LIBRO DE ABSTRACTS

XIII Reunión de la Red Glial Española

Las Palmas de Gran Canaria

3 de septiembre de 2025

XIII Reunión de la RGE

Las Palmas de Gran Canaria
Septiembre 3, 2025

RED GLIAL ESPAÑOLA
RGE-SENC

FINAL PROGRAMME

8:30 WEST **Welcome and Inauguration**
Arantxa Tabernero
Chair of the Spanish Glial Network

SHORT TALKS (Chairs: Maite Solas, José Gómez-Sánchez)

9:00 WEST **OPCs' inflammatory memory as a key factor in remyelination**
Sonia Cabeza Fernández
Instituto de Neurociencias UMH-CSIC. Instituto de Investigación Sanitaria y Biomédica de Alicante

9:15 WEST **Accumulation of PFAS in myelin sheaths: Long-term consequences on myelination and myelin stability**
Victor Valcárcel Hernández
Muséum National d'Histoire Naturelle (CNRS), Paris

9:30 WEST **Unveiling the dynamic link between proliferation and phagocytic efficiency in brain development: the role of IKAROS**
Marco González Dominguez
Achucarro Basque Center for Neuroscience, Bilbao

9:45 WEST **Beneficial effects of astrocytic GLUT1 ablation in Alzheimer's disease**
Paula Escalada Matute
Universidad de Navarra, Pamplona

10:00 WEST **Decoding THC-related impairments: the role of astrocytic ensembles in the nucleus accumbens**
Cristina Martín Monteagudo
Instituto Cajal (CSIC), Madrid

10:15 WEST **Neuronal ensembles encoding sensory behavior are defined by astrocyte excitability**
Andrea Misol Ortiz
Hospital Nacional de Parapléjicos, Toledo

LAIA ACARIN AWARD LECTURE (Chair: Juliana M. Rosa)

10:30 WEST **Microglia mitochondrial complex I deficiency during development induces glial dysfunction and early lethality**
Nicolás Capelo-Carrasco y Bella Mora Romero
Instituto de Biomedicina de Sevilla

11:00 WEST **COFFEE BREAK**

PLENARY LECTURE (Chair: Federico N. Soria)

11:30 WEST **Microglia modulate neurovascular responses in health and disease**
Ádám Dénes
Institute of Experimental Medicine, Budapest

12:30 WEST **Assembly of the Spanish Glial Network**

13:00 WEST **Concluding remarks**

Plenary Lecture

Speaker Ádám Dénes
Affiliation Institute of Experimental Medicine, Budapest, Hungary

MICROGLIA MODULATE NEUROVASCULAR RESPONSES IN HEALTH AND DISEASE

Microglial phenotypes are altered in common brain diseases, but how microglial modulation of neurovascular processes changes in diverse disease states, is not well understood. We have identified novel forms of microglia-neuron interactions, through which microglia sense neuronal activity and injury, while also modulate neuronal function. These purinergic interactions occur at specified areas of neuronal somata and are maintained in accordance with changes in neuronal metabolic states. Microglia also shape vascular responses via purinergic, compartment-specific actions, through which microglia modulate cerebral blood flow, neurovascular coupling and cerebral hypoperfusion. In the inflamed brain, altered microglia-neurovascular interactions are associated with perfusion changes and modulation of central leukocyte recruitment. We systematically assess the key molecules that contribute to neurovascular modulation by microglia in the mouse and the human brain, to understand how different neurological conditions affect microglial states and what functional consequences this may have on disease outcomes. Understanding the molecular mechanisms of microglia-neurovascular interactions is likely to help the identification of novel therapeutic targets in common neurological disorders.

