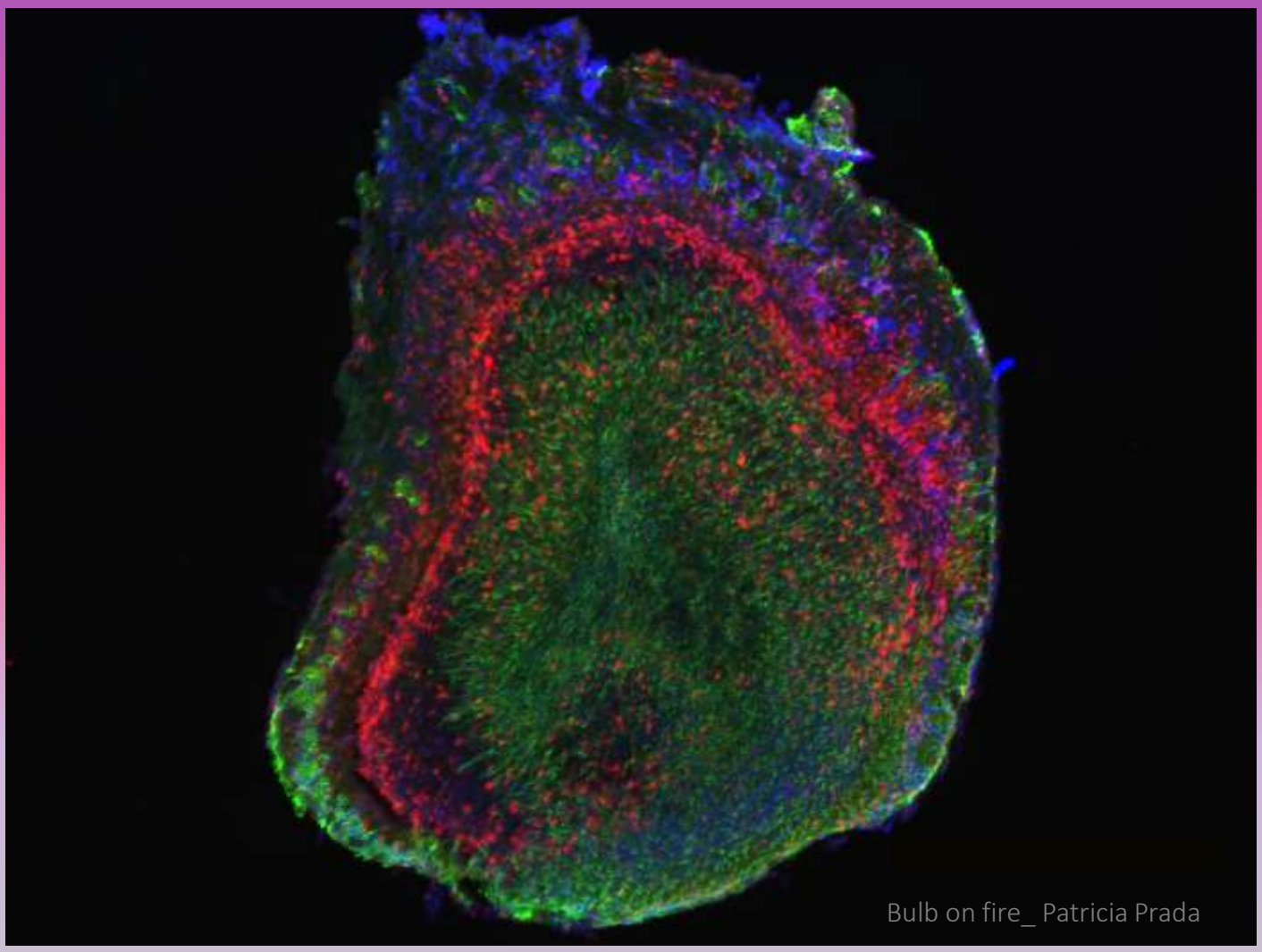
XIII Jornada del Departament de Biologia Cel·lular, Fisiologia i Immunologia

10 de juny del 2022



Millor fotografia científica de la XII Jornada del Departament BCFI 2021

CONFERÈNCIA

Harnessing NK cells for cancer immunotherapy.
Dra. Aura Muntasell. Unitat d'Immunologia.

CONFERÈNCIA

Molecular profiling of neuronal susceptibility to Mitochondrial Disease.
Dra. Elisenda Sanz. Unitat de Fisiologia Animal.

CONFERÈNCIA DE CLAUSURA DE LES BIOJORNADES

Nanotechnology for the Design of Next-Generation Therapeutics and Diagnostics.
Professor Kostas Kostarelos - ICN2.

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Microbiota seminal i integritat de l'ADN espermàtic.**Sergio Garcia Segura**.BCGM.

A roadmap for postnatal brain maturation: changes in white and grey matter compositionduring development. **Marta Peris Salas**.HM.

BETproteins as an epigenetic target to improve functional outcome after PNI. **Georgina Palomés Borrajo**.FM.

Severe cortical affectation after mitochondrial complex I subunit deletion in Cck-expressing cells. **Andrea Urpi Badell**.FA.

La oveja como modelo experimental en estudios de lesión y regeneración de nervio periéfrico. **Estefanía Contreras Carretón**.FV.

Funciones alternativas del Regulador Autoinmune (AIRE). **Adrián Tirado Herranz**.IBB.

Opto Electrical Nanoreactors for Wireless Cell Stimulation. **Nour al Hoda Al Bast**.BC.

Trip13 prevents precocious desynapsis during meitoc prophase. **Andros Maldonado-Linares**.CH.

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Àrea de Biologia Cel·lular

BC.1 RAD21L depletion alters the 3D genome architecture in the male germ line. **Laia Marín Gual.**

BC.2 Piezoelectric ZnO nanostructures integrated in microdevices for cell stimulation. **Laura Lefaix Fernández.**

BC.3 The co-culture of keratinocytes and fibroblasts on a multi-layered polyester nanofibrous membrane enriched with platelet lysate. **Andreu Blanquer Jerez**.

BC.4 Effect of moderate ethanol consumption on the ovarian reserve in mice and strategies to revert it. **Nikoleta Nikou**.

BC.5 Fatal COVID-19 compromises spermatogenesis in men. **Maria López Panadés**.

BC.6 Meiotic prophase I dynamics in reptiles. **Laura González Rodelas**.

BC.7 Evolutionary implications of 3D chromatin remodeling in the germ line. **Lucía Álvarez González.**

BC.8 Aïllament de cèl·lules germinals mitòtiques procedents de testicle de ratolí mitjançant selecció cel·lular activada per fluorescència (FACS). **Álvaro Pascual Bascuñana.**

BC.9 Functional and epigenetic implications of chromosomal fusions in the germline. **Cristina Marín García.**

BC.10 SIRT7 regulates PAX5 function and is required for proper B cell development. **Andrés Gámez García-Cervigón.**

BC.11 Role of SIRT7 in male meiosis and reproductive longevity. **Anna Guitart-Solanes**.

Àrea de Fisiologia

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FIS.2 Aberrant perineuronal nets alter spinal circuits, impair motor function, and increase plasticity. **Judith Sánchez Ventura**.

