Biofilm prevention and treatment were measured by biomass and viability assays. Synergy with phage FT2P, daptomycin, and ampicillin was assessed using checkerboard assays.

Results:
FT5P exhibited myovirus morphology with a 56 kb genome encoding 89 genes and no lysogeny, toxin, virulence, or antimicrobial resistance genes. It remained stable at pH 4.5–10.5 and physiological temperatures, retaining infectivity in inactivated serum but showing complement susceptibility at 24 h. FT5P infected 39% of E. faecium and 6% of E. faecalis strains. Lytic efficacy was strain-dependent, achieving complete inhibition in reference strains. Biofilm prevention reached 70%, while established biofilms showed up to 60% viability reduction. Synergy was observed with FT2P, additive effects with daptomycin, and antagonism with ampicillin.

Conclusion:
FT5P demonstrates a safe genomic profile and promising antibiofilm activity against VRE, supporting further exploration in personalized phage therapy approaches.

Key words: Phage Therapy; Antimicrobial Resistance, *Enterococcus faecuim*.

PhD Student Name and surname: Andrés Gómez Dávila
UAM PhD program: Pharmacology and Physiology
COMMUNICATION TYPE: ORAL

TITLE: A new strategic and collaborative model to enhance efficiency, performance and access to pediatric hemato-oncology clinical trials

Authors: Andrés Gómez-Dávila[1], María García-Llorente[1]; Pilar Guerra-García, MD[2]; Sira Alonso-Collado[1]; Antonio Pérez-Martínez, PhD, MD[2] ; Alberto M Borobia, PhD, MD[1]

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ABSTRACT (350 Word limit)

Background:
Pediatric Hemato-Oncology in Spain faces structural constraints that make it difficult to conduct high-quality clinical trials, including low incidence, treatment complexity, and fragmentation of the national ecosystem. Despite existing initiatives, inequalities in access and limited structured collaboration persist. International regulatory agencies promote more coordinated, efficient, and patient centered models. This project proposes a strategic and collaborative framework to enhance clinical trial efficiency in Pediatric Hemato-Oncology. The hypothesis is that an integrated model based on professionalized governance, stable networks, patient engagement, and optimized processes will improve the efficiency of the clinical trials, expanding access to innovative therapies. The Pediatric Hemato-Oncology Department and Central Clinical Trial Unit (UCICEC) at Hospital Infantil La Paz has extensive experience, conducting over 40 clinical trials, including early-phase and academic studies, and is accredited by ITCC as a center of excellence.

Methodology:
A four year mixed methods approach will be implemented. Year 1 focuses on literature review, regulatory analysis, and initial model design, including KPIs and organizational structure. Year 2 includes stakeholder engagement (industry and CROs), development of partnerships, and regulatory analysis. Year 3 centers on patient engagement programs and professional development. Year 4 involves model refinement and validation. Objectives include evaluating the national framework, strengthening alliances, enhancing patient participation, analyzing regulatory factors and promoting team development.

Results:
Expected outcomes include an innovative strategic model improving organizational efficiency, trial performance, and patient access to novel therapies. The project will deliver a governance framework, performance metrics, strengthened collaborations, and a patient-centered engagement program. It will also identify regulatory barriers and propose solutions to accelerate equitable access.

Conclusion:
This project presents the first comprehensive strategic model for pediatric hemato-oncology clinical trials, integrating governance, collaboration, regulation, and patient involvement. Its implementation may significantly improve research capacity and access to innovative therapies at national and international levels.

Key words: Pediatric Hemato-Oncology; UCICEC; Clinical Trials; Strategic Model; Patient Engagement; Regulatory Framework; Innovation; Collaboration.

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Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Wilfrido Arrúa
UAM PhD program: Pharmacology and Physiology
COMMUNICATION TYPE: ORAL

TITLE: Inhibition of serum and glucocorticoid regulated kinase-1 as novel therapy for cardiovascular diseases

Authors: Wilfrido Arrúa[1], Naoual Boukich[1], Enrique Madruga[2,3], Eduardo Oliver[2,4,5], Isabel Lastres-Becker[3,6], Ana Martínez[2,3], Ana García-Redondo[5,7,8], Ana M. Briones[1,5,8]

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ABSTRACT

Background:
The serum and glucocorticoid inducible kinase 1 (SGK1) is a member of the serine/threonine kinase gene family that plays an important role in cardiovascular diseases through complex signaling pathways by activating fibrotic, inflammatory, and oxidative pathways in the heart, vascular organs and kidney. Despite the validated biological functions of SGK1, which are strongly associated with various diseases, only a few small-molecule SGK1 inhibitors have been discovered, and none have progressed to clinical trials. Most SGK1 inhibitors have insufficient potency and complete kinome selectivity. Therefore, the objective of this study was to evaluate the effect of the administration of EMM3.20, a novel selective SGK1 inhibitor, on cardiovascular and kidney damage caused by angiotensin II (AngII).

Methodology:
Aorta, small mesenteric arteries, perivascular adipose tissue (PVAT), heart and kidney were taken from C57BL/6J male mice, infused or not with AngII (1.44 mg/kg/day, 14 days) in presence or absence of EMM3.20 (15mg/kg/day) starting 1 day before AngII infusion. Systolic blood pressure was measured in the animals using tail-cuff plethysmography. Thoracic aorta and mesenteric artery function or structure was analyzed using wire or pressure myography. Various markers of vascular, cardiac, and renal damage were determined using qPCR.

Results:
Preventive treatment with EMM3.20 partially avoided AngII-induced hypertension. Moreover, the SGK1 inhibitor improved endothelial function in the aorta, vascular remodeling in mesenteric resistance arteries, inflammation in the perivascular adipose tissue, cardiac hypertrophy, and markers of kidney damage caused by AngII. Specifically, the SGK1 inhibitor decreased markers of immune cells infiltration and proinflammatory cytokines, and extracellular matrix proteins in the aorta, heart, and kidney, increased by AngII.

Conclusion:
SGK1 inhibitor prevent the deleterious effects of AngII on the cardiovascular and renal systems by reducing inflammation and fibrosis.
Key words: angiotensin II, SGK1, inflammation, endothelial dysfunction.

PhD Student Name and surname: Irene Campaña Gómez
UAM PhD program: Microbiology
COMMUNICATION TYPE: ORAL

TITLE: Impact of ISG15 on MPXV Infection in the Context of Interferon Stimulation

Authors: Irene Campaña Gómez (1) and Susana Guerra (1,2).

AFFILIATIONS:

1. Department of Preventive Medicine, Public Health and Microbiology, Faculty of Medicine, Autonomous University of Madrid. 2. Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, New York, USA.

ABSTRACT (350 Word limit)

Background:
Monkeypox virus (MPXV), a member of the Poxviridae family, has recently re-emerged as a global health concern. Like other poxviruses, MPXV replicates in the cytoplasm and interacts closely with the host antiviral response. ISG15 encodes a ubiquitin-like modifier with antiviral activity, yet its role in MPXV infection remains unclear. As an interferon (IFN)-stimulated gene, ISG15 is induced as part of the IFN response, one of the main cellular defenses against viral infection. In this study, we explored how different MPXV strains behave in the presence or absence of ISG15, and then investigated how IFN pre-treatment influences the cellular response to infection, particularly in strains associated with recent human outbreaks.

Methodology:
HeLa cells, wild type (WT) or ISG15 knockout (KO), were used to infect with four different MPXV strains (2024, 2022, USA and WRAIR) to assess viral replication. In a second set of experiments, the analysis was focused on the two strains associated with recent human outbreaks (2022 and 2024). In this case, cells were pre-treated with IFN prior to infection in order to evaluate the impact of the antiviral response in both WT and KO backgrounds. We employed different approaches including viral titration assays, immunoblotting for viral protein detection, immunofluorescence microscopy, etc. In addition, proteomic and ISGylome analyses were performed to investigate cellular pathways and to identify ISG15-conjugated proteins.

Results:
ISG15 potently restrict replication of recent epidemic strains, whereas ISG15 deficiency enhances viral growth, establishing ISG15 as a restriction factor in humans. In contrast, IFN pre-treatment promotes antiviral protection specially in KO cells. Proteomic analysis revealed that MPXV infection triggers distinct host responses depending on viral strain and ISG15 status. ISGylome profiling identified a number of viral and cellular proteins conjugated to ISG15, suggesting that ISG15 modulates viral components and host defense machinery during infection.

Conclusion:
This work provides new insights into host–virus interactions, highlights the role of ISG15, and underscores the complexity of interferon-mediated antiviral responses. These findings may have important implications for understanding MPXV pathogenesis and for the development of antiviral strategies.

Key words: MPXV, ISG15, IFN, Host–virus interaction, Antiviral response.

PhD Student Name and surname: Javier García-Rodríguez
UAM PhD program: Pharmacology & Physiology
COMMUNICATION TYPE: ORAL

TITLE: **Preliminary observations in heart rate variability and vascular stiffness in 5 to 7-year-old children born preterm: sex and international cohorts' comparisons**

Authors: Javier García-Rodríguez[1], Ricardo Alonso de Celada[1], Jesús Blázquez Camacho[2], Lucia Deiros-Bronte[2], Silvia M. Arribas[1,3], David Ramiro-Cortijo[1,3]

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ABSTRACT

Background: Individuals born prematurely are at risk of cardiometabolic diseases (CMD). Given the high prevalence of prematurity and the socioeconomic burden of CMD, this represents a public health challenge, being essential its early detection. Heart rate variability (HRV), which reflects autonomic nervous system modulation of heart rate, is a marker of both cardiac and non-cardiac conditions. Arterial stiffness is another marker of CMD risk and can be assessed non-invasively using pulse wave velocity (PWV) and related hemodynamic parameters.

Methodology: A case-control study is being conducted in children aged 5–7 years born preterm (24–30 weeks of gestation), recruited from Hospital Universitario La Paz (Madrid, Spain). Participants are assessed body composition by bioimpedance analysis. HRV is analyzed using a H10 Polar band (V4-lead ECG). The arterial stiffness is determinated by SphygmoCor system. For the comparison of our cohort (CARDIOPREM), international reference populations of similar ages were used, but in no case were included premature infants.

Results: Significantly differences were observed between sexes in weight (Male: 14.9 [14.8; 15.1] kg, female: 19.6 [17.9; 22.8] kg), fat mass (male: 2.90 [2.85; 3.65] kg, female: 7.00 [6.50; 7.20] kg), muscle mass (male: 14.0 [13.7; 14.2] kg, female: 10.4 [9.95; 11.8] kg). In favor of female, the waist, arm and thigh circumferences also showed significantly differences with male. CARDIOPREM cohort shows low square root of the mean of successive differences (6.81 [4.85; 7.90] ms) and high low-to-high frequencies ratio (10.6 [6.90; 16.8] a.u.), suggesting reduced parasympathetic and increased sympathetic activity, consistent with the method of data collection. Related to arterial stiffness, PWV was significantly lower in CARDIOPREM (3.09 [2.82; 3.32] m/s) than international cohorts (Youth Vascular Consortium: 4.55 [4.07; 5.21] m/s P=0.002).

Conclusion: These findings suggest that early alterations in electrocardiographic and hemodynamic parameters may be associated with prematurity, potentially reflecting early cardiovascular dysregulation. These results support their utility in the development of predictive models for early identification of children at increased risk of cardiometabolic disease.

Key words: Prematurity; Cardiometabolic diseases; Autonomic nervous system; Vascular stiffness; Central hemodynamic.

PhD Student Name and surname: Paula Carretero Navarro
UAM PhD program: Molecular bioscience
COMMUNICATION TYPE: ORAL (or poster or any kind)

TITLE: Two immunometabolic worlds in high-grade gliomas: interaction between immune checkpoints and tumor metabolism.

Authors: Paula Carretero-Navarro[1], Rebeca Nestares de Kok[1], Pilar López-Larrubia[1], Jesús Pacheco-Torres[1]

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ABSTRACT

Background:
High-grade gliomas are currently the most lethal brain tumors. Those harboring the R132H mutation in isocitrate dehydrogenase 1 (IDH1) show a better prognosis in clinical settings. Nevertheless, standard treatments fail to significantly extend patients' survival, highlighting an urgent need to develop new therapeutic strategies. Immunotherapies based on immune checkpoint inhibition, such as those targeting PD-L1, have shown promising results in other tumor types but they have not been effective in gliomas. We hypothesize that one a potential contributing factor for this is the aberrant tumor metabolism. In this work, we aim to study the relationship between immunorresistance and glioma tumor metabolism.

Methodology:
To address this, we studied orthotopic murine models of high-grade glioma comprising IDH1 wild-type (GL261-WT) glioblastoma and IDH1 R132H-mutant glioma (GL261-mIDH). We treated them ip with Saline/ IgG2b, anti–PD-L1 or AGI-5198, a mutant IDH1–targeted metabolic modulator. Tumor growth was monitored using T1-w and T2-w MRI images with contrast in a 7T Bruker Biospec. Additionally, diffusion tensor imaging (30 directions, TR/TE = 3000/38.10 ms, δ/Δ = 4/25 ms, matrix = 100×100, slice thickness = 0.8 mm, b-values = 800 μm²/s and 2500 μm²/s) was performed to assess changes in tumor microenvironment.

Results:
We observed a significant reduction in tumor growth in GL261-mIDH compared to GL261-WT, successfully recapitulating clinical observations. GL261-WT did not respond to AGI-5198, but showed significant reduction in tumor volume with immunotherapy. In vivo monitoring revealed a significant increase in mean diffusivity, radial diffusivity, and axial diffusivity, indicating that anti–PD-L1 therapy induces necrosis. GL261-mIDH didn´t response to anti-PD-L1 but showed a significant reduction in tumor size when treated with AGI-5198. Finally, a decrease in fractional anisotropy was detected in this mutant model following treatment with the metabolic modulator, indicating reduced cellularity.

Conclusion:
Overall, our findings support previous preclinical evidence demonstrating that immune checkpoint blockade can induce robust responses in glioma models. Together, these findings support a stratified therapeutic approach combining immunotherapy and metabolic modulation based on tumor genotype. Furthermore, multiparametric MRI enabled non-invasive monitoring of tumor progression and treatment response, providing additional insight into tumor behavior in vivo.

Key words: IDH1, high-grade glioma, PD-L1, tumor metabolism, MRI

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Darwin Andrés Córdova Ascurra
UAM PhD program: Molecular Biosciencies
COMMUNICATION TYPE: ORAL

TITLE: TNF-α–Dependent Alterations in Magnetic Resonance Imaging (MRI) parameters during high-fat Diet–induced neuroinflammation

Authors: Darwin Córdova-Ascurra[1], Raquel González-Alday[1], Nuria Arias-Ramos[1], Jesús Pacheco-Torres[1] and Pilar López-Larrubia[1*].

AFFILIATIONS:
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ABSTRACT

Background:
Obesity due to high-fat diets (HFD) activate pro-inflammatory cascades in the brain because saturated fatty acids can cross blood-brain barrier. In this context, Tumor Necrosis Factor α (TNF-α) sits at the crossroads of neuroinflammation (NI) and obesity, shaping metabolic and neural outcomes. TNF-α is not only a cytokine, it is also a metabolic regulator. Our objective is to characterize *in vivo* the role of TNF-α in NI induced by obesity, with a TNF-αKO murine model.

Methodology:
Eight-week old C57BL/6J wild-type (WT) mice (n=30) and TNF-αKO mice with the same genetic background (n=52) were fed either with SD or HFD for 20 weeks. In weeks 10 and 20, multiparametric MRI studies were conducted using a Bruker Biospec 7T scanner; acquiring diffusion tensor imaging (DTI). Subsequently, parametric maps were processed and 4 brain regions of interest (ROIs) were selected and quantified using ImageJ: cortex (Cx), hippocampus (HPC), thalamus (Thal) and hypothalamus (HTH). Linear mixed effects models were used to statistically assess the impact of diet, sex and genotype across different areas. Indirect calorimetry analysis (Phenomaster) was performed after both temporal MRI studies, obtaining data on indirect calorimetry, motor activity and food intake, etc. Finally, we carried out immunofluorescence assays of every group after 20 weeks of diet diversification to validate selected findings.

Results:
WT mice gained weight faster than KO mice and every group with HFD exhibited a loss of circadian oscillations of respiratory exchange ratio. MRI studies revealed significant differences between genotypes in both temporal points: higher MD, AD and FA in WT mice than KO across all groups and ROIs in week 10 of diet, however most of these differences disappear in week 20.

Conclusion:
Data indicate that TNFαKO mice diverge from WT mice in early diet-induced MRI signatures of microstructural change associated with neuroinflammation. These effects are stronger after 10-week dietary diversification but diminish with longer exposure, suggesting early TNF-α–dependent modulation of brain diffusivity parameters across regions, possibly reflecting axonal or fiber reorganization or may indicate transient glial or vascular remodeling. By contrast, the attenuation of these differences at 20 weeks suggests possible compensation, or a plateau of the structural response over time.

Key words: Neuroinflammation, TNF-α knockout, obesity, MRI.

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Álvaro López Codina
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: ORAL

TITLE: Molecular and structural analyses of mTORC1 assembly and maturation by the HSP90-R2TP chaperone system

Authors: Alvaro L. Codina[1,3], Carmen García-Martín[2,3], Ana González-Corpas[3], Maria Martínez-Molledo[3], Johanne Le-Coq[4], Andrés López-Perrote[3], Jasminka Boskovic[4], Maria I. Dauden[3,*], Oscar Llorca[3,*]

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ABSTRACT (350 Word limit)

Background:
mTOR (mammalian target of rapamycin) is a large PIKK (phosphatidylinositol 3-kinase-related kinase) which controls cell growth and proliferation. Thus, its abnormal hyperactivation is an important therapeutic target in cancer. mTOR is only active as part of two 1-MDa multiprotein complexes, termed mTORC1 and mTORC2, with distinct subunit compositions and cellular functions. mTORC1 is comprised of mTOR, RAPTOR (regulatory-associated protein of mTOR) and mLST8 (mammalian lethal with SEC13 protein 8). Importantly, mTORC1 assembly is essential for its activation, requiring the HSP90 (heat shock protein 90) chaperone and the RUVBL1-RUVBL2-RPAP3-PIH1D1 (R2TP) co-chaperone complex. However, how HSP90 and R2TP handle mTOR to catalyze mTORC1 assembly is unknown. To understand this process, we aim to define its stepwise structural mechanism by a combination of cryo-electron microscopy (cryo-EM) and biochemical experiments.

