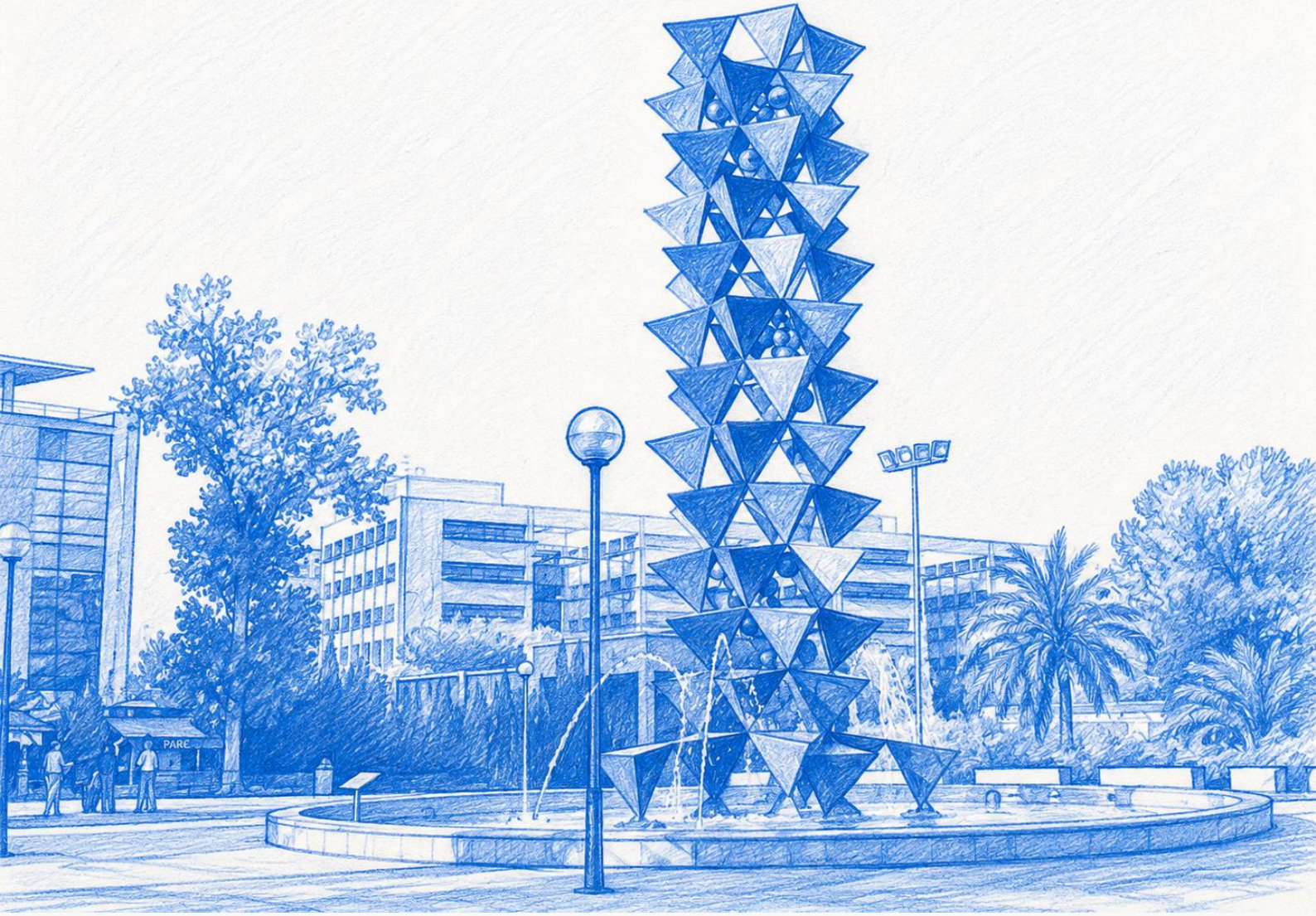
VNIVERSITAT DE VALÈNCIA

Institut Universitari de Biotecnologia i Biomedicina BIOTECMED

JORNADA ANUAL DEL INSTITUTO BIOTECMED

20 JULIO 2026

Salón de Grados – Facultad de Farmacia



Novogene

bioNova científica, s.l.

VNIVERSITAT DE VALÈNCIA Facultat de Ciències Biològiques

VNIVERSITAT DE VALÈNCIA Facultat de Farmàcia

VNIVERSITAT D VALÈNCIA Institut Universitari de Biotecnologia i Biomedicina BIOTECMED

JORNADA ANUAL DEL INSTITUTO BIOTECMED

Programa

20 de julio del 2026

08:45 – 09:00 Colocación de pósteres

09:00 – Bienvenida institucional

Isabel Fariñas

Vicerrectora de Investigación

Sacri R. Ferrón

Directora de Biotecmed

09:30-10:15 Charla plenaria de apertura

Daniel Ramón Vidal

Catedrático en la Universidad CEU Cardenal Herrera

"El futuro de la biotecnología en la industria agroalimentaria"

10:15- 10:45h Charla investigador invitado

Alfred Fillol

Investigador distinguido con experiencia Internacional

Instituto de Biología Integrativa de Sistemas (I2SysBio)

"Integrative mobilizable elements are pervasive throughout Pseudomonadota"

10:45- 11:00h Short talk Sponsor: Novogene

11:00-12:30 Pausa café y sesión de pósteres

Espacio para intercambio científico y networking.

12:30-13:20h Nuevas incorporaciones Biotecmed

Nicolás Gutiérrez Castellanos

Ramon y Cajal Investigator.

Grupo de Neurobiología. Social Plasticity lab.

"Hypothalamic circuits for the flexible control of social and sexual behavior"

Alba Timón Gómez

Marie Curie Postdoctoral Investigator

Grupo de Genómica Traslacional Humana

"Strategies to improve the delivery of synthetic therapeutic oligonucleotides"

13:20h-14:00 Conferencia *"Vidas en Ciencia"*

José Enrique Pérez Ortín

Catedrático en el Dpto. de Bioquímica y Biología Molecular

Grupo EGE:DtoP y Secretario de Biotecmed

"La carrera investigadora en Biología Molecular: la visión de un científico vocacional"

Clausura de la Jornada

Comida: Bar de Farmacia

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VNIVERSITAT D VALÈNCIA Facultat de Ciències Biològiques

VNIVERSITAT D VALÈNCIA Facultat de Farmàcia

JORNADA ANUAL DEL INSTITUTO BIOTECMED

20 JULIO 2026

Redes Sociales

BIOTECMED

Venue

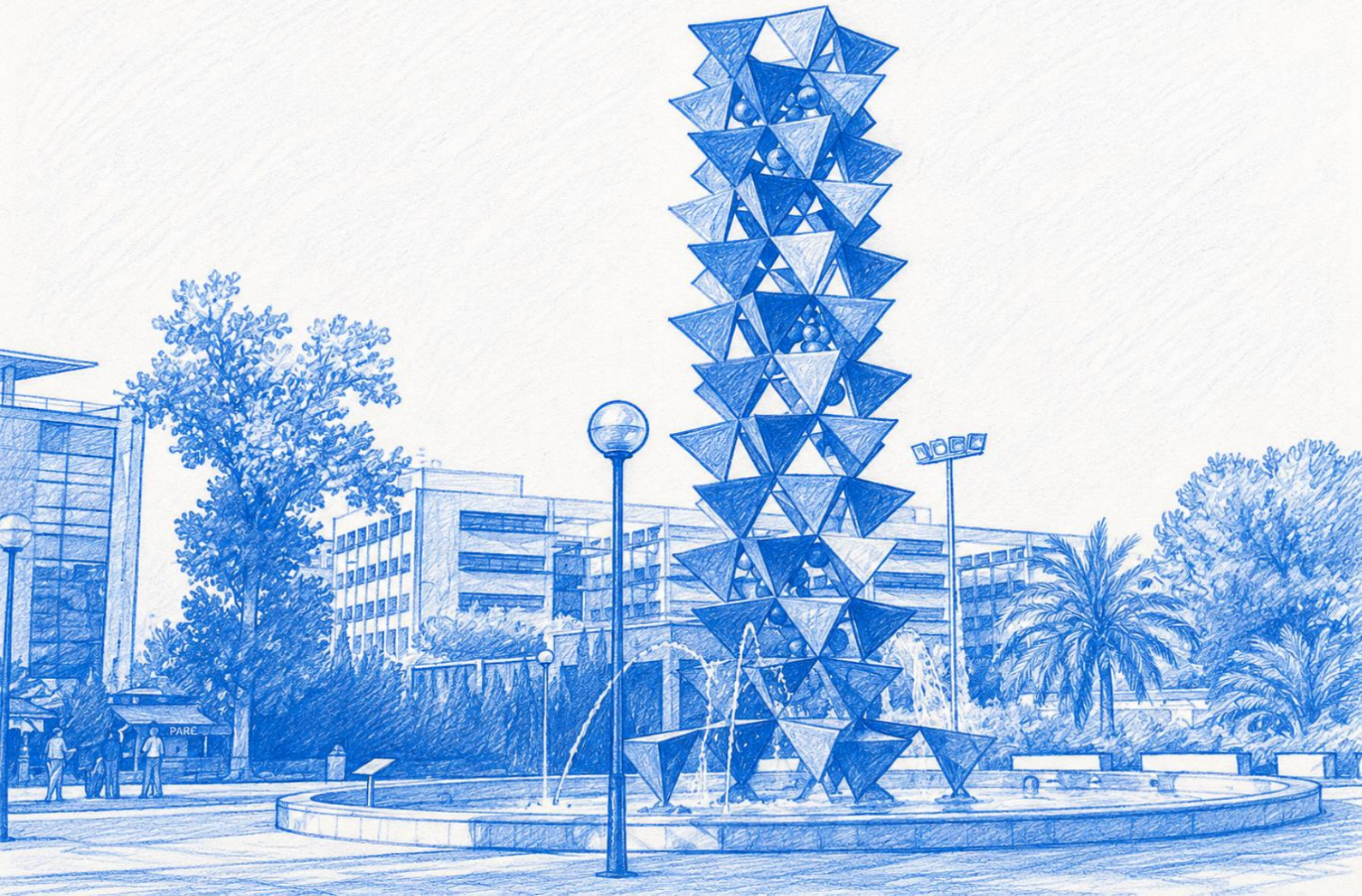
Facultad de Farmacia, University of Valencia