FIS.3 Assessment of IL-38 levels in Multiple Sclerosis. **Néstor López González.**

FIS.4 LSD1 inhibition improves functional outcome after spinal cord injury. **Raquel del Río Astorga.**

FIS.5 Novel graphene-based electrode for interfacing the peripheral nervous system. **Bruno Rodríguez Meana.**

FIS.6 Spinal cord control of manual dexterity in rats: a functional mapping study. **Diego López Santos.**

FIS.7 Modulation of VDAC promotes motoneuron survival after brachial plexus injury. **Carla Badia Puiggalí.**

FIS.8 Impact of calorie-restricted cafeteria feeding and treadmill exercise on sucrose intake, sensitivity and reactivity in diet-induced obese male and female rats. **Adam Álvarez Monell.**

FIS.9 Characterization of human induced pluripotent stem cell-derived microglia from a familial amyotrophic lateral sclerosis patient. **Joana Garcia Garcia.**

FIS.10 Effects of a cafeteria restricted diet and oleuropein supplementation on sweet taste modifications in a cafeteria diet-induced obesity rodent model**. Àlex Subias Gusils.**

FIS.11 Sigma-1 receptor is a pharmacological target to promote neuroprotection in the SOD1G93A ALS mica. **Núria Gaja Capdevila.**

FIS.12 Preclinical development of a therapy for Chronic Traumatic Spinal Cord Injury with Wharton's Jelly Mesenchymal Stromal Cells: proof of concept and regulatory compliance. **Quim Hernandez Martin.**

Àrea d'Immunologia

IMM.1 Plataforma modular de vacunas para administración oral: El caso de SVCV. **Mauricio Rojas Peña.**

IMM.2 Vacuna de subunidades de VHSV: Una nueva herramienta profiláctica con potencial de administración oral. **Patricia Aceituno Abarzúa.**

COMUNICACIONS ORALS

I. PARTICIPANT

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II. COMUNICACIÓ ORAL

Títol: Microbiota seminal i integritat de l'ADN espermàtic

Autors: Sergio Garcia Segura, Javier del Rey, Laia Closa, Iris Garcia Martínez, Carlos Hobeich, Ana Belén Castel, Francisco Vidal, Jordi Benet, Jordi Ribas Maynou, Maria Oliver Bonet

III. RESUM

El conjunt de microorganismes presents en un ambient determinat es coneix com a microbiota. Al cos humà hi habiten diverses colònies, principalment bacterianes, lligades a la salut de l'organisme. Recentment, la disbiosi de la microbiota del plasma seminal s'ha proposat com una causa potencial de la infertilitat masculina, tot i que el nombre d'estudis realitzats és encara limitat i mostren algunes discrepàncies. Diversos estudis recolzen que la microbiota seminal està composta per quatre fílums bacterians: Firmicutes, Bacteroidetes, Proteobacteria i Actinobacteria; i alguns dels gèneres més comuns són Lactobacillus, Corynebacterium, Prevotella, Veillonella, Streptococcus i Staphylococcus, entre d'altres. Alguns d'aquests bacteris han estat correlacionats amb paràmetres de qualitat espermàtica com la motilitat i concentració o amb paràmetres seminals com la viscositat. L'objectiu del present estudi ha estat analitzar la microbiota seminal de població mediterrània mitjançant la seqüenciació del gen 16S rRNA i avaluar la seva relació amb la integritat de l'ADN espermàtic i l'estrès oxidatiu seminal. Els resultats mostren que l'abundància de diversos bacteris correlaciona amb una disminució de la fragmentació d'ADN espermàtic, com Moraxella, Brevundimonas i Flavobacterium. En canvi, Actinomycetaceae, Ralstonia i Paenibacillus s'han correlacionat amb alteracions de compactació de la cromatina i amb un augment de la fragmentació d'ADN de cadena doble. Aquests efectes coincideixen en molts casos amb el metabolisme o les activitats enzimàtiques d'aquests grups bacterians. També s'han trobat diferències significatives entre homes fèrtils i infèrtils en la presència relativa de la família Propionibacteriaceae i els gèneres Cutibacterium, Rhodopseudomonas i Oligotropha. Aquestes troballes sostenen la hipòtesi que la microbiota seminal té un efecte sobre la fertilitat masculina.

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II. COMUNICACIÓ ORAL

Títol: A roadmap for postnatal brain maturation: changes in white and grey matter composition during development

Autors: Peris M., Zerpa O., Manich G., Almolda B., Benseny-Cases N., Perálvarez-Marín A., González B., Castellano B.

III. RESUM

Synchrotron based Fourier Transform Infrared microspectroscopy (µFTIR) is an emerging technique in the study of biochemical properties of biological samples. Specifically, the study of parameters such as lipid oxidation, protein structure or the lipid/protein ratio is widely used in the analysis of pathological (neurodegenerative diseases) or non-pathological processes (aging). However, there are no studies of this type in the normal postnatal development of the central nervous system (CNS). Here we show a first detailed roadmap of the biochemical composition of the CNS during postnatal development in mice. In this study, we describe changes in lipid and protein composition from postnatal day 0 (P0) to P28, and we compare white and grey matter areas of the mouse brain and cerebellum (strain C57BL/6). Furthermore, we checked the correlation of other known myelin study techniques with µFTIR, such as histochemical and immunohistochemical stainings. We found that, at birth, differences between white and grey matter were minimal, and were enhanced during development. In white matter, the presence of lipids was greater than in grey matter from P14 to adulthood, and these were poor in unsaturated olefinic and carbonyl groups. Lipid histochemical stainings (Luxol fast blue, Oil Red O and Sudan Black) reflected changes observed in white matter myelination using µFTIR. However, MBP and MOG immunohistochemical stainings did not reflect so well changes in the composition of white matter compared to µFTIR, but they did reflect the modifications in the composition of the secondary structure of the proteins (alfa-helix and beta-sheet) present in the sample. Our results lay a foundation for future studies with the µFTIR technique in developmental diseases in which changes in grey matter or white matter have been found, such as autism or perinatal white matter injury (WMI).

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II. COMUNICACIÓ ORAL

Títol: BET proteins as an epigenetic target to improve functional outcome after PNI

Autors: Georgina Palomés, Clara Penas, Xavier Navarro

III. RESUM

Peripheral nerve injury (PNI) results in functional loss and the raise of secondary problems, such as neuropathic pain (NP). Patients suffer from reduced quality of life and there is a lack of effective treatments. Thus, it is important to find novel strategies to promote functional recovery after injury. PNI leads to an immune-like process, known as Wallerian Degeneration (WD), that promotes distal axon degradation and debris clearance, which are necessary for regrowth of surviving neurons. However, the inflammatory environment produced in WD in the distal axon stump may also limit axonal regeneration and raise neural excitability and NP. BET proteins are epigenetic readers that can influence inflammatory gene expression. Thus, we inhibited BET proteins with the compound JQ1 to improve outcome after PNI. To assess the effects of BET inhibition on NP, we treated spared nerve-injured mice with JQ1 or vehicle. We found that treatment with JQ1 reduced mechanical hyperalgesia after injury in vivo. BET inhibition regulated cytokine expression, reduced microglial reactivity, and altered ion channel transcription after injury. Concerning regeneration, we found that treatment with JQ1 in crush-injured mice enhanced GAP-43, IL-4 and IL-13 transcription. But the treatment did not have effects on sensory and motor reinnervation. Ex vivo assays with dorsal root ganglia (DRG) explants demonstrated that JQ1 decreased neurite outgrowth, but conditioned media from JQ1-treated macrophages increased neurite growth of cultured DRGs through STAT6 pathway. Thus, macrophages could offset the negative effects of JQ1 in vivo by increasing anti-inflammatory cytokine secretion. These findings prove that BET inhibition reduces inflammation, NP, and enhance nerve regeneration, however a specific targeting on macrophages must be done to achieve functional outcome after PNI.

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II. COMUNICACIÓ ORAL

Títol: Severe cortical affectation after mitochondrial complex I subunit deletion in Cck-expressing cells

Autors: Andrea Urpi, Elisenda Sanz and Albert Quintana

III. RESUM

Leigh syndrome (LS) is a progressive neurodegenerative disorder caused by dysfunctional mitochondria resulting in failure to thrive, ataxia, respiratory problems, and early death. Although the clinical signs present in LS patients are highly heterogeneous, they are characterized by bilateral and symmetrical lesions in the brainstem and/or basal ganglia. However, around 18-25% of patients with LS also show alterations in the cerebral cortex, which has been mostly neglected. To determine the role of the cerebral cortex in the progression of the pathology, we set to generate a cerebral cortex-centered mouse model by removing the mitochondrial complex I subunit NDUFS4 in Cck-expressing cells, one of the most prominent cortical neuronal populations. Mitochondrial dysfunction in Cck neurons led to progressive cortical lesions accompanied by a glial scar formation and apparent neuroinflammation in the parietal cortex. Longitudinal monitoring by magnetic resonance imaging revealed the presence of cortical hyperintense signals along with a cytotoxic edema. Behaviorally, Ndufs4 deficiency in Cck neurons resulted in a severe motor phenotype and social deficits, related with part to the phenotype presented by LS patients. Additionally, molecular profiling revealed a characteristic synaptic organization and function of CCK neurons comparing parietal and temporal cortex, despite CCK neuropeptide is expressed in the whole cortex. Overall, our results demonstrates the implication of the cerebral cortex in the development of LS and particularly the cortical susceptibility to mitochondrial dysfunction in the parietal cortex.

