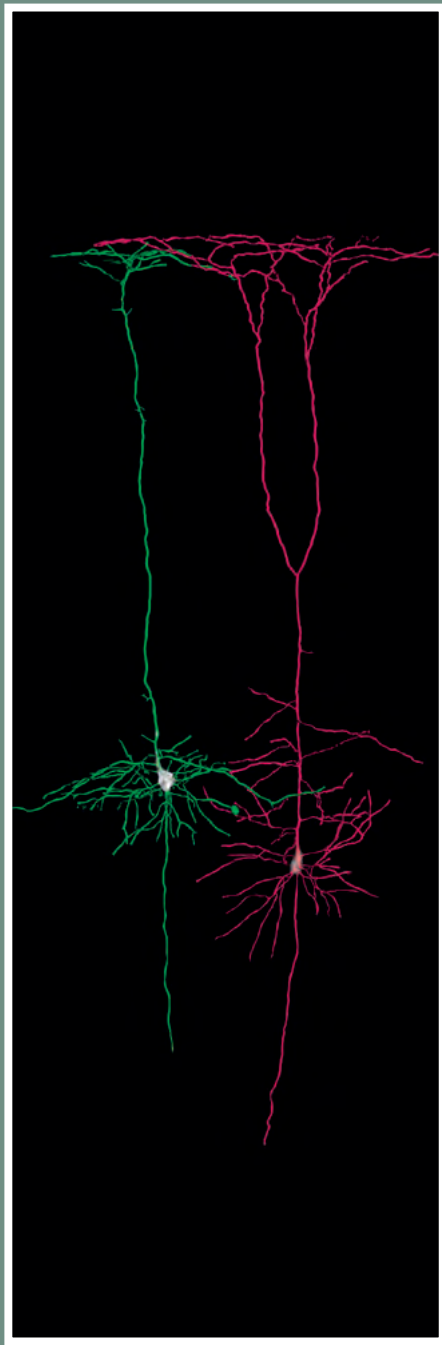


# CIPF 2020

Centro de  
Investigación  
Príncipe  
Felipe

# Annual Report





C I P F

CENTRO DE INVESTIGACIÓN PRÍNCIPE FELIPE



PRINCIPE FELIPE  
CENTRO DE INVESTIGACIÓN



GENERALITAT  
VALENCIANA  
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EUROPEAN UNION  
European Structural and Investment Fund



EUROPEAN UNION  
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Without a doubt, the health pandemic triggered by the emergence of SARS-CoV-2 shaped our personal lives and our research in 2020. How impressive that scientists around the globe responded rapidly to create diagnostic tools and effective vaccines against this virus in record time! Thus, 2020 was a year in which science played the leading role in society, providing a clear testament to the importance of funding research as a long-term investment in health and social stability. I am grateful to all of the staff and investigators of the CIPF for the courage and commitment to maintain the activity of the centre during these difficult months.

Our scientists at the CIPF also responded with their knowledge and skills to provide support to the local public health system: we were accredited by the ISCIII to perform PCRs to detect SARS-CoV-2. They devised and implemented a novel test based on a non-invasive sample of saliva that does not require extraction of RNA, thereby solving a bottleneck of the PCR procedure. Many, many thanks for a good well done to the whole CIPF COVID team: Laura, Amparo, Enric, Salva, Carmen, Bea, Begoña, Arancha, Cristina, and last but not least, Pilar who courageously organized the logistics for the team. Other investigators such as Dr. Francisco J. Iborra are collaborating in nationally-funded projects to understand more about how COVID19 alters cell biology.

Although the total number of our scientific publications declined very slightly in 2020, the gain of quality is evidenced by an increase in the average impact factor (5,89 versus 5,69 last year) and the fact that 74% of our results were published in Q1 journals. I would like to highlight an important publication from the group of Dr. Mar Orzáez in the journal *Proceedings of the National Academy of Science*. The article "Mcl-1 and Bcl-2 transmembrane domains: Unexpected players in the modulation of apoptosis" describes the novel observation that the formation of Mcl-1 homooligomers in the mitochondrial membrane induces cell death. Dysregulation of apoptosis is one of the underlying mechanisms of malignant transformation and tumour metastasis. Hence, the more we understand about the molecules involved in apoptotic pathways, the better we can design drugs to modulate this process in cancer, which is precisely the goal of Dr. Orzáez and her team.

Congratulations to Dr. Victoria Moreno who was awarded considerable funding from the highly competitive H2020-FET Open call. The aim of the RISEUP project is to develop a highly innovative system with micropulses and biomaterials for functional neuronal regeneration as a highly innovative strategy for treating patients with spinal cord injury. Dr. Moreno is an internationally-recognized leader in the field of cell therapy and spinal cord lesions. Also, many thanks to Dr. Moreno and her team for hosting and mentoring Dr. Hoda Elkhenany, a visiting scholar from Alexandria University. This was possible through our collaboration with the Women for Africa Foundation.



We also reached a key goal of our strategic plan: implementation of a new, more dynamic webpage. I want to congratulate our great IT team---Jhosland, Vicent, and Lucas-- for their dedication to the design and testing our new website, which was launched in November. This is an invaluable tool for both our image as well as our day-to-day operations Thanks to the efforts of Yolanda, we achieved another key communication milestone in October when we were awarded the Spanish Foundation for Science and Technology (FECYT) certification which identifies as a partner of the Network of Scientific Culture and Innovation Units.

The tremendous role of science in this pandemic reminds us that by promoting respect for science and by investing in scientists and their research, we can solve critical health problems. Finally, a word of gratitude and appreciation for our Consellera de Sanitat Universal i Salut Pública, Ana Barceló, who has tirelessly led the Valencian government's response to the COVID19 crisis: this disease has consistently had a lower impact in the Valencia region thanks to the leadership and planning of the Consellera and her team. This year our mantra is more meaningful than ever: more research, better health.