Methodology:
Human mTOR and HSP90 were recombinantly expressed in insect and bacterial cells, respectively, and purified by affinity chromatography and gel filtration. The HSP90-mTOR complex was reconstituted *in vitro*, and its formation was determined by pull-down and gel filtration. For cryo-EM experiments, the HSP90-mTOR complex was concentrated and purified by gel filtration prior to vitrification. A total of 1,558 micrographs were collected using a JEOL JEM-2200FS transmission electron microscope at 200 kV and processed in RELION and CryoSPARC. In parallel, human R2TP complex was produced by recombinant co-expression in bacterial cells and purified by affinity chromatography to assess its interaction with HSP90 *in vitro*.

Results:
mTOR was successfully expressed and purified in absence of mLST8, which has been reported to be critical for mTOR stability. Additionally, mLST8 was dispensable for the interaction between mTOR and HSP90 *in vitro*. Preliminary cryo-EM analysis suggested the presence of a molecular population compatible with the HSP90-mTOR complex.

Conclusion:
Our *in vitro* interaction assays suggest that neither mLST8 nor R2TP is required for the interaction between HSP90 and mTOR. However, further *in vitro* experiments are needed to discern whether mTOR can bind a pre-assembled HSP90-R2TP complex. Finally, our cryo-EM data provides the groundwork to understand how mTOR is assisted by HSP90 to assemble into mTORC1.

Key words: mTOR; assembly; HSP90; R2TP; chaperone; cryo-EM.

PhD Student Name and surname: Paula Diez Roda
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: ORAL

TITLE: In vivo communication through extracellular microRNA carriers and their role in metabolic diseases

Authors: Paula Diez-Roda[1] and Ruben Garcia-Martin[1]

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ABSTRACT

Background:
Intercellular communication is essential for the coordinated regulation of complex biological processes such as metabolism. microRNAs (miRNAs) are short non-coding RNAs that modulate gene expression by the association with Argonaute (AGO) proteins, mainly AGO2, forming the RNA-induced silencing complex (RISC). Despite the abundance of RNases in biofluids, circulating miRNAs remain stable in them through the association with multiple transporters such as AGO proteins, extracellular vesicles, and lipoproteins, being AGO2 the predominant carrier.

Emerging evidence suggests extracellular AGO2 is not derived from cell death, as other miRNA-processing proteins are absent in biofluids and AGO2-carried miRNAs profile differs from the intracellular pattern. Alterations in circulating miRNAs have been linked to various pathological conditions. Although not much studied, signature of AGO2-carried miRNAs is altered in several diseases such as amyotrophic lateral sclerosis and cancer. In obesity, circulating miRNAs are largely altered, although the contribution of AGO2 as a carrier for them has not been studied yet.

This project hypothesizes that circulating miRNAs bound to AGO2 and act as signaling molecules that mediate intercellular communication, contributing to metabolic regulation and disease progression. The main objective is to investigate the role of AGO2-associated miRNAs released by hepatocytes in metabolic regulation and their involvement in metabolic diseases.

Methodology:
The laboratory has developed and employed a set of tissue-specific animal models in which AGO2 is tagged with HaloTag, enabling its selective capture. In this case, an specific model for hepatocytes (Alb-AGO2Halo) was used. After the capture of released AGO2, its carried miRNAs were profiled and analysed.

Results:
Preliminary results indicate that AGO2 is capable of transporting miRNAs outside the cell and likely into the circulation, influencing key metabolic pathways. To determine this, specific AGO2-associated miRNAs have been identified and characterized, and their potential target pathways analyzed. Between them, miR-137-3p, has been shown to affect the insulin pathway, as evidenced by its impact on key signaling nodes such as ERK1/2 and AKT. Notably, cells treated with this miRNA exhibit insulin resistance, supporting its functional role in modulating this pathway.

Conclusion:
These analyses suggest that AGO2-bound miRNAs may regulate metabolic processes by

modulating signaling networks relevant to insulin response, supporting their role as mediators of intercellular communication.

Key words: AGO2, intercellular communication, insulin signalling.

PhD Student Name and surname: Greys María Rodelo Olmos
UAM PhD program: Epidemiology and Public Health
COMMUNICATION TYPE: Oral

TITLE: Initial steps of a Scoping Review on Artificial Intelligence in the diagnosis and treatment of Rare Hematological Diseases

Authors: G Rodelo-Olmos [1,2,3], L Arzuza-Ortega[3], V Alonso-Ferreira [1,4], M Posada-de la Paz [5], G Arias-Merino [1]

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ABSTRACT (350 Word limit)

Background:
Artificial Intelligence (AI) could have the potential to optimize clinical workflows, enhance decision-making and accelerate the diagnosis and treatment of Rare Hematological Diseases (RHDs). However, current evidence regarding the scope and characteristics of AI applications in this field remains unclear. The aim of this work is to show the initial steps of a scoping review (ScR) about how AI has been applied in the diagnosis and treatment of RHDs.

Methodology:
This ScR follows the methodological framework proposed by the Joanna Briggs Institute and is reported according to PRISMA-ScR guidelines. A comprehensive literature search was conducted in four electronic databases: PubMed, Web of Science, EMBASE, and COCHRANE. The protocol is publicly available in the Open Science Framework (v4ykp). The ScR is structured around the Population, Concept, and Context (PCC) framework. Study selection was performed in two phases (title/abstract and full-text screening) according to predefined criteria. Citation searching was undertaken during full-text review. The screening process was conducted independently and in a blinded manner using Rayyan software, with a third reviewer resolving disagreements. Inter-reviewer agreement was calculated using the Kappa index.

Results:
The database search identified 296 records, with 16 duplicates removed prior to screening. Of the 280 records screened, 230 were excluded. 50 full-text reports were assessed, and eight additional studies were identified through citation searching. Following eligibility assessment, 20 records were excluded. The evaluation of the 38 included studies yielded a Kappa index of 0.72 during both the title/abstract and full-text screening phases, indicating a good level of agreement.

Conclusion:
Given the evolving nature of AI in RHDs, a ScR is appropriate to map a research area and identify gaps. This will help other researchers avoid repeating similar studies. Findings are expected to inform researchers and clinicians about the AI potential in RHDs management and supporting evidence-based decision-making.

Key words: rare hematologic disease, artificial intelligence, scoping review, rare diseases

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Laura Bravo Robles
UAM PhD program: Biociencias moleculares
COMMUNICATION TYPE: ORAL

TITLE: High-dimensional spectral flow cytometry profiling reveals systemic immune dysregulation in pediatric patients with cystic fibrosis

Authors: Laura Bravo-Robles[1,2], Pablo Mata-Martínez[1,2], Laura Hurtado-Navarro[1,3], Gülce Bıçakcıoğlu[1,2] Olivia Fernández-Medina[4], Paula Almellones-Araiz[4], Luna Minute[1,2], Verónica Terrón[1,3], Jaime Fernández[1,2], Eduardo López-Collazo[1,3,5,6,7], Cristina de Manuel Gómez[8], Marta Ruiz de Valbuena Maiz[8], Cristina Calvo[9], Carlos del Fresno[1,2,10]

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ABSTRACT

Background:
Cystic fibrosis (CF) is a rare, life-limiting genetic disorder affecting 1 in 5000 newborns in Spain. CF arises from mutations that disrupt or abolish Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) protein function. The lungs are most severely affected due to thick mucus that impairs mucociliary clearance, leading to a self-perpetuating cycle of infection and inflammation.
CFTR modulators have improved protein function and quality of life, but airway inflammation often persists, and their effect on immune-mediated inflammation remains unclear. Children with CF also exhibit intrinsic innate immune abnormalities; innate cells may be developmentally immature or functionally impaired, reducing bacterial clearance and promoting chronic inflammation from early life. Understanding these early immune alterations is crucial for novel therapies.

Methodology:
In this study, we evaluated the immunological profile of circulating immune cells in pediatric patients with CF. Using 1mL of peripheral blood from pediatric patients followed at La Paz University Hospital, we performed a comprehensive immunophenotyping with a 37-color full-spectrum flow cytometry panel designed for this study, rendering 371 immunological variables per patient. This panel assesses lineage, activation, and immune checkpoints (ICs) across T and B lymphocytes, NK and NKT cells, monocytes, dendritic cells, neutrophils, and myeloid-derived suppressor cells (MDSCs).

Results and conclusion:
Comparison with healthy donors identified over 50 immune parameters that differed significantly in pediatric CF patients, including a generalized downregulation of the PD-1/PD-L1 axis and other ICs, while population frequencies were unchanged. Therefore, these spectral cytometry analyses distinguish pediatric CF patients from healthy children at the systemic level, revealing immune features that reflect clinically relevant aspects of disease. This work provides the foundation for future translational and therapeutic studies.

Key words: cystic fibrosis, spectral flow cytometry, immunophenotyping.

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PhD Student Name and surname: Irati Higuera
UAM PhD program: Medicina y cirugía
COMMUNICATION TYPE: POSTER

TITLE: Benefits, limitations and potential solutions for defining good practices in Online Counselling Chat Services for Youth

Authors: Irati Higuera-Lozano [a] [b], Ana M. Ramirez [a], Noortje Breugelmans [c], Elke Denayer [c], Alexis Dewaele [c], Katalin Felvinczi [d], Lien Goossens [c], Zsuzsa Kaló [d], Tuuli Pitkänen [e], Mónika Rényi [d], Virvatuli Uusimäki [e], María Cabello [a] [b] [f]

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ABSTRACT (350 Word limit)

Background:
Online Chat Counselling Services (OCCS) provide accessible mental health support for young people. However, systematic, cross-cultural research from the perspective of service providers is needed to improve current practices, guide future development, and share best practices. This study explores the experiences of OCCS providers and counsellors in four European countries, identifying benefits, limitations, and potential solutions to improve services and inform future best practices.

Methodology:
62 counsellors or chatline coordinators from 33 OCCS in Belgium, Finland, Hungary, and Spain were interviewed online. A thematic analysis of the output from these interviews focused on the benefits, limitations and proposed solutions.

Results:
Most of the participants were female (80 %). Nearly half of the services (48 %) worked with both paid counsellors and volunteers. Eighteen percent of OCCSs did not request any user information at login. In almost half of the OCCSs, counsellors were able to see whether a user had made contact previously. Six key benefits of OCCS were identified: improved accessibility, anonymity-facilitated disclosure, future-oriented services, chat-based communication advantages, positive counsellor experience, and meaningful user support.

Five main limitations emerged: unclear communication, limited resources, anonymity as a barrier, uncertainty-related negative perceptions, and low visibility and utilization. Proposed solutions included conventional strategies (e.g., enhanced training, referrals, inter-service collaboration) and innovative approaches (e.g., AI integration for risk assessment, translation, and chatbot functionalities). Certain limitations were considered intrinsic to the OCCS model and accepted accordingly.

Conclusion:
This study explored the experiences of a diverse group of counsellors to identify the key benefits, challenges, and potential solutions within OCCS. The proposed strategies provide a valuable foundation for the cross-national implementation of best practices in this field. Future research should evaluate these recommendations, incorporating the perspectives of service users.

Key words: Online chat, Helpline, Youth, Mental health, Europe, Qualitative study.

PhD Student Name and surname: Mikel Blanco Otaegui
UAM PhD program: Medicina y cirugía
COMMUNICATION TYPE: ORAL

TITLE: Structural Deletions in HTLV-1 Proviruses Correlate with Disease Severity in Adult T-cell Leukemia

Authors: Mikel Blanco[1], Rafael Muñoz[1], Ariadna Rando[2], Diego Ortega[3], Paloma Liendo[4], Mª José Pena[5], Andrea Huertas[1], Alejandro Muñoz[1], José Manuel Ramos[6], Vicente Soriano[7] & Carmen de Mendoza[1] on behalf of HTLV Spanish Study Group

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ABSTRACT (350 Word limit)

Background:
HTLV-1 is a neglected retrovirus associated with severe neurological and lymphoproliferative diseases, including tropical spastic paraparesis/HTLV-1-associated myelopathy (HAM/TSP) and adult T-cell leukemia/lymphoma (ATLL). Although Spain is a non-endemic country, more than 550 individuals with HTLV-1 infection had been reported up to date. A national HTLV-1 registry has existed since 1989. Most cases are migrants from endemic regions in Latin America and Equatorial Africa. There is a high diagnostic delay, reflected by a high proportion of cases (22%) presenting with clinical symptoms. Virological factors contributing to HTLV-1 disease progression remain poorly understood.

Methodology:
Peripheral blood mononuclear cells (PBMCs) from 30 HTLV-1-infected individuals (8 ATLL, 12 HAM/TSP, and 10 asymptomatic carriers) were analyzed. Proviral DNA was sequenced using Next Generation Sequencing (NGS) with 149 biotinylated probes and 1 million reads per sample. Demographic and clinical data including disease status, proviral load, and treatment history were examined along with proviral genomic structure.

Results:
The cohort was predominantly female (70%) with a median age of 46 years. Most participants were from Latin America (93%), with one from Ivory Coast and one native Spaniard. Proviral load was significantly higher in ATLL and HAM/TSP patients compared to asymptomatic carriers (median 16.44%, 7.25%, and 4.35%, respectively; p=0.037). No significant differences were found in the number of mutations across structural, accessory, or regulatory genes including tax and HBZ. However, 75% of ATLL patients showed defective proviruses, primarily Type I deletions (loss of gag, pol, and env), associated with acute/lymphoma forms. One patient with a smoldering cutaneous form exhibited a Type II deletion (loss of gag). Post-treatment analysis of two patients revealed partial restoration of deleted proviral regions from 4.2% to 62.1% in one and from 0.2% to 14.5% in another, suggesting clonal replacement or shifts in dominant proviral subpopulations.

Conclusion:
Defective HTLV-1 proviruses are significantly associated with ATLL, particularly with aggressive clinical forms. Type I deletions may contribute to oncogenesis and immune evasion. The dynamic nature of proviral structure following treatment highlights the importance of longitudinal genomic sequence monitoring in HTLV-1-infected individuals.

Key words: HTLV-1, Proviral deletions, ATLL, NGS.

PhD Student Name and surname: Diego M. Conti
UAM PhD program: Medicine and Surgery
COMMUNICATION TYPE: Oral communication

TITLE: New Chronic Rhinosinusitis Control Tests: Development and Validation

Authors: D.M. Conti[1,2]; W.J. Fokkens[3]; G.K. Scadding[4,5]; V. Backer[6]; S. Lau[7]; X. Bertels[8]; K. Aanaes[9]; M.P. Aguilera Quezada[10]; A. Alani[11]; I. Alobid[12]; E. Anisman[11]; Y. Chan[13]; J. Constantinidis[14]; M. Corbò[15,16]; M.E. Cornet[17]; E.J. Correa[18]; L.M. D´auria[19]; E. De Corso[15,16]; A. Del Cuvillo[20]; M. Doulaptsi[21]; A. García-Lliberós[22]; F. García Río[23,24,25]; P. Gevaert[26]; J. Han[27]; J. Lee[28,29]; S. Lee[30]; K. Limage[11]; G. Liva[21]; D.R. Lobo[31,32]; A. Manole[33]; F. Manole[33]; F. Mariño-Sanchez[34]; J. Maza-Solano[35,36,37]; C. Montuori[15,16]; R. Moreno-Luna[38]; X.I. Mota Rojas[39]; G.B. Patel[40]; A. Peters[40]; E. Prokopakis[21,41]; S. Quirce[24,42]; D. Ramdhani[43]; S. Reitsma[3]; A. Sánchez Barrueco[44]; A. Santamaría-Gadea[45]; S. Sánchez Gómez[46]; T. Sarafidou[47]; S. Snoeks[48]; W. Thorley[49]; E. Toskala[11]; M. Tucciarone[50]; J.M. Villacampa Aubá[51]; I.M. Villarreal Patiño[52]; M. Wagenmann[53]; L.W. Wang[54]; A. Belmans[55]; P.W. Hellings[56,57,58]

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ABSTRACT

Background:
Measuring control in Chronic Rhinosinusitis (CRS) was introduced by the European Position Paper on Chronic Rhinosinusitis and Nasal Polyps (EPOS) in 2012 and adapted in EPOS 2020. We developed and validated 2 new tests for the evaluation of control in CRS, CRS Control Test (CCT) and CRS Patient Control Test (CPCT) and investigated their correlations with existing tools.

Methodology:
An international survey was conducted in 1,102 CRS patients in 19 centres in 7 countries using a questionnaire including the newly developed CCT and CPCT, VAS scores for CRS severity and control, the EPOS control test (EPOSCT) assessed by patient and HCP, the Sino-Nasal Outcome Test 22 (SNOT-22) and the Patient Global Assessment Tool (PGAT). We evaluated convergent and discriminative validity, internal consistency and cross-cultural validity. Sub-analyses were performed for CRS patients with and without nasal polyps.

Results:
Both CCT and CPCT demonstrated a high correlation with SNOT-22 and the PGAT. Moderate correlations were observed for all other comparisons like with patient and physician control (VAS), severity (VAS) and EPOSCT by physician. CPCT also correlated highly with the severity VAS and the EPOSCT by patient. Both tests showed good internal consistency, discriminative validity and cross-cultural validity.

Conclusion:
The brief CCT and the longer CPCT are new CRS control tests that show moderate to high correlations with existing tools. Both instruments demonstrated good psychometric properties and therefore can be recommended for use in clinical practice and research.

Key words: Chronic rhinosinusitis; Nasal Polyposis; CRS Control Test; EPOS; CRS Patient Control Test.