Laia Acarin Award

Candidate Nicolas Capelo Carrasco, Bella Mora Romero
Affiliation Instituto de Biomedicina de Sevilla / Universidad de Sevilla
Position PhD students

MICROGLIA MITOCHONDRIAL COMPLEX I DEFICIENCY DURING DEVELOPMENT INDUCES GLIAL DYSFUNCTION AND EARLY LETHALITY

Nature Metabolism, 2024

Bella Mora-Romero (*,1,2,3), Nicolas Capelo-Carrasco (*,1,3,4), Juan J Pérez-Moreno (*,#,5,6,7), María I Alvarez-Vergara (1,2,3,8), Laura Trujillo-Estrada (3,9), Carmen Romero-Molina (1,3,4,10), Emilio Martinez-Marquez (1,3,11), Noelia Morano-Catalan (1,3), Marisa Vizuete (1,3,4), Jose Lopez-Barneo (1,3,11), Jose L Nieto-Gonzalez (1,3,11), Pablo Garcia-Junco-Clemente (1,3,11), Javier Vitorica (1,3,4), Antonia Gutierrez (3,9), David Macias (1,11), Alicia E Rosales-Nieves (1,3,4), Alberto Pascual (#,12,13)

(1) Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain.
(2) Department of Biología Celular, Facultad de Biología, Universidad de Sevilla, Seville, Spain.
(3) Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain.
(4) Department of Bioquímica y Biología Molecular, Facultad de Farmacia, Universidad de Sevilla, Seville, Spain.
(5) Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain. jpmoreno@us.es.
(6) Department of Biología Celular, Facultad de Biología, Universidad de Sevilla, Seville, Spain. jpmoreno@us.es.
(7) Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain. jpmoreno@us.es.
(8) Institute for Neurovascular Cell Biology, University Hospital Bonn, Bonn, Germany.
(9) Department of Biología Celular, Genética y Fisiología, Facultad de Ciencias, Instituto de Investigacion Biomedica de Malaga (IBIMA), Universidad de Málaga, Málaga, Spain.
(10) Ronald M. Loeb Center for Alzheimer's Disease, Icahn School of Medicine at Mount Sinai, New York, NY, USA.
(11) Departamento de Fisiología Médica y Biofísica, Universidad de Sevilla, Seville, Spain.
(12) Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain. apascual-ibis@us.es.
(13) Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain. apascual-ibis@us.es.
**Contributed equally; #Corresponding authors.*

Primary mitochondrial diseases (PMDs) are associated with pediatric neurological disorders and are traditionally related to oxidative phosphorylation system (OXPHOS) defects in neurons. Interestingly, both PMD mouse models and patients with PMD show gliosis, and pharmacological depletion of microglia, the innate immune cells of the brain, ameliorates multiple symptoms in a mouse model. Given that microglia activation correlates with the expression of OXPHOS genes, we studied whether OXPHOS deficits in microglia may contribute to PMDs. We first observed that the metabolic rewiring associated with microglia stimulation in vitro (via IL-33 or TAU treatment) was partially changed by complex I (CI) inhibition (via rotenone treatment). In vivo, we generated a mouse model deficient for CI activity in microglia (MGcCI). MGcCI microglia showed metabolic rewiring and gradual transcriptional activation, which led to hypertrophy and dysfunction in juvenile (1-month-old) and adult (3-month-old) stages, respectively. MGcCI mice presented widespread reactive astrocytes, a decrease of synaptic markers accompanied by an increased number of parvalbumin neurons, a behavioral deficit characterized by prolonged periods of immobility, loss of weight and premature death that was partially rescued by pharmacologic depletion of microglia. Our data demonstrate that microglia development depends on mitochondrial CI and suggest a direct microglial contribution to PMDs.