Deborah Burks

**#sciencewillwin**





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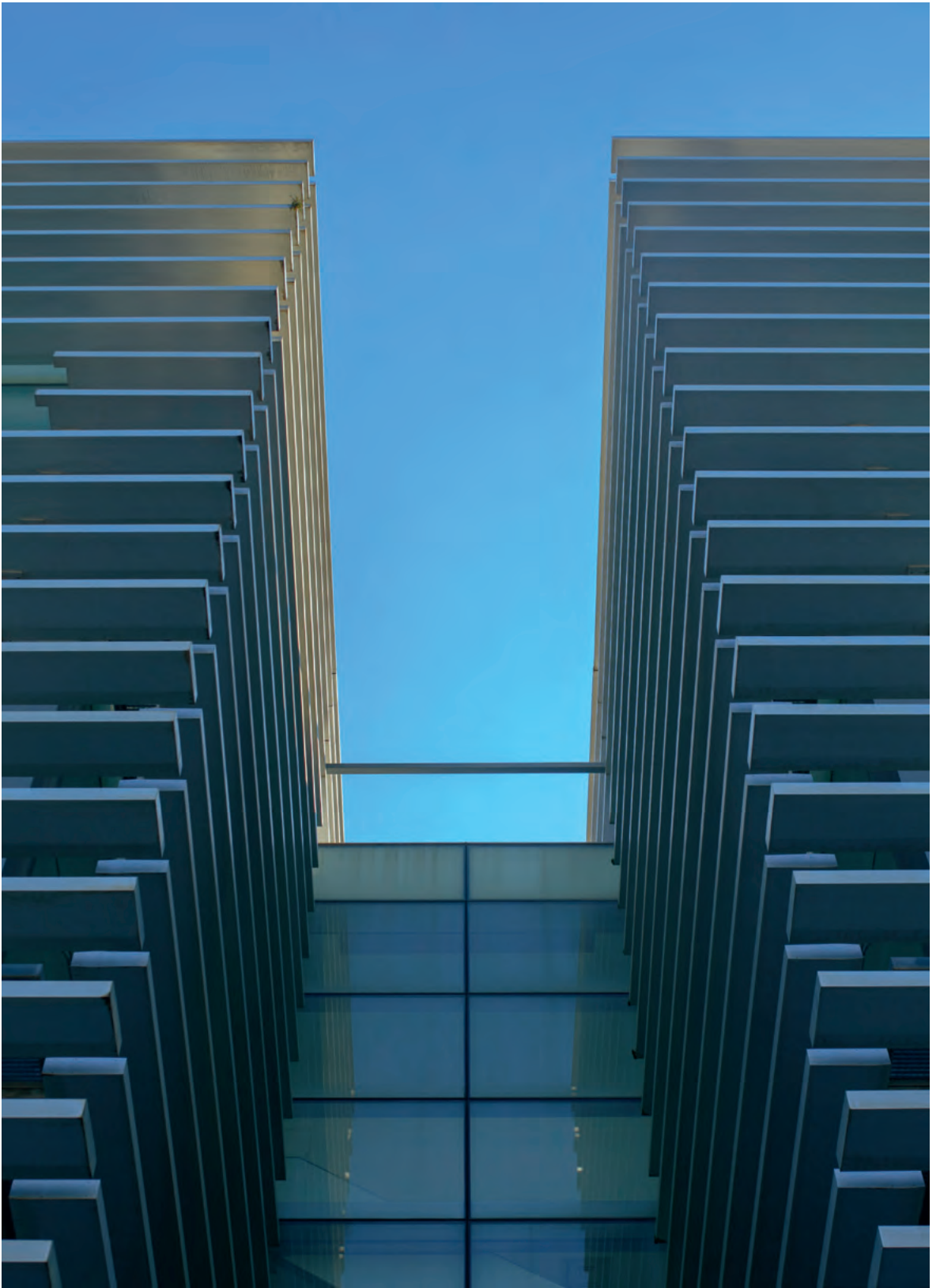
#### SECRETARY

Deborah J. Burks

*CIPF Director.*

The Board of Trustees celebrated two meetings in 2020  
12th of June and the 15th of December.

In accordance with the Spanish Transparency Legislation (Spanish Royal Decree 451/2012 of March 5) and the By- Laws of the CIPF Foundation, the Board of Trustees are not remunerated.







## MOLECULAR NEUROENDOCRINOLOGY

### TEAM MEMBERS

Deborah Burks *Principal investigator*

M<sup>a</sup> Amparo Galán, Arantxa Leal, Carlos Acosta, Esperanza Irles

TOTAL PUBLICATIONS

2

IMPACT FACTOR

12.1

AVERAGE IF

6.05

## OVERVIEW

The overall goal of our laboratory is to understand the role(s) of insulin receptor substrate (IRS) proteins in health and metabolic diseases, particularly diabetes and obesity. The IRS2 signaling pathways are essential for glucose homeostasis and the proper action of insulin in regulating cell growth and survival, and CNS functions such as learning and memory. During 2020, our efforts have centered on the validation and characterization of a new tool for defining the expression and regulation of the *Irs2* gene during development and during a variety of biological processes including metabolic stress and ageing. This reporter mouse model where *Irs2* expression can be monitored by GFP or luciferase activity is a novel tool which will permit us to determine the spatial-temporal expression of *Irs2* and to explore factors and drugs which may modulate *Irs2* expression. Using cytometry as well as imaging techniques, we have confirmed the enriched expression of IRS2 in pancreatic beta cells. By using agents that elevate cAMP, we have demonstrated that the transgene responds correctly by upregulating the levels of cellular IRS2. Our plans for the next include the detailed characterization of *Irs2* regulation, with the goal of identifying physiological factors which modulate this gene.

## SELECTED PUBLICATIONS

Taberner-Cortés A, Vinué Á, Herrero-Cervera A, Aguilar-Ballester M, Real JT, Burks DJ, Martínez-Hervás S, González-Navarro H. Dapagliflozin Does Not Modulate Atherosclerosis in Mice with Insulin Resistance. *Int J Mol Sci*. 2020 Dec 3;21(23):9216. doi: 10.3390/ijms21239216. PMID: 33287201

In Collaboration with the University of Valencia and the Unit for Gender in Biomedicine: Sentandreu-Mano, T., L. Badenes-Ribera, I. Fernandez, A. Oliver, D. Burks and J. Tomas (2020). Frailty in the Old Age as a Direct Marker of Quality of Life and Health: Gender Differences. *Social Indicators Research* (online first) DOI: 10.1007/s11205-019-02246-1.



## STEM CELL THERAPIES IN NEURODEGENERATIVE DISEASES

### TEAM MEMBERS

Slaven Erceg *Principal investigator*

Francisco Javier Rodríguez Jiménez, Ana Artero-Castro, María Amparo Pérez Arago, Francisca Selles Sorlí, Candela Machuca Arellano.