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Juan Carlos Lizarzaburu Robles
UAM PhD program: Medicina y Cirugía
COMMUNICATION TYPE: ORAL

TITLE: Cardiometabolic risk factors for type 2 diabetes across early and late postmenopausal stages in prediabetic women

Authors: Juan Carlos Lizarzaburu-Robles[1,2], Ignacio Mahíllo-Fernández[3], Clotilde Vázquez-Martínez[4], Sebastián Mas-Fontao[2,5], Amalia Paniagua[4], Maite Ortega[4], Blanca Timón[4], Sacramento Martínez-Albaladejo[2,5], Oscar Lorenzo[2,5]

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ABSTRACT (350 Word limit)

Background:

Prediabetes is increasingly prevalent, and women transitioning through menopause may face a particularly elevated risk of progressing to type 2 diabetes (T2DM). Estrogen deficiency promotes visceral adiposity, insulin resistance, and systemic inflammation, potentially amplifying the metabolic burden of aging and obesity. However, the cardiometabolic determinants of T2DM across menopausal stages remain insufficiently characterized.

Methods:

This retrospective cohort study included 229 prediabetic women evaluated at a tertiary-care hospital and followed for up to 5.5 years. Prediabetes was defined according to ADA criteria and women were classified as premenopausal (< 51 years), early postmenopausal (51-60 years), or late postmenopausal (> 60 years). Clinical and biochemical variables were extracted from medical records. Relative risks (RRs) for T2DM were estimated using Poisson regression, and time-to-event analyses were performed using Kaplan-Meier curves.

Results:

During follow-up, 18% of premenopausal and 35% of postmenopausal women developed T2DM. Higher BMI predicted T2DM in both groups. In postmenopausal women, hypertension (RR: 3.03), lower HDL-C (RR: 0.96), lower vitamin D (RR: 0.94), and reduced eGFR (RR: 0.97) were independently associated with T2DM. Stratification revealed that early postmenopause carried the highest incidence of T2DM (HR: 2.94). In early postmenopause, higher BMI and lower vitamin D were independent predictors, whereas in late postmenopause, reduced eGFR was the strongest determinant.

Conclusions:

Cardiometabolic risk factors for T2DM in prediabetic women vary across menopausal stages. While excess adiposity is a universal driver, early postmenopause represents a particularly vulnerable period in which vitamin D deficiency adds significant risk. In late

postmenopause, declining renal function becomes the predominant predictor. These findings support stage-specific risk assessment and tailored preventive strategies for prediabetic women.

Key words: Prediabetes, menopause, aging, type 2 diabetes

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Mario Ricciardi Serra
UAM PhD program: Medicine and Surgery
COMMUNICATION TYPE: ORAL

TITLE: Enlarged perivascular spaces reflect neuropathological severity of cerebral amyloid angiopathy in Alzheimer's disease dementia

Authors: Mario Ricciardi Serra[1,2], Iván Burgueño-García[1], Elizabeth Valeriano-Lorenzo[1], María Ascensión Zea-Sevilla[1], Meritxell Valentí[1], Belén Frades[1], Isabel López Torres[1], Marta Anton-Moreno[1], Francisco López-González[1], Paloma Ruiz[1], Laura Saiz[1], Alicia Uceda Heras[1], Linda Zhang[1], Mabel Torres Llacsa[1], Eva Alfayate Sáez[1], Marta Molero Cartón[1], María José López-Martínez[1], Teodoro Del Ser[1], Michel Grothe[1], Alberto Rábano[1], Pascual Sánchez-Juan[1]

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2 Faculty of Medicine, UAM

ABSTRACT

Background:
Cerebral amyloid angiopathy (CAA) contributes to neurodegeneration and impaired perivascular clearance in Alzheimer's disease (AD) and has important clinical and emerging therapeutic implications. Enlarged perivascular spaces in the centrum semiovale (CSO-PVS) have emerged as an MRI marker of CAA; however, direct clinicopathological evidence linking CSO-PVS burden to neuropathological CAA severity in AD remains limited. We investigated the association between neuropathological CAA severity and CSO-PVS burden in AD, and explored the influence of APOE ε4 status and AD-related neuropathological staging.

Methodology:
We included 68 individuals from the VARS clinicopathological cohort of the Alzheimer's Centre Reina Sofía-CIEN Foundation with moderate-to-advanced dementia, no history of intracranial haemorrhage, and pathological AD (Thal IV-V; Braak V-VI). All participants underwent antemortem brain MRI (T1, T2, FLAIR, GRE), with a median MRI-to-death interval of 2.6 years (IQR 0.7-4.9). Mean age at MRI was 84.7 ± 7.0 years, and 85.3% were female. Neuropathological CAA severity was assessed using the VCING criteria (0-4), and CSO-PVS were rated according to STRIVE criteria using the Potter scale (0-4). Associations were analysed using partial Spearman correlations and ordinal logistic regression adjusted for age at MRI and MRI-to-death interval. Exploratory analyses examined relationships with Thal amyloid phase, Braak tau stage, and APOE ε4 allele load.

Results:
Greater neuropathological CAA severity was associated with higher CSO-PVS burden. CAA severity correlated with CSO-PVS after adjustment for age ($\rho = 0.31$, $p = 0.011$) and MRI-to-death interval ($\rho = 0.26$, $p = 0.035$). Each one-point increase in VCING score was associated in ordinal logistic regression with 50% higher odds of greater CSO-PVS burden (OR 1.50, 95% CI 1.02-2.24; $p = 0.042$), independent of age. APOE ε4 allele load was associated with increasing CAA severity (OR 2.16 per allele), but not with CSO-PVS burden. CSO-PVS were not associated with Thal amyloid phase or Braak tau stage.

Conclusion:

CSO-PVS dilatation on MRI is independently associated with increasing neuropathological severity of CAA in AD, supporting CSO-PVS as an in vivo marker of CAA severity, likely reflecting impaired perivascular clearance mechanisms.

Key words: Cerebral amyloid angiopathy (CAA); Alzheimer's disease (AD); Perivascular spaces in the centrum semiovale (CSO-PVS); MRI; APOE ε4.

PhD Student Name and surname: Ana Ortiz-Tallo
UAM PhD program: Medicina y cirugía.
COMMUNICATION TYPE: ORAL (or poster or any kind)

TITLE: Childhood loneliness and disability in first-episode psychosis: exploring mechanisms and transdiagnostic effects

Authors: Ana Ortiz-Tallo[1,2] and María Cabello[1,2]

AFFILIATIONS:

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ABSTRACT (350 Word limit)

Background:
Adverse childhood experiences (ACEs) are well-established predictors of long-term mental and functional impairment. While ACEs have been linked to psychotic disorders, less is known about the specific mechanisms linking early social adversity to functional outcomes in first-episode psychosis (FEP).

Objective:
To examine the association between childhood loneliness and disability in FEP, and to explore potential mechanisms, including psychotic symptomatology, premorbid adjustment, and transdiagnostic effects across groups.

Participants and Setting:
A total of 381 individuals with FEP from the AGES-CM multicenter cohort in Madrid, Spain, along with siblings and controls for comparative analyses.

Methods:
ACEs were assessed retrospectively using a modified Childhood Experience of Care and Abuse interview. Disability was measured with the WHODAS 2.0. Generalized linear models (gamma distribution, log link) were used to estimate associations. Additional analyses examined mediation by psychotic symptoms (PANSS), differential effects of positive and negative symptoms, independence from premorbid adjustment (PAS), and interactions across groups.

Results:
Childhood loneliness was independently associated with higher disability in adulthood. This association remained significant after adjusting for other ACEs and premorbid functioning. Psychotic symptomatology partially attenuated the effect, with evidence suggesting a specific role of positive symptoms, but not negative symptoms. No significant association was found for cumulative ACE exposure. The effect of loneliness on disability did not differ significantly between patients, siblings, and controls.

Conclusions:
These findings highlight childhood loneliness as a robust and specific predictor of functional impairment. The partial mediation by positive psychotic symptoms suggests involvement of

social-cognitive mechanisms, while the persistence of the effect beyond premorbid adjustment supports its independent role. The absence of group differences points to a potential transdiagnostic mechanism linking early social disconnection to later disability.

Keywords: Childhood loneliness; First-episode psychosis; Disability; Adverse childhood experiences; Psychotic symptoms; Transdiagnostic mechanisms; Social cognition; Positive symptoms; Mediation; Functional outcomes; Early adversity; Premorbid adjustment; WHODAS 2.0.

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Lucía Lomba Riego
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: ORAL

TITLE: TARGETING THE KRAS-RAF1 INTERACTION IN LUNG CANCER USING INTRABODIES AND BIOPROTACS

Authors: Lucía Lomba-Riego[1], Mariano Barbacid[1], Sara García-Alonso[1]

AFFILIATIONS:
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ABSTRACT

Background:
RAF1 is a critical effector downstream of KRAS in the MAPK signaling pathway. Unlike other RAF isoforms, genetic ablation of RAF1 induces tumor regression without significant toxicity in *KRAS^{G12V}; Trp53^{KO}* lung cancer mouse models. The interaction between KRAS and RAF1 is mediated by the RAS-binding domain (RBD) of RAF1, and its disruption, such as through the R89L mutation, abolishes binding, supporting this interface as a promising therapeutic target. We aimed to develop intracellular nanobodies (intrabodies) targeting RAF1-RBD to block its interaction with KRAS.

Methodology:
Nanobodies against RAF1-RBD were selected using a phage display library. Binding affinities were measured by surface plasmon resonance. A yeast two-hybrid screen was used to identify clones capable of intracellular folding and binding. Disruption of the KRAS-RAF1 interaction in mammalian cells was evaluated by an optimized NanoBRET assay. The lead intrabody was fused to E3 ligases to generate bioPROTACs for targeted protein degradation. Additionally, doxycycline-inducible stable lung cancer cell lines were generated to assess phenotypic effects.

Results:
Thirteen nanobodies were initially identified by ELISA. The lead candidate displayed nanomolar affinity for RAF1-RBD and shared the same sequence as the best clone in the yeast assay. This intrabody reduced the KRAS^{G12V}-RAF1 interaction by 52% in the NanoBRET assay and decreased cancer cell viability by 25% after 72 hours of induction.

To further exploit this RAF1-RBD-binding intrabody, bioPROTAC-mediated RAF1 degradation was employed, which effectively reduced RAF1 protein levels and decreased cancer cell viability by approximately 40% after 72 hours of induction.

Current efforts are focused on improving intracellular delivery of these agents by incorporating cell-penetrating peptides (CPPs) into the intrabody design. In parallel, *in vivo* validation using mouse xenograft models will be performed to assess therapeutic efficacy and tumor regression.

Conclusion:
We have developed a first-in-class functional intrabody and derived bioPROTACs that effectively disrupt the KRAS-RAF1 interaction and reduce lung cancer cell viability. These findings support RAF1 as a promising therapeutic target and highlight the potential of intrabody-based approaches in KRAS-driven cancers.

Key words: Intrabodies, KRAS-RAF1 interaction, bioPROTACs.

PhD Student Name and surname: Rosa Andreu Martínez
UAM PhD program: Biociencias Moleculares
COMMUNICATION TYPE: ORAL

TITLE: Transcriptomic Profiling of Human Pulmonary Artery Smooth Muscle Cells: Impact of COPD and Emphysema Phenotypes

Authors: Rosa Andreu-Martínez[1,2]Jorge Rodríguez-Pérez[1,2], , Leila Pérez Sánchez[2], Ramón Moreno-Balsalobre[2], Héctor Milian[2], Luis del Peso[2,] Cecilia Muñoz-Calleja[1,2], María J. Calzada[1,2,4,*]

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ABSTRACT (350 Word limit)

Background:
Chronic Obstructive Pulmonary Disease (COPD) is frequently associated with pulmonary vascular alterations, even in early stages. Human pulmonary artery smooth muscle cells (hPASMCs) play a pivotal role in the structural remodeling of the pulmonary vasculature. This study aims to characterize the transcriptomic profile of HPASMCs derived from oncological patients undergoing thoracic surgery at the Hospital Universitario de La Princesa. The primary objective was to identify differential gene expression patterns between non-COPD and COPD patients, as well as to distinguish specific signatures between COPD patients with and without emphysema.

Methodology:
Primary hPASMCs were isolated from pulmonary arteries samples obtained during thoracic surgery. Patients were stratified into two main cohorts: non-COPD (control) and COPD. The COPD group was further sub-stratified based on the presence or absence of emphysema. High-throughput RNA sequencing (RNAseq) was performed to analyze the transcriptome. The bioinformatic analysis included differential expression analysis to identify statistically significant upregulated and downregulated genes, as well as to identify differentially expressed pathways.

Results:
The analysis revealed distinct molecular signatures between the groups. Compared to non-COPD controls, hPASMCs from COPD patients exhibited significant dysregulation in pathways associated with inflammation, OXPHOS, and mTORC signaling. Furthermore, the sub-analysis of COPD patients highlighted a unique transcriptomic fingerprint in those with emphysema,

Conclusion:
The transcriptomic landscape of hPASMCs is significantly altered by the presence of COPD and emphysema. These findings suggest that the pulmonary vasculature undergoes specific molecular shifts depending on the clinical phenotype of the patient. Identifying these differentially expressed pathways provides a foundation for discovering novel therapeutic targets to mitigate vascular remodeling in COPD.

Key words: hPASMC, transcriptomics, COPD, pulmonary emphysema

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PhD Student Name and surname: Elena Moya Ruiz
UAM PhD program: Biociencias Moleculares (Ciencias)
COMMUNICATION TYPE: Oral Communication

TITLE: Mitochondria control the identity of heart resident macrophages, which protect during anthracycline-induced cardiotoxicity through insulin-like growth factor 1 (IGF-1)

Authors: Elena Moya-Ruiz [1,2*], Miguel Galán [1,*] , Vanessa Núñez [1], Pau Figuera-Belmonte [1], Diego Mañanes [1,2] , Stefanie K Wculek [3], Iñaki Robles-Vera [1], David Sancho [1,4].

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ABSTRACT (350 Word limit)
Doxorubicin-induced cardiotoxicity is a major cardiovascular complication that affects a substantial proportion of cancer patients treated with anthracyclines, often leading to irreversible myocardial injury. Among cardiac immune cells, heart-resident macrophages (rMFs) play a crucial role in maintaining tissue homeostasis by clearing cellular debris, supporting cardiomyocyte function, and orchestrating repair processes following injury. These macrophages exhibit a distinct metabolic profile that supports their specialized functions, suggesting that metabolic integrity may be key to their cardioprotective role.

To investigate the impact of mitochondrial dysfunction in rMFs during anthracycline-induced cardiotoxicity, we generated *Cx3cr1*-Cre *Tfam* f/f mice to selectively target *Cx3cr1*-lineage macrophages, including cardiac rMFs. Flow cytometry and single-cell RNA sequencing (scRNA-seq) analyses revealed a significant reduction of $TIMD4^{+}$ $CCR2^{-}$ heart-resident macrophages in adult *Cx3cr1*-Cre *Tfam* f/f mice, whereas this depletion was not yet evident at 3 weeks of age.

Transcriptomic analysis using bulk RNA sequencing showed downregulation of genes associated with macrophage identity and residency, accompanied by upregulation of cellular stress and apoptosis pathways and suppression of proliferation-related genes, suggesting impaired development and survival of this macrophage subset.

To evaluate the consequences of rMF loss on cardiac function during chemotherapy, mice were treated with doxorubicin for 5 weeks. *Cx3cr1*-Cre *Tfam* f/f mice exhibited markedly reduced survival and severe cardiac dysfunction with echocardiography, together with elevated serum CK-MB and troponin levels and extensive fibrosis.

To uncover potential protective mediators derived from rMFs, we conducted scRNA-seq two weeks after the first doxorubicin dose. Among the top candidates, insulin-like growth factor 1 (IGF-1) emerged as a key cardioprotective molecule. Remarkably, exogenous administration of IGF-1 improved survival, reduced fibrosis, and decreased circulating cardiac damage markers.

Together, these findings demonstrate that mitochondrial integrity is essential for the maintenance and cardioprotective function of heart-resident macrophages. Moreover, they identify IGF-1 as a crucial macrophage-derived factor mediating resilience against anthracycline-induced cardiotoxicity.

Key words: Heart resident macrophages, Insulin-like growth factor 1, doxorubicin-induced cardiotoxicity.

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PhD Student Name and surname: Mª Aránzazu Gómez Díaz
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: ORAL

TITLE: Rank-Driven Metabolic Reprogramming in Postmenopausal Breast Cancer

Authors: María Aránzazu Gómez-Díaz[1], Macarena Pozo-Morales[1], Marina Ciscar[1], María Jimenez[1], Sergi Velasco[1], Víctor Lopez-Díaz[1], Andrés Méndez-Lucas[2], Eva Gonzalez-Suarez[1,3]

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ABSTRACT (350 Word limit)

Background:
Breast cancer is the most commonly diagnosed cancer worldwide, and its prognosis and treatment are significantly influenced by the patient's menopausal status, largely due to associated metabolic changes. Our research has identified RANK receptor expression in breast cancer tumor cells as an independent biomarker of poor prognosis in postmenopausal patients, where RANK signaling is heightened and may influence tumor metabolism. This project aims to elucidate how RANK signaling modulates tumor and systemic metabolism, contributing to the poor prognosis of postmenopausal breast cancer.

Methodology:
Using RANK+/RANK− breast cancer cells implanted into ovariectomized mice—a preclinical model of postmenopause—together with complementary in vitro models, we evaluated RANK functionality through mechanistic, metabolomic, and transcriptomic analyses.

Results:
RANK+ tumors exhibited enhanced aggressiveness in postmenopausal contexts, accompanied by profound metabolic rewiring at both the tumor and systemic levels. Tumor-intrinsic changes included alterations in glucose metabolism and TCA cycle flux, together with marked alterations in mitochondrial number, size, and morphology in tumor cells, consistent with impaired mitochondrial fitness. These changes were exacerbated by the postmenopausal environment. Beyond tumor-intrinsic effects, RANK signaling also rewired systemic metabolism: RANK+ tumors coexisted with an inflammatory environment, characterized by elevated levels of circulating inflammatory cytokines and enhanced inflammatory responses in multiple organs. These inflammatory alterations were accompanied by energetic metabolite imbalances and impaired glucose and insulin tolerance in tumor-bearing ovariectomized mice.