Salón de Grados

Avda. Vicent Andrés Estellés, s/n 46100, Burjassot (Valencia).

Sponsors

SPEAKERS



Opening Plenary Talk

"El futuro de la biotecnología en la industria agroalimentaria"

Catedrático en la Universidad CEU Cardenal Herrera

Daniel Ramón Vidal is one of Spain's leading biotechnology scientists, internationally recognized for his contributions to microbial biotechnology, food innovation, and the transfer of scientific knowledge to industry. He earned his degree and PhD in Biological Sciences from the University of Valencia, receiving the Extraordinary Doctoral Award in 1987, and completed postdoctoral training at Wageningen University in the Netherlands. Throughout his academic career, he held research and leadership positions at the Spanish National Research Council (CSIC), including Scientific Researcher, Research Professor, Director of the Institute of Agrochemistry and Food Technology (IATA), National Coordinator for Food Science and Technology, and Institutional Coordinator of CSIC in the Valencian Community. He also served as Professor of Food Technology at the University of Valencia.

In 2011, he became Chief Scientific Officer and CEO of Biopolis, a biotechnology company he helped create to translate cutting-edge research into industrial applications. He also co-founded and led LifeSequencing, a company specializing in large-scale genomic sequencing. Both companies were acquired by Archer Daniels Midland (ADM) in 2017, after which he became Vice President of Research & Development for Nutrition and Health at ADM. His research has focused on microbial biotechnology, systems biology, and microbial genomics, with applications in the food, nutrition, and health industries. He has published more than 150 peer-reviewed scientific papers and is the inventor of over 400 patents, most of which have been commercially exploited.

Professor Ramón has received numerous prestigious national and international awards, including the Spanish National Research Award "Juan de la Cierva", and was elected a Full Member of the Royal Academy of Engineering of Spain in 2020. Throughout his career, he has also served on numerous national and international scientific advisory boards, playing a key role in promoting innovation, biotechnology, and collaboration between academia, industry, and public institutions.

Invited Speaker

"*Integrative mobilizable elements are pervasive throughout Pseudomonadota*"

Investigador Distinguido con experiencia Internacional (I2SysBio)

Alfred Fillol

Investigador distinguido con experiencia Internacional

Instituto de Biología Integrativa de Sistemas (I2SysBio)

Alfred Fillol Salom is an internationally recognized microbiologist whose research focuses on bacteriophages, the viruses that infect bacteria, and their applications in biotechnology, microbial ecology, and human health. He is a Distinguished Researcher at the Institute for Integrative Systems Biology (I2SysBio), a joint research center of the University of Valencia and the Spanish National Research Council (CSIC).

After earning his PhD in Microbiology, Dr. Fillol carried out research at leading international institutions, where he developed expertise in microbial genomics, phage biology, and host–virus interactions. His work combines experimental and computational approaches to understand the role of bacteriophages in shaping microbial communities and their potential as alternatives to antibiotics and as tools for biotechnology.

His research has been published in high-impact international journals, and he has established himself as a leading scientist in the rapidly expanding field of phage biology. In recognition of his scientific achievements, he was awarded a Distinguished Researcher position under Spain's international talent recruitment program, joining I2SysBio to strengthen its research in microbial systems biology and virology.

BIOTECMED 2025 New Researchers

Ramón y Cajal Researcher

(BIOTECMED)

Nicolás Gutiérrez Castellanos obtained his B.Sc. in Biology from the University of Valencia and an M.Sc. in Experimental Biomedicine from the University of Castilla La Mancha. He completed his Ph.D. in Neuroscience at the Netherlands Institute for Neuroscience (NIN-KNAW, Amsterdam) as a Marie Skłodowska-Curie Fellow, where he investigated the neural mechanisms underlying cerebellar learning and synaptic plasticity. He then carried out postdoctoral research at the Champalimaud Foundation in Lisbon, working in the laboratories of Zach Mainen and Susana Lima, where he expanded his research to the neural circuits underlying decision-making, adaptive learning, and social behavior using state-of-the-art systems neuroscience approaches.

In 2025, he joined the Institute of Biomedicine and Biotechnology (BIOTECMED) at the University of Valencia as a Ramón y Cajal Researcher, where he established the Social Plasticity Laboratory. His research combines behavioral neuroscience, electrophysiology, imaging, and computational approaches to investigate how experience reshapes neural circuits to drive learning, memory, decision-making, and social interactions.