TOTAL PUBLICATIONS

5

IMPACT FACTOR

40

AVERAGE IF

8

## OVERVIEW

We are developing new therapeutic cell-based treatment approaches for neurodegenerative diseases by using adult stem cells or pluripotent stem cells such as human embryonic stem cells (hESCs) and induced human pluripotent stem cells (hiPSCs). Our aim is to develop clinically acceptable protocols for neural differentiation and to test them in different animal models as potential therapeutic tools to help treat spinal cord injuries and different types of ataxias. We also apply combinatorial approaches using small molecules in order to increase the success of cell-based therapies.

Hereditary retinal dystrophies are another subject of interest in our laboratory. In particular, we are focusing on creating new human cell models using patient-specific hiPSCs, and especially, retinal pigment epithelial (RPE) cells derived from them. We are using these cells to investigate the mechanisms driving these diseases, develop treatments, perform toxicity screens, and model development in cells affected by these diseases. Moreover, we intend to correct the faulty genes in these cells using Crispr/Cas9 technology and to optimize the derivation of RPE cells from corrected hiPSCs as a cell source for transplantation therapies in animal models with retinal degeneration diseases. In collaboration with other laboratories, we are developing new cell therapies using RPE and photoreceptor cells transplanted into degenerated retina in small and large animal models.

## SELECTED PUBLICATIONS

Activation of Neurogenesis in Multipotent Stem Cells Cultured In Vitro and in the Spinal Cord Tissue After Severe Injury by Inhibition of Glycogen Synthase Kinase-3. Rodriguez-Jimenez FJ, Vilches A, Perez-Arago MA, Clemente E, Roman R, Leal J, Castro AA, Fustero S, Moreno-Manzano V, Jendelova P, Stojkovic M, Erceg S. *Neurotherapeutics*. 2020 Sep 30. doi: 10.1007/s13311-020-00928-0. Online ahead of print. PMID: 33000422

Glaucoma as a Neurodegenerative Disease Caused by Intrinsic Vulnerability Factors. Artero-Castro A, Rodriguez-Jimenez FJ, Jendelova P, VanderWall KB, Meyer JS, Erceg S. *Prog Neurobiol*. 2020 Oct;193:101817. doi: 10.1016/j.pneurobio.2020.101817. Epub 2020 Apr 29. PMID: 32360241

Chronic hyperammonemia induces peripheral inflammation that leads to cognitive impairment in rats: Reversed by anti-TNF- $\alpha$  treatment. Balzano T, Dadsetan S, Forteza J, Cabrera-Pastor A, Taoro-Gonzalez L, Malaguarnera M, Gil-Perotin S, Cubas-Nuñez L, Casanova B, Castro-Quintas A, Ponce-Mora A, Arenas YM, Leone P, Erceg S, Llansola M, Felipe V. *J Hepatol*. 2020 Sep;73(3):582-592. doi: 10.1016/j.jhep.2019.01.008. Epub 2019 Jan 14. PMID: 30654069



## RARE NEURODEGENERATIVE DISEASES LABORATORY

### TEAM MEMBERS

Carmen Espinós *Principal investigator*

Vincenzo Lupo, Dolores Martínez-Rubio, Isabel Hinarejos, Candela Machuca,  
Ana Sánchez-Montegudo, Paula Sancho, Amparo Andrés.

TOTAL PUBLICATIONS

10

IMPACT FACTOR

40.29

AVERAGE IF

4.03

## OVERVIEW

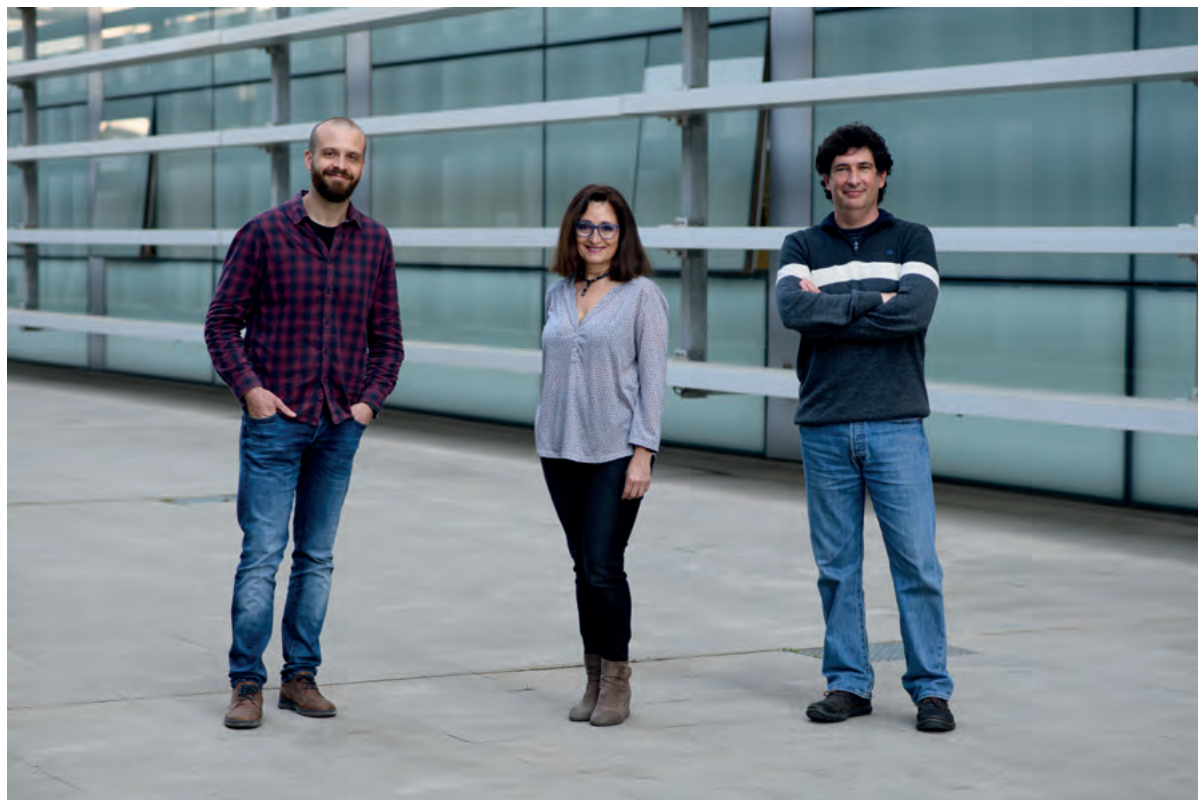
Molecular bases of movement disorders (ataxia, dystonia, parkinsonism, spastic paraplegia, NBIA). We researched a series of 124 cases and identified the genetic bases in 89 probands. We characterized a second case of *PLEKHG2*, a gene involved in leukodystrophy with microcephaly and dystonia; we broadened the clinical picture associated with NR4A2, a syndrome with parkinsonism-dystonia; and we discovered a novel gene responsible for an early-onset ataxia, *PRDX3*. Biomarkers of Wilson's disease. Using RNAseq we detected five miRNAs significantly dysregulated in patients: miR-485-3p, miR-340-3p, miR-122-5p, miR-192-5p, and miR-885-5p. The latter three miRNAs are related to hepatic function and, in our series, they correlated with abnormal levels of transaminases and triglycerides. Characterization of MORC2 involved in Charcot-Marie-Tooth disease. By performing proteomics in infected rat sensory neurons, we investigated two *MORC2* mutations (p.R252W and p.S87L). Proteins belonging to several pathways (synaptic transmission, intracellular transport, lipid metabolism, fatty acid metabolism, and apoptosis) exhibited significantly altered expression.