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II. COMUNICACIÓ ORAL

Títol: La oveja como modelo experimental en estudios de lesión y regeneración de nervio periférico

Autors: Estefanía Contreras, Sara Traserra, Félix García, Eduardo José-Cunilleras, Ignacio Delgado, Joaquim Forés, Esther Udina, Xavier Navarro, Patri Vergara

III. RESUM

Las lesiones nerviosas ocurren con frecuencia afectando tanto a humanos como a animales. No se ha establecido una terapia eficaz que promueva la regeneración del nervio periférico lesionado y permita la completa recuperación funcional, por lo que el desarrollo de modelos animales sigue siendo una necesidad. El modelo ovino se considera una buena opción traslacional ya que presenta nervios periféricos con características anatómicas y fisiológicas, incluyendo su longitud, similares a los humanos.

El objetivo de este estudio es establecer un protocolo quirúrgico para efectuar lesiones del nervio peroneal en oveja, optimizar la metodología de supervisión, pruebas funcionales, ecográficas y electromiográficas para evaluar la regeneración nerviosa.

Bajo anestesia se realizó una resección del nervio peroneal en 20 ovejas ripollesas hembras. Mediante una incisión lateral longitudinal de la piel a lo largo del muslo, y posterior disección de los músculos semitendinoso y bíceps femoral, se expuso el nervio. Se resecó un segmento del mismo que se reparó mediante un autoinjerto, usando suturas epineurales. Las pruebas funcionales se realizaron mensualmente mediante la evaluación de la locomoción, la propiocepción y el reflejo flexor de retirada, mientras que las pruebas electromiográficas y ecográficas se realizaron en el músculo tibial anterior a días 120 y 180 post operación.

Los resultados obtenidos indican que la oveja es un buen modelo para la realización de procedimientos microquirúrgicos de lesiones de nervios de larga longitud. En cuanto al post operatorio, el 20% de los animales presentaron complicaciones debido a la falta de propiocepción y la parálisis muscular provocadas por la denervación, que fueron resueltas mediante la colocación de una férula. Las pruebas funcionales permitieron la evaluación periódica de la reinervación y regeneración nerviosa. Las pruebas electrofisiológicas y ecográficas permitieron obtener una evaluación cuantitativa para el análisis comparativo entre grupos experimentales. Al acabar el seguimiento funcional se obtuvieron muestras de nervio, músculo y piel inervados por el nervio peroneal para su análisis histológico.

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II. COMUNICACIÓ ORAL

Títol: Funciones alternativas del Regulador Autoinmune (AIRE)

Autors: Adrián Tirado Herranz, Iñaki Álvarez

III. RESUM

Durante la maduración de las células T en el timo se adquiere tolerancia hacia las proteínas propias (tolerancia central). En el proceso denominado selección negativa se eliminan los timocitos autorreactivos. Este proceso ocurre principalmente en la médula tímica y requiere la expresión de, idealmente, todas las proteínas del organismo. Son las células epiteliales tímicas medulares (mTECs) gracias a la expresión de AIRE, las que permite la expresión ectópica de un amplio repertorio de antígenos restringidos a órganos y tejidos (TRAs). AIRE se encuentra involucrado en otras funciones: reconocimiento de marcas epigenéticas, diferenciación de mTECs, inducción de apoptosis o regulación de la división celular. Asimismo, se describió un papel como E3 Ubiquitin ligasa, aunque en experimentos posteriores no se pudo confirmar dicha función.

En un trabajo previo de nuestro grupo se comparó cuantitativamente los proteomas de células la línea celular de origen tiroideo HT93 sin transfectar o transfectada con AIRE. Se observó un aumento de chaperonas y una disminución de proteínas relacionadas con citoesqueleto, así como un aumento de la apoptosis. En este trabajo se ha comparado cuantitativamente los proteomas de la línea celular HEK293 y un transfectante de AIRE, HEK293-AIRE. Los resultados son similares a los obtenidos en otra línea celular: Incremento en expresión de chaperonas; incremento de apoptosis en células que expresan AIRE; aumento o disminución de proteínas relacionadas con el citoesqueleto y su efecto a nivel funcional. Asimismo se ha comprobado la expresión de SIP en este transfectante estable, lo que sugiere un papel de AIRE en la función de SIAH1. Se ha caracterizado la interacción de la proteína AIRE con dos E3 ubiquitín ligasa SIAH1 y SIAH2. Actualmente se está intentando determinar la funcionalidad de esta interacción.

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II. COMUNICACIÓ ORAL

Títol: Opto Electrical Nanoreactors for Wireless Cell Stimulation

Autors: Nour al Hoda Al Bast, Carme Nogues, Maria Jose Esplandiu and Borja Sepulveda

III. RESUM

In this study, we aim to develop opto-electric nanomaterials with high performance for wireless cells stimulation. The device used is based on Au/Si nanowires fabricated on silicon wafer with p-n junction for enhance opto-electrical characteristics.

The electrical properties of the nanowires, i. e., photovoltage and photocurrent, were tested in phosphate buffer saline solution using two light sources corresponding to the biological windows (810 nm and 1050 nm). Results showed no significance difference regarding the photovoltage obtaine with nanowires compared to flat p-n Si wafer. However, photocurrent was higher in both biological windows with nanowires than with flat Si wafer. In addition, wafer nanowires showed higher photocurrent at 810 nm than at 1050 nm. In order to translate the device performance at the cellular level, a human osteosarcoma Saos2 cell line was used, which expresses voltage gated calcium channels. First, we confirmed the biocompatibility of these nanowires through cell viability assays. then, using the confocal laser scanning microscope, we recorded the opening of these channels in response to light illumination at 810 nm in both flat and Au/Si nanowires samples.

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II. COMUNICACIÓ ORAL

Títol: TRIP13 PREVENTS PRECOCIOUS DESYNAPSIS DURING MEIOTIC PROPHASE

Autors: Andros Maldonado-Linares , Cristina Madrid-Sandín , Judith Fuentes-Lázaro, Ana Martinez-Marchal, Ricardo Benavente, Riccardo Zenezini-Chiozzi and Ignasi Roig.

III. RESUM

At the beginning of the meiotic prophase, double-strand breaks (DSBs) are produced by the Spo11 protein, and their repair by meiotic recombination promotes the pairing and synapsis of the homologous chromosomes. The synaptonemal complex (SC) proteins are recruited to chromosome axes at the onset of the meiotic prophase, something fundamental to correctly complete the meiotic recombination. TRIP13, also known as Pch2 in non-vertebrate species, is a AAA+ ATPase involved in DNA repair, synapsis, and chromosome segregation. Previous studies have shown that TRIP13 is required to complete homologous chromosome synapsis. However, it is still unclear how TRIP13 mediates synapsis in mouse spermatocytes. To learn more insights about this and other TRIP13 meiotic functions, we immunoprecipitated TRIP13 from mouse testis protein extracts and identified its interacting partners by liquid chromatography-tandem mass spectrometry (LC-MS/MS). The results comparing wild-type and *Trip13*$^{-/-}$ mutant samples revealed that the chaperone HSPA2 is one of the strongest interactors of TRIP13 in the testis. It had been previously described that HSPA2 is required to disassemble the synaptonemal complex during diplonema. Interestingly, HSPA2 location in mouse spermatocytes is dependent on TRIP13, since *Trip13*$^{-/-}$ spermatocytes show a precocious loading of HSPA2. Accordingly, *Trip13* mutant spermatocytes display an incomplete synapsis, present fewer SC initiation sites and premature loading of other desynapsis factors like Plk1. Thus, we propose TRIP13 is responsible for preventing precocious SC disassembly during meiotic prophase by regulating desynaptic factors presence in the chromatin of mouse meiocytes.