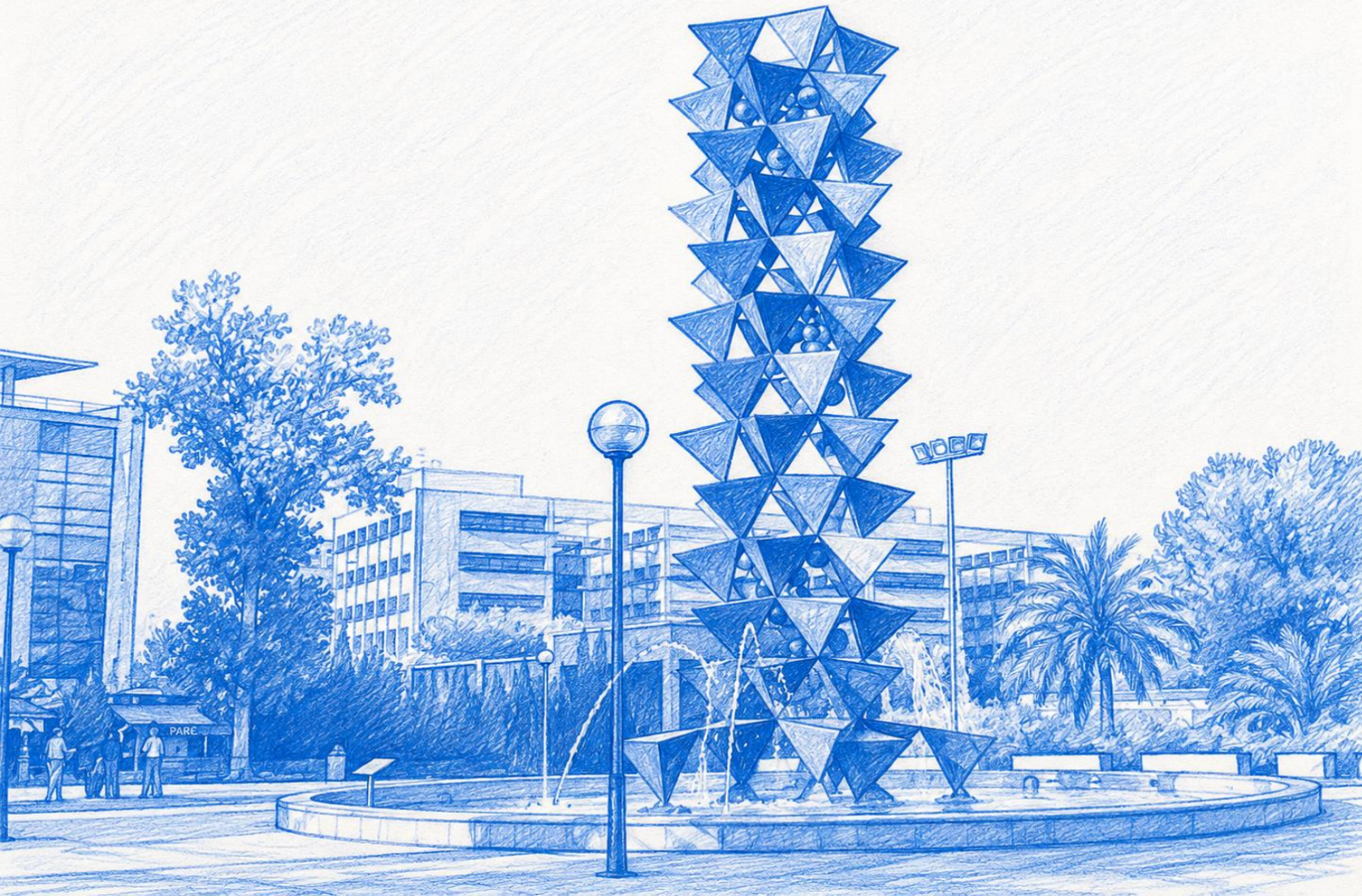
Marie Curie Postdoctoral Researcher

(BIOTECMED)

Alba Timón Gómez obtained her B.Sc. in Biotechnology and her Ph.D. in Biotechnology from the Universitat Politècnica de València (UPV), where she investigated the molecular mechanisms regulating mitochondrial function and cellular bioenergetics. She subsequently carried out postdoctoral research at the University of Miami (USA), studying the assembly and regulation of the mitochondrial respiratory chain and its role in oxygen sensing, followed by a second postdoctoral appointment at Oroboros Instruments (Austria), where she specialized in high-resolution respirometry and advanced approaches to mitochondrial physiology. In recognition of her scientific excellence, she was awarded a prestigious Marie Skłodowska-Curie Postdoctoral Fellowship.

In 2025, she joined the Institute of Biomedicine and Biotechnology (BIOTECMED) at the University of Valencia as an ARISTOS postdoctoral researcher. Her research focuses on mitochondrial biology, cellular bioenergetics, and the development of innovative nucleic acid-based therapies for genetic disorders, combining molecular biology, genomics, and metabolic analysis to better understand disease mechanisms and identify new therapeutic strategies.

POSTERS ABSTRACTS



P1. The Phosphorylated Pathway of Ser Biosynthesis (PPSB) is essential for the rhizobium–legume symbiosis in Lotus japonicus

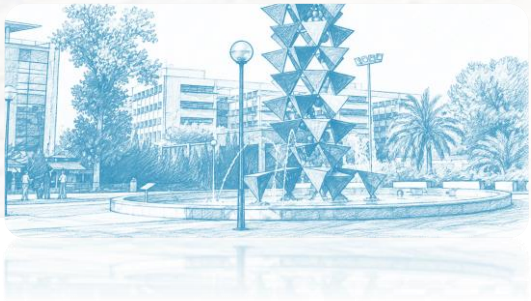
Martínez-Serra C, Doghri Maroua, García-Calderón M, Márquez AJ. Betti M, Muñoz-Bertomeu J, Torres-Moncho A, Renau-Morata B, Blancato G, Rosado-Souza L, Fernie A, Ros R and Rosa-Téllez S

*Metabolismo Primario e Ingeniería (**ROC ROS GROUP**)*

Legumes form a mutualistic association with rhizobia, which reduce atmospheric N_2 into ammonium for the plant. The development of nitrogen-fixing root nodules depends on two tightly regulated host processes: de novo organogenesis of nodule primordia and rhizobial colonization[1,2]. The amino acid L-serine (Ser) participates in the biosynthesis of several biomolecules, including one-carbon (1C) units essential for methylation reactions, purine and pyrimidine synthesis, which are critical for cell differentiation and proliferation. In plants, Ser is synthesized mainly through the Phosphorylated Pathway of Ser Biosynthesis (PPSB) and the glycolate pathway. We recently described the Ser–Gly–1C network as a metabolic hub regulating sulfur metabolism and root development[3]. In legumes, sulfur metabolism and root architecture are crucial for symbiotic nitrogen fixation4. Here, we characterized PGDH (3-phosphoglycerate dehydrogenase) genes in L. japonicus and identified three orthologs: LjPGDH1, LjPGDH2-1 and LjPGDH2-2. Expression analyses showed that LjPGDH1 and LjPGDH2-1 are expressed in roots and nodules. Using mutant lines from the LORE1 collection5, we found that single mutants for LjPGDH1 (p1p1) do not display the embryo-lethal phenotype observed in Arabidopsis6, suggesting functional redundancy. Segregation analysis of crosses between LjPGDH1 and LjPGDH2-1 mutants revealed lethality of double homozygous individuals, with deviations from Mendelian expectations pointing to a predominant role for LjPGDH1. Phenotypic characterization of individuals derived from double heterozygous lines (P1p1/P2p2) revealed a gene-dosage effect: plants homozygous for LjPGDH1 and heterozygous for LjPGDH2-1 (p1p1/P2p2) showed the greatest biomass reduction, particularly under symbiotic conditions, where nodule organogenesis was compromised. Metabolome analysis of p1p1/P2p2 mutants revealed altered Ser/Gly contents, potentially affecting 1C supply and cell differentiation during nodule maturation. Transcriptome analysis showed functional enrichment of genes involved in organ senescence, protein catabolism and cysteine-type peptidase activity, pointing to a premature nodule senescence process and demonstrating the essential role of the PPSB in the establishment of the rhizobium–legume symbiosis.

References

1. Crespi M et al. (2008) Sci. Signal. 1(49): re11
2. Zhang X et al. (2024) *Plant Commun.* 5(11):101045
3. Rosa-Téllez *et al.* (2023) *Plant Cell.* 2023:1-23
4. Becana M *et al.* (2018) *Front. Plant Sci.* 9(1434):1-10
5. Małolepszy A *et al.* (2016) *Plant J.* 88:306-317
6. Toujani W et al. (2013) Plant Physiol. 163(3):1164-78



P2. Microtubule dynamics as a key modulator in the response to heat stress in plants.

Eva Hoyas-Sánchez, María Sáez-Díaz, Jose Casañ, Diego Herencias-Mateos, Juan Carlos Montesinos.

*Respuesta celular al estrés ambiental (**MONTESINOS LAB**)*

Plants are constantly exposed to environmental stresses such as high temperature, salinity, drought, and UV radiation. Since plants cannot relocate, they have evolved mechanisms that enable them to rapidly adapt to adverse conditions, a process known as the fast cellular response. This response is key to triggering and adjusting the subsequent responses necessary for the acclimatization phase. In our research, we investigate the still poorly understood role of microtubules (MTs) in the cellular response to heat stress, one of the abiotic stresses expected to have a major impact on plant survival in the coming years.

We found that heat stress rapidly induces depolymerization of cortical MTs in root epidermal cells and reduces root growth in Arabidopsis thaliana seedlings. Heat stress also alters MTs dynamics, decreasing MTs polymerization rates and promoting a reorientation from a transverse to an oblique array during the recovery phase. Experiments using the MTs-stabilizing drug Taxol have demonstrated that the MTs-depolymerization is not an unspecific response to heat shock damage. Preventing MTs depolymerization after heat shock led to an altered physiological response, with significantly stronger inhibition of root growth under heat stress. These results suggest that preventing MTs depolymerization could hinder part of the cellular response necessary to confront stress and achieve acclimatization.

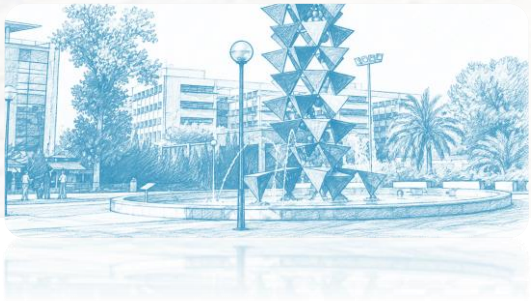
Cortical MTs depolymerization during heat stress is followed by the formation of dot-like MTs structures at the cortex-cytoplasm interface, compatible with heat stress-induced liquid-liquid phase separation (LLPS). These condensates may act as dynamic compartments that transiently sequester MTs-associated components, thereby contributing to the rapid reorganization of the MTs cytoskeleton during stress. We are currently investigating the role of MTs-associated LLPS in this cellular response.