LINK: https://www.nature.com/articles/s42255-024-01081-0

Short Talks – Abstract #1

Speaker Andrea Misol Ortiz
Affiliation Hospital Nacional de Parapléjicos, Toledo, España
Position PhD student
Main interest Astrocytes

NEURONAL ENSEMBLES ENCODING SENSORY BEHAVIOR ARE DEFINED BY ASTROCYTE EXCITABILITY

Misol-Ortiz A (1,2), Zaforas M (2,3), Fernández-López E (2,3) Alonso-Calviño E (2,3) Aguilar J (2,3) Rosa JM (1,3)

(1) Grupo de Circuitos Neuronales y Comportamiento, Hospital Nacional de Parapléjicos, Toledo, Spain
(2) Grupo de Neurofisiología Experimental, Hospital Nacional de Parapléjicos, Toledo, Spain
(3) Instituto de Investigación Sanitaria de Castilla-La Mancha, Toledo, Spain

How the primary somatosensory cortex (S1) discriminates and processes simultaneous information from four different modalities (touch, temperature, pain and proprioception) remains a longstanding question in neuroscience. Here, we hypothesize that cortical astrocytes fine-tune the spatially and temporally organized activity of neuronal ensembles encoding sensory modalities, thereby influencing behavior. To investigate this, we employed in vivo chemogenetic manipulation of astrocytes and behavioral assessment combined with microendoscopic calcium imaging (miniscope), to record the simultaneous activation of neuronal sensory ensembles across S1 layers. Our in vivo imaging data, obtained from freely moving animals, showed that peripheral tactile and thermal stimulation activate distinct neuronal ensembles across the cortical layers, with a small subset of multimodal neurons participating in both tactile and thermal ensembles. Furthermore, in vivo modulation of astrocyte Ca activity using Gq-DREADDs enhanced the number of multimodal neurons, indicating increased flexibility of single neurons to shift from ensemble to ensemble in the presence of a disrupted astrocytic network. However, rather than being beneficial, the induced multimodality impaired texture and temperature discrimination in behavior tests, suggesting that neuronal ensembles recruited under disrupted astrocyte activity are broadly tuned and less specialized to discriminate the arriving inputs. Thus, our results demonstrate that S1 ensures the activation of the appropriate neuronal ensembles to process sensory modalities, thereby enabling accurate behavioral responses.

Short Talks – Abstract #3

Speaker Paula Escalada Matute
Affiliation Universidad de Navarra, Pamplona, España
Position PhD student
Main interest Astrocytes

BENEFICIAL EFFECTS OF ASTROCYTIC GLUT1 ABLATION IN ALZHEIMER'S DISEASE

Escalada P (1,2), Ardanaz C G (1,2), Ramírez M J (1,2), Solas M (1,2)

(1) Department of Pharmaceutical Sciences, University of Navarra, Pamplona, Spain; (2) IdISNA, Navarra Institute for Health Research, Pamplona, Spain.

Aberrant brain bioenergetics is proposed as one of the underlying mechanisms in Alzheimer's disease (AD) pathology. Indeed, a prominent drop in brain glucose uptake is observed prior to the manifestation of AD symptoms. Glucose is the main energy source of the brain, and its supply from the blood to the brain is controlled by the glucose transporter GLUT1, highly present in astrocytes. Thus, astrocytes are located at the interface between vessels and neurons, putting them in a privileged position to control brain glucose uptake. In the present work, we hypothesized that astrocyte-specific GLUT1 deletion could accelerate the onset of AD.

To explore the role of astrocytic GLUT1 in AD, we generated an astrocytic GLUT1 knockout (KO) mouse model at 2 months of age and assessed its effects at 8 months. Surprisingly, astrocytic GLUT1 deletion decreased the elevated mortality of APP/PS1 mice. Moreover, astrocytic GLUT1 ablation rescued the cognitive impairments shown by APP/PS1 mice in the Morris water maze and fear conditioning memory tests. These effects were unrelated to Aβ pathology, as both amyloid plaques and Aβ levels were unchanged. Interestingly, our data showed a higher baseline Ca2+ event probability and duration of GLUT1 depleted astrocytes, indicating elevated Ca2+ activity levels. Noteworthy, chemogenetic perturbation of astrocytic Ca2+ activity totally abrogated the cognitive improvement elicited by astrocytic GLUT1 ablation.