PÒSTERS
Àrea de Biologia Cel·lular

BC_01

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II. PÒSTER

Títol: RAD21L depletion alters the 3D genome architecture in the male germ line

Autors: Laia Marín-Gual, Covadonga Vara, Natalia Felipe-Medina, Yasmina Cuartero, Lucía Álvarez-González, François Le Dily, Francisca Garcia, Elena Llano, Marc A. Marti-Renom, Alberto M. Pendás, Aurora Ruiz-Herrera

III. RESUM

During meiotic prophase I, cohesin complexes participate in synapsis and recombination of homologous chromosomes by keeping the two sister chromatids together and holding chromatin loops to the synaptonemal complex (SC). RAD21L is a meiotic-specific cohesin subunit essential for synapsis and male fertility but its implications on the spatial folding of chromosomes during meiosis remain unclear. Here, we study the impact of RAD21L depletion on the 3D genome architecture in the male germ line by combining fluorescence activated cell sorting (FACS) and the chromosome conformation capture technique (Hi-C). We demonstrate that the loss of RAD21L prevents proper chromatin condensation during meiosis, with changes in the inter- and intra-chromosomal interactions ratio and the A/B compartmentalization in pre-meiotic (spermatogonia) and meiotic (primary spermatocytes) cells. We detected defects in the bouquet formation and an increase in telomeric interactions between heterologous chromosomes in primary spermatocytes, resembling telomere aberrations detected in other cohesin deficient models. Overall, our results show how the three-dimensional genomic structure is affected in the absence of the meiotic cohesin subunit RAD21L during mouse spermatogenesis.

BC_02

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II. PÒSTER

Títol: Piezoelectric ZnO nanostructures integrated in microdevices for cell stimulation

Autors: Laura Lefaix, Marc Navarro, Andreu Blanquer, Lucie Bacakova, Gonzalo Murillo

III. RESUM

Cells respond to electrical stimuli by proliferating, differentiating and migrating. Also, other specific electrical signals such as the nerve impulse and muscle contraction happen due to electrical processes. Electrical devices are currently used to improve these electrical properties of the cell and establish a way of communication between the electrical signal delivered and the final stimulus produced. To safely deliver the electrical signal, the use of piezoelectric materials is being implemented. In this kind of applications, their ability to generate an electric dipole between their surfaces when mechanically stressed is exploited. Ultrasounds, in the biomedical range (MHz), can be used to actuate the piezoelectric materials, communicating with the microdevices inside our body from the outside of it.
In this work, we have developed a microdevice with piezoelectric nanostructures capable of stimulating a single cell. First, microparticles were defined by microfabrication techniques; a template to chemically grow zinc oxide nanosheets (ZnO NSs) on their surface. Then, they were peeled off and suspended in a biocompatible liquid. ZnO NSs have previously been tested as substrate for Saos-2 cell cultures: the electromechanical interaction between the cells and the NSs can increase spontaneously the calcium concentration in the cell cytoplasm. Our microdevices have been proved cytocompatible and a study to know the internalization and the positioning with respect to the cells has been carried out. The electrical field generated by the NSs in contact with the cell membrane seems to be enough to trigger the opening of voltage-gated calcium channels (VGCCs), according to our finite element model. Currently, we are performing biological experiments using ultrasonic pulses to stimulate the microdevices and study the calcium peak pattern produced by the activated cells.

BC_03

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II. PÒSTER

Títol: The co-culture of keratinocytes and fibroblasts on a multi-layered polyester nanofibrous membrane enriched with platelet lysate

Autors: Andreu Blanquer, Elena Filova, Vera Jencova, Antonin Broz, Eva Kuzelova Kostakova, Maxim Lisnenko, Renata Prochazkova, Lucie Bacakova

III. RESUM

The prevalence of chronic wounds is increasing due to the population ageing and specific illnesses like diabetes mellitus and vascular diseases. Nanofibrous membranes fabricated using synthetic polymers are promising materials to enhance skin wound healing. PCL and PVA membranes are being studied to be used as scaffolds for skin tissue engineering and hydrogels for controlled drug delivery, respectively. The present study considers the development of a multi-layered membrane made of PCL and PVA loaded with platelet lysate (PL). PCL nanofibers allowed cell adhesion and growth, whereas PVA acted as a hydrogel that releases the bioactive compounds of platelet lysate. The cytocompatibility of the membranes containing PL and without it was demonstrated on two cell types involved in wound healing, i.e. keratinocytes and fibroblasts. Both cell types were able to adhere and proliferate on the membranes. In addition, the membrane containing PL enhanced the proliferation of fibroblasts. A co-culture study was also performed by seeding each cell type on one side of the membrane. The cells were co-cultured for 7 days and the results showed that PL increased the proliferation of cells achieving a monolayer of keratinocytes or fibroblasts on each side of the membrane. Thus, the beneficial effect of PCL-PVA+PL membranes on monocultures and co-cultures of skin cells was demonstrated, and these membranes can be considered potential scaffolds for treatment of chronic wounds.

BC_04

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II. PÒSTER

Títol: EFFECT OF MODERATE ETHANOL CONSUMPTION ON THE OVARIAN RESERVE IN MICE AND STRATEGIES TO REVERT IT.

Autors: Nikoleta Nikou, Maria López Panadés, and Ignasi Roig

III. RESUM

In mammals, oocyte development and maturation are critical processes for female fertility1. Lifestyle and diet habits seem to affect these processes significantly, resulting in differences in the fertility capability among populations2. Nevertheless, the genetic mechanisms regulating the follicle reserve are just beginning to be described3 . Moderate alcohol consumption has been linked to a diminished ovarian reserve in humans.4,5 Since ethanol causes oxidative stress, which has been associated with a decline in the quality of aging oocytes6,7, we wondered if a moderate alcohol consumption could damage the ovarian reserve in mice and if treatment with the antioxidant SKQ1 could revert it. To test this hypothesis, four-week-old C57BL/6JOlaHsd mice were administered for 14 weeks with a water solution containing 0.1% ethanol or supplemented with the 4,632 mg/ml SkQ1. Our preliminary findings reveal a significant negative effect of daily alcohol consumption on the follicles' quality and development. Also, the treatment with SkQ1 could revert these effects on the ovarian reserve. Based on our data, we propose that the daily consumption of EtOH, even in small doses, could significantly affect the fertility status of mammalian females. However, an antioxidant treatment could counterbalance the ethanol effect and preserve the ovarian reserve.

References
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BC_05

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II. PÒSTER

Títol: Fatal COVID-19 compromises spermatogenesis in men

Autors: López-Panadés, Maria; Maldonado-Linares, Andros; Madrid-Sandín, Cristina; Martínez-Marchal, Ana; Brieño-Enríquez, Miguel; Roig-Navarro, Ignasi

III. RESUM

The SARS-CoV-2 virus has infected more than 500 million people worldwide in the last two years. SARS-CoV-2 uses the TMPRSS2 protease and ACE2 receptor to infect host cells. Even though it is mainly a respiratory disease, these are expressed in many tissues, such including several testicular cell types. Abnormal levels of sex hormones and a decrease in the sperm quality have been observed in patients during and after recovery from COVID-19. Furthermore, severe damage caused by inflammation has been detected in the testes. In addition, the SARS-CoV-2 has been found in the testis. Thus, the possibility that COVID-19 affects the male reproductive system deserves further research. First, we analyzed the morphology of testis sections from patients deceased by COVID-19 and compared them to control samples of similar ages. Overall, COVID-19 samples displayed various anomalies commonly associated with compromised spermatogeneses, such as vacuolization of the Sertoli Cells, detachment of the germinal epithelium, or thickening of the basal lamina. Next, we studied the presence of different relevant biomarkers of spermatogenic cells, DNA damage, and leukocytes in these samples. A higher fraction of T lymphocytes and macrophages were detected in the peritubular spaces of COVID-19 samples compared to controls, thus confirming the infiltration of immune cells in the peritubular tissue of the testis. In addition, the seminiferous tubules of COVID-19 samples showed fewer UTF1-positive spermatogonia, which represents the spermatogonial stem cell population from which all sperm derive. Moreover, these presented more DNA damage than control cells, suggesting that COVID-19 could compromise spermatogenesis even after recovery. However, more studies are needed to understand the impact of COVID-19 in spermatogenesis, especially in those patients that have recovered from the infection.