P3. Using a mouse model of antibody-based hematopoietic progenitor-depletion to study Candida albicans-induced central innate memory in neutrophils

Andrea Guiu, María Sobén, Paula Guerrero, M. Luisa Gil and Alberto Yáñez

*Inmunología de las infecciones fúngicas (**IMMUNOSTEM**)*

Candida albicans is an opportunistic pathogen with the potential to cause from superficial to life-threatening systemic infections. Neutrophils are crucial to the defense against C. albicans as they are the first immune cells recruited to the site of infection. Neutrophils have recently been discovered as key effector cells of the innate immune memory (IIM), a transient, non-specific protective state induced by previous pathogen encounters. When IIM is initiated in hematopoietic stem and progenitor cells (HSPCs) is called central innate memory (CIM), especially relevant in neutrophils given their short lifespan. The study of CIM relies on transplantation-based assays, which present its very own problematics, encouraging new methodologies to emerge. In order to study the C. albicans-induced CIM, we have developed a mouse model of antibody-based hematopoietic progenitor-depletion and tested it in the evaluation of the functional phenotype of neutrophils differentiated from transplanted HSPCs exposed to different strains of C. albicans. In this work, we have produced, purified and in vivo tested the monoclonal antibody anti-c-Kit (clone ACK2), which specifically depletes HSPCs enhancing the engraftment of a subsequent HSPCs-transplant, without the side effects of the classical immunosuppressive procedures. Using this mouse model, we have found that HSPCs in vitro exposed to live C. albicans cells can differentiate in vivo to generate trained neutrophils (with enhanced production of TNF-α) in the bone marrow and spleen, and that, HSPCs in vivo exposed to live C. albicans generate neutrophils with a better ability to be recruited to the site of infection. This work introduces a robust and minimally invasive method to study CIM and also provides evidence that HSPCs can retain and transmit antifungal training cues to their neutrophil progeny. These findings highlight the therapeutic potential of harnessing trained immunity in hematopoietic progenitors to enhance host defense mechanisms to combat invasive fungal infections.



P4. *Candida albicans* activated hematopoietic stem and progenitor cells (HSPCs) produce trained neutrophils in a Dectin-1- and TLR2-dependent manner

María Sobén, Paula Guerrero, Andrea Guiu, Alberto Yáñez and M. Luisa Gil

*Inmunología de las infecciones fúngicas (**IMMUNOSTEM**)*

Central trained immunity, induced via reprogramming of hematopoietic stem and progenitor cells (HSPCs), mediates sustained heightened responsiveness of mature myeloid cells to secondary challenges. We have previously demonstrated that HSPCs use TLR2 and Dectin-1 to sense Candida albicans to induce the production of trained monocytes/macrophages to fight against secondary infection. However, the potential role of trained neutrophils in protection during candidiasis remains unexplored, despite the essential role of this cell type in protection against C. albicans infection.

In this work, we used an in vitro model of mouse HSPC differentiation to investigate the functional phenotype of neutrophils derived from HSPCs exposed to various pathogen associated molecular patterns (PAMPs) and C. albicans cells. We found that neutrophils derived from HSPCs stimulated by a TLR2 agonist exhibit reduced inflammatory cytokine production (tolerized neutrophils) whereas neutrophils generated from a Dectin-1 agonist or C. albicans stimulated HSPCs produce higher amounts of cytokines (trained neutrophils). We further demonstrated that a transient exposure of HSPCs to live C. albicans cells is sufficient to induce a trained phenotype of the neutrophils they produce in a Dectin-1- and TLR2-dependent manner. These trained neutrophils exhibited higher phagocytosis and microbicidal capacity than control neutrophils.

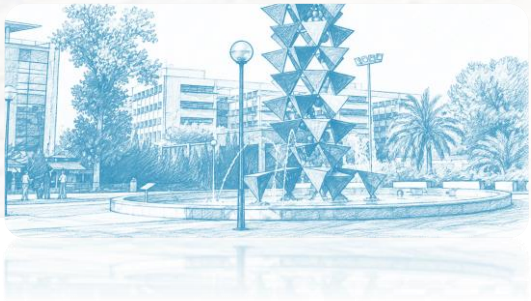
Overall, these results demonstrate that HSPCs can sense live C. albicans cells to generate trained neutrophils. Targeting this mechanism may provide a therapeutic strategy to boost neutrophil function and treat or prevent infectious diseases.

P5. Afadin couples cell–cell adhesion to molecular regulation of Radial Glial Cells during corticogenesis.

Alba Marín-Garnes, Laura Veintimilla-Escot, David de Agustín-Durán, Ana Pérez-Villalba, Jaime Fabra-Beser, Isabel Mateos-White, Carmen María Mateos-Martínez, Cristina Gil-Sanz.

*Neurobiología Molecular (**NEURAL DEVELOPMENT**)*

The neocortex is a highly organized brain structure whose proper formation is essential for its correct function. Higher cognitive functions such as language, sensory perception or cognition rely on this evolutionary recent acquisition of the mammalian brain. Although major efforts have been made to understand the regulatory mechanisms governing its development, many of these processes remain incompletely characterized. Radial glial cells (RGCs) are the embryonic neural stem cells that drive the generation, positioning, and specialization of neural cells. A tightly regulated balance between their proliferation and differentiation is crucial for proper neocortical formation, and its disruption can lead to structural and functional abnormalities. Previous studies have highlighted the importance of cell-cell adhesion molecules and their associated proteins in neocortical morphogenesis. Early inactivation of genes such as Cdh2 or Afadin in the dorsal telencephalon leads to cellular and molecular defects, including loss of apical attachment, abnormal delamination, and increased RGC proliferation. These alterations shift differentiation toward a major production of neurons expressing upper-layer markers and impair neuronal migration, ultimately disrupting neocortical developmental trajectories. Consequently, the neocortex exhibits marked disorganization, increased size, and double cortex formation. Interestingly, similar features have been described in certain mouse models of autism spectrum disorder (ASD) as well as in some ASD patients, and our extensive behavioral analyses revealed social impairments in Afadin mutant mice. In this study, we investigate the molecular mechanism regulated by Afadin during cortical development. To address this, we performed RNA sequencing-based transcriptomic analyses of RGCs and more differentiated neural cell populations from control and mutant mice at early (E13.5) and late (E16.5) stages of corticogenesis. Our analysis revealed significant changes in gene expression programs that coordinate mitotic dynamics and the balance between cortical progenitor maintenance and differentiation. These changes were further validated by RT-qPCR, immunohistochemistry, and RNAscope in situ hybridization. Together, these findings shed light on the essential role of Afadin in maintaining cortical organization and identify molecular pathways that may also be disrupted in neurodevelopmental disorders characterized by abnormal progenitor behavior.



P6. Investigating PCDH19 synaptic function in mouse embryonic stem cell-derived neurons

E. Stebleva, J. Griffiths, R. Gómez-Villafuertes, F. Ortega and I. Martinez-Garay

*Neurobiología Molecular (**NEUROADHESION**)*

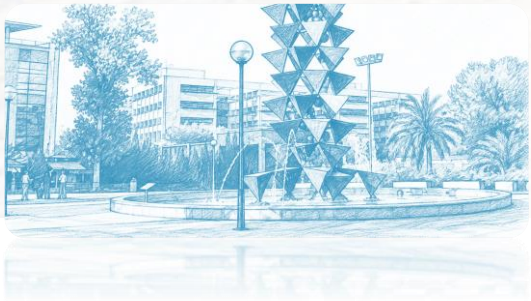
Protocadherin-19 (PCDH19), an X-linked cadherin superfamily member, is associated with early-onset epilepsy characterized by infantile seizures, cognitive impairment, and neuropsychiatric comorbidities. The disorder predominantly affects heterozygous females, most likely due to cellular interference arising from mosaic expression of PCDH19 in the brain. We have uncovered a reduced calcium response in mouse embryonic stem cell (mESC)-derived neurons lacking PCDH19 (PCDH19 knockout, KO) compared with wild-type (WT) neurons, and a similar reduction in WT neurons when co-cultured with PCDH19 KO neurons; however, the molecular mechanisms underlying this effect remain unknown. We aim to investigate the molecular mechanisms by which PCDH19 regulates synaptic function using mESC-derived neurons cultured as WT, PCDH19 KO, and WT/KO mixed populations to model mosaicism in vitro. Experiments are performed on mature neurons at day in vitro 12. Plasma membrane protein–enriched samples and synaptosomal fractions are analyzed using data-independent acquisition mass spectrometry to assess changes in the levels of membrane and synaptic proteins, respectively. Preliminary differential expression analysis has revealed significant changes in protein abundance between mutant, wild-type, and mixed populations. We will now use these proteomic data to formulate hypotheses regarding possible mechanisms underlying the reduced intracellular calcium response, which we will test and validated using calcium imaging and western blotting. Together, this work aims to link PCDH19-dependent proteomic alterations to functional changes in calcium signalling and synaptic activity in a cellular model of PCDH19-related epilepsy.