## SELECTED PUBLICATIONS

Sánchez-Monteaagudo A, Álvarez-Sauco M, Sastre I, Martínez-Torres I, Lupo V, Berenguer M, Espinós C. Genetics of Wilson disease and Wilson-like phenotype in a clinical series from eastern Spain. *Clinical Genetics* 2020; 97(5):758-763.

Correa-Vela M, Lupo V, Montpeyó M, Sancho P, Marcé-Grau A, Hernández-Vara J, Darling A, Jenkins A, Fernández-Rodríguez S, Tello C, Ramírez-Jiménez L, Pérez B, Sánchez A, Sobrido MJ, Martínez-Vicente M, Pérez-Dueñas B, Espinós C. Impaired proteasome activity and neurodegeneration with brain iron accumulation in FBXO7 defect. *Annals of Clinical and Translational Neurology* 2020; 7(8): 1436-1442.

Hinarejos I, Machuca-Arellano C, Sancho P, Espinós C. Mitochondrial dysfunction, oxidative stress and neuroinflammation in neurodegeneration with brain iron accumulation (NBIA). *Antioxidants* 2020; 9



## CELLULAR AND MOLECULAR IMMUNOLOGY LABORATORY

### TEAM MEMBERS

Enric Esplugues *Principal investigator*  
Salvador Meseguer, Beatriz Pérez, Mari Paz Rubio.

TOTAL PUBLICATIONS

1

IMPACT FACTOR

12.12

AVERAGE IF

12.12

## OVERVIEW

New therapeutic strategies against infectious diseases. We studied the role of viral non-coding RNA (ncRNA) in COVID-19 patients. Many RNA viruses synthesise their own ncRNAs which can play a multitude of functions in the host cell during infection. We are in the process of validating their function to be able to use them as therapeutic targets in SARS-CoV-2-infected patients. Anti-inflammatory fate of TH17 cells. We showed that the capacity of TH17 cells to acquire an anti-inflammatory fate is necessary to sustain immunological tolerance, even though it impairs immune protection against *Staphylococcus aureus*. Our data indicate that TH17 cell plasticity plays a key function in maintaining immune homeostasis, and we dissected the molecular mechanisms explaining the functional flexibility of TH17 cells with regard to environmental changes.

## SELECTED PUBLICATIONS

The induction and function of the anti-inflammatory fate of TH17 cells. Xu H, Agaloti T, Zhao J, Steglich B, Wahib R, Vesely MCA, Bielecki P, Bailis W, Jackson R, Perez D, Izbicki J, Licona-Limón P, Kaartinen V, Geginat J, Esplugues E, Tolosa E, Huber S, Flavell RA, Gagliani N. Nat Commun. 2020 Jul 3;11(1):3334



## ONCOGENIC SIGNALLING LABORATORY

### TEAM MEMBERS

Rosa Farràs Rivera *Principal investigator*

Carolina Gandía Ventura, Arantxa Martínez Férriz, Alihamze Fathinajabadi  
Nasresfahani.

TOTAL PUBLICATIONS

2

IMPACT FACTOR

8.57

AVERAGE IF

4.28

## OVERVIEW

Despite great advances, lung cancer remains the leading cause of cancer-related death in developed countries. Metastasis and drug resistance are the main factors contributing to relapse and death in these patients. The developmental program known as mesenchymal epithelial transition (EMT) has become a possible candidate mechanism to explain tumour metastasis. Our research focuses on studying the changes induced by the TGF-beta signalling pathway at two different levels. First, at the transcriptional level through the activity of AP-1 transcription factors. Second, we also studied alterations at the translational level through the activity of the eIF5A translation factor, which promotes EMT in non-small cell lung cancer. Understanding the EMT process will help define new treatment strategies to counteract tumour progression and drug resistance. To investigate lung tumour biology, we are currently generating *in vivo* cancer experimental models (organoids and patient-derived xenografts) in collaboration with local hospitals that can adequately represent tumour heterogeneity and predict drug sensitivity *in vivo*. Through our expertise in protein degradation, our group is a member of the UBIred network dedicated to the study of ubiquitin and ubiquitin-like proteins and their roles in cell proliferation, differentiation, and cancer.

## SELECTED PUBLICATIONS

Pérez-Díez I, Hidalgo MR, Malmierca-Merlo P, Andreu Z, Romera-Giner S, Farràs R, de la Iglesia-Vayá M, Provencio M, Romero A, García-García F. Functional Signatures in Non-Small-Cell Lung Cancer: A Systematic Review and Meta-Analysis of Sex-Based Differences in Transcriptomic Studies. *Cancers (Basel)*. 2021 Jan 5;13(1):143. doi: 10.3390/cancers13010143. PMID: 33526761; PMCID: PMC7796260.

Pérez-Benavente B, Nasresfahani AF, Farràs R. Ubiquitin-Regulated Cell Proliferation and Cancer. *Adv Exp Med Biol*. 2020;1233:3-28. doi: 10.1007/978-3-030-38266-7\_1. PMID: 32274751.