BC_06

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II. PÒSTER

Títol: MEIOTIC PROPHASE I DYNAMICS IN REPTILES

Autors: Laura González-Rodelas, Laia Marín-Gual, Maria Magdalena Garcias, Lukas Kratochvil, Nicole Valenzuela, Arthur Georges, Paul D Waters, Aurora Ruiz-Herrera

III. RESUM

During meiotic prophase I, tightly regulated processes take place, from pairing and synapsis, of homologous chromosomes to recombination, which are essential for the generation of variable haploid gametes. These processes have canonical meiotic features conserved across different phylogenetic groups. However, our knowledge of the dynamics of meiotic prophase I in non-model vertebrates is still very limited. Here, we compare four different species from the Sauropods clade to understand the regulation of meiotic prophase I in reptiles, including the bearded dragon (*Pogona vitticeps)*, two geckos (*Paroedura picta* and *Coleonyx variegatus)* and the painted turtle (*Chrysemys picta*). Firstly, we performed a histological characterization of the spermatogenesis process in both the bearded dragon and the painted turtle. Secondly, we performed a cytological analysis of prophase I dynamics, including chromosome pairing and synapsis and the formation of double stand breaks (DSB). Our preliminary results show that reptiles species have a similar pattern of prophase I progression forming the “bouquet”. Pairing of chromosomes initiates at the micro-chromosomes at early stages of prophase I. Finally, our analyses detected low levels of meiotic DSB formation in reptiles. Overall, our results provide new insights into meiotic progression in reptiles.

BC_07

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II. PÒSTER

Títol: Evolutionary implications of 3D chromatin remodeling in the germ line

Autors: Lucía Álvarez-González, Frances Burden, Dadakhalandar Doddamani, Roberto Malinverni, Cristina Marín-García, Laia Marin-Gual, Albert Gubern, Covadonga Vara, Andreu Paytuví-Gallart, Marcus Buschbeck, Peter Ellis, Marta Farré, Aurora Ruiz-Herrera

III. RESUM

The spatial folding of chromosomes and their organization in the nucleus has profound regulatory impacts on gene expression and genome architecture, whose evolutionary consequences are far from being understood. Here we explore the evolutionary plasticity of the 3D chromatin remodelling in the germ line given its pivotal role in the transmission of genetic information. Using a comprehensive integrative computational analysis, we (i) reconstruct ancestral rodent genomes analyzing whole-genome sequences of 14 rodent species representatives of the major phylogroups, (ii) detect lineage-specific chromosome rearrangements and (iii) identifica the dynamics of the structural and epigenetic properties of evolutionary breakpoint regions throughout mouse spermatogenesis by applying integrative computational analyses. Our results show that evolutionary breakpoint regions are devoid of programmed meiotic DSBs and meiotic cohesins in primary spermatocytes but associated with functional long-range interaction regions and sites of DNA damage in post-meiotic cells. Moreover, we detect the presence of long-range interactions in spermatids that recapitulate ancestral chromosomal configurations. Overall, we propose a model, which integrates evolutionary genome reshuffling with DNA damage response mechanisms and the dynamic spatial genome organization of germ cells.

BC_08

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II. PÒSTER

Títol: Aïllament de cèl·lules germinals mitòtiques procedents de testicle de ratolí mitjançant selecció cel·lular activada per fluorescència (FACS).

Autors: Á. Pascual, M. Solé, J. Blanco, E. Anton i Z. Sarrate.

III. RESUM

Durant la fase mitòtica de l'espermatogènesi dels ratolins, els espermatogonis realitzen un procés gradual de diferenciació i passen d'espermatogonis A, considerats les cèl·lules mare espermatogèniques, a espermatogonis tipus B que són els que finalment es diferenciaran a espermatòcits i iniciaran la meiosi. Un procés essencial de l'espermatogènesi és l'aproximació i alineament dels cromosomes homòlegs amb la finalitat de dur a terme l'aparellament, la sinapsi i la recombinació. Mentre la dinàmica i els mecanismes que regulen els processos de sinapsi i recombinació són àmpliament coneguts, existeixen molts interrogants en relació als mecanismes i la temporalitat de l'aparellament dels cromosomes homòlegs.
Emmarcat en un projecte de recerca que té l'objectiu principal de realitzar una cara,cterització espai-temporal de l'aparellament del cromosomes homòlegs, en aquest estudi presentem els resultats preliminars de la metodologia dissenyada per a la selecció de diferents poblacions de cèl·lules germinals com a requeriment previ a la seva anàlisi cromosòmica. El disseny experimental consisteix en tres etapes: 1) disgregació del teixit testicular; 2) identificació mitjançant immunofluorescència dels espermatogonis As, espermatogonis Apr i Aal i espermatogonis diferenciats (A1 fins a B) i 3) selecció de les diferents fraccions cel·lulars mitjançant FACS.
Els resultats preliminars mostren la possibilitat de seleccionar la població d'espermatogonis diferenciats, mitjançant la detecció de c-KIT. Pel que fa la resta de poblacions, s'està optimitzant la detecció combinada de PAX7 i GFRα-1 per seleccionar diferencialment espermatogonis As i espermatogonis Apr-Aal.

Agraïments: PI21/00564 (Instituto de Salud Carlos III, Gobierno de España), GJ515013 (UAB), 2017-SGR-1624 (Generalitat de Catalunya). Álvaro Pascual Bascuñana, PIF/2021 (UAB).

BC_09

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II. PÒSTER

Títol: FUNCTIONAL AND EPIGENETIC IMPLICATIONS OF CHROMOSOMAL FUSIONS IN THE GERMLINE

Autors: Cristina Marín-García, Keren Yam, Carolina Buza, María Magdalena Garcías-Ramis, Laia Marín-Gual, Covadonga Vara, Jacint Ventura, Aurora Ruiz-Herrera

III. RESUM

Spermatogenesis is a tightly regulated process and includes several checkpoints to ensure success in the transmission of genetic information through generations. Misregulation due to structural genomic variants (i.e., chromosomal fusions) is linked in humans to recurrent miscarriages, aneuploid offspring and infertility. Here, we take advantage of wild mice populations carrying Robertsonian (Rb) chromosomal fusions as a model system to study the impact of structural genomic variants on spermatogenesis. To this aim, we performed a comprehensive cytological analysis of primary spermatocytes to analyze (i) patterns of constitutive heterochromatin (i.e., the H3K9me3 immunostaining), (ii) recombination maps (i.e., MLH1 immunostaining), combined with (iii) an in-depth study of sperm head morphology, the product of spermatogenesis. Our results show differences between wild populations studied, but even more critical differences between inbred and wild populations (standard mice versus carriers of Rb fusions), in terms of sex chromosomes silencing, MLH1 chromosomal distribution, and sperm morphology. Taking it all together, our results provide new insights into the functional consequences of chromosomal rearrangements affecting germline genetic regulation.

BC_10

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II. PÒSTER

Títol: SIRT7 regulates PAX5 function and is required for proper B cell development

Autors: Andrés Gámez-García, Joshua Thackray, Clara Berenguer, Elisenda Alari-Pahissa, Jose Luis Sardina, Lourdes Serrano, Berta Vazquez*, Alejandro Vaquero *

III. RESUM

B cells develop through the coordinated action of multiple epigenetic and transcription factors. During B lymphopoiesis, functional immunoglobulins are raised in the B cell surface through VDJ recombination. Inactivating mutations in B lineage-specific transcription factors and chromosomal translocations produced during VDJ are the leading cause of B cell progenitor Acute Lymphoblastic Leukemia (B-ALL), the most common cancer in children.
Sirtuins are epigenetic enzymes that catalyze NAD+-dependent deacylation and ADP-rybosilation of protein substrates and are pivotal in the cellular stress response. In cancer, sirtuins can be either protective against malignant transformation or instrumental for cancer cell survival.
Here, we describe that B lymphopoiesis is highly dependent on SIRT7 function. SIRT7 protein levels increased as B cells mature and peaked in pre-B cells, suggesting an important role for SIRT7 at this stage. Consistently, in Sirt7-/- mice, B cell differentiation was partially arrested at the pro-B cell stage. SIRT7 was dispensable for VDJ recombination, as B lymphopoiesis was not rescued by the rearranged IgHEL transgene. Instead, RNA-Seq indicated that Sirt7-/- B cell progenitors showed impaired cell cycle and lineage commitment. Mechanistically, SIRT7 regulated the transcription factor PAX5, a tumor suppressor pivotal for the establishment of B cell identity, in vivo and in cell lines. The PAX5 motif was one of the most enriched in SIRT7-regulated genes, and we identified a gene set regulated by both SIRT7 and PAX5. In B-ALL, PAX5 is frequently mutated, which is associated with adverse prognosis. In B-ALL cells, SIRT7 and PAX5 protein levels were positively correlated. Remarkably, 31% of Sirt7-/- mice showed splenomegaly, suggesting the development of spontaneous leukemias. Our data reveals an unexpected role for SIRT7 in B cell identity and leukemia.