P7. Role of Pcdh9 in adult neural stem cells in the context of glioblastoma formation

Saray Calvo Parra, Olaya de Dios, Pau Garcia Bolufer, Tomás Viuda, Adrián Tarazona, Antonio Jordán Pla, Javier Gilabert Juan, Pilar Sanchez Gomez, Isabel Farinas, Andrzej W Cwetsch

*Grupo Neurobiología Molecular (**FARIÑAS LAB**)*

The subependymal zone (SEZ) of the adult brain constitutes a major neurogenic niche and plays a dual role in physiological neurogenesis and brain tumor pathophysiology. Neural stem cells (NSCs) within the SEZ generate interneurons for the olfactory bulb and transition through quiescent, primed, and activated states. Importantly, the SEZ has also been proposed as a source of cells that give rise to glioblastoma multiforme (GBM), a highly aggressive brain tumor, with glioblastoma stem cells (GSCs) sharing key properties with normal NSCs. Protocadherin 9 (Pcdh9), a member of the Protocadherin family, has been identified as a potential tumor suppressor whose downregulation has been reported in multiple cancers, including gliomas. Due to its structural features, Pcdh9 plays a pivotal role in regulating cell-cell adhesion and modulating signaling pathways involved in proliferation and differentiation. Loss of Pcdh9 expression has been associated with increased tumor growth and invasiveness in GBM; however, the mechanisms underlying its contribution to tumor progression remain poorly understood. Here, we employed single-cell RNA sequencing to reveal dynamic Pcdh9 expression across the NSC lineage. Pcdh9 is highly expressed in quiescent and primed NSCs, while its expression is reduced in activated NSCs and neural progenitor cells, suggesting a role in regulating NSC state transitions within the SEZ. We further demonstrate that Pcdh9 downregulation alters NSC proliferation and cell-cycle dynamics. Using an innovative three-electrode SEZ electroporation approach, we show that reduced Pcdh9 expression modifies NSC differentiation trajectories and affects signaling pathways commonly dysregulated in GBM. Finally, we characterize the impact of Pcdh9 downregulation on proliferation and invasion in murine GBM cell lines. Collectively, our findings identify Pcdh9 as a key regulator of NSC dynamics and suggest that its dysregulation may contribute to GBM pathogenesis.



P8. From adult neural stem cells to glioblastoma: exploring the miRNA imprintome

Daniel Samper-Llavador, Jennifer Díaz-Moncho, Jordi Planells and Sacri R. Ferrón

*Grupo Neurobiología Molecular (**NEUROIMPRINT**)*

Glioblastoma multiforme (GBM) is the most aggressive brain tumor in humans and has the poorest survival rate after diagnosis. Neural stem cells (NSCs) are responsible for neurogenesis in the subventricular zone (SVZ) of the adult brain, giving rise to neurons, astrocytes and oligodendrocytes. According to the cancer stem cell theory, GBM may originate from the transformation of NSCs into glioblastoma stem cells, which drive tumor initiation, progression and therapy resistance. MicroRNAs (miRNAs) are small non-coding RNA molecules that post-transcriptionally repress the expression of target mRNAs. Dysregulated miRNA expression, has been described in multiple cancers, including GBM, reporting that they can act both as oncogenes and tumor suppressors. Notably, DNA methylation regulates miRNA biogenesis and expression, linking monoallelic expression of imprinted miRNAs to the global genomic hypomethylation characteristic of GBM. This work explores the potential role of imprinted miRNAs in GBM initiation and progression using NSCs derived from the murine SVZ and a GBM cell line generated from NSCs carrying multiple mutations observed in human GBM. Whole transcriptome sequencing revealed a highly altered miRNome, with 16% of miRNAs differentially expressed in GBM cells compared to adult NSCs. More strikingly, most expressed miRNAs within imprinting clusters exhibited significant expression changes. Importantly, we identified miR-296-3p and miR-298-5p, located at the Gnas cluster, as candidates with a potential shared role in quiescence and activation of adult NSCs and GBM cells. These results provide insights into how imprinted miRNAs may contribute to GBM malignancy as key regulators of gene expression in the adult brain.

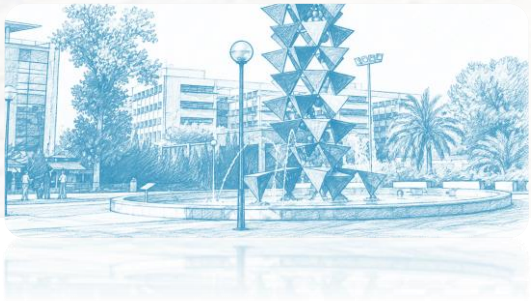
P9. Alterations in the formation of new neurons in the adult brain of a Prader-Willi Syndrome mouse model

Esteban Jiménez-Villalba, Jordi Planells, Laura Lázaro-Carot and Sacri R. Ferrón

*Grupo Neurobiología Molecular (**NEUROIMPRINT**)*

While most genes are expressed biallelically, a subset known as imprinted genes are expressed from only one allele in a parent-of-origin–dependent manner. These genes are typically organized in clusters, and their monoallelic expression is mainly driven by DNA methylation at specific regions called imprinting control regions (ICRs), which are differentially methylated (DMRs) between maternal and paternal chromosomes. Alterations in genomic imprinting underlie several diseases known as imprinting disorders, such as Prader–Willi syndrome (PWS), a neurodevelopmental disorder caused by loss of expression of paternally expressed genes within the Prader–Willi/Angelman syndrome (PWS/AS) cluster on human chromosome 15q11–13. In approximately 70% of cases, this loss is due to the deletion of some of these imprinted genes. Mapping patient deletions identified a critical region (PWScr) sufficient to produce a PWS-like phenotype, containing the orphan small nucleolar RNA gene SNORD116 and the noncoding gene IPW.

Gene dosage control by genomic imprinting plays a key role in adult neural stem cell (NSC) biology and niche regulation, and its disruption alters homeostasis. Here, we characterize the two main adult neurogenic niches – the subventricular zone (SVZ) lining the lateral ventricles, and the subgranular zone (SGZ) of the dentate gyrus of the hippocampus – in a PWS mouse model (PWScrm+/p–) carrying a paternal deletion of the murine orthologous PWScr. Regarding the SVZ, in vitro differentiation of NSCs showed that neurons obtained from PWScr deficient mice were less complex and branched than the ones obtained from wild-type SVZ-derived NSCs. On the other hand, transcriptomic analysis of the hippocampus of PWScrm+/p– mice revealed enrichment of Gene Ontology (GO) terms related to neuronal development and synaptogenesis. Further in vivo studies of adult neurogenesis in the SGZ showed an increased number of newborn neurons in PWS model mice compared to their wild-type littermates. Together, these findings suggest an important role of the PWScr in the formation and development of neurons in the adult brain.



P10. Impact of maternal separation and post-weaning social isolation on the reticular thalamic nucleus inhibitory circuits and microglia in a murine double-hit model.