In conclusion, GLUT1-ablated astrocytes maintain the ability to metabolically cope with Aβ challenge, and far from worsening AD pathology, astrocyte-specific GLUT1 ablation prevents both the increased mortality and impaired cognition exhibited by APP/PS1 mice.

Short Talks – Abstract #5

Speaker Cristina Martín Monteagudo
Affiliation Instituto Cajal, CSIC, Madrid, Spain
Position PhD student
Main interest Astrocytes

DECODING THC-RELATED IMPAIRMENTS: THE ROLE OF ASTROCYTIC ENSEMBLES IN THE NUCLEUS ACCUMBENS.

Martín-Monteagudo C1 , Navarrete M1

1 Cajal Institute - CSIC, Madrid, Spain

Cannabis is the most commonly used illicit drug among adolescents. Although it is often perceived as harmless, emerging evidence shows that it impairs spatial learning—a process that primarily depends on the coordinated activity between the ventral hippocampus (vHip) and the Nucleus Accumbens (NAc). The NAc integrates motor and limbic information from various glutamatergic inputs, such as medial prefrontal cortex, basolateral amygdala, and vHip. Regarding this, our group has previously identified pathway-specific neuron-astrocyte networks in the NAc. Moreover, astrocytic CB1Rs have been shown to modulate synaptic transmission and long-distance communication between neuronal populations. Here, our goal is to investigate the role of astrocytic ensembles in the NAc in impairments related to the use of tetrahydrocannabinol (THC), the psychoactive component of cannabis. Using fiber photometry, we analyzed astrocytic calcium and glutamate dynamics in NAc after chronic administration of 1mg/kg THC in wild-type and p38αMAPK-/- (Astrop38α) mice. We also conducted electrophysiological experiments to examine synaptic plasticity. Furthermore, the Barnes Maze test was employed to evaluate the effects of THC on spatial learning. Finally, using a combination of AstroLight, a new tool developed in our group, and optogenetics, we identified and selectively manipulated the astrocytic ensemble within the NAc involved in vHip–NAc circuit to analyze its behavioral implications. We observed: (1) THC increases astrocytic calcium activity and glutamatergic tone within the NAc; (2) the THC-induced glutamatergic alterations are absent in Astrop38α mice, implicating p38αMAPK signaling in astrocyte-mediated plasticity; (3) astrocytic glutamate release within the vHip->NAc ensemble is required for THC-induced cognitive deficits; and (4) targeted attenuation of THC-induced calcium activity in this ensemble prevents both spatial learning and synaptic plasticity impairments. These results highlight a critical role for astrocytic ensembles in shaping behavior and emphasize their potential as therapeutic targets for mitigating the cognitive consequences of THC exposure.

Short Talks – Abstract #10

Speaker Marco Gonzalez Dominguez
Affiliation Achucarro Basque Center for Neuroscience, Leioa (Spain)
Position PhD student
Main interest Microglia

UNVEILING THE DYNAMIC LINK BETWEEN PROLIFERATION AND PHAGOCYTIC EFFICIENCY IN BRAIN DEVELOPMENT: THE ROLE OF IKAROS

González-Domínguez, M (1,2); Pereira-Iglesias, M(1,2); Wiebke, M(3); Ballasch, I(4, 5, 6); Maldonado-Teixido, J(1,7); García-Moreno, F(1,2,8); Giralt, A(4, 5, 6); Greter, M(3); Sierra, A(1,8,9).

1 Achucarro Basque Center for Neuroscience, Scientific Park of the University of the Basque Country (UPV/EHU), 48940, Leioa, Spain.
2 Department of Neuroscience, Faculty of Medicine and Odontology, UPV/EHU, Barrio Sarriena s/n, 48940 Leioa, Bizkaia, Spain.
3 Institute of Experimental Immunology, University of Zurich, Zurich, Switzerland.
4 Departament de Biomedicina, Facultat de Medicina, Institut de Neurociències, Universitat de Barcelona, 08036, Barcelona, Spain.
5 Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, (Spain).
6 Centro de Investigación Biomédica en Red Sobre Enfermedades Neurodegenerativas (CIBERNED), 28031, Madrid, Spain.
7 Department of Pharmacology, Faculty of Pharmacy, UPV/EHU, Barrio Sarriena s/n, 48940 Leioa, Bizkaia, Spain.
8 IKERBASQUE Foundation, María Díaz de Haro 3, 6th Floor, 48013 Bilbao Spain.
9 Biochemistry and Molecular Biology Department, University of the Basque Country UPV/EHU, Leioa (Spain).