Conclusion:
Altogether, these data suggest that RANK-driven metabolic reprogramming, both within the tumor and at the systemic level, may underlie the increased aggressiveness of RANK+ postmenopausal breast cancer. Understanding these mechanisms could uncover novel metabolic vulnerabilities and offer therapeutic opportunities, with direct translational relevance given the availability of approved RANK pathway inhibitors.

Key words: RANK; Postmenopause; Breast cancer; Metabolism.

PhD Student Name and surname: Miryam Polo Hernández
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: ORAL (or poster or any kind)

TITLE: Uncovering the crucial role of the 3' NCR stem-loops in Foot-and-Mouth disease virus biology: insights from the ΔSL2 mutant

Authors: Miryam Polo Hernández[(1)], Miguel Rodríguez-Pulido[(1)], Samuel J. Dobson[(2)], Rosario Francisco-Velilla[(1)], Nicola J. Stonehouse[(2)], Andrew Tuplin[(2)], Encarnación Martínez-Salas[(1)] and Margarita Sáiz[(1)]

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(2) Astbury Centre for Structural Molecular Biology, University of Leeds. LS2 9JT. Leeds (United Kingdom)

ABSTRACT (350 Word limit)

Background:
Foot-and-mouth disease virus (FMDV) causes a highly contagious disease in livestock, necessitating the development of safer and more effective vaccine candidates. The ~8,500-nt positive-sense RNA genome contains structured non-coding regions (NCRs) at both termini, with the 3' NCR folding in two conserved stem-loops, SL1 and SL2, that play relevant roles for the expression of the viral genome. While deletion of SL1 yields a viable although attenuated virus, deletion of SL2 is lethal in cell culture.This work aimed to characterize the functional contribution of these domains to FMDV replication and their potential as targets for attenuation.

Methodology:
An infectious FMDV-ΔY mutant was generated via RNA trans-complementation in cell culture. To further comprehend the trans-complementation basis, RNA-RNA interaction analyses (EMSA) were performed. Replication and translation kinetics were then analyzed via live-cell imaging of FMDV replicons (GFP/mCherry) to compare mutants against the WT and to evaluate the importance of RNA secondary structure through targeted disruptions induced by Locked Nucleic Acids (LNAs). Viral growth phenotype was evaluated through plaque assays and RT-qPCR and plaque assays during serial passages in swine cells. Additionally, the innate immune response (IFN-β induction) was quantified, and the viral quasispecies evolution was analyzed through high-throughput RNA-seq.

Results:
The lethal ΔY phenotype was successfully rescued *in trans*, supported by EMSA data showing specific RNA–RNA interactions between the SL1 and SL2 domains. Live-cell imaging of replicons provided real-time evidence of differential kinetics in ΔSL1/2 mutants and confirmed that LNA-induced structural disruptions differentially altered the replication dynamics. Although the ΔSL2 mutant initially showed reduced titers, it achieved wild-type levels after serial passage, indicating rapid adaptation. Furthermore, the ΔSL2 mutant maintained the ability to elicit a robust IFN-β response in host cells, similar to the parental virus. RNA-seq analysis unveiled a distinct variant spectrum in ΔSL1/2 mutants compared to the wild-type virus, reflecting unique evolutionary trajectories.

Conclusion:
our results indicate that 3'NCR SLs plays a central role in the FMDV viral cycle, integrating structural, functional and evolutionary layers of genome regulation. These findings provide new mechanistic insights into RNA virus biology and suggest the potential of FMDV-ΔSL2 as a new viral tool for further vaccine development.

Key words: Foot-and-mouth disease virus (FMDV), RNA trans-complementation, Live-cell imaging, Viral attenuation

PhD Student Name and surname: Laura Fernández Rosa
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: ORAL

TITLE: CRISPR-Cas9 Gene Editing in Hematopoietic Stem and Progenitor Cells for the treatment of Congenital Dyserythropoietic Anemia Type II

Authors: Laura Fernandez[1,2], Miruna Giurgiu[1,2], Mercedes Dessy-Rodriguez[1,2],Jose Carlos Segovia[1,2] and Oscar Quintana-Bustamante[1,2]

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ABSTRACT (350 Word limit)

Background:

Congenital Dyserythropoietic Anemia type II (CDAII) is a rare inherited disorder with an incidence of about 0.71 cases per million. It is characterized by ineffective erythropoiesis and accumulation of binucleated erythroblasts in the bone marrow. CDAII is caused by mutations in the *SEC23B* gene, essential for the vesicular trafficking between the endoplasmic reticulum and the Golgi apparatus. Main clinical features include varying degrees of anemia and splenomegaly, among others. Current treatments are mainly palliative, such as transfusions. Allogeneic stem cell transplantation is the only curative option but is limited by severe associated risks and donor availability. Gene editing in hematopoietic stem and progenitor cells (HSPCs) offers a promising alternative. This study aims to develop a clinically applicable CRISPR–Cas9 therapy for CDAII**.**

Methodology:

We developed a knock-in strategy to insert a promoterless SEC23B cDNA into its endogenous locus in human mobilized peripheral blood HSPCs (mPB-HSPCs). Cells were electroporated with a Cas9/sgRNA ribonucleoprotein complex (RNP) and transduced with an AAV6 vector carrying the repair template. To optimize efficiency and mitigate AAV6-associated toxicity, we evaluated the Homologous Directed Repair (HDR) enhancer i53BP1 at various concentrations (6.25–25 µM). This small molecule increases gene targeting by blocking the Non-Homologous End Joining (NHEJ) pathway, thereby HDR. Editing frequency was assessed by digital droplet PCR, while cell functionality was validated via colony-forming unit (CFU) assays and transplantation into immunodeficient mice.

Results:

High AAV6 doses are detrimental to HSPC fitness and increase manufacturing costs. Our results demonstrate that adding i53BP1 significantly improves efficiency. At a concentration of 12.5 µM, the i53BP1 addition almost doubled the knock-in frequency, reaching 37.35%. *In vitro* HSPC functionality was preserved, as confirmed by CFU assay. Human hematopoietic reconstitution in immunodeficient mice is currently under evaluation to confirm long-term safety and efficacy.

Conclusion:
The use of i53BP1 increases therapeutic cDNA knock-in efficiency at the *SEC23B* locus

without compromising the clonogenic capacity of mPB-HSPCs. This optimized approach provides a more efficient and safer gene-editing strategy, representing a significant step toward a viable therapy for CDAII patients.

Key words: Gene editing; Hematopoietic Stem and Progenitor Cells; Homology Directed Repair; 53BP1 inhibitor.

PhD Student Name and surname: Carmen Campa
UAM PhD program: Medicina y Cirugía
COMMUNICATION TYPE: POSTER

TITLE: The relationship between chronic diseases, pain and loneliness

Authors: Carmen Campa[a,b], María Cabello[b,c,d], Marta Miret[b,d]

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ABSTRACT (350 Word limit)

Background: Chronic conditions are increasingly linked to higher levels of loneliness. This study investigated the complex relationships between chronic diseases, pain intensity, and social isolation.
Methods: Data were drawn from the Spanish Longitudinal Study on Aging and Health, focusing on a 2019 cross-sectional baseline of 3,002 adults in Madrid and Barcelona. Interviews were conducted via computer-assisted personal interviewing (69.9% response rate) between 2019 and 2021. Loneliness was evaluated using the UCLA scale, with data analyzed via ordinal logistic regression.
Results: Preliminary analysis showed that chronic diseases were associated with significantly higher loneliness (OR=1.68; 95%CI 1.30, 2.17). However, once the model accounted for pain intensity over the previous 30 days, the direct association between multiple chronic diseases and loneliness was no longer statistically significant (OR=1.10; 95%CI 0.82, 1.47). Instead, pain intensity emerged as a primary factor:

- **Mild pain:** OR=1.43 (95%CI 1.10, 1.85)
- **Moderate to extreme pain:** OR=1.51 (95%CI 1.14, 2.01)

Conclusions: Physical pain appears to be a key mediator in the relationship between chronic illness and loneliness. These results suggest that clinical interventions focused on pain management may be a viable strategy for reducing social isolation. Further longitudinal research is required to confirm these pathways.
Keywords: loneliness, chronic diseases, pain, disability

PhD Student Name and surname: María Redondo Moya
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: Poster

TITLE: **New insights in the modulation of the electrophysiology of $K_V1.5/K_V\beta2.1$ channels by Lgi4**

Authors: María Redondo-Moya[1,2*], Paula G. Socuéllamos[1,3], Alejandro Gutiérrez-Yeves[1], Marta Gutiérrez-Rodríguez[4] & Carmen Valenzuela[1,5]

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ABSTRACT (350 Word limit)

Background:
The leucine-rich glioma-inactivated protein family is a four-member family (Lgi1-4) that are best known in neurons, where they interact with different members of the ADAM protein family: ADAM23/22/11. They are part of a larger multiprotein complex that includes K_V channels. Lgi proteins act as regulatory subunits of K_V1 and K_V4 channels, modifying their trafficking and biophysical properties in neurons. However, little is known about the expression and impact of Lgis in the heart. We demonstrated that Lgi3-4 are the only Lgi proteins present in human myocardium, so we focused on studying their effects on cardiac potassium currents. In atrial cardiomyocytes, $K_V1.5$ channels generate the I_{Kur}, which is essential in human atrial repolarization. To generate this current, $K_V1.5$ interacts with several regulatory subunits, such as $K_V\beta$s, forming signaling complexes (*channelosomes)*. Previous patch-clamp experiments conducted by our laboratory on transfected cells show that Lgi3-4 do not induce any effect on the $K_V1.5$ channel on its own, but if $K_V\beta$s are also expressed, Lgi3-4 impair the $K_V1.5/K_V\beta$ interaction causing, in the case of $K_V1.5/K_V\beta2.1$: i) a decrease in the current amplitude, ii) a shift in the activation curve towards more positive potentials, and iii) a reduction in the degree of C-type inactivation induced by $K_V\beta2.1$. Given the well-documented role of Lgis as secreted molecules through their interaction with ADAM proteins, some of these effects might be attributable to an extracellular function of Lgis.

Methodology:
The culture media were analyzed using Western Blot assays to verify that Lgi4 is also secreted in our heterologous system. Next, we conducted conditioned-medium experiments by incubating cells expressing $K_V1.5/K_V\beta2.1$ (with or without ADAM23) with medium derived from cells expressing Lgi4. Subsequently, we registered the currents generated by these cells using the whole-cell configuration of the patch-clamp technique.

Results:

Our results showed that the presence of Lgi4 in the culture medium replicates the reduction in the degree of slow inactivation previously observed, being this effect enhanced when

ADAM23 is also expressed, while the current amplitude and the activation curved remain unchanged.

Conclusion:
These results suggest that Lgi proteins may exert their effects on the $K_V1.5/K_V\beta$ *channelosome* through a combination of extracellular and intracellular mechanisms.

Key words: Kv1.5; Kvβ; Lgi; ADAM

PhD Student Name and surname: Laura de la Bastida Casero
UAM PhD program: Biociencias Moleculares
COMMUNICATION TYPE: POSTER

Targeting β3-Adrenergic Receptors as a Novel Therapeutic Approach for Endothelial Dysfunction and Cardiopulmonary Impairment in Pulmonary Arterial Hypertension

Laura de la Bastida-Casero[1], Yolanda Sierra-Palomares[1], Bertha García-León[1], Lola Navarro-Llinares[1], María Villalba-Orero[2, 3], Eduardo Oliver[1, 3, 4].

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ABSTRACT

Background:
Pulmonary arterial hypertension (PAH) is a progressive and potentially fatal disease characterized by endothelial dysfunction, pulmonary vascular remodelling, and a sustained elevation of pulmonary arterial pressure. These alterations increase right ventricular (RV) afterload, ultimately leading to RV hypertrophy, heart failure, and premature mortality. Endothelial activation also promotes the expression of adhesion molecules that favor leukocyte recruitment, inflammation, and structural changes in the pulmonary vasculature. Therefore, addressing endothelial dysfunction could represent an effective therapeutic strategy. In this study, we evaluated the effects of the β3-adrenergic receptor (β3-AR) agonists -Mirabegron and Vibegron, currently approved for overactive bladder-, as potential treatments for PAH.

Methodology:
PAH was induced in mice using the hypoxia + Sugen model. Subsequently, the animals were treated with β3-AR agonists to evaluate their effects on the lungs and heart. To investigate molecular changes in lung tissue, protein expression was analyzed by Western blot and immunofluorescence, paying particular attention to markers of endothelial activation and vascular remodelling, including E-selectin, VCAM-1, GDF15 and α-SMA. Hemodynamic assessment was also performed to measure right ventricular systolic pressure (RVSP), and RV hypertrophy was determined. Finally, cardiac structure and function were examined using magnetic resonance imaging (MRI), while positron emission tomography (PET) was used to evaluate metabolic alterations in both the heart and lungs.

Results:
Treatment with β3-AR agonists reduced pulmonary expression of E-selectin, VCAM-1, GDF15 and α-SMA compared to untreated mice with PAH. These molecular changes were associated with lower RVSP and attenuation of RV hypertrophy. Imaging analyses showed a trend toward less RV dilation and improved cardiac function. Furthermore, 18F-FDG PET imaging suggested a partial reduction of cardiac and pulmonary glucose uptake. These findings are consistent with our previous observations, which support a protective effect of mirabegron on the pulmonary endothelium.

Conclusion:
β3-AR agonists demonstrate promising therapeutic effects in PAH by improving hemodynamic parameters, reducing vascular remodelling, and modulating endothelial dysfunction and inflammation. Furthermore, biomarkers such as E-selectin, VCAM-1, and

GDF15 can help stratify disease severity and support precision medicine approaches. Taken together, these results reinforce the potential for repurposing β3-AR agonists as a novel strategy for PAH.

Key words: Pulmonary arterial hypertension; endothelial dysfunction; Vascular remodelling; β3-adrenergic receptor; Mirabegron.

PhD Student Name and surname: Adriana Ferreiro De Aguiar
UAM PhD program: Biociencias Moleculares
COMMUNICATION TYPE: POSTER

TITLE: Longitudinal MRI and Spectroscopy study of Bariatric Surgery Induced Brain Changes in obese mice

Authors: Adriana Ferreiro[1], Maya Holgado[1], Pilar López-Larrubia[1] and Blanca Lizarbe[1,2]

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ABSTRACT

Background:
Obesity is a chronic disease associated with several pathologies, including type 2 diabetes, cardiovascular disease, and neurodegenerative diseases. Bariatric surgery (BS) is one of the most effective approaches for achieving a non-obese body mass index in an increasing proportion of the population. Beyond weight reduction, BS alters metabolism, gut microbiota, and brain function. Among available techniques, vertical sleeve gastrectomy (VSG) is one of the most common, removing 70–80% of the stomach. This study investigates the effects of VSG on the brain in a rodent model of diet-induced obesity using diffusion kurtosis imaging (DKI).

Methodology:
26 C57BL/6 mice (male and female) were fed a high-fat, high-sugar (HFHS; 45 kcal% fat, 30 kcal% sucrose) diet. After 20 weeks, obese mice were assigned to either a sham-operated group or a BS group. Post-surgery, animals were maintained on a liquid diet for 1 week, followed by a chow diet for 6 weeks. Body weight (BW) was monitored daily. Brain diffusion magnetic resonance imaging was acquired pre-surgery and at 3 and 6 weeks post-surgery. Immunofluorescence analysis was performed to assess glial markers, and high-resolution magic angle spinning spectroscopy (HR-MAS) was used to quantify neurometabolite concentrations related to glial activity, membrane turnover, energy metabolism, and neuronal integrity.

Results:
A significant reduction in body weight was observed in both groups; however, this decrease was more pronounced in the BS group. DKI analysis in the hypothalamus and hippocampus showed significant *Type:State* effects on RD ($p < 0.001$; $p < 0.01$), with increased RD in the BS group and decreased RD in the sham group (Pre vs. Post6w). In the hippocampus, fractional anisotropy (FA) showed a significant interaction ($p < 0.001$), with lower FA in the BS group at week 6. Qualitative analysis indicated more ramified microglia in the BS group and a more amoeboid morphology in the sham group.

Conclusion:
In summary, treatment with BS, which effectively reduced body weight, resulted in decreased FA values and increased RD, in agreement with reversal of the inflammatory state induced by obesity. Significant differences in microglial cell morphology were also observed. HR-MAS data are currently being processed and analyzed.

Key words: Obesity, Neuroinflammation, Bariatric Surgery, Magnetic resonance imaging, HR-MAS spectroscopy

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PhD Student Name and surname: Gonzalo Soria Alcaide
UAM PhD program: Biociencias Moleculares
COMMUNICATION TYPE: poster

TITLE: Integration of scRNA-seq and Topological Data Analysis for the Study of Leukemic Niches

Authors: Soria-Alcaide Gonzalo[1,2], Marta Portasany-Rodriguez[1,2], Jaanam Lalchandani[1,2], Elena G. Sánchez[1], Ramírez-Orellana Manuel[1,3,4], García-Martínez Jorge[5]

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ABSTRACT (350 Word limit)

Background:
The heterogeneity of pediatric **Acute Lymphoblastic Leukemia (ALL)** presents a biological challenge where traditional diagnostics often fall short by failing to fully account for the tumor ecosystem. The dynamic interaction between leukemic cells, the stroma, and biophysical factors generates **"protective niches"** that drive therapeutic resistance and relapse. We propose an integrative framework that fuses **scRNA-seq** with mathematical models based on **Topological Data Analysis (TDA)**. This approach enables the characterization of the microenvironment and the identification of latent patterns prior to clinical manifestation.

Methodology:
Bone marrow scRNA-seq profiles from murine models (**WT and Pax5+/-** before and after disease onset) were analyzed. Following single-cell processing via the ***Crocketa* pipeline**, TDA was applied using the **giotto-tda** library on low-dimensional projections to compute **Persistent Homology**. We quantified the "shape" of the ecosystem through **Betti curves** and **topological entropy**, correlating geometric structures with biological realities: stable subpopulations (β0), cellular transition cycles (β1), and the architecture of microenvironmental niches (β2).