## CORTICAL CIRCUITS IN HEALTH AND DISEASE

### TEAM MEMBERS

Pietro Fazzari *Principal investigator*

M<sup>a</sup> Carmen Navarro González, Ángela Rodríguez Prieto, Ana González Manteiga,  
Yaiza Domínguez Canterla.



TOTAL PUBLICATIONS

1

IMPACT FACTOR

5.61

AVERAGE IF

5.61

## OVERVIEW

Our group studies the development of the cerebral cortex and investigates innovative strategies to promote the regeneration of cortical neurons upon brain injury. We found that Nrg1 intracellular signalling regulates neuronal development and is neuroprotective upon stroke, both in vitro and in vivo. Our work suggests that stimulation of Nrg1 may be a promising target for the treatment of cortical damage. Notably, brain damage is the most common cause of permanent disability and recovery is very limited. We are currently investigating the hypothesis that Nrg1 may promote the regeneration and recovery of cortical circuits after brain damage. In addition, we recently studied the role of brain expansion during embryonic development. We showed that this process contributes to the distribution of different neurons in specific regions of the cortex. This process defines the function of different cortical areas and it is often altered in neurodevelopmental disorders.

## SELECTED PUBLICATIONS

Cortical distribution of GABAergic interneurons is determined by migration time and brain size. Pietro Fazzari, Niall Mortimer, Odessa Yabut, Daniel Vogt, Ramon Pla. Development 2020 147: dev185033 doi: 10.1242/dev.185033 Published 22 July 2020



## LABORATORY OF NEUROBIOLOGY NEUROCIPF

### TEAM MEMBERS

Vicente Felipo *Principal investigator*

Marta Llansola, Amparo Urios, Carla Giménez Garzó, María Sancho, Paula Izquierdo, Paola Leone, Yaiza Arenas, Gergana Ivaylova, Teresa Rubio, Mar Martínez, Mari Carmen Castro, Alejandra Hernández, Alberto Sabio, Álvaro Gómez Pérez, María Castelló Pons, Zulema Rodríguez Hernández, Borja Gómez Cabañes.

TOTAL PUBLICATIONS

7

IMPACT FACTOR

49.93

AVERAGE IF

7.13

## OVERVIEW

The Neurobiology Laboratory performs basic and translational research on the mechanisms, diagnosis, and treatment of cognitive and motor impairment in animal models of hyperammonemia and minimal hepatic encephalopathy (MHE). We study the mechanisms responsible for cognitive and motor impairment in patients with MHE in rat models. We also analyse the role of peripheral inflammation, how it induces neuroinflammation, how neuroinflammation alters neurotransmission, and how this leads to cognitive and motor impairment. Once we identify the mechanisms involved, we design and test new therapeutic treatments to reverse neuroinflammation and restore neurotransmission and cognitive and motor function. Within the framework of the Joint Unit for Neurological Impairment with INCLIVA, we perform parallel studies in cirrhotic patients with MHE to analyse in detail the cognitive and motor alterations, cerebral alterations (by magnetic resonance, neurophysiology, and neuropathology), and role of changes in the immune system in triggering these alterations. Thus, we look for new, early, and more sensitive procedures to diagnose MHE.

## SELECTED PUBLICATIONS

Balzano T, Dadsetan S, Forteza J, Cabrera-Pastor A, Taoro-Gonzalez L, Malaguarnera M, Gil-Perotin S, Cubas-Nuñez L, Casanova B, Castro-Quintas A, Ponce-Mora A, Arenas YM, Leone P, Erceg S, Llansola M, Felipe V. Chronic hyperammonemia induces peripheral inflammation that leads to cognitive impairment in rats: Reversed by anti-TNF- $\alpha$  treatment. *Journal of Hepatology*. 2020 Sep;73(3):582-592. doi: 10.1016/j.jhep.2019.01.008.. PMID: 30654069.

Arenas YM, Cabrera-Pastor A, Juciute N, Mora-Navarro E, Felipe V. Blocking glycine receptors reduces neuroinflammation and restores neurotransmission in cerebellum through ADAM17-TNFR1-NF- $\kappa$ B pathway. *Journal of Neuroinflammation*. 2020 Sep 11;17(1):269. doi: 10.1186/s12974-020-01941-y. PMID: 32917219; PMCID: PMC7488331.

Balzano T, Arenas YM, Dadsetan S, Forteza J, Gil-Perotin S, Cubas-Nuñez L, Casanova B, Gracià F, Varela-Andrés N, Montoliu C, Llansola M, Felipe V. Sustained hyperammonemia induces TNF- $\alpha$  IN Purkinje neurons by activating the TNFR1-NF- $\kappa$ B pathway. *Journal of Neuroinflammation*. 2020 Feb 22;17(1):70. doi: 10.1186/s12974-020-01746-z. PMID: 32087723; PMCID: PMC7035786.



## BIOINFORMATICS AND BIOSTATISTICS UNIT

### TEAM MEMBERS

Francisco García García *Head of Unit*

Marta Hidalgo García, Rubén Sánchez García, Sandra Alandes Esteve, José F. Català Senent, Rubén Grillo Risco, Pablo M. Malmierca Merlo, Sergio Romera Giner, Adolfo López Cerdán, Irene Pérez Díez.

TOTAL PUBLICATIONS

11

IMPACT FACTOR

48.8

AVERAGE IF

4.4

## OVERVIEW

The Bioinformatics and Biostatistics Unit aims to develop innovative methods and tools for big data analysis from different sources in Biomedicine, allowing us to better characterise human diseases and their treatments. Our main lines of work are focused on (1) the generation of clinical predictors based on high-throughput technologies and artificial intelligence methods; (2) the detection and understanding of the molecular mechanisms associated with spinal cord injuries; and (3) the study of gender and sex differences in biomedical studies using computational approaches based on omic data meta-analysis to detect and characterise the specific molecular mechanisms of disease in men and women in several groups: (i) cardiovascular diseases (aortic stenosis and ischemic heart disease); (ii) neurodegenerative diseases (Parkinson, Alzheimer, and multiple sclerosis); (iii) autoimmune diseases (rheumatoid arthritis, dermatitis, and psoriasis); (iv) hepatic diseases; and (v) different tumour groups (ovarian, breast, lung, and pancreatic cancer).

## SELECTED PUBLICATIONS

*Unveiling Sex-Based Differences in the Effects of Alcohol Abuse:*

*A Comprehensive Functional Meta-Analysis of Transcriptomic Studies.*

Casanova Ferrer F, Pascual M, Hidalgo MR, Malmierca-Merlo P, Guerri C, García-García F. *Genes* (Basel). 2020 Sep 21;11(9). doi: 10.3390/genes11091106. PubMed PMID: 32967293.