Beltran M, Muñoz-Menzinger C, Ávila JC, Klimczak P and Nacher J

*Neuroplasticidad (**NACHER LAB.**)*

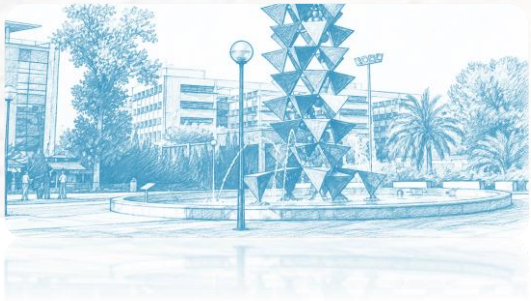
Exposure to aversive experiences during early life has been associated with alterations in brain maturation and may contribute to the development of psychiatric disorders such as major depression or schizophrenia. Previous animal models have reported behavioral changes linked to early-life stressors, which coincide with key neurodevelopmental processes occurring during the early postnatal period in mice, such as the closure of critical periods in inhibitory circuits. While these stress-induced alterations have been well described in the cortex, their impact on subcortical regions, such as the thalamus, remains poorly understood. The thalamus plays a crucial role in sensory information processing and higher cognitive functions, and its information flow is tightly regulated by inhibitory neurons located in the thalamic reticular nucleus (TRN). Most of these GABAergic neurons express parvalbumin (PV+), and are surrounded by a specialized extracellular matrix known as perineuronal nets (PNNs), which regulate neuronal plasticity. Microglia, the brain's immune cells, are also key regulators of circuit refinement during development and may mediate the effects of early-life stress. This study aims to explore how early-life adversities influence TRN inhibitory circuitry and microglia using a murine double-hit model. The model combines maternal separation (MS) from postnatal day 7 (P7) to weaning (P21) as an early life stressor, with post-weaning social isolation as a chronic stressor. Given the sex differences observed in psychiatric disorders, adult male and female mice were analyzed both grouped and separately. We found a significant reduction in the area occupied by microglial somata and decreased Iba1 fluorescence intensity in males, but not in females. Conversely, females showed increased immunofluorescence of PV+ neurons and PNNs, possibly indicating enhanced neuronal activity and reduced plasticity, respectively. These findings highlight the TRN as a relevant structure in the long-term effects of early-life adversity and emphasize the importance of including both sexes in neurodevelopmental studies.

P11. Distinct afferent signatures onto anterior and posterior VMHvl subdomains and their progesterone receptor-expressing neurons

Pablo Ruiz-Campillos, Julija Raudyte, Diogo F.M. Matias, Pablo Drees-Gimenez1, Inês C. Dias, Liliana Ferreira, Susana Q. Lima, Nicolas Gutierrez-Castellanos

*Neuroplasticidad (**NICO GUTIÉRREZ LAB.**)*

Female sexual behavior is tightly coupled to reproductive state and requires the coordinated regulation of sexual receptivity and rejection across the estrous cycle. In mice, these opposing behaviors are controlled by distinct anteroposterior subdomains of the ventrolateral ventromedial hypothalamus (VMHvl): the posterior VMHvl (pVMHvl) promotes sexual receptivity, whereas the anterior VMHvl (aVMHvl) drives sexual rejection. Although progesterone receptor–expressing (PR^+) neurons in both subregions are essential for these behaviors, the circuit mechanisms underlying this anteroposterior functional segregation remain poorly understood. Here, we investigated whether anterior and posterior VMHvl subdomains receive distinct afferent inputs that could support their divergent roles. Using classic retrograde tracing combined with whole-brain, machine learning–assisted quantification, we mapped the afferent connectivity of the anterior and posterior VMHvl. We found that while the two subdomains share a majority of their inputs, they also receive distinct and biased projections. The aVMHvl preferentially receives inputs from the anterior hypothalamic nucleus, paraventricular and peripeduncular thalamic nuclei, and the parabrachial nucleus, whereas the posterior VMHvl is preferentially innervated by the preoptic area, ventral premammillary nucleus, anteroventral periventricular nucleus, and lateral septum. To determine whether these afferents target behaviorally relevant neurons, we performed monosynaptic rabies tracing from PR^+ VMHvl neurons, which corroborated these domain-specific input signatures. Together, our results reveal distinct afferent architectures onto anterior and posterior PR^+ VMHvl neurons, providing a circuit-level framework for understanding how hormonal state flexibly biases female sexual behavior toward receptivity or rejection.



P12. Motivated behaviour, astrocytes and corticolimbic plasticity in a rodent model of inflammatory pain

Paula Andrés-Herrera, María De Jorge, Javier Cuitavi, Ana Polache and Lucía Hipólito

*Grupo Dolor Recaída y Alcoholismo (**DOREAL Laboratory**)*

Context:
Both pain and AUD engage overlapping neural circuits, including glutamatergic projections between the PFC and NAc, suggesting interacting mechanisms. Indeed, PFC-NAc projection is critical in the context of alcohol consumption and relapse but also in the development of chronic pain. Our previous preclinical studies have shown that inflammatory pain alters alcohol drinking behaviour; however, the underlying mechanisms remain unclear.

Goal:
This study investigates how inflammatory pain modulates astrocytic activation and glutamatergic signalling in the PFC–NAc pathway, aiming to clarify how pain-induced neuroplasticity could contribute to increased vulnerability to alcohol consumption.

Method:
Male and female Sprague Dawley rats received a hindpaw injection of Complete Freund's Adjuvant (CFA) to induce chronic inflammatory pain. We tested rats under progressive ratio (PR) schedule for sucrose and alcohol self-administration post-injection. Brain tissue was collected to analyse astrocytic markers (GFAP, S100β) and glutamatergic/neuroplasticity-related proteins (EGR1, mGluR2, NMDA receptor subunits) in PFC and NAc via immunohistochemistry and western blot.

Results:
Inflammatory pain decreased sucrose motivated behaviour in a sex- and time-dependent manner but had no significant impact in alcohol responding under PR. Additionally, inflammatory pain increased astrocytic markers in specific PFC subregions and induced differential expression of NR2A and NR2B subunits in both PFC and NAc.

Conclusion:
Our findings reveal inflammatory pain induces significant astrocytic activation and glutamatergic remodelling in the PFC–NAc pathway, which may modulate reward-related behaviours such motivation for sucrose. However, alcohol motivated behaviour was not directly affected under our protocol.

P13. Caracterización funcional, estructural y fenotípica de la unión de ligando al sistema Rcs de *Salmonella.*

Ignacio Francés-Castillo, Daniel Martí-Montón, Rebeca García-Lucena, Francisco García-Del Portillo and Patricia Casino.

Proteínas de membrana **(LABORATORIO DE BIOLOGÍA ESTRUCTURAL)**

Salmonella enterica serovar Typhimurium es una enterobacteria patógena que causa gastroenteritis1. El sistema Rcs es un sistema complejo de fosfotransferencia conservado en enterobacterias, el cual responde al estrés de membrana, regula positivamente la producción de cápsula de exopolisacárido, reprime motilidad, y participa en virulencia2. Este sistema está constituido por los receptores periplásmicos RcsC y RcsD conectados funcionalmente con el regulador transcripcional RcsB mediante una cascada de fosfotransferencia. La actividad del sistema se modula negativamente por la proteína de membrana IgaA y positivamente por la lipoproteína de membrana externa RcsF3. La identidad de las señales que activan el sistema es todavía desconocida. Nuestro objetivo es identificar posibles ligandos que activen el sistema Rcs de S. Typhimurium caracterizando su unión y efecto mediante aproximaciones funcionales, estructurales y fenotípicas. Hemos determinado la estructura cristalina del dominio periplásmico de RcsD. Tiene similitud a dominios doble-CACHE, forma un dímero de arquitectura no descrita previamente, y responde a un catión divalente formando un tetrámero. Hemos caracterizado funcionalmente esta dimerización y el sitio de unión de ligando mediado por dos residuos de His y dos de Asp. Sorprendentemente, RcsB también une catión divalente con dos sitios de unión identificados que implican dos residuos de His. Mediante estudios estructurales se visualiza uno de estos sitios en una estructura hexamérica de RcsB determinada previamente4 cuyo papel era hasta ahora desconocido.

Además, se han realizado estudios fenotípicos en cepas de S. Typhimurium con pérdida parcial de función en el represor IgaA (alelo igaA1) y deleccionadas en rcsB ó rcsD endógenos y complementadas con variantes mutantes de RcsB ó RcsD en los residuos de unión de ligando. La cepa igaA1-ΔrcsB complementada con RcsB silvestre muestra producción de cápsula y represión de la motilidad, mientras que los mutantes no producen cápsula, lo que indica que dichos residuos son relevantes para función. En cambio, la cepa igaA1-ΔrcsD complementada con las variantes mutantes de RcsD no se diferencia de la RcsD silvestre. En conjunto, nuestros resultados identifican la unión de un mismo ligando a dos componentes del sistema Rcs y sugieren que esta interacción está relacionada con la producción de cápsula.

Referencias:

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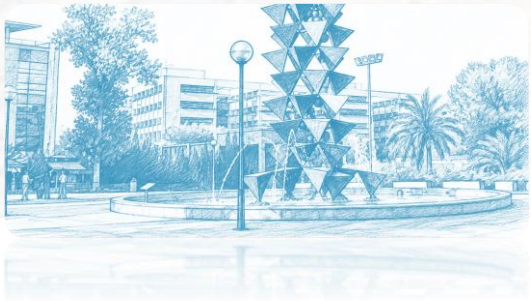


P14. Selección de cepas de *Lachancea thermotolerans* y evaluación de su potencial acidificante y bioprotector.