Results:
The analysis effectively differentiated healthy from leukemic states at both the global and population levels. Betti curves revealed a distinctive peak in dimensions **β1 (cycles)** and **β2 (voids)** exclusive to leukemic samples, coinciding with significantly reduced topological entropy. These findings indicate an **"ecosystem homogenization,"** directly correlated with the massive expansion of topologically similar B-cell clones and the structural alteration of critical progenitor subpopulations.

Conclusion:
Our results validate topological analysis as a robust tool for unequivocally differentiating healthy and pathological states across global and subpopulation

scales. The inclusion of **pre-leukemic models** offers a unique opportunity to isolate the evolution of specific functional niches. This analytical framework could facilitate the identification of novel **topological biomarkers** applicable to early-stage diagnostics.

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PhD Student Name and surname: Sara Ruiz Buceta
UAM PhD program: Biociencias moleculares
COMMUNICATION TYPE: Poster

TITLE: MAFG-driven melanomagenesis is partially recapitulated by the ECM remodeler LOXL2

Authors: Sara Ruiz Buceta[1], Cesar Lumbreras[1], María José Beato[3], Ander Mayor[4], Michael Martinez[2], Florian A. Karreth[2], Inmaculada Ibañez de Cáceres[1], César Casado Sánchez[5], Olga Vera[1]

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ABSTRACT (350 Word limit)

Background:.

Melanoma is a highly aggressive cancer that affected over 325,000 people in 2020. Although activating mutations in BRAF and NRAS occur in over 80% of cases, they are not sufficient on their own to induce full melanomagenesis; further epigenetic and transcriptional alterations are required for tumor progression. In this context, MAFG has emerged as a potential oncogene capable of reshaping the transcriptomic and epigenomic landscape of melanoma cells. Data from The Cancer Genome Atlas revealed frequent amplification and/or overexpression of MAFG, whose stability is enhanced via ERK-mediated phosphorylation following MAPK pathway hyperactivation. This transcription factor promotes DNA hypermethylation and induces a phenotypic shift away from melanocytic traits via interaction with MITF. However, its role in melanoma remains poorly characterized.

Methodology:

We investigated the functional role of MAFG in melanoma progression, focusing on its regulation of extracellular matrix and adhesion-related genes. Transcriptomic analyses were performed to identify downstream targets, followed by gain- and loss-of-function approaches to validate gene expression changes. Epigenetic reactivation assays using 5-AZA-citidine were conducted to evaluate transcriptional regulation. Functional in vitro assays, including overexpression, silencing, and rescue experiments, were used to determine the contribution of key targets. Additionally, protein secretion into conditioned media and correlation with patient plasma levels were assessed.

Results:

Transcriptome analyses identified LOXL2, COL4A1, LAMA2, JUP, CNTN4, and SPOCK1 as potential downstream targets of MAFG. Modulation of MAFG expression altered LOXL2, JUP, and SPOCK1 levels in agreement with RNA-sequencing data, with similar expression patterns observed in melanoma patient datasets. Epigenetic reactivation experiments

demonstrated that MAFG suppresses JUP expression through transcriptional silencing mechanisms. Functional assays showed that LOXL2 overexpression in LOXL2Low cells phenocopied MAFG oncogenic activity, whereas LOXL2 silencing in LOXL2High cells did not fully recapitulate the effect. Rescue assays suggested cooperative activity between LOXL2 and MAFG. Furthermore, LOXL2 secretion was increased in MAFG-expressing cells and correlated with MAFG levels in patient plasma.

Conclusion:
Overall, our study reveals that MAFG and its downstream gene network play key roles in melanomagenesis and extracellular matrix regulation, highlighting MAFG, LOXL2, and JUP as promising biomarkers and potential therapeutic targets in melanoma.

Key words: melanoma; MAFG; LOXL2; extracellular matrix; epigenetic regulation; biomarkers

Note: Please send this fully completed abstract as a PDF file, including your surname in the filename, to vicedecanato.medicina.investigacion@uam.es, using "Abstract Workshop 2026" as the email subject.

PhD Student Name and surname: Andrea Rodríguez-San Pedro
UAM PhD program: Molecular Biosciences (Science)
COMMUNICATION TYPE: Poster

Surface Functionalization of Multimodal Iron Oxide Nanotracers with Glioblastoma-Targeting Ligands for Theranostic Applications

Authors: Andrea Rodríguez-San Pedro[1], Fernando Herranz Rabanal[2]

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ABSTRACT

Background:
Radiopharmaceuticals that combine diagnostic and therapeutic isotopes are at the forefront of next-generation cancer theranostics. Recently, our group demonstrated that citrate-coated ultrasmall iron oxide nanotracers (IONT) act as a universal chelator platform, enabling rapid incorporation of a wide range of radiometals while preserving consistent physicochemical and biological properties across PET, SPECT, and therapeutic applications.[1] In addition, these nanoparticles exhibit intrinsic contrast properties for magnetic resonance imaging, supporting their use as multimodal imaging agents.[1] Building on this platform, the present study explores the incorporation of glioblastoma-targeting ligands onto the surface of IONP as a preliminary step toward the development of targeted nano-radiotracers.

Methodology:
Surface functionalization was optimized under "cold" conditions on non-radiolabeled nanoparticles. The IONP were synthesized using the microwave-assisted reaction that was previously reported.[1] Two independent targeting approaches were selected based on complementary biological mechanisms in glioblastoma.

First, IONP-tetrazine were functionalized with glucuronic acid-TCO via tetrazine/ trans-cyclooctene (TCO) bioorthogonal ligation. This approach exploits the overexpression of glucose transporters (GLUT1/GLUT3) in glioblastoma, which has been previously demonstrated to enable metabolically driven uptake and transcytosis of IONP.[2]

In a second approach, a lysine-extended T7 peptide (K-T7; sequence: K-HAIYPRH) was selected for targeting the transferrin receptor, which has been found to be overexpressed in glioblastoma and brain endothelial cells and is known to mediate transcytosis across the blood–brain barrier.[3] Conjugation was accomplished via carbodiimide-mediated coupling using EDC/sulfo-NHS chemistry. This method results in the formation of stable amide bonds between surface-exposed carboxyl groups from the citrate coating of the nanoparticles and the primary amines of the K-T7 peptide.

Results:
Fluorescence-based quantification studies suggest the successful incorporation of K-T7 and glucuronic acid onto the surface of our IONP, supported by complementary characterization techniques including thermogravimetric analysis (TGA) and FTIR spectroscopy. Both conjugation strategies proved to be effective and compatible with the IONP platform.

Conclusion:
The feasibility of functionalizing IONPs with glioblastoma-targeting ligands under "cold" conditions has been demonstrated. These results provide a basis for future translation to radiolabeled systems. Overall, this work supports the development of targeted IONT as a

versatile theranostic platform combining radiometal incorporation with biologically driven tumor targeting.

Key words: *Iron Oxide Nanoparticles, Nano-radiopharmaceuticals, Glioblastoma*

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PhD Student Name and surname: Pilar Rodriguez-Martin
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: Poster

TITLE: Hippocampal function alterations in mouse models of Lamb-Shaffer syndrome

Authors: P. Rodriguez-Martin[1], A. Sanz[1], A. Segovia[1], J. Gómez[1], E. Cintado[1], P. Tirado-Melendro[1], E. Monserrat[1], C. Domínguez[1], J.L. Trejo[1], A.V. Morales[1]

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ABSTRACT

Background:
Lamb-Shaffer Syndrome (LAMSHF; OMIM #616803) is a rare genetic disorder caused by mutations in the SOX5 gene, affecting multiple organ systems. Many of the manifestations in LAMSHF patients are of neurological origin, including intellectual disabilities, generalized delays in speech and learning, loss of memory, anxiety, and behaviors associated with autism spectrum disorders (ASD), such as social deficits and stereotypical behavior. Understanding the pathophysiology of this complex syndrome demands the development of robust animal models to study the individual neural components involved.

Methodology:
In this study, we examined hippocampal function using two distinct LAMSHF mouse models: i) a conditional loss-of-Sox5 model during embryonic development specifically in the CA2 region of the hippocampus (Amigo2-cre/$Sox5^{fl/fl}$; $Sox5^{Amigo2}$), a region crucial for social memory; and ii) a tamoxifen-inducible conditional loss-of-Sox5 model specific to the central nervous system (Sox2-$creER^{T2}$ /$Sox5^{fl/fl}$ /YFP+; $Sox5^{icKO}$), which enables Sox5 depletion in neural stem cells (NSCs) of the subgranular zone of the dentate gyrus, responsible for adult neurogenesis maintenance, a process crucial for spatial memory. With these two models, we combined cellular characterization strategies and transcriptomic tools with an extensive battery of behavioral assays.

Results:
We found that: i) $Sox5^{Amigo2}$ mice exhibited alterations in social memory related to ASD traits, and ii) $Sox5^{icKO}$ model displayed impaired adult neurogenesis and delay in granule neuron maturation, leading to deficits in spatial and contextual memory, both common features in LAMSHF.

Conclusion:
These findings provide valuable insights into the neurological mechanisms underlying the syndrome and highlight the potential of these mouse models for the future exploration of therapeutic approaches.

Key words: Lamb-Shaffer syndrome; Hippocampus; Spatial memory; Adult Neurogenesis; Autism Spectrum Disorder

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PhD Student Name and surname: Pooria Mohammadi Arvejeh
UAM PhD program: Molecular Bioscience
COMMUNICATION TYPE: Poster

TITLE: Immune Organ–Targeted MicroRNA Delivery Systems for Cancer Nanoimmunotherapy

Authors: Pooria Mohammadi Arvejeh[1], Guillermo González Salso[1], Miguel Fernandez de la Torre[2], Clara Gomez-Cruz[3], Daniel Garcia-Gonzalez[2], Lola Fernandez-Messina[4], Milagros Castellanos[1]

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ABSTRACT (350 Word limit)

Background:
Tumors evade immunity by limiting T cell priming and driving macrophages toward suppressive phenotypes (1). MicroRNAs can rebalance these pathways but require carriers that reach immune organs (2). Protein nanocages such as encapsulins are programmable, biocompatible, and efficiently internalized by phagocytes, supporting macrophage targeting (3). Alternatively, RBC biodistribution depends on membrane mechanics, as reduced deformability promotes spleen retention (4, 5). We hypothesize that i) nanocage-mediated miRNA delivery can activate macrophages, while ii) AuNP hitchhiking on RBCs may tune spleen-directed biodistribution.

Methodology:
Enc nanocages were expressed in *Escherichia coli*, purified by ultracentrifugation and chromatography. MiRNA cargo was loaded by controlled disassembly–reassembly. MiRNA loading was assessed by nuclease challenge and gel mobility assay readouts. Macrophages will be treated with Enc–miRNA formulations. Uptake, viability and immune (M1) reprogramming will be assessed further. On the other hand, we assessed the mechanical features of RBCs under different conditions to determine how changes in membrane rigidity influence nanoparticle loading and biodistribution, aiming to establish a future correlation between AuNP–RBC loading and preferential spleen delivery.

Results:
Encs formed well-defined nanocage–like particles after purification, as proved by negative-stain TEM and AFM, and supported miRNA association under optimized loading conditions. *In vitro*, preliminary assays showed activation of human J77 T cells following Enc exposure, while encapsulin–miRNA uptake, viability, and the activation and polarization shift of macrophages toward an antitumor phenotype (M1) are currently under evaluation. If confirmed, these findings would provide proof-of-concept that encapsulin–based miRNA delivery can reprogram immune cells, motivating further evaluation across complementary delivery routes and more complex tumor-relevant models in vitro/in vivo. Moreover, mechanical actuation increased RBC stiffness and elongation, reduced circularity, and lowered deformability. These effects are expected to scale with AuNP–miRNA loading and shifted RBCs toward spleen-enhanced NP delivery, preparing them to step forward the in vivo analyses.

Conclusion:
This work introduces two novel, bio-inspired organ–targeted strategies for nucleic acids delivery, to our knowledge not previously explored, for miRNA-based immunomodulation. If successful, the platforms could enable broad immune reprogramming and be readily extended to multiple immune-related conditions beyond the initial models studied.

Key words: Immune reprogramming; Protein Nanocages; RBC hitchhiking; Gold nanoparticle; miRNA delivery.

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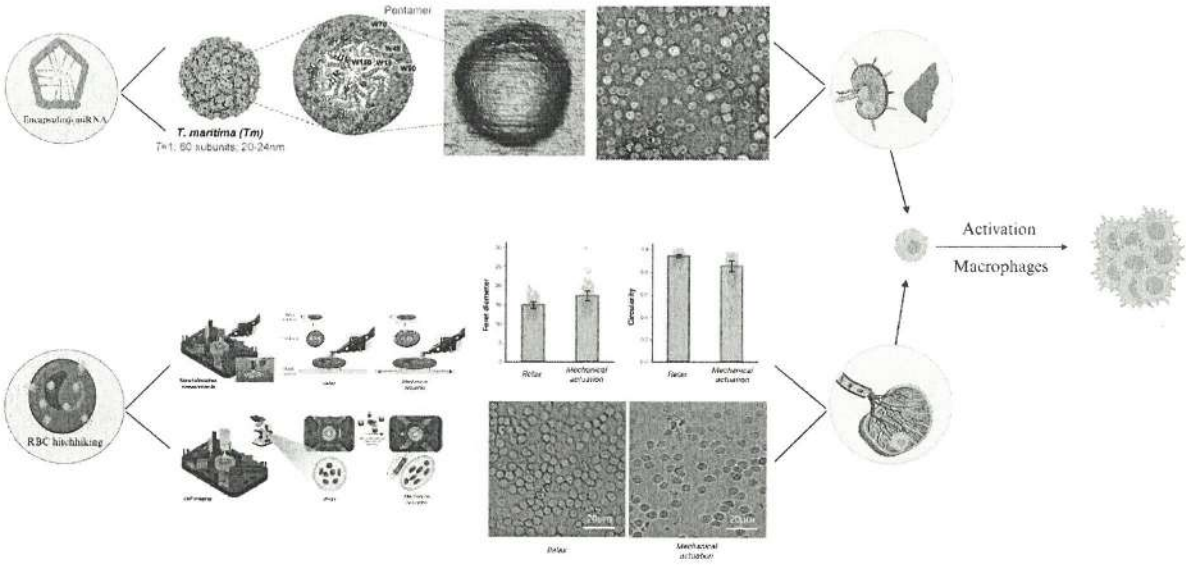

PhD Student Name and surname: Lucía Miranda Alcaraz
UAM PhD program: Biociencias Moleculares
COMMUNICATION TYPE: POSTER

TITLE: Identification of Structural Variants in *BMPR2* by whole-genome sequencing in patients with pulmonary arterial hypertension

Authors: Lucía Miranda-Alcaraz[1,2,3,4], Mónica Mora-Gómez [1,2,3], Natalia Gallego-Zazo [1,2,3], Alejandro Cruz-Utrilla [5,6,7], María Jesús del Cerro Marín [8], Spanish PAH Consortium [1,2,3,5], Juan Andrés Jiménez-Estrada [1,2,3], Tomás Valle [1,2,3], Mario Cazalla [1,2,3], Manuel Rodríguez-Canó [1,2,3], Cristina Silván [1,2,3], Valeria Vásquez-Amell [1,2,3], Pedro Arias [1,2,3], Julián Nevado [1,2,3], Pilar Escribano-Subías [5,6,7], Pablo Lapunzina [1,2,3] and Jair Tenorio-Castano [1,2,3]

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ABSTRACT (350 Word limit)

Background:
Pulmonary arterial hypertension (PAH) is a severe disease characterized by high pulmonary artery pressure. Without treatment, PAH can lead to heart failure and premature death. Genetic factors play a significant role in PAH, and several genes have been associated with its development. *BMPR2* is the most frequently mutated gene among patients with idiopathic or heritable PAH. This study aimed to identify structural variants (SVs) affecting *BMPR2* in patients with idiopathic or heritable PAH who had previously undergone inconclusive genetic testing.

Methodology:
We analyzed a cohort of 158 individuals (101 PAH patients and 57 relatives) using whole-genome sequencing (WGS). Variants were prioritized using a custom in-house pipeline and classified according to ACMG guidelines.

Results:
Six patients with idiopathic PAH (5.95%) were identified as carrying clinically significant SV encompassing the *BMPR2* gene, affecting either coding or non-coding regions. The detected SVs included two duplications and four deletions.

Conclusion:
These findings highlight the increased diagnostic yield achieved by whole-genome sequencing, which enables the detection of SV that may be missed by standard-of-care approaches such as exome sequencing. In addition, we developed an in-house pipeline specifically optimized for SV analysis from WGS data in patients with PAH.

Key words: Copy-number variation (CNV); whole genome sequencing (WGS); pulmonary arterial hypertension (PAH).

PhD Student Name and surname: Diego Matas Aguado
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: POSTER

TITLE: **Deciphering the role of *NOTCH2* on Endocrine Pancreas Development**

Authors: Diego Matas-Aguado[1], Mario Hernanz[1], Marta G. de la Fuente[1] and Alberto Bartolomé[1,2]

AFFILIATIONS:
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[2]CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Madrid, Spain.

ABSTRACT

Background:
Notch is an evolutionarily conserved pathway critical for cell-fate decisions in most tissues, playing an important role in the proliferation and differentiation of pancreatic progenitors during embryonic development. Single nucleotide polymorphisms (SNPs) within the NOTCH2 locus have been associated with increased risk of type 2 diabetes (T2D), according to genome-wide association studies (GWAS). Expression Quantitative Trait Loci (eQTL) point towards lower NOTCH2 expression in adult pancreas. Although we know Notch signaling is orders of magnitude more active in the developing pancreas, there is no database in which we could assess the impact of T2D risk associated SNPs during human embryonic development. Our goal is to characterize the role of NOTCH2 during endocrine pancreas differentiation.

Methodology:
We utilized human pluripotent stem cells (hPSCs) and differentiation protocols as a platform to model human endocrine pancreas development. *NOTCH2* loss-of-function hPSC lines were generated using CRISPR/Cas9. Transcriptomics and other techniques were employed to gauge differences along the differentiation process.

Results:
Step-wise differentiation of hPSCs to β-like mature cells revealed peak Notch activity at the pancreatic progenitor stage. Differentiation from *NOTCH2*-deficient hPSCs resulted in less proliferative pancreatic progenitor cells and furthermore reduced insulin-expressing cells at mature β cell stage. Genomic, transcriptomic and functional analyses revealed altered expression of canonical markers.