*Sex is a strong prognostic factor in stage IV non-small-cell lung cancer patients and should be considered in survival rate estimation.* Barquin M, Calvo V, García-García F, Nuñez B, Sánchez-Herrero E, Serna-Blasco R, Auglytė M, Carcereny E, Rodríguez-Abreu D, López Castro R, Guirado M, Camps C, Bosch-Barrera J, Massutí B, Ortega AL, Del Barco E, Gonzalez-Larriba JL, Aguiar D, García-Campelo R, Dómine M, Agraso S, Sala MA, Oramas J, Bernabé R, Blanco R, Parejo C, Cruz A, Menasalvas E, Royuela A, Romero A, Provencio M. *Cancer Epidemiol.* 2020 Aug;67:101737. doi: 10.1016/j.canep.2020.101737. PubMed PMID: 32450544.

*Uterine disorders affecting female fertility: what are the molecular functions altered in endometrium?.* Devesa-Peiro A, Sebastian-Leon P, García-García F, Arnau V, Aleman A, Pellicer A, Diaz-Gimeno P. *Fertil Steril.* 2020 Jun;113(6):1261-1274. doi: 10.1016/j.fertnstert.2020.01.025. PubMed PMID: 32482256.





## MOLECULAR AND CELLULAR PATHOLOGY

### TEAM MEMBERS

Consuelo Guerri Sirera *Principal investigator*  
Maria Pascual Mora, Juan Ureña Peralta, Francesc Ibañez Cabañes,  
Carlos Manuel Cuesta Díaz. Marina Sanchez Petidier  
(shared with Dr. V.Moreno), Susana Mellado.

TOTAL PUBLICATIONS

4

IMPACT FACTOR

4.75

AVERAGE IF

4.12

## OVERVIEW

Adolescence is an important brain maturation period during which some brain regions undergo remodelling and functional changes. Activation of TLR4 receptors during binge alcohol drinking in adolescent animals leads to astrogliosis and microgliosis, increases cytokines and inflammatory mediators, and causes neuroinflammation and brain damage. Current studies show evidence of the role of miRNAs in extracellular vesicles (EVs) as key regulators of pathological processes, including neuroinflammation and neurodegeneration. Using astrocyte-derived EVs, we demonstrated that astroglial EVs can act as cellular transmitters of inflammatory signalling by spreading and amplifying the neuroinflammatory response induced by ethanol through the TLR4 response. Since, EVs can cross the blood brain barrier and EV miRNAs are highly stable in peripheral circulation, we evaluated the potential sex differences in the levels of inflammatory-regulated miRNAs in human and murine plasma EVs derived from alcohol-intoxicated female and male adolescents, and whether these miRNAs could be used as biomarkers of this neuroinflammation. We demonstrated that while alcohol intoxication reduces the levels of anti-inflammatory miRNAs (mir-146a-5p, mir-21-5p, and mir-182-5p) in plasma EVs from human and mouse female adolescents, these EV miRNAs were increased in males. In mouse brain cortices, ethanol treatment reduces the levels of mir-146a-5p and mir-21-5p, and triggers higher expression of inflammatory target genes (Traf6, Stat3, and Camk2a) in adolescent female mice. These results indicate that the effects of ethanol associated with the EV profile of inflammatory-related plasma miRNAs differ in female and male adolescents, and suggest that the former are more vulnerable than the latter to the inflammatory effects of binge alcohol drinking. These findings also suggest that circulating miRNAs in EVs could be useful biomarkers to screen ethanol-induced neuroinflammation and brain damage in adolescence.

## SELECTED PUBLICATIONS

Ibáñez F, Ureña-Peralta JR, Costa-Alba P, Torres JL, Laso FJ, Marcos M, Guerri C, Pascual M. *Circulating MicroRNAs in Extracellular Vesicles as Potential Biomarkers of Alcohol-Induced Neuroinflammation in Adolescence: Gender Differences* *Int J Mol Sci.* 14;21(18):6730, 2020 (4,66)

Casanova Ferrer F, Pascual M, Hidalgo MR, Malmierca-Merlo P, Guerri C, García-García F. *Unveiling Sex- Based differences in the effects of alcohol abuse : A Comprehensive Functional Meta-Analysis of Transcriptomic Studies.* *Genes (Basel).* 11(9):1106, 2020

Ureña-Peralta JR, Pérez-Moraga R, García-García F, Guerri C *Lack of TLR4 modifies the miRNAs profile and attenuates inflammatory signaling pathways.* *PLoS One.* 15(8):e0237066, 2020

Pascual M, Ibáñez F, Guerri C. *Exosomes as mediators of neuron-glia communication in neuroinflammation.* *Neural Regen Res.*15(5):796-801,2020

Montagud-Romero S, Montesinos J, Pavón FJ, Blanco-Gandia MC, Ballestín R, Rodríguez de Fonseca F, Miñarro J, Guerri C, Rodríguez-Arias M. *Social defeat-induced increase in the conditioned rewarding effects of cocaine: Role of CX3CL1* *Prog Neuropsychopharmacol Biol Psychiatry* 10;96:109753,2020



## NEURONAL AND TISSUE REGENERATION LABORATORY

### TEAM MEMBERS

Victoria Moreno Manzano *Principal investigator*

Esther Giraldo Reboloso, Carlos Sánchez Huertas, Hoda Elkhenany, Ana Alastrue Agudo, Marina Sánchez Petidier, Pablo Bonilla Villamil, Beatriz Martínez Rojas, Sonia Prakash, M<sup>a</sup> del Mar Sánchez Martín, Maravillas López Mellado, Eric López Mocholi, David Palmero Cantón, Celia Calvo Fernández, Angela Molines Signes.