Microglia are the specialized phagocytes of the brain, and they play a key role in maintaining its homeostasis. They derive from yolk sac progenitors that invade the brain parenchyma at embryonic stages. However, the spatiotemporal dynamics and molecular mechanisms by which microglia acquire their functionality are largely unknow. Here we show that microglia are not born-efficient phagocytes. Using confocal imaging to visualize mice brain slides from P2 to P60, we found that microglia colonized the brain in the first two postnatal weeks and achieved final number by P28 in the hippocampus and P21 in the cerebellum. This increase was driven by highly proliferative cells during the first postnatal week, which progressively became quiescent. We next studied the relationship between microglial colonization and phagocytosis and found that its efficiency increased progressively in postnatal mice until P21 whereas developing microglia were not able to respond to apoptotic challenges until P14. These findings showed microglial phagocytic efficiency increased after they colonized the brain. Microglial proliferation and phagocytosis efficiency were negatively correlated, suggesting that they are exclusive processes. To test whether colonization was required for phagocytosis maturation, we impaired microglial proliferation using both an IL34 KO mice model and pharmacologically inhibiting CSF1R, founding that phagocytic efficiency was reduced. We are further exploring the functional effects of impairing microglial proliferation during development using a mouse model deficient in IKAROS, an inhibitor of KDM5B which regulates proliferation. Our preliminary data shows that IKAROS KO mice have reduced microglial proliferation and density, resulting in impaired phagocytosis. These results underscore the tight link between proliferation and phagocytosis and highlight the fact that microglia need to proliferate and colonize the brain before acquiring full phagocytic efficiency. This is highly relevant as microglia are long-lived cells and early impairments on their maturation may have an impact in the long term.

Short Talks – Abstract #19

Speaker Victor Valcárcel Hernández
Affiliation CNRS - Muséum National d'Histoire Naturelle, Paris, France
Position Postdoc
Main interest Oligodendrocytes and OPCs

ACCUMULATION OF PFAS IN MYELIN SHEATHS: LONG-TERM CONSEQUENCES ON MYELINATION AND MYELIN STABILITY

Víctor Valcarcel-Hernández (1), Lucile Butruille (1), Dominique Langui (2), Patricia Bassereau (3), Bernard Zalc (2), Sylvie Remaud (1).

[1]*Laboratory Molecular Physiology and Adaptation, CNRS UMR 7221, Department Adaptations of Life, Muséum National d'Histoire Naturelle, Paris, France.*
[2]*Sorbonne Université, Inserm, CNRS, ICM-GH Pitié-Salpêtrière, Paris, France.*
[3]*Institut Curie, Université PSL, Sorbonne Université, CNRS UMR168, Physics of Cells and Cancer, Paris, France.*