Conclusion:
The link between reduced NOTCH2 expression and T2D diabetes may originate from disrupted Notch signaling in early pancreatic progenitors, which could lead to altered endocrine pancreas differentiation, impaired beta cell specification, and ultimately suboptimal beta cell mass acquisition, predisposing to glucose homeostasis defects.

Key words: T2D, transcriptomics, endocrine pancreas, insulin, SNPs

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PhD Student Name and surname: Noelia Martín Bermejo
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: Poster

TITLE: Generation of a Model to Study Early Stages of Non-Syndromic Thoracic Aortic Disease

Authors: **Noelia Martín-Bermejo *[1,2]**, Iván Alarcón-Ruiz *[2,3], Marta Toral[2,4], Sara Martínez-Martínez[2,3], María José Méndez-Olivares[2,3], Miguel R. Campanero [#,2,3] and Juan Miguel Redondo [#,2,3].

AFFILIATIONS:

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4 Department of Pharmacology, School of Pharmacy, University of Granada, 31 Granada, Spain.

**These authors contributed equally to this work*

#These authors jointly directed this work

ABSTRACT (350 Word limit)

Background:

Thoracic aortic aneurysms and dissections (TAADs) are severe cardiovascular diseases characterized by progressive aortic dilation and high risk of acute dissection, leading to significant morbidity and mortality. TAADs are classified as syndromic or non-syndromic depending on the presence of systemic manifestations. Currently, no effective pharmacological treatments are available for non-syndromic TAADs. Although several molecular targets have been identified in syndromic forms, few have been associated with non-syndromic aortopathies, partly due to the lack of appropriate experimental models to study early disease mechanisms. Mutations in *ACTA2*, encoding α-smooth muscle actin (αSMA), a key component of the vascular smooth muscle cell (VSMC) contractile apparatus, are strongly associated with disease development. A better understanding of early molecular and structural alterations is essential to identify novel therapeutic targets. This study aims to develop an experimental model to investigate early stages of non-syndromic TAAD associated with *ACTA2* mutations.

Methodology:

A deficiency mouse model was generated via intrajugular injection of lentiviral vectors carrying shRNAs targeting *Acta2*. To mimic the human condition, highly penetrant ACTA2 mutations were overexpressed in the aorta of wild-type mice using lentiviral particles with aortic tropism, enabling targeted *in vivo* gene modulation. VSMCs were used for *in vitro* validation. *In vivo*, aortic diameters were monitored by ultrasound imaging (Vevo 2100) at baseline and during follow-up; systolic blood pressure was measured longitudinally using a tail-cuff system (BP-2000); transduction efficiency was assessed by qPCR and immunofluorescence; and Verhoeff–Van Gieson staining was used to evaluate aortic wall integrity.

Results:
In vivo, targeted silencing of *Acta2* and overexpression of *ACTA2* mutations induced early aortic alterations, including elastic fiber fragmentation and progressive aortic dilation, as assessed by ultrasound imaging. In addition, sh*Acta2*-treated mice showed hypotension compared to controls. These findings recapitulate key structural and functional features of non-syndromic thoracic aortic disease.

Conclusion

Silencing of *Acta2* and overexpression of *ACTA2* mutations in the aorta of wild-type mice using intrajugularly delivered lentiviral vectors recapitulate key features of human aortic disease associated with *ACTA2* defects. This approach enables disease induction at any stage of life, establishing a novel and versatile mouse model for studying early-stage disease mechanisms.

Key words: Non-syndromic TAADs; Mouse model; Lentivirus; *Acta2*

PhD Student Name and surname: Clara Gordillo Gayo
UAM PhD program: Biociencias moleculares (Medicina)
COMMUNICATION TYPE: poster (or poster or any kind)

TITLE:

Characterization of pathogenic mutations and CIN signatures in tumor from high-risk BRCAX ovarian cancer patients

Authors:_
Clara Gordillo Gayo[1], Noelia Sánchez[1] & María José García Pérez[1]

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ABSTRACT (350 Word limit)

Introduction:
Epithelial ovarian cancer is the most lethal gynecologic malignancy, with poor prognosis driven by late diagnosis and frequent relapse. Around 20% of cases stem from hereditary predisposition involving DNA repair genes such as BRCA1/2, yet many high-risk families remain genetically unexplained ("BRCAX or non-BRCA families"). Recent advances have facilitated the identification of patterns (signatures) of chromosomal instability (CIN) associated to the specific putative CIN-causal mechanisms. Since most BRCAX tumors exhibit CIN, by characterizing their CIN-associated signatures we aim to uncover previously unexplored biological mechanisms and identify new ovarian susceptibility genes.

Methods:
This retrospective study analyzed 33 FFPE epithelial ovarian tumors from BRCAX high-risk patients and 7 BRCA1/2 or RAD51C tumors from carriers included as controls. Tumor DNA was extracted using standard procedures and characterized by using a customized targeted NGS gene panel and low-depth shallow Whole Genome Sequencing (sWGS). Pathogenic variants in driver genes were called using a three-caller pipeline followed by stringent filtering. Absolute Copy Number Variants (CNV) profiles were derived and five key CIN features and Bayesian NMF over 43 components were applied to identify copy-number signatures and quantify their activities. tumors were then grouped according to shared signatures.

Results:
At least one pathogenic driver variant was detected in all samples. Previously reported mutations in control tumors and typical histotype-associated driver genes were consistently identified, supporting the robustness of the technical and bioinformatic pipelines. Several tumors carried pathogenic *BRCA1/2* variants with high allele frequencies that supported a germline origin and that were likely missed in previous less sensitive testing procedures. Most samples clustered with signatures associated with homologous recombination deficiency, replication stress, and chromosome missegregation via defective mitosis. Whole-exome sequencing (WES) will be performed on the normal matched samples corresponding to tumors representing the three most enriched biological pathways.

Conclusions:
Our preliminary data provides a foundation for an innovative approach that uses CIN signatures to uncover novel mechanisms behind non-BRCA familial ovarian

cancer. This approach will help group samples by altered molecular pathways, facilitating the discovery of novel genes in a non-biased manner.

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PhD Student Name and surname: Marta Alonso Moreno
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: POSTER

TITLE: Regional differences in dendritic spine morphology and innervation of the trisynaptic circuit of a mouse model of GSK-3β overexpression.

Authors: Marta C. Alonso-Moreno[1,2,3]; Julia Terreros-Roncal[1,2]; Carla B. Rodríguez-Moreno[1,2]; Jesús Ávila[1,2]; María Llorens-Martín[1,2,3].

AFFILIATIONS:
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[2]*Centro de Investigación Biomédica en Red (CIBERNED), Madrid, España.*
[3]*Departamento de Biología Molecular, Facultad de Ciencias, Universidad Autónoma de Madrid (UAM), Madrid, España*

ABSTRACT (350 Word limit)

Background:
The trisynaptic circuit, which includes the entorhinal cortex (EC), dentate gyrus (DG), and Cornu Ammonis (CA1, CA2, and CA3) of the hippocampus, is among the regions first affected by Alzheimer's disease (AD). Glycogen synthase kinase-3β (GSK-3β) has emerged as a key enzyme in AD pathology. Indeed, a mouse model of AD that overexpresses GSK-3β displays decreased dendritic spine density in the DG. However, the effects of GSK-3β overexpression on the remaining regions of the trisynaptic circuit are still unknown.

Methodology:
Here, we analyzed dendritic spine morphology and density in apical and basal dendrites of CA1, CA3, and EC pyramidal neurons in wild-type (WT) and GSK-3β-overexpressing (GSK-3β-OE) mice using intracellular Lucifer Yellow injections.

Results:
WT mice showed intrinsic differences in spine density and spine-type distribution between apical and basal dendrites across regions. GSK-3β overexpression induced region-specific alterations. The EC showed subtle morphological changes, suggesting partial structural resilience despite its early involvement in AD. The CA3 region presented minimal alterations overall, with basal dendrites being more affected than their apical counterparts, likely due to the differential input they receive. In contrast, CA1 was the most affected region, consistent with its known vulnerability to AD pathology. Finally, a reduced percentage of area occupied by Vesicular glutamate transporter 1 (VGlut1+) boutons in both CA1 and basal CA3 dendrites indicated a loss of excitatory innervation in GSK-3β-OE mice, thereby suggesting disrupted synaptic plasticity.

Conclusion:
The regional variability in the observed alterations in dendritic spines suggests a selective vulnerability of certain hippocampal areas during the progression of the disease.

Key words: Alzheimer's disease; dendritic spines; GSK-3β; hippocampus; trisynaptic circuit; pyramidal neuron.

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Sofía Inés Martínez Centeno
UAM PhD program: Biociencias Moleculares
COMMUNICATION TYPE: Póster

TITLE: Hippocampal LTP

Authors: Sofía Inés Martínez-Centeno[1], Laura García-Redondo[1], Aixa Victoria Morales-García[1].

AFFILIATIONS:
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ABSTRACT (350 Word limit)

Background: Adult neurogenesis is highly restricted in the adult mammalian brain. One of the two main regions where it occurs is the subgranular zone (SGZ) of the dentate gyrus (DG) and is attributed to a population of neural stem cells (NSCs) that are in a quiescent state. Through regulated mechanisms, these NSCs are activated (aNSCs) and produce intermediate progenitor cells (IPCs) that generate granule neurons. Neurogenesis and astrogliogenesis occur simultaneously during early postnatal DG development. Astrocytes are key components of the neurogenic niche of the hippocampus, and multiple lines of evidence suggest that they have a significant impact on DG plasticity by positively regulating NSC function. Previous results from our lab have shown that transcription factor Sox5 is expressed in aNSCs and astrocytes in the adult GD and that the loss of Sox5 in those populations does not affect the number or distribution of astrocytes. However, it is unknown if astrocytes might influence the emergence of adult NSC during the development of DG.

Methodology: Using a Nestin-Cre-mediated Sox5 deletion mouse model in NSCs, we have determined that Sox5 is necessary during embryonic/postnatal development to prevent excessive astrogliogenesis. Furthermore, using astrocyte specific inducible Aldh1L1-CreERT2 mediated deletion of Sox5 at postnatal P3 (young model) and P60 (adult model), we are analysing the possible astrocyte participation.

Results: Our preliminary results confirm that the Aldh1L1-CreERT2 line can drive cre-mediated recombination specifically in astrocytes, with minimal effect on other cell types. Moreover, we can confirm that using Aldh1L1 as a driver results in high recombination efficiency, with most of the recombined cells being astrocytes.

Conclusion: Sox5 plays a crucial role during early development is in the dentate gyrus. Additionally, astrocytes appear to be important contributors to this process, and the validated experimental models will help further clarify their role in adult neurogenesis.

Key words: Dentate gyrus; NSCs; Astrocytes; Hippocampus.

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PhD Student Name and surname: Ana Victoria Prádanos Senén
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: POSTER

TITLE: Longitudinal study of the adult hippocampal neurogenic niche homeostasis in a mouse model of Alzheimer's disease

Authors: Ana Victoria Prádanos-Senén [1,2], Carla B. Rodríguez-Moreno [1,3], María Llorens-Martín [1,2,3]

AFFILIATIONS:

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2. Department of Molecular Biology, Faculty of Sciences, Universidad Autónoma de Madrid, Madrid, Spain.
3. Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED), Madrid, Spain.

ABSTRACT (350 Word limit)

Background:
In the hippocampal dentate gyrus (DG), adult hippocampal neurogenesis (AHN) occurs within a specialized environment, the neurogenic niche, comprising an extensive vascular network and glial cells. This study aims to identify the cellular mechanisms underlying AHN failure in Alzheimer's disease (AD) by longitudinally studying the components of the DG neurogenic niche.

Methodology:
We used a mouse model of AD (mice that overexpress glycogen synthase kinase 3 beta (GSK-3β)), and conducted a study at four different time points: 4, 12, 18, and 30 months of age (mo) to study the glial populations and vasculature of the neurogenic niche.

Results:
Our results reveal significant alterations in glial populations and vascularization. In AD mice, astrocyte and microglia densities increase in the granule cell layer (GCL) at 4 mo but decrease in the subgranular zone (SGZ) by 12 mo, accompanied by morphological changes observed through 3D reconstructions. Oligodendrocyte precursor cells (OPCs) decrease in the GCL at 4 mo, while mature oligodendrocytes remain stable in the GCL but decline in the SGZ from 12 mo onwards.

These glial changes correlate with increased DG vascularization, particularly in the SGZ at 12 and 18 mo and the GCL at 12 mo. GCL blood vessels exhibit increased thickness at 12 and 30 mo, with elevated CD31 immunoreactivity at 30 mo.

The putative interaction of newborn dentate granule cells with glial cells was also examined. Astrocytes show increased overlapping with 1-week-old neurons in the AD model, which decreases in 8-week-old neurons in both AD and wild-type conditions. Conversely, overlap with UEA1+ blood vessels increases in 8-week-old neurons compared to 1-week-old ones in AD mice.

Finally, a detailed analysis of the hippocampal expression of 96 cytokines revealed a variable imbalance between pro- and anti-inflammatory signals in the AD model.

Conclusion:
These findings bring to light the disruption of the DG neurogenic niche homeostasis in this mouse model of AD, potentially contributing to AHN impairments.

Key words: Adult hippocampal neurogenesis; Hippocampus; Neurogenic niche; Microglia; Vasculature; Astrocytes; Neuroinflammation; Aging.

UAM Universidad Autónoma de Madrid | Escuela de Doctorado | Facultad de Medicina

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Ana Arauzo Cabrera
UAM PhD program: Biociencias Moleculares
COMMUNICATION TYPE: poster

TITLE: Evaluation of Epigenetic Biomarkers of Risk and Progression of NSCL in COPD Patients: Focus on Hypoxia-Driven microRNAs and Cancer-Associated Fibroblasts

Authors: Ana Arauzo[1,2], Olga Pernía [1,2], Miranda Burdiel [1,2], Alvaro García-Guede [1,2], Elisabet Martinez Cerón [3], Raúl Galera [3], Oliver Higuera [4], Itsaso Losantos-García [5], Javier de Castro [4], Francisco García-Rio [3], Inmaculada Ibañez de Caceres [1,2], Olga Vera [1,2].

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ABSTRACT (350 Word limit)

Background:
Non-small cell lung cancer (NSCLC) is the leading cause of cancer-related mortality worldwide, mainly due to late diagnosis and treatment resistance. Despite therapeutic advances, only 15% of patients benefit from targeted therapies, underscoring the need for early biomarkers, especially in high-risk populations such as patients with chronic obstructive pulmonary disease (COPD), where hypoxia promotes a more aggressive tumor microenvironment. Previously, our group identified six overexpressed microRNAs (miRNAs) in extracellular vesicles (sEVs) derived from NSCLC tumor explants using small RNA sequencing.

Methodology:
To validate their clinical relevance, we analyzed their expression in tumor and adjacent non-tumor tissues from 36 early-stage lung adenocarcinoma patients. We also evaluated non-invasive detection by analyzing pharyngeal epithelium samples from 119 mild COPD patients enrolled in a lung cancer screening program. Primary cultures were established from tumor and non-tumor tissues, isolating epithelial cells, cancer-associated fibroblasts (CAFs), and normal fibroblasts (NFs) from each patient. Total RNA was extracted from all samples, reverse transcribed using miRNA-specific primers, and quantified by qRT-PCR. Expression of hypoxia-related genes (HIF1A, VEGFA) was assessed to explore functional relationships with the miRNAs.

Results:
Immunofluorescence confirmed successful CAF isolation for future 3D functional models and statistical analysis ($p < 0.05$) revealed that three of the six miRNAs showed potential as tumor biomarkers. Notably, one miRNA was associated with lung cancer development in COPD patients who were cancer-free at the time of sample collection (2019–2020) but developed cancer in 2024.

Conclusion:
These findings support the potential of these miRNAs as non-invasive biomarkers for early detection of NSCLC, particularly in high-risk COPD populations.

Key words: miRNA; biomarker; epigenetic; CAFs; hypoxia; NSCLC; COPD.

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Mario Hernanz
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: POSTER

TITLE: Reevaluating KLF11 in Human Endocrine Pancreas Development: Implications for Monogenic Diabetes Pathogenesis

Authors: Mario Hernanz[1], Diego Matas-Aguado[1], Marta G. de la Fuente[1] and Alberto Bartolomé[1,2]

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[2] *CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Madrid, Spain.*

ABSTRACT (350 Word limit)

Background and aims: Maturity Onset Diabetes of the Young (MODY) is driven by mutations specific genes. MODY7, in particular, has been associated with variants in KLF11, a transcription factor whose role in diabetes pathogenesis remains still unclear. Some studies have questioned its candidacy as a monogenic diabetes driver due the relatively high prevalence of these variants in the general population. Moreover, previous animal model studies have yielded inconclusive results regarding the role of KLF11 in the endocrine pancreas, highlighting the need for research in a human context. This study aims to elucidate the function of KLF11 during human endocrine pancreas development and in mature β-cell function, to clarify its contribution to MODY.

Material and Methods: Human pluripotent stem cells (hPSCs) were used in differentiation protocols to model human endocrine pancreas development. We generated KLF11 loss-of-function hPSC lines, as well as lines carrying single-nucleotide variants identified in MODY7 patients, using CRISPR/Cas9 genome editing. Endocrine differentiation efficiency, transcriptional profiles, and glucose-stimulated insulin secretion were assessed to determine the impact of KLF11 alterations.

Results: Comparative analyses between KLF11-edited lines and isogeneic controls revealed no significant differences in endocrine differentiation. No significant differences were observed across endocrine differentiation between KLF11-deficient and control lines. Transcriptional profiling and immunofluorescence assays demonstrated that KLF11 disruption did not impair the formation of insulin-producing cells.

Conclusion: Our findings indicate that KLF11 is not a key regulator of endocrine pancreatic development nor essential for the formation of functional β-cells. These results support current recommendations to exclude KLF11 as a primary causative gene for monogenic diabetes. However, the potential for KLF11 to interact with other genetic factors in an oligogenic form of diabetes cannot be completely ruled out.