TOTAL PUBLICATIONS

8

IMPACT FACTOR

46.68

AVERAGE IF

5.83

## OVERVIEW

In the Neuronal and Tissue Regeneration laboratory we aim to tackle currently incurable spinal cord injuries (SCIs) by the implementation of novel combinatorial strategies that harness multiple independent mechanisms for optimal functional regeneration. Interesting data was recently obtained by the use of optogenetics, leading to significant benefits for the use of neural precursor cells (NPCs) for cell therapy applications. Engineering NPCs to ectopically express the excitatory light-sensitive protein channelrhodopsin-2 (ChR2-NPCs), prompted an influx of cations and a subsequent increase in proliferation and differentiation into oligodendrocytes and neurons, as well as the polarization of astrocytes from a pro-inflammatory phenotype to a pro-regenerative/anti-inflammatory phenotype. These results highlight the enormous potential of optogenetically stimulated NPCs as a means to increase neuroregeneration and improve cell therapy outcomes by enhancing engraftment and cell specification upon transplantation into hostile conditions such as in cases of SCI.

## SELECTED PUBLICATIONS

Optogenetic Modulation of Neural Progenitor Cells Improves Neuroregenerative Potential. Giraldo E, Palmero-Canton D, Martinez-Rojas B, Sanchez-Martin MDM, Moreno-Manzano V. *Int J Mol Sci.* 2020 Dec 31;22(1):365. doi: 10.3390/ijms22010365

tappAS: a comprehensive computational framework for the analysis of the functional impact of differential splicing. de la Fuente L, Arzalluz-Luque Á, Tardáguila M, Del Risco H, Martí C, Tarazona S, Salguero P, Scott R, Lerma A, Alastrue-Agudo A, Bonilla P, Newman JRB, Kosugi S, McIntyre LM, Moreno-Manzano V, Conesa A. *Genome Biol.* 2020 May 18;21(1):119. doi: 10.1186/s13059-020-02028-w

Human adipose-derived mesenchymal stem cells accelerate decellularized neobladder regeneration. Moreno-Manzano V, Mellado-López M, Morera-Esteve MJ, Alastrue-Agudo A, Bisbal-Velasco V, Forteza-Vila J, Serrano-Aroca Á, Vera-Donoso CD. *Regen Biomater.* 2020 Mar;7(2):161-169. doi: 10.1093/rb/rbz049. Epub 2019 Dec 22.



## TARGETED THERAPIES ON CANCER AND INFLAMMATION

### TEAM MEMBERS

*Mar Orzáez Principal investigator*

Mónica Sancho Medina, Diego Leiva Yust, Paula Soriano Teruel, Estefanía Lucendo Gutiérrez, Alicia García Jareño, María Marco Salvador, Alba Amparo Ortuño Bernal.

TOTAL PUBLICATIONS

5

IMPACT FACTOR

40.95

AVERAGE IF

8.19

## OVERVIEW

The Targeted Therapies Laboratory works on the identification and preclinical development of new modulators for cell death and inflammation. In terms of cell death, our main targets are the transmembrane interactions between proteins of the Bcl-2 family. Deregulation of the Bcl-2 interactome is associated with tumour development and chemotherapy resistances. We work to resolve which mitochondrial membrane interactions are responsible for cancer resistances and to develop new drugs to trigger cancer cell death. In terms of inflammation, our main goal is to develop new inflammasome modulators. The inflammasome is one of the main components of the pro-inflammatory signalling pathway that protects our body from injury and infections. Deregulation of this protein complex is associated with the pathophysiology of autoimmune disorders, inflammatory diseases, and cancer. We work on the characterisation of new inflammasome inhibitors as therapeutic agents and as chemical tools to understand the molecular mechanisms responsible for these diseases.

## SELECTED PUBLICATIONS

Lucendo E, Sancho M, Lolicato F, Javanainen M, Kulig W, Leiva D, Duart G, Andreu-Fernández V, Mingarro I, Orzáez M. Mcl-1 and Bok transmembrane domains: Unexpected players in the modulation of apoptosis. *Proc Natl Acad Sci U S A*. 2020 Nov 10;117(45):27980-27988. doi: 10.1073/pnas.2008885117. Epub 2020 Oct 22. PMID: 33093207; PMCID: PMC7668047.

Galiana I, Lozano-Torres B, Sancho M, Alfonso M, Bernardos A, Bisbal V, Serrano M, Martínez-Máñez R, Orzáez M. Preclinical antitumour efficacy of senescence-inducing chemotherapy combined with a nanoSenolytic. *J Control Release*. 2020 Jul 10;323:624-634. doi: 10.1016/j.jconrel.2020.04.045. Epub 2020 May 4. PMID: 32376460.

Lozano-Torres B, Blandez JF, Galiana I, García-Fernández A, Alfonso M, Marcos MD, Orzáez M, Sancenón F, Martínez-Máñez R. Real-Time in Vivo Detection of Cellular Senescence through the Controlled Release of the NIR Fluorescent Dye Nile Blue. *Angew Chem Int Ed Engl*. 2020 Aug 24;59(35):15152-15156. doi:10.1002/anie.202004142. Epub 2020 Jun 8. PMID: 32416002



## POLYMER THERAPEUTICS LABORATORY

### GROUP MEMBERS

María J. Vicent *Principal investigator*

Ana Armiñán de Benito, Inmaculada Conejos-Sánchez, Zoraida Andreu, Alessio Malfanti, Katia Maso, María Medel, Stuart P. Atkinson, Irene Dolz, Oleksandr Zagorodko, Sonia V. Ruiz, Fernanda Rodríguez-Otormin, Tetiana Melnyk, Snežana Đorđević, Paz Boix, Antoni Serrano, Paula Soriano (co-supervised with Dr Mar Orzáez), Camilla Pegoraro, Inés Domingo Ortí, Esther Masiá, David Charbonnier, M<sup>a</sup> Helena Ferrandis, Susana Vila.

PUBLICATIONS	PATENTS	IMPACT FACTOR	AVERAGE IF
15	1	107.12	7.65

## OVERVIEW

The Polymer Therapeutics Lab develops nanopharmaceuticals as solutions for unmet clinical needs, including metastasis and neurodegeneration. Our interdisciplinary strategy begins with controlled polymer chemistry, supramolecular assembly, optimised conjugation, and physico-chemical characterisation, but also extends to in vivo preclinical evaluation. The ERC-Co-MyNano project, which aims to develop anticancer combination nanoconjugates, has established a family of self-assembled polypeptide carriers. We characterised patient-derived three-dimensional breast cancer models and identified optimal personalised nanoconjugates/functional biomarkers. We also strengthened our research efforts in immuno-oncology by designing lymphotropic nanoconjugates that enhance immunomodulation in melanoma ('ERC-PoC-Polymune') and pancreatic cancer (La Caixa 'HR-NanoPanTher') as single-agent and multivalent nanovaccines. Research supported by MICINN and AECC-CV demonstrated how polypeptide-based nanocarriers bypass the blood-brain barrier after intravenous or intranasal administration to provide treatment opportunities for disorders including Alzheimer disease, multiple sclerosis, paediatric tumours, and brain metastases. Finally, demonstrated the benefits of locally administered newly developed polypeptide-based nanoconjugates as single agents and combination therapies in skin-related pathologies ('RTC-PolypepSkin') and spinal cord injury (Marató TV3).