Isidoro Olmeda Hurtado, Sergi Ferrer Soler and Isabel Pardo Cubillos

Microbiología y Biotecnología Enológica **(ENOLAB)**

El cambio climático provoca aumento del pH de los vinos, lo que favorece la presencia de microorganismos alterantes y compromete la calidad y seguridad del vino. Se requieren estrategias que aseguren la estabilidad microbiológica y preserven las características organolépticas evitando así los sulfitos. El objetivo de este trabajo es seleccionar cepas de Lachancea thermotolerans con capacidad acidificante y actividad antimicrobiana como alternativa sostenible a los aditivos químicos.

Metodología

Se aislaron 19 cepas de L. thermotolerans de bodegas españolas y se evaluó su capacidad acidificante en mosto blanco Moscatel. Se adaptaron en 10 mL de: 1) mosto sintético, 2) mosto comercial estéril al 50% y 3) mosto Moscatel. En este último, a los 15 días se midieron ácido láctico y pH final, seleccionando las cepas con mayor producción de láctico y descenso de pH. Con ellas se realizó co-inoculación con S. cerevisiae (Aroma White, Enartis), añadida 24 h después en 10 mL de mosto. La cepa con mayor producción de láctico y menor pH se ensayó en 4 L. Se hicieron tres fermentaciones (4 L): L. thermotolerans CDS12, L. thermotolerans comercial (Excellence X-Fresh, Lamothe-Abiet) y control con solo S. cerevisiae.

La capacidad bioprotectora y acidificante se evaluó mediante recuentos en WL, MRS y MLO (levaduras, bacterias lácticas y acéticas) a los 1, 2, 3, 4, 7 y 15 días. La identificación se realizó por secuenciación del gen 16S (bacterias) y del ITS (levaduras). La producción de ácidos se determinó por HPLC.

Resultados

En el ensayo inicial se seleccionaron 4 cepas por su mayor producción de ácido láctico (>8.3 g/L) y mayor descenso de pH (entre 0.57 y 0.63), tras 15 días. En la co-inoculación en 10 mL, el aislado CDS12 mostró los mejores resultados (17.32 g/L de ácido láctico; disminución pH 0.49). En 4 L, Excellence X-Fresh el pH disminuyó 1.41 unidades y CDS12 1.34 ; sin embargo, CDS12 produjo menos ácidos acético y succínico que Excellence X-Fresh durante los primeros 7 días. En bioprotección, ambas cepas de L. thermotolerans redujeron las poblaciones de Komagataeibacter saccharivorans y Gluconobacter sp. entre los días 1 y 7.

Conclusión

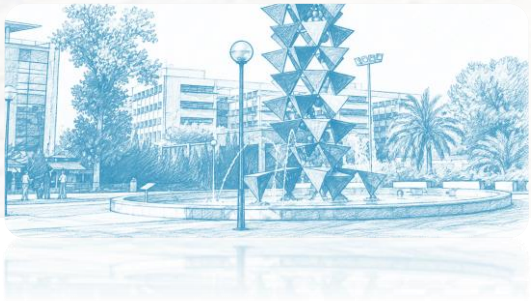
La cepa CDS12 logró un descenso de pH similar al de la cepa comercial, con menor producción de ácido acético y succínico. Ambas cepas de L. thermotolerans redujeron la población de Komagataeibacter saccharivorans y Gluconobacter sp.

P15. Biogenesis of the SARS-CoV-2 membrane protein

Juan Ortiz-Mateu, Pearson GJ., Alonso-Romero J, Rius-Salvador M, Sedighian S., Pavlova A., De Gregorio A., González-Dominguez I., Metola A., García-Murria MJ, Gumbart JC, von Heijne G, Carlton JG, Sánchez-Del Pino MM*, Martínez-Gil L, Mingarro I.

*Proteínas de Membrana (**MemProt Lab**)*

Viral protein biogenesis underpins every viral life cycle stage, and elucidating these processes could reveal fundamental principles of virus–host interaction, and vulnerabilities amenable to therapeutic targeting. Here we apply biophysical, molecular, and cell biology techniques to investigate the insertion, folding, and oligomerization of the SARS-CoV-2 M protein. We describe the sequential co-translational insertion of the hydrophobic core, and demonstrate that the cytosolic C- terminal domain undergoes slower adoption of its tertiary structure. Additionally, we characterize how the transmembrane domain bundle facilitates M-protein oligomerization. Our results reveal a hydrophobic residue cluster that is essential for protein folding and co-translational dimerization. Additionally, we identify the cellular machinery responsible for targeting and inserting the M protein into the ER membrane, and chaperones and cofactors that may contribute to proper folding.



P16. Receptor profiling of Spodoptera exigua for Vip3A protein from Bacillus thuringiensis.

Júlia Gironés Ases, Luis Benavent-Albarracín, Leopoldo Palma, Patricia Hernández-Martínez, Juan Ferré

Control biotecnológico de plagas **(CBP)**

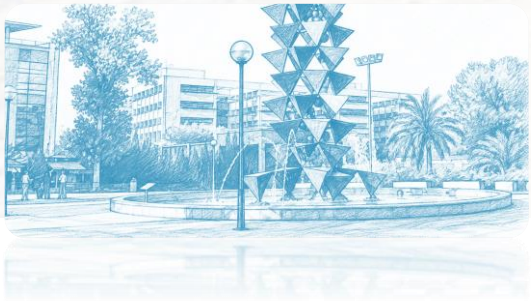
We investigated potential receptors for Bacillus thuringiensis Vip3 protein in Spodoptera exigua using immunoprecipitation assays with brush border membrane vesicles (BBMV). Using this methodology, some candidate proteins capable of binding to the Vip3Aa protein were identified. For the present work, the V-type ATPase, a membrane-associated proton pump, was chosen to validate its role as a functional receptor protein. For this purpose, the gene encoding the membrane-integrated aC subunit of the V-ATPase was disrupted using CRISPR/Cas9. As controls, we used two insect lines from our insectary: 1) Vip3-susceptible S. exigua larvae, and 2) CRISPR-edited larvae with a targeted disruption of the chs2 gene, which encodes chitin synthase 2. Bioassays revealed that larvae lacking V-ATPase did not show increased resistance to Vip3, suggesting that this protein may bind Vip3 in vitro but is not essential for its toxicity. In contrast, chs2-disrupted larvae exhibited high levels of resistance to Vip3, surviving concentrations exceeding 2000 ng/cm² (LC_{50} in susceptible larvae ~20 ng/cm²). These findings indicate that while V-ATPase may function as a binding partner, chs2 disruption strongly reduces Vip3 susceptibility in S. exigua. Further studies will be necessary to fully characterize the role of chs2 and to identify functional Vip3 receptors in S. exigua.

P17. Comparative characterization of two related viruses in different parasitoid species

Rosalía García García, Jesica Pérez-Rodríguez, Salvador Herrero and Laila Gasmi

Control Biotecnológico de Plagas **(CBP)**

Parasitoids are key players in biological control strategies and essential components of terrestrial ecosystems. Despite their importance, little is known about how parasitoids and viruses interact, except for domesticated endogenized DNA viruses (DEVs) that have developed an obligatory, mutualistic interaction with their parasitoid hosts. Within this interaction, DEVs benefit from the host machinery for their replication and propagation, meanwhile the successful development of the parasitoid progeny within the parasitoid's host depends on the DEV immunosuppressive genes. In contrast, RNA viruses associated with parasitoids are often overlooked. Herein, we aim to characterize the association between RNA viruses, parasitoids and their respective mealybug hosts. In a previous study, we identified the RNA virome of two mealybug–parasitoid systems relevant to Mediterranean Basin citriculture: the native Planococcus citri–Anagyrus vladimiri system and the invasive Delotococcus aberiae–Anagyrus aberiae system, native to South Africa and employed in a classical biological control strategy. Despite their original geographical distribution, the two parasitoid species are each infected with a distinct phasmavirus sharing around 70% sequence homology. Each phasmavirus is injected by its respective parasitoid through oviposition suggesting a potential role in parasitism success. Herein, we aim to obtain insights into the interaction Phasmavirus-parasitoid-host by assessing: viral prevalence within populations, tropism, transmission and implication in the parasitism success. Adding to this, we explored whether the phasmaviruses dynamics and effects are conserved between both parasitoid species



P18. Dual regulation of the levels and function of Start transcriptional repressors drives G1 arrest in response to cell wall stress

Mihai Spiridon Bodi, J. Carlos Igual, Mercè Gomar-Alba.