BC_11

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II. PÒSTER

Títol: Role of SIRT7 in male meiosis and reproductive longevity

Autors: Anna Guitart-Solanes, Mayra Romero, Karen Schindler, Alejandro Vaquero*, Berta Vazquez*

III. RESUM

Meiosis is the specific type of cell division that occurs during gametogenesis and leads to the generation of haploid germ cells. Sirtuins, a family of NAD+-dependent deacetylases and ADP-ribosylases, play key roles in the maintenance of genome integrity, metabolic homeostasis and aging in many biological contexts, among them, meiosis. In this regard, our group has recently unveiled a relevant role for Sirtuin 7 (SIRT7) in meiosis and reproductive longevity. Sirt7-/- oocytes present increased regions with unsynapsed chromosomes which results in a diminished oocyte pool that leads to a rapid age-dependent decline in fertility. However, what is the underlying molecular mechanism and whether SIRT7 plays a similar role in males remains unknown. High expression of SIRT7 in human spermatogonia and spermatocytes suggests an important role in early spermatogenesis. In fertility trials, crosses with Sirt7-/- male mice produced significantly smaller litters. Besides, aged Sirt7-/- males present a reduction in testicular volume, suggesting an important role of SIRT7 in the control of the reproductive lifespan. Interestingly, we have found that SIRT7 is the most significantly reduced Sirtuin in aged mice testicular samples. SIRT7 functions as an epigenetic factor by deacetylating lysine 36 at histone H3 (H3K36ac). As expected, total levels of H3K36ac in Sirt7-/- testicular samples increased compared to the WT. In addition, through SIRT7 immunoprecipitation we identified several SIRT7 interactors related to chromosome organization during meiotic prophase I. Taken together, our data points to SIRT7 as a new regulator of male meiosis through epigenetics and chromosome organization. Future investigations will provide deeper insights on the functional mechanisms by which SIRT7 contributes to the meiotic progression and to the prevention of reproductive aging.

PÒSTERS
Àrea de Fisiologia

FIS_01

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II. PÒSTER

Títol: Alzheimer's disease pathogenesis is influenced by selective brain IL-6 overexpression

Autors: Carla Canal, Gemma Comes, Kevin Aguilar, Iain L. Campbell, Juan Hidalgo

III. RESUM

Increasing evidence suggests that neuroinflammation has a strong contribution in Alzheimer's disease (AD) pathogenesis. Understanding and controlling the mechanisms underlying the interaction between the immune system and the nervous system might be key at the therapeutic level. Interleukin-6 (IL-6) is involved in numerous physiological functions, as it plays a critical role in the homeostasis of the neural tissue and in the pathogenesis of inflammatory disorders including AD. We have examined the role of cerebral IL-6 overexpression in a mouse model of AD, the Tg2576, which courses with progressive loss of brain functions and strong inflammatory processes that accompany the neuropathology of the disease. The effects of IL-6 overexpression on the progression of AD were examined at different levels, including physiology, behavior and neuropathology. Aged Tg2576 mice showed enhanced locomotor activity and exploration, decreased anxiety-like behavior, and impaired working memory. Overexpression of IL-6 had sex-dependent changes at the behavioral level, affecting locomotion, anxiety-like behavior and working memory. When assessing the effect of chronic neuroinflammation on motor performance, IL-6 overexpressing mice revealed deteriorated motor function. Neuropathological analysis revealed extensive plaque-associated chronic glial activation, that has been hypothesized to further promote beta-amyloid accumulation and neuroinflammation. IL-6-induced neuroinflammation in AD may promote neurodegeneration, but the evidence suggests that could also play a neuroprotective role by decreasing the amyloid load. Collectively, our results reveal the behavioral and neuropathological impact of brain IL-6 overexpression and suggest that regulating this cytokine may be relevant for the pathogenesis of AD.

FIS_02

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II. PÒSTER

Títol: Aberrant perineuronal nets alter spinal circuits, impair motor function, and increase plasticity

Autors: Sánchez-Ventura J, Canal C, Hidalgo J, Penas C, Navarro X, Torres-Espin A, Fouad K, Udina E

III. RESUM

Perineuronal nets (PNN) are a specialized extracellular matrix that have been extensively studied in the brain. Cortical PNN are implicated in synaptic stabilization, plasticity inhibition, neuroprotection, and ionic buffering. However, the role of spinal PNN, mainly found around motoneurons, is still unclear. Thus, the goal of this study is to elucidate the role of spinal PNN on motor function and plasticity in both intact and spinal cord injured mice. We used transgenic mice lacking the link protein 1 (cartilage link protein 1 (Crtl1) KO mice), which is implicated in PNN assembly. Crtl1 KO mice showed disorganized PNN with an altered proportion of their components in both motor cortex and spinal cord. Behavioral and electrophysiological tests revealed motor impairments and hyperexcitability of spinal reflexes in Crtl1 KO compared to WT mice. These functional outcomes were accompanied by an increase in excitatory synapses around spinal motoneurons. Moreover, following spinal lesions of the corticospinal tract, Crtl1 KO mice showed increased contralateral sprouting compared to WT mice. Altogether, the lack of Crtl1 generates aberrant PNN that alter excitatory synapses and change the physiological properties of motoneurons, overall altering spinal circuits and producing motor impairment. This disorganization generates a permissive scenario for contralateral axons to sprout after injury.

FIS_03

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II. PÒSTER

Títol: Assessment of IL-38 levels in Multiple Sclerosis

Autors: Néstor López González, Andrea Vera Barrón, Jose Martínez Rodríguez, Rubèn López Vales

III. RESUM

Multiple Sclerosis (MS) is chronic inflammatory disease of the central nervous system with an increasing prevalence last years. Interleukin 38 (IL-38) is the most recently discovered cytokine of the IL-1 family with reported anti-inflammatory effects. However, little is known about the changes in IL-38 expression in MS.

Aims
In this work we aimed to investigate the changes in IL-38 levels in serum samples from MS patients, as well as in the spinal cord of experimental autoimmune encephalomyelitis mice, a murine model of MS.

Methods
Human Serum samples of patients with MS and healthy individuals were collected and IL-38 levels were quantified by ELISA. Spinal cords from EAE mice were harvested at different stages of the disease and IL-38 levels were assessed by QPCR.

Results
Despite IL-38 has potent anti-inflammatory actions, the protein levels of this cytokine were not increased in MS patients. Similarly, IL-38 transcripts were not detected in the spinal cord of EAE mice at the onset and peak of the disease. However, we observed that IL-38 mRNA levels were induced in the spinal cord of EAE mice at the remission phase of the disease, coinciding with the attenuation of the neuroinflammatory response.

Conclusions
These results suggest that IL-38 could be involved in attenuating inflammation in EAE mice, and that the induction of this cytokine is defective in MS patients.

FIS_04

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II. PÒSTER

Títol: LSD1 inhibition improves functional outcome after spinal cord injury

Autors: Raquel del Río Astorga, Xavier Navarro Acebes, Clara Penas Pérez

III. RESUM

Spinal cord injury (SCI) is a major cause of sensorial, motor and autonomic dysfunction worldwide. The primary impact causes neuronal damage and blood-brain barrier disruption, leading to the activation of secondary neurodegenerative mechanisms such as inflammatory processes, excitotoxicity and oxidative stress. Lysine specific demethylase 1 (LSD1) is an epigenetic eraser that promotes and represses gene transcription by removing methyl groups from histone 3, being involved in a wide range of biological processes. LSD1 inhibition reduces neuronal death caused by glutamate neurotoxicity and oxidative stress and has also been related with neuroplasticity. However, studies of this demethylase after nervous system trauma are scarce. Therefore, we aimed to analyze the effects of LSD1 inhibition on neuroprotection, regeneration, and functional recovery after a SCI. Spinal cord injured mice were treated with the LSD1 inhibitor RN1. Locomotor function assessed using both the basso mouse scale and the walking track showed that the RN1-treated group had an enhancement of the functional outcome compared to vehicle-treated animals. Electrophysiological analysis suggested a better preservation of the spinal cord descending pathways after LSD1 inhibition. Injured mice treated with RN1 also presented a decrease in neuropathic pain compared to the vehicle group. However, histological analysis did not show significative changes in neuronal death nor glial reactivity. Finally, by analyzing protein levels in the spinal cord after LSD1 inhibition, we identify GLT-1 as a possible LSD1 target involved in neuroprotection after SCI. These findings suggest that LSD1 inhibition may be a therapeutic approach to enhance functional recovery after SCI.