Over the past three decades, developed countries have reported a rising incidence of multiple sclerosis (MS), potentially linked to environmental factors. We investigated whether persistent organic pollutants, specifically perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS), disrupt myelin formation and remyelination. We hypothesized that these per- and polyfluoroalkyl substances (PFAS) could accumulate in lipid-rich structures such as myelin, compromising sheath integrity.
Accordingly, we recently published by LC-MS/MS that PFOS – and to a lesser extent PFOA - accumulated into the myelin sheath of offsprings exposed to PFOS via the mother drinking water during late gestation and lactation. Furthermore, using both in vivo and ex vivo models, we demonstrated that PFOS, but not PFOA, impairs functional remyelination (Butruille et al., 2023). In the present work, we explored the long-term impact of perinatal PFAS exposure on oligodendrogenesis and myelination.
First, we showed that perinatal PFOS exposure, but not PFOA, disrupts neurogliogenesis in the adult subventricular zone and inhibits oligodendrocyte precursor cell (OPC) maturation in the corpus callosum. Transmission electron microscopy (TEM) studies in the corpus callosum revealed that PFOS exposure results in persistent thinning and ultrastructural abnormalities of the myelin sheath., suggesting permanent alterations in myelin integrity and stability. To analyze this hypothesis, we have developed in-vitro and in silico systems based on the production of myelin giant unilamellar vesicles (GUVs) and in simulations of the biophysical properties of the myelin membrane, that allowed us to observe that PFOS, even at near to legal doses, enters the myelin sheath compromising its stability and making it more fragile and less resistant to tension.
In summary, our data demonstrate that perinatal exposure to PFOS, and in a lesser extent to PFOA, induces lasting myelin abnormalities, which may increase vulnerability to demyelinating diseases such as MS.

Short Talks – Abstract #21

Speaker Sonia Cabeza Fernández
Affiliation Instituto de Investigación Sanitaria y Biomédica de Alicante. Instituto de Neurociencias UMH-CSIC, Alicante
Position PhD student
Main interest Oligodendrocytes and OPCs

OPCS' INFLAMMATORY MEMORY AS A KEY FACTOR IN REMYELINATION

Sonia Cabeza-Fernández(1,2), Sergio Niñerola(2), Ángela Armengol-Gomis(1,2), Juan Paraíso-Luna(2), José Antonio Gómez Sánchez(1,2), Hugo Cabedo(1,2), Ángel Barco(2), Alerie G de la Fuente(1,2,3)

(1) Instituto de Investigación Sanitaria y Biomédica de Alicante (ISABIAL), Alicante, Spain
(2) Instituto de Neurociencias CSIC-UMH, San Juan de Alicante, Spain
(3) Wellcome-Wolfson Institute for Experimental Medicine, Queen's University Belfast, Belfast, UK

Oligodendrocyte Progenitor Cells (OPCs) are the main drivers for central nervous system remyelination. Upon demyelination, OPCs migrate to the damaged area, proliferate and differentiate into oligodendrocytes that regenerate the lost myelin, preventing axon degeneration and functional impairment. Successful remyelination relies on a controlled inflammatory response. However, chronic inflammation like that observed in multiple sclerosis (MS) and aging hinders OPC remyelination capacity. Recent studies have demonstrated that some tissue-specific stem cells can undergo inflammation-driven long lasting epigenetic reprogramming that modifies their response to subsequent stimuli. This phenomenon is known as inflammatory memory.

Our work investigated the short- and long-term impact of inflammatory stimulus on OPC biology to explore whether OPCs retain an inflammatory memory that modifies their response to demyelinating insults. To address this question, we are investigating OPC response to acute lipopolysaccharide (LPS)-mediated systemic inflammation in vivo. Transcriptomic analysis of OPCs 24 hours after LPS treatment revealed an increased expression of several immune- and disease-associated genes. 5 weeks after LPS injection, OPCs revert to their homeostatic state, and no longer express disease-associated markers. Notably, ATAC sequencing data coupled with super-resolution microscopy showed a persistently altered chromatin accessibility profile in OPCs 5 weeks after LPS treatment.

Our results reveal enduring epigenetic reprogramming of OPCs after LPS injection, which may represent OPC inflammatory memory. However, whether this reprogramming alters OPC response to subsequent stimuli and their regenerative properties is yet to be elucidated. Our ongoing and future work aims to understand how inflammatory memory influences OPCs response to demyelination. Exploring the role of OPC inflammatory memory and the underlying molecular pathways will provide new insights into remyelination failure in chronic inflammatory conditions, such as MS and aging. Altogether, this will help to developing new therapeutic approaches aimed at boosting remyelination.