Regulación del ciclo celular en eucariotas

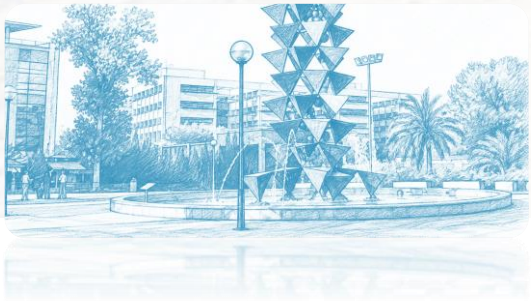
Many different stress signaling pathways converge in a common response: slowdown or arrest cell cycle in the G1 phase. The G1/S transition, or Start, is a key checkpoint controlled by positive and negative regulators. Among them, Whi7 and Whi5 are transcriptional repressors of the G1/S transcriptional program, yeast functional homologs of the Retinoblastoma family proteins in mammalian cells. Under standard conditions, Whi7 plays a lesser role than Whi5 in Start inhibition. However, under cell wall stress, Whi7 is induced and plays a more important role in G1/S control. In this work, we investigated the functional hallmarks of Whi7 and Whi5, which determine their strength as Start inhibitors under cell wall stress. We found that cell wall stress promoted the specific upregulation of the Whi7 Start repressor. First, although cell wall stress increases Whi7 protein levels, this is not the only determinant behind the Whi7 function in promoting G1 arrest. Indeed, artificial induction of Whi5 at the same protein level resulted in a lower G1 block. Second, under cell wall stress, Whi7 was specifically recruited to SBF-target promoters, independent of the increase in its protein levels or cell cycle stage. Finally, we found that Whi7 protein instability further increased during cell wall stress and that Whi7 degradation triggered advanced cell cycle re-entry. Here, we show that cell wall stress signaling specifically enhances Whi7 function as a Start transcriptional repressor. Importantly, we identified new Whi7-specific regulatory mechanisms that do not operate in the Whi5 repressor. Our results indicate that cells may benefit from stress-specific repressors to ensure the stress-induced G1 arrest and that Whi7 rapid degradation may be particularly important to resume cell cycle upon adaptation.

P19. Unmasking Essentiality: How Yeast Bypasses eIF5A Dysfunction Through Transcriptional Rewiring

Samoa Prieto-Diez, Alejandro Aguilar, Luis Araque, David Peris and Paula Alepuz

Expresión génica en eucariotas: del DNA a las Proteínas ***(EGE:DtoP)***

The eukaryotic translation initiation factor 5A (eIF5A) is essential and highly conserved from archaea to eukaryotes. eIF5A binds to ribosomes to facilitate translation of specific peptide motifs, e.g. consecutive prolines, that would otherwise cause ribosome stalling. eIF5A is involved in proliferation, differentiation, autophagy and mitochondrial function and has been implicated in cancer, viral infection, neurodegenerative diseases and aging. In most eukaryotes, including the yeast Saccharomyces cerevisiae, there are two eIF5A isoforms encoded by two highly conserved paralogous genes, TIF51A and TIF51B. The expression of these genes is tightly regulated: under aerobic conditions, TIF51A is activated by the transcription factor Hap1, which is also the activator of the TIF51B repressors, Rox1 and Mot3; whereas under anaerobic conditions TIF51B is expressed while TIF51A is repressed. To further investigate the function of eIF5A, we used thermosensitive mutants of eIF5A, tif51A-1 and tif51A-3, containing one or two point mutations in the Tif51A protein, and isolated suppressors able to grow at the restrictive temperature of 37ºC. All suppressors from these strains showed upregulated expression of TIF51B under aerobic conditions, allowing cells to grow at 37ºC, where the mutant Tif51A protein is degraded. Genomic sequencing of the suppressors revealed mutations in Rox1 or Mot3, lifting their repressive effect on TIF51B. On the other hand, suppressors from tif51A-1 and tif51A-3 strains lacking the TIF51B gene showed reversions or additional mutations in the TIF51A gene itself, restoring stability at 37ºC. In conclusion, our results provide a collection of mutations in the Rox1 and Mot3 repressors, revealing how their inactivation enables the expression of TIF51B under aerobic conditions. Furthermore, our results highlight the essential role of eIF5A in yeast, showing that no alternative mechanism can compensate for the loss of TIF51A other than upregulation of its paralog gene.



P20. Caracterización del miRNome en la distrofia miotónica tipo 2

Àngela Natividad-Mateu, Luis Orduña-Rubio, Javier Poyatos-García, Juan Vilchez, Rubén Artero-Allepuz, Arturo Lopez-Castel, Ariadna Bargiela-Schönbrunn.

Genómica Traslacional Humana

A pesar de los importantes avances en el esclarecimiento de la patogénesis de la distrofia miotónica tipo 1 (DM1), la distrofia miotónica tipo 2 (DM2) sigue siendo relativamente poco estudiada en comparación con la DM1, lo que pone de manifiesto la necesidad de comprender mejor sus bases moleculares y desarrollar terapias eficaces. La DM1 está causada por una expansión de repeticiones CTG en el gen DMPK, mientras que la DM2 se debe a una expansión de repeticiones CCTG en el gen CNBP. En ambas enfermedades, estas expansiones generan transcritos de ARN tóxicos que se acumulan formando focos nucleares y secuestran proteínas de unión al ARN de la familia Muscleblind-like (MBNL), reguladores clave del splicing, lo que provoca alteraciones generalizadas del procesamiento del ARN. Sin embargo, el secuestro de MBNL en la DM2 es menos pronunciado y presenta una correlación más débil con la gravedad clínica que en la DM1, lo que sugiere que existen mecanismos adicionales implicados en la enfermedad.

En la DM1, además del secuestro de MBNL, la desregulación de múltiples microARN contribuye a los mecanismos patogénicos. Entre ellos, miR-23b y miR-218 se encuentran sobreexpresados y actúan como represores endógenos que agravan aún más la depleción de MBNL. Se ha demostrado que los antimiRs dirigidos contra estos microARN restauran los niveles funcionales de MBNL, corrigen los defectos de splicing y reducen los focos nucleares de ARN en modelos preclínicos. Basándonos en estas observaciones y en evidencias previas de desregulación de microARN en DM2 detectadas mediante microarrays, planteamos la hipótesis de que los microARN podrían desempeñar un papel clave en la patogénesis de la DM2. Para comprobarlo, realizamos secuenciación de ARN pequeño (Small RNA-seq) en seis biopsias musculares de pacientes con DM2 y controles, seguida de análisis bioinformáticos y de ontología génica para identificar microARN desregulados con posible relevancia funcional. Paralelamente, llevamos a cabo secuenciación de ARN mensajero (mRNA-seq) en las mismas muestras, lo que permitió obtener un perfil transcriptómico global que incluye tanto cambios en la expresión génica como eventos de mis-splicing, estos últimos reconocidos como biomarcadores pronósticos de la fuerza y la función muscular en la DM1. La integración de ambos conjuntos de datos proporciona un marco para relacionar la desregulación de microARN con los defectos de splicing y las alteraciones transcriptómicas en la DM2, aportando información sobre los mecanismos de la enfermedad, su posible relación con la gravedad clínica e identificando nuevas dianas moleculares con potencial terapeútico.

P21. Microfluidics-free PIP-seq Reveals a Senescence-to-Fibrosis Signalling Axis in the Ageing Human Liver

Liwei Zhang, Ioannis K Deligiannis, Safiah Olabi, **Lona Lion**, Celia P Martinez-Jimenez.

Envejecimiento molecular en enfermedades crónicas

Single-nucleus RNA sequencing has advanced the study of human liver ageing, but droplet-based platforms such as 10x Genomics remain costly for extending existing cohorts. This study shows that PIP-seq, a microfluidics-free single-nucleus platform, recovers the same hepatic cell populations as 10x Genomics once matched quality-control thresholds are applied. Benchmarking of integration methods showed that the Seurat-CCA successfully integrated the two platforms into a single atlas that mixes cleanly. Marker gene expression is indistinguishable between platforms, while shifting clearly with donor age, indicating that PIP-seq matches 10x in sensitivity to genuine biological signal without introducing technical noise. Applying the combined atlas to young (under 20 years) and aged (over 60 years) human liver identifies fibrosis-associated markers and a macrophage-centred signalling circuit similar in tissue that is histologically non-fibrotic in both age groups. This points to a shared mechanism linking ageing and fibrosis in the liver. Together, these results support PIP-seq as a cost-effective complement to droplet-based platforms for expanding single-cell liver cohorts.