FIS_05

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II. PÒSTER

Títol: Novel graphene-based electrode for interfacing the peripheral nervous system

Autors: Rodríguez-Meana B, Del Valle J, Viana D, Walston ST, Garrido JA, Navarro X.

III. RESUM

Neuroprostheses aim to restore the lost function after a limb amputation or severe neural injuries. Within a peripheral neuroprosthesis, the interface between nerve and machine is intended to record neural signals and stimulate selective populations of nerve fibers, constituting a bidirectional interface. In this work, a new generation of neural interfaces that replaces metals by engineered graphene has been tested. This new device is based on modified reduced-graphene oxide, named EGNITE.
The biocompatibility of EGNITE devices was tested in vitro and in vivo. In vitro, cell viability of dorsal root ganglia and cortical neurons seed on top of the material was analyzed. In vivo, polyimide devices coated with EGNITE were longitudinally implanted in the sciatic nerve of rats for 8 weeks. EGNITE had no impact on cell viability and did not produce any significant functional deficit or axonal damage in the implanted animals.
To test the functionality of EGNITE devices, transverse intrafascicular multichannel electrodes containing 16 EGNITE active sites were implanted in the sciatic nerve of rats for 90 days. EGNITE devices were able to stimulate nerve fascicles to produce selective muscle activation. Compared with standard electrodes using metal conductors, EGNITE devices needed about 2 times less current to produce the same muscle activation.
The biocompatibility of EGNITE together with its superior electrical capabilities may have relevant implications in the field of neuroprostheses by reducing potential tissue damage and lowering the energy consumption of the devices, thus extending the window of effective stimulation after implantation.

FIS_06

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II. PÒSTER

Títol: Spinal cord control of manual dexterity in rats: a functional mapping study

Autors: López-Santos D, Flores Á, García-Alías G.

III. RESUM

Manual dexterity, such as object “reaching and grasping” (R&G), is essential to conduct daily tasks. Stereotypic features of these movements suggest that some level of control may be exerted from the spinal cord (SC). In this project, we aimed to unveil the presence of these networks and their rostrocaudal location within the SC. The approach consisted of inflicting excitotoxic injuries to rats at different SC levels covering from C3 to T3 using kainic acid, for exclusively affecting spinal networks while preserving descending commands. Motor deficits were evaluated by comparing the performance, before vs after the intervention, in multiple behavioural tests of forelimb muscles’ function that likely require distinct neuronal networks. One-week post-intervention, C3-injured animals showed a significant impairment in R&G, staircase and horizontal ladder tests, but not on other tasks. The performance of rats receiving more caudal injuries remained grossly unaffected. Histological analysis revealed a grey matter loss that correlated with the segments of injection, and which presumably is accompanied by the loss of spinal premotor circuits. To dismiss the possibility of the concomitant loss of motoneurons and/or sensory feedback being the cause of the behavioural deficits observed, a subsequent experiment was conducted in which the C3 dorsal and ventral roots were sectioned, therefore eliminating all its direct afferences and efferences but preserving spinal networks’ integrity. Those animals did not suffer manual dexterity impairments. Our results suggest the presence, at spinal segment C3, of a neuronal network necessary for properly executing forelimb skilled movements.

FIS_07

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II. COMUNICACIÓ ORAL

Títol: Modulation of VDAC promotes motoneuron survival after brachial plexus injury

Autors: Carla Badia-Puiggalí, Neus Solanes, Mireia Herrando-Grabulosa, Xavier Navarro

III. RESUM

Traumatic lesions of the spinal roots cause severe loss of neural functions, leading to dysfunctions that result in social and labor impairment. The preservation of the motoneurons after axotomy is essential to allow successful axonal regeneration and recovery. Here we set up a model of brachial plexus injury in adult mice that represents a traumatic lesion often observed after road accidents. We focused on strategies to preserve motoneurons after brachial plexus injury by modulating components of the complex located at the mitochondria associated membranes (MAMs), in which Sigma-1 receptor (Sig1R), voltage dependent anion channel 1 (VDAC1) and inositol 1,4,5- trisphosphate receptor type 3 (IP3R3) are involved. Brachial plexus injury induced motoneuron loss to 28% after 3 weeks, increased reactive gliosis and accumulation of VDAC1 in the motoneuron. Treatment with DIDS, a pan-inhibitor of VDAC oligomerization, promoted motoneuron survival to 86% and reduced microglial reactivity to 56% and astrocytic activity to 40% of untreated mice values. VDAC1 seems to induce survival of motoneurons through the downregulation of pro-apoptotic proteins, such Cytochrome c (Cyt C) and Apoptotic inducing factor (AIF), showing a distinct decrease in cytosolic levels of both proteins after treatment. Therefore, our data suggest that, in a spinal nerve injury, the modulation of VDAC induces a neuroprotective effect.

FIS_08

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II. PÒSTER

Títol: Impact of calorie-restricted cafeteria feeding and treadmill exercise on sucrose intake, sensitivity and reactivity in diet-induced obese male and female rats

Autors: Alvarez-Monell A, Subias-Gusils A, Noemí Boqué, Antoni Caimari, Josep M. Del Bas, Roger Casadó-Mariné, Escorihuela RM, Solanas M

III. RESUM

We aimed to study how a previously characterized calorie-restricted cafeteria diet (CAFR) and moderate treadmill exercise (12-17 m/min) affects the sweet taste and biometrical and metabolic parameters in obese male and female rats. Animals were fed standard chow (STD) or cafeteria (CAF) diet for 8 weeks to induce obesity. Afterwards, animals were either maintained with ad libitum CAF or switched to CAFR diet. Dietary groups were subdivided into control (C) and exercise (E) groups. Biometric measures (body weight, Body mass index and abdominal perimeter) were recorded periodically. After 8 weeks of treatment, animals performed a two-bottle preference test, a brief-access licking test and a taste reactivity test with sucrose (0.01M-1M).

CAFR feeding decreased all biometrical parameters measured compared with CAF only in females. CAF diet in both sexes decreased sucrose intake compared with STD, while CAFR diet partially reverted this effect in females. Exercise in CAF fed males decreased sucrose intake compared with the CAF-C group. In the brief-access test, CAF feeding decreased sucrose sensitivity and CAFR feeding reverted this effect in both sexes. Exercise also decreased sucrose sensitivity in CAF fed females. Hedonic behaviour elicited by sucrose was decreased in CAF fed males compared to the STD fed.

These results indicate that the cafeteria diet-induced obesity decreases intake and sensitivity to sucrose, possibly through the development of an anhedonic state associated with obesity. This effect can be partially reverted by CAFR feeding. Additionally, treadmill exercise might decrease sucrose intake and its rewarding value in CAF-induced obese rats.

FIS_09

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II. PÒSTER

Títol: Characterization of human induced pluripotent stem cell-derived microglia from a familial amyotrophic lateral sclerosis patient

Autors: Garcia-Garcia Joana, Hernández-Martín Joaquim, López-Vales Rubèn

III. RESUM

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder characterized by motor neuron degeneration, whose cause remains unknown in 95% of ALS patients. The most common ALS mouse model, which expresses the mutant G93A superoxide dismutase 1 (SOD1G93A), have provided important insights about the detrimental microglial role in its pathogenesis. However, rodent mouse models have strong limitations since they represent a small proportion of ALS cases. Moreover, mouse microglial transcriptome is divergent compared to the human, being an important obstacle for the study of microglia. The development of humanized mouse models with human microglia have become a promising tool to understand better the role of ALS-associated risk genes in microglial cells, since engrafted human microglia in the mouse CNS mimic more closely the primary human microglia transcriptome rather than cultured microglial cells.

In the present study, we characterized in vitro human induced pluripotent stem cells (iPSCs)-derived microglia from a familial ALS patient, carrier for the SOD1I114T mutation, as preliminary data to further develop a humanized ALS microglia mouse model. The obtained microglial cells expressed the main microglial markers (CD45low, CD11b, Iba1, P2RY12), exhibited a ramified morphology and responded to a proinflammatory stimulus. Additionally, human SOD1I114T iPSC-derived microglia released neurotoxic factors able to induce motor neuron degeneration in the spinal cord of C57Bl/6 mice. Finally, transplantation of human SOD1I114T iPSC-derived microglial precursors differentiate into microglia in the mouse spinal cord, being a starting point to further optimize our chimeric mice with human ALS microglia.