Acknowledgements: Funded by PID2021-122284NA-I00 (Ministerio de Ciencia, Innovación y Universidades, Spain) and Sociedad Española de Diabetes.

Key words: Monogenic diabetes, stem cells, endocrine development, genetics.

PhD Student Name and surname: Laura Pérez Gómez
UAM PhD program: Biociencias Moleculares
COMMUNICATION TYPE: Poster

TITLE: Role of BRCA2 in the prevention and repair of replication stress-induced DNA lesions: implications for chemotherapy response

Authors: Laura Perez[1], Yodharaudshani Wijesekarahanthi[2], Natividad Bellido[1], Vincenzo Costanzo[2], Aura Carreira[1]

AFFILIATIONS:

1 *Centro de Biología Molecular Severo Ochoa (CBM) CSIC-UAM, Madrid, España*
2 *DNA Metabolism Laboratory, IFOM-ETS, The AIRC Institute of Molecular Oncology, Milan, Italy*

ABSTRACT (350 Word limit)

Background:
Chronic replication stress is a hallmark of cancer cells, particularly in those harboring BRCA2 mutations, leading to the accumulation of single-stranded DNA (ssDNA) gaps. While these lesions represent a source of genomic instability, they also create therapeutic vulnerabilities. DNA damage tolerance (DDT) pathways, including template switching (TS) and translesion synthesis (TLS), enable replication to proceed despite DNA damage. However, how different types of replication stress influence DDT pathway choice, and how BRCA2 contributes to these processes, remains poorly understood.

Methodology:
To address this, we use isogenic human cell lines expressing BRCA2 N-terminal (NTD) variants associated with breast cancer. Replication dynamics and ssDNA gap formation are analyzed using DNA fiber assays, including S1 nuclease–based detection, and electron microscopy to visualize replication intermediates. PARP1 activation is assessed by immunofluorescence of poly(ADP-ribose) chains. DDT pathway usage is investigated through biochemical approaches and functional assays, including drug sensitivity (MTT and clonogenic assays) and modulation of TLS (REV1 inhibition) and repriming (PRIMPOL depletion).

Results:
Our results show that BRCA2 NTD variants accumulate ssDNA gaps under replication stress, which may arise from defective lagging strand processing, as suggested by increased PARP1 activation. These cells display reduced fork progression, indicative of replication stress. Electron microscopy analyses reveal that fork reversal is not impaired but rather increased in the C315S variant, suggesting preserved fork remodeling capacity. However, ssDNA gaps persist, indicating a defect in gap suppression rather than fork protection. Furthermore, these cells exhibit efficient fork restart, potentially through alternative pathways such as TLS.

Conclusion:
Altogether, our findings indicate that BRCA2 N-terminal variants uncouple fork protection from ssDNA gap suppression, leading to altered replication stress responses. We propose that these cells rely on compensatory DDT mechanisms, potentially favoring TLS, which may contribute to chemoresistance. This work provides insight into BRCA2 domain-specific functions and identifies potential therapeutic targets to selectively exploit replication stress in BRCA2-mutant tumors.

Key words: BRCA2, replication stress, ssDNA gaps, DNA damage tolerance, translesion synthesis, template switching, fork reversal, PARP1.

PhD Student Name and surname: Marta Olazabal Chias
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: Poster

TITLE: *Functional evaluation of novel activating compounds targeting NRF2.*

Authors: Marta Olazabal Chias[1], Raquel Fernádez Ginés[2], Daniel Carnicero Senabre[2], Antonio Cuadrado[1] and Ana I Rojo Sanchís[1]

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ABSTRACT (350 Word limit)

Background:

Alzheimer's disease is a multifactorial disease with only symptomatic treatments available. NRF2 is a transcription factor in charge of the regulation of antioxidant and electrophilic stress at a cellular level, that has emerged as a potential protector in neurodegenerative disorders. NRF2 inducers are mostly electrophilic compounds directed against KEAP1 (the main degradation pathway) with poor selectivity and off-target effects. Our group is trying to get a new set of compounds activators of NRF2 that could have a beneficial effect on the brain, with anti-inflammatory properties.

Methodology:
Mouse microglial immortalized cells were used to analyze the NRF2 activation and the anti-inflammatory properties of 3 different compounds. Cells were treated with different doses and at different time points to establish the best one, assessed by western blot by the activation of NRF2. Once it was determined we looked by RT-qPCR for the activation of different genes related with the transcription machinery of NRF2. And anti-inflammatory properties were analyzed by western blot and RT-qPCR after 9h of treatment with the last 3h of LPS (10ng/ml) treatment to induce inflammation.

Results:
Results showed that the 3 compounds tested, increase NRF2 activity and different NRF2 target genes in microglial cells at a dose of 9μM and 9h of treatment. And decrease inflammatory response in vitro against a proinflammatory stimulus such as bacterial Lipopolysaccharide.

Conclusion:
New NRF2 inducers have demonstrated beneficial effects in an in vitro brain model, giving us the opportunity to move on to an in vivo model of Alzheimer's disease.

Key words: NRF2; Alzheimer's disease; Microglia; Inflammation.

Poster · Biocaucas Moleculas

AbstractWorkshop 2026

A Novel Skeletal Muscle ETFDH Knockout Model Demonstrates Systemic Consequences of FAO Deficiency

Beñat Salegi Ansa [a, c*], Laura Naharro Naharro [a], Jose Maria Lanza Arnaiz [a, c], Tzoline Topdjian Panosian [a], PabloSanchez-Aguilera [a], Laura Formentini [a, b, c]

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The electron transfer flavoprotein dehydrogenase (ETFDH) is a mitochondrial ubiquinone reductase that connects fatty acid oxidation (FAO), choline and branched-chain amino acid catabolism to the oxidative phosphorylation (OXPHOS).Pathogenic mutations in ETFDH cause multiple acyl-CoA dehydrogenase deficiency (MADD; ORPHA:26791), a rare autosomal recessive disorder. Despite its critical role in mitochondrial energy balance, ETFDH remains poorly understood, partly because its complete deletion results in embryonic lethality.

Here, we present a novel conditional and skeletal muscle-specific ETFDH knockout (Etfdh-/-) mouse model to investigate the in vivo consequences of FAO inhibition in muscle. These mice develop myopathy, intramuscular lipid accumulation, and display fasting-induced hypoglycemia and hyperketonemia, alongside altered circulating lipid profiles. Remarkably, despite the muscle-specific deletion of ETFDH, the model reproduces key systemic features of MADD, making it a promising tool for preclinical research. Furthermore, we uncover an unexpected axis of communication between skeletal muscle and liver. Through both in vivo and in vitro approaches, we show that muscle-specific loss of ETFDH triggers the secretion of a protein factor that finally impairs hepatic mitochondrial function. Liver tissue analysis revealed a reduction in mitochondrial number and cristae density, with cristae appearing shorter and wider. Hepatocytes displayed compromised glucose and fatty acid oxidation, linked to decreased OXPHOS activity resulting from mitochondrial complex III inhibition.

Altogether, this model highlights a FAO-driven muscle-liver intercommunication, where dysfunction in muscle signals to the liver inducing secondary mitochondrial alterations, tush offering new insights into the systemic impact of FAO disorders.

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Irene Camacho-Olmos
UAM PhD program: Biociencias moleculares
COMMUNICATION TYPE: Poster

TITLE: Aβ pathology reduction and safety validation of hE2F4DN-based gene therapy for Alzheimer's disease

Authors: I.Camacho-Olmos[1,2], C.Sánchez-Puelles[1,2], A.Garrido-García[1,2], J.M.Frade[2]

AFFILIATIONS:

[1] *Tetraneuron, Madrid, Spain.*

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ABSTRACT (350 Word limit)

Background:
Alzheimer's disease (AD) is a major global health challenge affecting more than 50 million people worldwide. Current therapies provide limited symptomatic benefit and do not effectively halt disease progression. We developed a multifactorial gene therapy based on hE2F4DN, a non-phosphorylatable mutant form of the human transcription factor E2F4 that cannot be modified by the stress kinase p38MAPK, an early pathological driver in AD. Neuronal expression of hE2F4DN is designed to preserve brain homeostasis under stress conditions. This therapeutic strategy is currently licensed by Tetraneuron S.L..

Methodology:
The disease-modifying potential of AAV.hSyn1.hE2F4DN was evaluated in homozygous 5xFAD mouse mice. The vector was administered intracisternally at two stages: 6 weeks of age (pre-symptomatic stage) and 3 months of age (symptomatic stage with memory deficits). Amyloid pathology was analyzed at 6 months of age by measuring soluble Aβ monomers, oligomers (oAβ), and hippocampal plaque burden. Safety was assessed in wild-type mice through neuronal morphology and dendritic complexity analyses. Translational validation was performed in human induced pluripotent stem cells-derived neurons.

Results:
hE2F4DN treatment significantly reduced soluble Aβ monomers and oAβ levels, as well as the average hippocampal Aβ plaque area, independently of the age of administration. These findings indicate efficacy in both preventive and therapeutic intervention settings. Safety studies demonstrated that hE2F4DN expression did not alter neuronal morphology or dendritic complexity in wild-type mice. Importantly, equivalent safety outcomes were confirmed in human iPSC-derived neurons, supporting translational relevance and cross-species tolerability.

Conclusion:
AAV.hSyn1.hE2F4DN shows strong disease-modifying potential by reducing amyloid pathology while preserving neuronal integrity. This multifactorial gene therapy represents a promising and safe candidate for the treatment of AD and supports further preclinical and clinical development.

Key words: Alzheimer's disease; gene therapy, E2F4, amyloid-beta

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PhD Student Name and surname: Daniel Alba Olano
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: poster

TITLE:

Validation of plasma lyophilisation as an alternative to deep-freezing

Authors:

Daniel Alba[1], Carmen Ortega[1], Maria-Jesús Artiga[1], Ana Hernández[2], Miguel G. Álvarez[2], Mario Morgado[2]

AFFILIATIONS:

[1]*CNIO Biobank*[2], *300K Solutions*

ABSTRACT (350 Word limit)

Background:
A more sustainable alternative to freezing for preserving samples stored in biobanks and research centres is lyophilization, a method of dehydrating biological samples that allows them to be kept at room temperature for long periods of time. The objective of the study was to validate plasma lyophilisation as a room-temperature storage format equivalent to freezing, evaluating the quality and functionality of samples in the context of a prospective biobank collection.

Methodology:
Plasma samples collected in tubes with different anticoagulants, such as EDTA and citrate, from 20 donors from the CNIO Biobank were studied. Samples were stored by freezing (−80 °C) and at room temperature, after being lyophilised using the S3 system (300K Solutions). Cytokines IL-8 and IL-16 were determined as plasma quality markers by ELISA at three storage times (0, +2 and +6 months). Overall protein integrity was assessed by polyacrylamide gel electrophoresis.

Results:
Cytokines showed no significant differences over time or by type of anticoagulant after 6 months of storage. No significant interaction between anticoagulant and time was observed. Although nor frozen or lyophilised samples were fully comparable with fresh samples (gold standard) for cytokine quantification, no significant differences were detected between lyophilisation and freezing in most of the conditions evaluated. Overall protein profiles remained comparable between storage methods and storage times.

Conclusion:
Plasma stabilisation by lyophilisation with the S3 system and storage at room temperature maintains analytical quality parameters comparable to freezing at −80 °C for the biomarkers studied, supporting its use as a viable and reliable alternative to freezing in biobanks and research centres, with potential impact on the sustainability and logistics of multicentre studies.

Key words: Lyophilization, Sample preservation, Biospecimen science, Sustainability

PhD Student Name and surname: Daniel Alba Olano
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: Poster

TITLE:

Circadian Rhythms Disruption and Occupational Health: Microbiome Alterations in Cabin Crew

Authors:

Daniel Alba-Olano[1], Maria-Jesús Artiga[1], Elizabeta Gorbunova[2], Silke Kiessling[2]

AFFILIATIONS:

[1]*Spanish National Cancer Research Centre (CNIO) Biobank*
[2] *University of Surrey (UK), Chronobiology Section*

ABSTRACT (350 Word limit)

Background:
Circadian rhythm disruption is associated with metabolic and immunological alterations, as well as an increased risk of chronic diseases. Flight workers, particularly long-haul cabin crew, are highly exposed to chronic jet lag, irregular shifts, and frequent time zone changes, being those factors that may impact the gut microbiota. However, the underlying biological mechanisms and associated early biomarkers remain insufficiently characterized. The aim of this study is to analyze microbiome alterations associated with chronic circadian disruption through the comparison of metagenomic and metabolomic profiles within this professional group.

Methodology:
Three groups were defined for the study: short-haul crew, long-haul crew, and controls. Samples were processed using an *ex vivo* culture system that simulates the human colon, with sampling every 4 hours over a 48-hour period to assess temporal dynamics and microbial rhythmicity. In addition, metabolomic analyses will be performed. Multi-omics data will be integrated with occupational, lifestyle, and clinical variables using bioinformatic and statistical analyses, enabling the evaluation of differences among the study groups.

Results:
Differences were observed among the three groups, particularly in long-haul workers compared to short-haul crew and controls. Alterations in microbial diversity and composition were identified, including changes in taxa and attenuation or loss of rhythmic patterns in the microbiota assessed *ex vivo*. We expect to see a link between these changes and the metabolic and immunoregulatory, including distinct metabolomic profiles, including variations in microbial metabolites involved in inflammation, metabolism, and immune regulation.

Conclusion:
Characterizing microbiome alterations associated with chronic jet lag may transform how the health of flight personnel is monitored, enabling early detection of biological dysregulation prior to disease onset. The identification of biomarkers linked to circadian disruption would facilitate the development of tailored prevention, surveillance, and monitoring strategies adapted to these occupational risks, with potential applicability to other professional groups exposed to similar conditions, thereby reinforcing its relevance in occupational health and chronic disease prevention.

Key words: Chronobiology, Microbiome, Chronodisruption, Occupational Health, Cabin Crew

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PhD Student Name and surname: Marina Bejarano Franco
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: POSTER

TITLE: BP-Flow: a novel method to measure DNA supercoiling

Authors: Marina Bejarano Franco [1], Jose Terrón Bautista [1, 2], Felipe Cortés Ledesma [1]

AFFILIATIONS:

[1] Spanish National Cancer Research Centre
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ABSTRACT (350 Word limit)

Background:
Supercoiling is a fundamental property of DNA that refers to the transition of the DNA double helix from a relaxed state to one that is underwound or overwound. It is primarily generated during strand-opening processes such as transcription and replication. To resolve the resulting topological stress, cells rely on DNA topoisomerases, enzymes that introduce transient strand breaks to relieve torsional strain. Current methods to measure DNA supercoiling, such as psoralen-based assays, often lack sensitivity, specificity, and reproducibility.

Methodology:
We developed a new method termed BP-Flow (biotinylated psoralen flow cytometry) to quantify negative DNA supercoiling by measuring the signal from biotinylated psoralen incorporated into fixed nuclei using flow cytometry. The method was validated in RPE1 Cas9 cells subjected to treatments known to alter DNA supercoiling.

Results:
In vitro treatment with *E. coli* Top1 enzyme, which selectively removes negative supercoiling, significantly reduced BP incorporation. Similarly, treatment with triptolide, a transcription inhibitor, decreased BP incorporation. In contrast, treatment with ICRF, a Top2B inhibitor, increased BP incorporation.

Conclusion:
BP-Flow provides a sensitive and reproducible approach for measuring negative DNA supercoiling in mammalian cell lines. This method offers a rapid and quantitative tool to study DNA topology changes under different cellular conditions.

Key words: DNA supercoiling; DNA topology; biotinylated psoralen; flow cytometry; topoisomerase; transcription;

PhD Student Name and surname: Alejandro Sánchez Juan
UAM PhD program: Biociencias Moleculares
COMMUNICATION TYPE: Poster

TITLE:

Identity Crisis! RANK-Driven Luminal Plasticity Promotes a Thymic Epithelial-like Program in the Mammary Gland

Authors:

Alejandro Sánchez[1], Jaime Redondo-Pedraza[1], María Jimenez[1], Víctor Lopez[1] and Eva Gonzalez-Suarez[1,2]

AFFILIATIONS:

[1] *Molecular Oncology, Spanish National Cancer Research Centre (CNIO), Madrid, Spain.*
[2] *Oncobell, Bellvitge Biomedical Research Institute (IDIBELL), Barcelona, Spain.*

ABSTRACT (350 Word limit)

Background:

In the mammary gland, RANK signalling is a key regulator of epithelial expansion during pregnancy. Luminal progenitor (LP) cells that express RANK respond to RANKL, which is produced primarily by mature luminal cells under the influence of progesterone. Previous data from our group linked RANK overexpression to a senescent and stem-like phenotype in epithelial cells. Furthermore, RANK signalling is associated with the development of breast cancer in BRCA1-mutant patients. This study aims to elucidate how the RANK pathway dictates luminal cell identity and plasticity, uncovering functional mechanisms that could be exploited as novel therapeutic targets in breast cancer.

Methodology:

We employed an inducible, luminal-specific mouse model (K8-Rank) to overexpress RANK in the mammary luminal compartment. Senescent-like populations were identified using DDAOG, a fluorescent probe for lysosomal beta-galactosidase activity in live cells. We characterized these populations through a multi-omics approach, including proteomics, flow cytometry, immunohistochemistry (IHC), qPCR, and single-cell RNA-seq (scRNA-seq).

Results:

RANK overexpression triggered an expansion and increased proliferation of luminal progenitors. Surprisingly, these cells displayed a luminal-to-basal transformation and a "senescence-like" signature. Transcriptomic analyses revealed a paradoxical state: these cells remained highly proliferative (Ki67-high) despite lacking classical tumor suppressors ($p16^{Ink4a}$-low and $p19^{Arf}$-low). High-resolution scRNA-seq analysis identified a novel subpopulation within the luminal cluster that closely resembles medullary thymic epithelial cells (mTECs), characterized by an inflammatory and senescent signature.

Current efforts focus on unraveling the RANK-dependent mechanisms of plasticity and stemness by integrating transcriptomic (bulk RNA-seq) and epigenetic (ATAC-seq) profiling of senescent-like luminal progenitors and their hybrid basal progeny.

Conclusion:

Our findings reveal that RANK-driven plasticity induces a thymic epithelial-like program in the breast. These mTEC-like cells may act as drivers of the luminal-to-basal transition and may contribute to local immune tolerance. Overall, this work provides new insights into how RANK signalling modulates epithelial homeostasis and the immune microenvironment in the mammary gland.

Key words: RANK; mammary gland; senescence; plasticity; luminal epithelial cells; thymic epithelial cells.

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: JaeJun Lee
UAM PhD program: Molecular Bioscience
COMMUNICATION TYPE: Poster

TITLE: Multi-feature predictive modeling of novel cancer predisposition genes using pan-cancer data

Authors: Jaejun Lee[1,2] , A-Reum Nam[2] and Solip Park[2]

AFFILIATIONS:

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[2]*Centro Nacional de Investigaciones Oncológicas, Madrid, España*

ABSTRACT (350 Word limit)

Background

Cancer predisposition genes (CPGs) are defined as genes whose inherited variants increase cancer risk. Despite their central role in tumorigenesis, the number of identified CPGs remains limited, largely due to the rarity of pathogenic germline variants and the limitations of traditional case–control approaches.

Methodology

We developed a machine learning–based predictive model integrating 13 diverse biological features—including germline genomic characteristics, transcriptomic profiles, and results from unbiased screening—to identify novel CPGs. We individually assessed the predictive power of each feature known to be associated with CPGs, evaluating their contribution at both cancer-type-specific and pan-cancer levels.

Results

While multiple single features possessed moderate predictive power individually, our integrative model outperformed all single-feature models (AUC = 0.74 vs. 0.53–0.58), demonstrating the value of multi-feature integration. We further applied the model across individual cancer types to discover cancer-type-specific candidate CPGs. We identified 8 high-confidence CPG candidates at both pan-cancer and cancer-type-specific levels, several of which were validated using an independent familial cancer cohort.

Conclusion

This approach provides a scalable framework for uncovering novel CPGs, offering a direct pathway for understanding the genetic basis of cancer susceptibility.

Key words: Cancer predisposition gene; Machine learning; Genomics.

PhD Student Name and surname: Raquel González-Alday
UAM PhD program: Molecular Biosciences
COMMUNICATION TYPE: Poster

TITLE: Diet-Induced Obesity and Sex Alter the Neuroinflammatory Landscape in Glioblastoma

Authors: Raquel González Alday[1], Nuria Arias-Ramos[1], Blanca Lizarbe[1,2] and Pilar López-Larrubia[1]

AFFILIATIONS:

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[2] *Departamento de Bioquímica, Universidad Autónoma de Madrid. Madrid, Spain.*

ABSTRACT (350 Word limit)

Background:
Obesity is a complex, chronic condition influenced by sex and associated with alterations in brain microstructure. While obesity has been linked to increased risk of several cancer types, its specific role in the progression of brain tumors, particularly glioblastoma (GBM), remains unclear. We aim to investigate magnetic resonance imaging (MRI) biomarkers that reflect the impact of high-fat diet exposure on GBM characteristics in a preclinical mouse model, assessing potential sex-dependent differences.

Methodology:
Adult C57BL/6 mice were divided in four groups based on diet type and duration: high-fat diet (HFD) or standard diet (SD), for either 10 weeks or 20 weeks. Then, GBM was induced via stereotactic injection of GL261 cells into the brain parenchyma. A multiparametric MRI protocol was conducted once tumors reached around 70 mm^3, including T_2 and T_2* mapping, magnetization transfer ratio (MTR), and diffusion tensor imaging (DTI). Brain samples were used for immunofluorescence assays with GFAP and Iba1 to visualize astrocytes and microglia.

Results and discussion:
First of all, expected differences in all MRI parameters reflected the presence of edema and haemorrhage in tumor areas, as well as slight edema in the peritumoral zone (PZ). Increased fractional anisotropy (FA) in the PZ reflected recruitment of astrocytes surrounding the tumor, observed with immunofluorescence. Moreover, sex, diet and diet duration effects were found in all MRI parameters, specially in the non-tumoral regions, suggesting differential impact of GBM on the whole brain, possibly linked to its neuroinflammatory state. In mean diffusivity (MD), at 10 weeks, differences between sexes on HFD mice were found on the contralateral brain (CL). At 20 weeks same sex differences were found but on SD mice, in the CL and PZ. Lower MD values on female mice respect to males, in the case of SD mice of 20 weeks could be related to less recruitment of astrocytes and microglia in the PZ and of microglia in the CL. At 10 weeks, the presence of less microglia on HFD males in the CL could also explain the increased MD. A more thorough multivariate analysis is being performed to understand the underlying causes of these sex differences and how tumor edema could also be masking neuroinflammatory effects.

Key words: Glioblastoma; MRI; Neuroinflammation.

PhD Student Name and surname: Inés de Cáceres Renovell
UAM PhD program: Biociencias Moleculares (Ciencias)
COMMUNICATION TYPE: Póster

TITLE: Development of new cellular immunotherapies against cancer based on bacteria reprogrammed T lymphocytes

Authors: Inés de Cáceres Renovell[1,2], Daniel Gómez Garrido[1,2], Nikolás Valencia[3], Andrés M. Acosta Moreno[1], Laura Jiménez Gracia[4], Juan C. Nieto [4], Holger Heyn [4], Jaume Mora[5], Jose Ramón Regueiro[3], Esteban Veiga Chacón[1]

AFFILIATIONS:

1 *Bacteria-based Immunotherapies Against Cancer Group. Molecular and Celular Biology. National Center for Biotechnology (CNB-CSIC). Madrid. Spain.* || ***2*** *Escuela de Doctorado, Universidad Autónoma de Madrid* || ***3*** *Universidad Complutense de Madrid.* || ***4*** *Centro Nacional de Análisis Genómico (CNAG)* || ***5*** *Hospital Sant Joan de Déu*

ABSTRACT (350 Word limit)

Over the past 15 years, novel biological cancer treatments —particularly **immune checkpoint inhibitors** (ICI) and **adoptive cell therapies** (ACT)— have transformed oncology. Agents such as pembrolizumab, ipilimumab, CAR-T therapies (e.g., Carvikty) and TIL products (e.g., lifileucel) have increased response rates and enabled unprecedented long-term remissions. However, major limitations persist: 40–95% of patients do not respond to ICI, CAR-T cells fail to effectively infiltrate or persist in solid tumors, and TIL therapies often underperform due to low yields of tumor-reactive lymphocytes. These challenges highlight the need for new ACT strategies (Cole et al. 2023; Chen and Mellman 2013; Mao et al., 2023; Pedrazzoli et Haanen, 2022; Kristensen et al., 2022).

T-Boost BacB cells represent a novel, malleable ACT platform composed of potent, antigen-specific CD8+ cytotoxic T cells. Their innovation lies in the reprogramming of T-cell phenotype using engineered *E. coli* expressing selected tumor antigens.

Methodology

1. CD8+ T cells from C57BL/6 mice were activated using different methods — transphagocytosis via CD4+ or B cells (Cruz-Adalia A. et al., 2017; García R. et al., 2023), or CD3/CD28 activator beads— expanded and administered at 1.5–4 million cells per mouse across six doses. Four groups (PBS control, CD8+ Beads, T-Boost BacT, T-Boost BacB) were evaluated in mice inoculated with B16-F10-OVA melanoma. Tumor growth was monitored for 19 days, after which tumor infiltrates were analyzed using scRNA-seq.
2. CD8+ T cells from C57BL/6 and BALB-C mice were similarly activated and assessed by advanced flow cytometry for specific activation (CD25+) and exhaustion (LAG3+) against melanoma (B16-F10) or osteosarcoma (K7M2) antigens. Controls included "empty" engineered *E. coli* versus bacteria expressing tumor-specific antigens.

Results and Conclusion

T-Boost BacB cells effectively **controlled tumor growth**, showed **strong persistence and infiltration** within the solid tumor microenvironment, and maintained a robust **Tc1 effector phenotype** with **minimal exhaustion**, outperforming CD8+ T cells expanded with CD3/CD28 beads. *In vitro* testing in melanoma and osteosarcoma models have shown the possibility of generating **20–70% specifically activated CD8+ T cells**, far exceeding the ~5% threshold associated with favorable clinical outcomes.

These findings suggest that **T-Boost BacB–based immunotherapies** could significantly enhance patient response rates while reducing relapse risk.

Key words: T-Boost BacB; ACT therapies; exhaustion; tumor-recognizing lymphocytes; melanoma; osteosarcoma.

PhD Student Name and surname: Cristina González Bragado
UAM PhD program: Molecular Bioscience
COMMUNICATION TYPE: POSTER

TITLE: Analysis of the effect of a mutant variant of E2F4 in oligodendrocytes in a mouse model of Alzheimer´s disease

Authors: C. González-Bragado[1], A. Lozano-Ureña[1], J.M. Frade[1]

AFFILIATIONS:
[1] *Cajal Neurosciences Center, Avenida de Léon, 1, 28805, Alcalá de Henares, Spain*

ABSTRACT

Background:
Alzheimer's disease (AD) is the most common form of age-related dementia and is characterized by progressive neurodegeneration. In recent years, increasing attention has been given to the role of non-neuronal cells in disease progression. Oligodendrocytes (OLs), the cells responsible for myelin formation, are continuously generated throughout life from oligodendrocyte progenitor cells (OPCs), making them a potential source for myelin repair in AD. Previous studies from our laboratory have shown that the expression of a dominant-negative form of the transcription factor E2F4 (E2F4DN), unable to become phosphorylated in a threonine-conserved motif, reduces microgliosis and astrogliosis in homozygous 5xFAD (h5xFAD) mice, a model of AD. However, its effects on the oligodendroglial lineage have not yet been explored.

Methodology:
In this study, we characterized the oligodendrocyte lineage in h5xFAD and wild-type (WT) mice and evaluated the impact of E2F4DN expression. Mice at three months of age were systemically injected with viral vectors expressing either E2F4DN or EGFP. One month later, brain tissues were analyzed using fluorescence-based immunohistochemistry. Specific markers were used to identify different cell populations: PDGFR-α for OPCs, ASPA for mature oligodendrocytes, and Olig2 for the entire oligodendrocyte lineage. In addition, OPCs proliferation was assessed using 5-Ethynyl-2′-deoxyuridine (EdU), a thymidine analog incorporated into DNA during the S phase of the cell cycle.

Results:
The results revealed a significant decrease in the population of mature OLs in the cortex of h5xFAD mice and a decreasing trend in the CA1 region. In contrast, an increase in OPCs numbers was observed in the cortex and corpus callosum, along with a similar trend in the CA1 region of the hippocampus, suggesting a compensatory mechanism. Notably, E2F4DN expression attenuated these alterations, restoring OPCs and OLs levels toward those observed in control animals.

Conclusion:
Overall, these findings, together with previous results from our laboratory, suggest that E2F4DN may represent a promising multifactorial therapeutic strategy for AD. Nevertheless, further studies are needed to better understand the alterations affecting OPCs and OLs and to clarify the specific role of E2F4DN in this context.

Key words: Alzheimer; oligodendrocytes; OPCs; E2F4; h5xFAD.

UAM Universidad Autónoma de Madrid | Escuela de Doctorado | Facultad de Medicina

Semana del Doctorado, Facultad de Medicina 28th May 2026

PhD Student Name and surname: Ana Ferrández Múrtula
UAM PhD program: Molecular bioscience
COMMUNICATION TYPE: Poster

TITLE: Identification of chromosomal integration sites in Escherichia coli Nissle 1917 for expression of therapeutic protein cargoes in a safe bacterial chassis

Authors: Ana Ferrández Múrtula [1], Elena M. Seco[1] and Luis Ángel Fernández[1]

AFFILIATIONS:

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ABSTRACT (350 Word limit)

Background:
Escherichia coli is widely used as a host in synthetic biology, and non-pathogenic variants allow therapeutic applications without additional attenuation. Among them, *E. coli* Nissle 1917 (EcN) has emerged as a promising live biotherapeutic chassis due to its probiotic safety profile and clinical use history. However, the design of modular EcN-based therapies requires well-defined chromosomal loci that permit stable and safe integration of therapeutic payloads. This study aimed to identify non-essential genetic regions in EcN associated with adhesins, fimbriae, autotransporters, and toxin-related factors, and to assess their potential as genomic insertion sites for heterologous protein expression.

Methodology:
We used a conjugation-based workflow developed in our lab that employs suicide integration vectors carrying homologous recombination arms flanking a *Ptac*-GFP reporter cassette. Vectors were mobilized into EcN via a donor–recipient conjugation system and resolved through double homologous recombination, generating scarless, markerless chromosomal insertions devoid of antibiotic resistance genes and plasmid backbone sequences. Each targeted locus was confirmed by PCR and fluorescence-based screening, ensuring integration accuracy and stability. Expression profiling was performed under both induced and non-induced conditions to evaluate promoter responsiveness and identify loci offering suitable dynamic ranges for protein expression.

Results:
Successful integration events were obtained across multiple chromosomal loci linked to adhesion-related and virulence-associated genes. The GFP reporter system enabled precise quantification of basal and induced expression levels from each genomic site, revealing variability among loci in expression strength and regulation efficiency. Several integration points exhibited stable, controllable expression without compromising bacterial growth or probiotic characteristics, suggesting their suitability for future loading of therapeutic payloads.

Conclusion:
This work establishes a conjugation-driven, markerless strategy for targeted genome engineering in *E. coli* Nissle 1917. By combining scarless integration with expression profiling, we delineate chromosomal sites compatible with therapeutic protein expression, thus advancing EcN as a safer, genome-programmable bacterial chassis for biomedical and synthetic biology applications.

Key words: *Escherichia coli* Nissle 1917, chromosomal integration, conjugation, therapeutic protein expression, synthetic biology.

PhD Student Name and surname: Violeta Araque
UAM PhD program: Neuroscience
COMMUNICATION TYPE: POSTER

TITLE: Regulating fear conditioning in wild type mice and FMR1KO mice

Authors: V Araque, R Garcia, I.B. Maroto, M Guzman, R. Ammar, H. Fetoui and, D. Fernández de Sevilla

AFFILIATIONS:

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Laboratory of Toxicology-Microbiology and Environmental Health (17ES06), Faculty of Sciences of Sfax, University of Sfax, BP1171, 3000 Sfax, Tunisia

ABSTRACT (350 Word limit)

Background:

Autism is a neurological disorder characterized by anxiety-like behavior, deficits in associative learning, and in social interaction. The FMR1KO mice is one of the most studied models of monogenic autism. Fear conditioning is a form of associative learning and memory that has been the focus of numerous studies centered on the neuronal functionality and connectivity of the brain regions involved in this learning process. However, the regulation of this associative learning process by neuromodulators is largely unexplored. Astrocytes modulate synaptic transmission, and IGF-1 plays a key role in synaptic plasticity, spatial learning, and anxiety-like behavioral processes. We have found that optogenetic activation of astrocytes in the prelimbic area of the medial prefrontal cortex, a brain area involved in fear conditioning, increases fear expression in wild-type mice. This increase in fear levels correlates with an increase in the AMPA/NMDA ratio of the prelimbic layer 5 pyramidal neurons, suggesting an increase in synaptic efficacy as the cellular mechanism of this effect. Interestingly, although IGF-1 decreases fear levels by favoring fear extinction in the wild-type mice, we found that IGF-1 increases fear expression in FMR1KO mice. The aim of this research was to test the effects of insulin-like growth factor-1 (IGF-1) and CuO NPs as neuromodulators to regulate associative learning behavior in wild-type mice and FMR1KO mice.

Methodology:

Two-month-old C57BL6/J and FMR1KO mice were fear habituated, conditioned and tested in a chamber of 25x31x25 cm with aluminum and Plexiglas walls. The floor consisted of stainless-steel bars that could be electrified to deliver a mild shock. A speaker was mounted on the outside wall and illumination was provided by a single overhead light. The chamber was situated inside a sound-attenuating box with a ventilating fan, which produced an ambient noise level of 80 db. The conditioning stimulus (CS) was a 4 kHz tone during 30 s at a 80 dB intensity. The unconditioned stimulus (US) was a 0.4 mA scrambled foot shock during 2s, which co-terminated with the tone during the conditioning phase. Animals were divided into two groups, according to the treatment received, saline, Cu-NPs or IGF1 (20mg/kg) applied intraperitoneally. On day one all animals received the first conditioning trial (tone paired with shock; conditioned phase). The next two following days, mice were exposed to a different context (triangle box with no steel bars on the floor) for 300s with the same tone every 30 seconds but no sock was applied. Behavior was video recorded,

and freezing was analyzed. The total freezing time during the 30s tone was measured and converted to percentage of freezing. Freezing was defined as the cessation of all movements except respiration. The percentage of freezing time was used as a measure of conditioned fear (Blanchard DC, 1972). The behavioral data were analyzed by manual evaluation of the videos and/or using the image J free software with the pulgging developed for this purpose (Shoji et al., 2014). No differences were observed with both methods.

Results:
Results showed that contextual fear conditioning differs in wild-type vs FMR1KO female mice compared to contextual fear conditioning is not significant different in wild-type vs FMR1KO male mice. Also, we found that intraperitoneal injection of IGF1 alters the contextual fear learning of wild-type female mice but it does not affect contextual fear learning in FMR1KO female.

On the other hand, intraperitoneal injection of CuO-NPs does not alter the contextual fear learning of either wild-type female or FMR1KO female but it alters contextual fear learning in wild-type male mice.

Conclusion:
The contextual fear conditioning differs in wild-type vs FMR1KO female mice

The contextual fear conditioning is not significant different in wild-type vs FMR1KO male mice

Intraperitoneal injection of IGF1 alters the contextual fear learning of wild-type female mice

Intraperitoneal injection of IGF1 does not affect contextual fear learning in FMR1KO female

Intraperitoneal injection of CuO-NPs does not alter the contextual fear learning of either wild-type female or FMR1KO female

Intraperitoneal injection of CuO-NPs alters contextual fear learning in wild-type male mice

Key words: LTP; Autism, Fear conditioning, IGF1, CuO NPs