FIS_10

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II. PÒSTER

Títol: Effects of a cafeteria restricted diet and oleuropein supplementation on sweet taste modifications in a cafeteria diet-induced obesity rodent model

Autors: Subias-Gusils A, Álvarez-Monell A, Boqué N, Caimari A, Del Bas JM, Casadó-Mariné R, Solanas M, Escorihuela RM

III. RESUM

Diet-induced obesity models are widely used to investigate dietary interventions for treating obesity. This study was aimed to test whether a dietary intervention based on a calorie-restricted cafeteria diet (CAF-R) and a polyphenolic compound (Oleuropein, OLE) supplementation modified sucrose intake, preference and taste reactivity in a cafeteria diet (CAF)-induced obese rats.
Male Sprague-Dawley rats fed standard chow (STD) or CAF diet were compared with obese rats fed CAF-R diet, alone or supplemented with an olive tree leaves extract (25 mg/kg*day) containing a 20.1% of OLE (CAF-RO). Two-bottle preference and taste reactivity tests were performed to evaluate the sweet preference and the hedonic responses to sucrose solutions, respectively. Also, biometric, food consumption, and serum parameters were measured.
As expected, CAF diet increased body weight, food and energy consumption and obesity-associated metabolic parameters. Interestingly, CAF-R and CAF-RO diets significantly attenuated body weight gain and BMI, diminished food and energy intake and improved biochemical parameters such as triacylglycerides and insulin resistance, which did not differ between CAF-RO and STD groups. The three cafeteria groups diminished sucrose intake and preference compared to STD group. CAF-RO also diminished the hedonic responses for the high sucrose concentrations compared with the other groups.
These results indicate that CAF-R diet may be an efficient strategy to restore obesity-associated alterations, whilst OLE supplementation seems to have an additional beneficial effect on sweet taste function.

FIS_11

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II. PÒSTER

Títol: Sigma-1 receptor is a pharmacological target to promote neuroprotection in the SOD1G93A ALS mice

Autors: Núria Gaja-Capdevila, Neus Hernández, Mireia Herrando-Grabulosa, Xavier Navarro

III. RESUM

There is no available cure for amyotrophic Lateral Sclerosis (ALS), thus, novel therapeutic targets are urgently needed. Sigma-1 receptor (Sig-1R) has been reported as a target to treat experimental models of degenerative diseases and, importantly, mutations in the Sig-1R gene cause several types of motoneuron disease (MND). In this study we compared the potential therapeutic effect of three Sig-1R ligands, the agonists PRE-084 and SA4503 and the antagonist BD1063, in the SOD1G93A mouse model of ALS. Pharmacological administration was from 8 to 16 weeks of age, and the neuromuscular function and disease progression were evaluated using nerve conduction and rotarod tests. At the end of follow up (16 weeks), samples were harvested for histological and molecular analyses. The results showed that PRE-084, as well as BD1063 treatment was able to preserve neuromuscular function of the hindlimbs and increased the number of surviving MNs in the treated female SOD1G93A mice. SA4503 tended to improve motor function and preserved neuromuscular junctions (NMJ), but did not improve MN survival. Western blot analyses revealed that the autophagic flux and the endoplasmic reticulum stress, two pathways implicated in the physiopathology of ALS, were not modified with Sig-1R treatments in SOD1G93A mice. In conclusion, Sig-1R ligands are promising tools for ALS treatment, although more research is needed to ascertain their mechanisms of action.

FIS_12

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II. PÒSTER

Títol: Preclinical development of a therapy for Chronic Traumatic Spinal Cord Injury with Wharton's Jelly Mesenchymal Stromal Cells: proof of concept and regulatory compliance

Autors: Joaquim Vives, Joaquim Hernández, Clémentine Mirabel, Maria Puigdomenech-Poch, David Romeo-Guitart, Sara Marmolejo-Martínez-Artesero, Raquel Cabrera-Pérez, Jessica Jaramillo, Hatice Kumru, Joan García-López, Joan Vidal, Xavier Navarro, Ruth Coll Bonet

III. RESUM

Spinal Cord Injury is a devastating condition resulting in loss of sensory and/or motor function. The use of multipotent Mesenchymal Stromal Cells (MSC) in emerging therapies for the treatment of spinal cord injury may hold the potential to contribute to sensory and/or motor function improvements in the patients. However, the development of cell-based medicines is challenging and a series of preclinical studies addressing quality and safety aspects, in addition to signs of efficacy, need to be performed prior to receiving regulatory approval for clinical testing in humans. Herein we present a series of in vitro and in vivo studies addressing the characterization of the quality attributes of MSC derived from the Wharton's jelly of the umbilical cord, safety of intrathecal infusion of MSC, and their effect in a rat model of spinal cord injury by controlled impaction after single (at day 7 post-injury) and repeated dose of 1x106 MSC (at days 7 and 14 post-injury). Animals were monitored for 70 days using a broad panel of tests including electrophysiological tests, motor function assessment and histology evaluation. Remarkably, recovery of locomotion was promoted at early time points and safety of repeated doses was demonstrated. The relevance of the data resulting from these studies is discussed in terms of their scientific significance as well as their suitability for being included in the Investigational Medicinal Product Dossier for further consideration by the competent Regulatory Authority.

PÒSTERS
Àrea d'Immunologia

IMM_01

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II. PÒSTER

Títol: Plataforma modular de vacunas para administración oral: El caso de SVCV

Autors: Mauricio E. Rojas, Patricia E. Aceituno, Marlid Garcia-Ordoñez, Mariana Teles, María E. Salvador, María del Mar Ortega-Villaizan, Luis Perez and Nerea Roher

III. RESUM

A la fecha, las herramientas profilácticas antivirales contra virus que afectan a los peces de piscifactorías son escasas y con protección insuficiente. En este contexto, estamos trabajando en una nueva plataforma modular de vacunas antivirales para administración oral elaborada con antígeno de proteína recombinante basada en cuerpos de inclusión (denominados “NPs”). Las proteínas recombinantes en base a cuerpos de inclusión presentan ventajas tales como; estables con un versátil diseño, totalmente funcionales y sin necesidad de encapsulación adicional, fáciles de producir y purificar, y estables en condiciones extremas de temperatura y pH. En el presente estudio, presentamos una caracterización morfológica y funcional de una nueva proteína recombinante modular antiviral elaborada con glicoproteína G del virus de la Viremia Primaveral de la Carpa (SVCV, siglas en inglés) combinada con un módulo de interferón gamma (IFNγ) recombinante de pez cebra, con el objetivo de evaluar si el dominio IFNγ induce un aumento de la respuesta inmune antiviral en comparación con el antígeno G recombinante sin IFNγ.

IMM_02

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II. PÒSTER

Títol: Vacuna de subunidades de VHSV: Una nueva herramienta profiláctica con potencial de administración oral.

Autors: Patricia E. Aceituno, Mauricio E. Rojas, Marlid Garcia-Ordoñez, and Nerea Roher

III. RESUM

A pesar del impacto y consecuencias de las enfermedades virales en la acuicultura, a la fecha hay pocas vacunas comerciales efectivas contra enfermedades virales relevantes. En base a esto, actualmente nuestro grupo está desarrollando una nueva vacuna para administración oral basada en proteínas recombinantes modulares nanoestructuradas denominadas Nanopellets (NPs). Esta plataforma biotecnológica de vacunas ya ha sido probada con diferentes antígenos virales recombinantes con resultados prometedores para SVCV y VNNV (Rojas-Peña et al., 2022; Thwaite et al, 2018; 2020). Estos biomateriales son biológicamente activos, no tóxicos, económicos y estables a pH gastrointestinal, por lo que no necesitan una mayor encapsulación. Para aumentar la respuesta antiviral, desarrollamos una nueva vacuna oral elaborada con un antígeno viral VHS más un dominio de proteína funcional adicional que codifica interferón-gamma recombinante (IFNγ). Aquí presentamos la caracterización estructural y funcional de $VHSV^{NP}$ y $VHSV\text{-}INF\gamma^{NP}$ testeado *in vitro* en macrófagos primarios (RT-HKM), e *in vivo* a partir de una intubación en truchas arcoíris lo que proporciona información relevante sobre la vía de administración y su biodistribución en tejidos inmunitarios clave.