## SELECTED ARTICLES

A Duro-Castano, C. Borrás, V. Herranz-Pérez, M. C. Blanco-Gandía, I. Conejos-Sánchez, A. Armiñán, C. Mas-Bargues, M. Inglés, J. Miñarro, M. Rodríguez-Arias, J. M. García-Verdugo, J. Viña, M. J. Vicent\*. Targeting Alzheimer's disease with multimodal polypeptide-based nanoconjugates. *Science Advances* 2021, 7, eabf9180.

D. Van Lysebetten, A. Malfanti, K. Deswarte, K. Koynov, B. Golba, T. Ye, Z. Zhong, S. Kasmi, A. Lamoot, Y. Chen, S. Van Herck, B. N. Lambrecht, N. N. Sanders, S. Lienenklaus, S. A. David, M. J. Vicent, S. De Koker, B. G. De Geest. Lipid-Polyglutamate Nanoparticle Vaccine Platform. *ACS Applied Materials & Interfaces* 2021, 13, 5, 6011–6022.

Melnyk T, Dordevic S, Conejos-Sánchez I.\*, Vicent MJ\* Therapeutic Potential of Polypeptide-Based Conjugates: Rational Design and Analytical Tools That Can Boost Clinical Translation. *Advanced Drug Delivery Reviews* 2020; 160: 136-169.

## PATENT

M.J. Vicent, V. Moreno-Manzano et al. Polymeric conjugates and uses thereof. Application number: PCT/EP2020/058940 Application date: 30/03/20. CIPF & Step by Step.



#### NEW JUNIOR GROUP LEADERS

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## HOST-MICROBE INTERACTIONS IN METABOLIC HEALTH LABORATORY

#### TEAM MEMBERS

Alfonso Benítez-Páez PhD *Principal investigator*  
Sonia Cárdenas Brito, Pedro Sánchez Sánchez.



## TOTAL PUBLICATIONS

1

## IMPACT FACTOR

7.74

## AVERAGE IF

7.74

## OVERVIEW

Our group started our research activity at the CIPF in 2020 as a novel laboratory studying the influence of microbiota on human health. Our lab aims to integrate clinical data with advanced multidimensional omics readouts to establish reliable diet-host-microbe interactions from the metabolic point of view. We also performed advanced experimental approaches to characterise human gut microbes as potential probiotics which can be formulated into innovative synbiotic products. Our group's major outcomes in 2020 consisted of clinical assessments to unveil potential microbiota-based biomarkers used to anticipate patient treatment evolution and disease onset, as well as the in-depth evaluation of controlled dietary interventions with a view towards personalised medicine. The lines of investigation in our laboratory have allowed us to advance already existing solutions for studying complex microbial communities, adapting them for predictive biomarker discovery and to propose cost-effective methods based on third-generation sequencing platforms used to assess strain-level diversity.

## SELECTED PUBLICATIONS

Christensen L, Sørensen CV, Wøhlk FU, Kjølbaek L, Astrup A, Sanz Y, Hjorth MJ, Benítez-Páez A. Microbial enterotypes beyond genus level: *Bacteroides* species as predictive biomarker for weight change upon controlled intervention with arabinoxylan oligosaccharides in overweight subjects. *Gut Microbes* 2020;12:e1847627. doi: 10.1080/19490976.2020.1847627 [Quality indicator: D1/Q1 Microbiology, IF = 7.740, JCR 2019].

Agudelo-Ochoa GM, Valdés-Duque BE, Giraldo-Giraldo NA, Jaillier-Ramírez AM, Giraldo-Villa A, Acevedo-Castaño I, Yepes-Molina MA, Barbosa-Barbosa J, Benítez-Páez A. Gut microbiota profiles in critically ill patients, potential biomarkers and risk variables for sepsis. *Gut Microbes* 2020;12:e1707610. doi: 10.1080/19490976.2019.1707610 [Quality indicator: D1/Q1 Microbiology, IF = 7.740, JCR 2019].

Benítez-Páez A, Gómez del Pulgar EM, López-Almela I, Moya-Pérez A, Codoñer-Franch P, Sanz Y. Depletion of *Blautia* species in the microbiota of obese children relates to intestinal inflammation and metabolic phenotype worsening. *mSystems* 2020;5:e00857-19. doi: 10.1128/mSystems.00857-19. [Quality indicator: Q1 in Microbiology, IF = 6.633, JCR 2019].



#### NEW JUNIOR GROUP LEADERS

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## NEURAL PLASTICITY LABORATORY

#### TEAM MEMBERS

Isabel del Pino Pariente *Principal investigator*

Andrés Aylón, Álvaro Ballesteros, Candela Barettino, Selene Díaz, Leticia Orti.



TOTAL PUBLICATIONS

3

IMPACT FACTOR

16.04

AVERAGE IF

5.34

## OVERVIEW

Our lab is unveiling mechanisms of neural circuit plasticity underlying abnormal developmental trajectories in neurological and neuropsychiatric disorders. Using mice as animal models of neurodevelopmental disease, we recently revealed that genetic predisposition to infantile encephalopathy leads to early alterations in the network and intrinsic neuronal activity of the immature cerebral cortex through abnormal expression of ion channels (Del Pino et al., 2020 Cerebral Cortex). In addition, our work contributed to a better understanding of the molecular code that guides the connectivity between excitatory and inhibitory neurons in the cerebral cortex (Exposito-Alonso et al., 2020, eLIFE). Thanks to this interdisciplinary work, we have started to unveil periods during brain development that are susceptible to major irreversible changes which underly the pathophysiology of neurodevelopmental disorders such as intellectual disability, autism, and schizophrenia. We provided a recent review and our perspectives on this topic in Dehorter & Del Pino 2020 (Front Cell Neurosci.).

## SELECTED PUBLICATIONS

Exposito-Alonso D, Osório C, Bernard C, Pascual-García S, Del Pino I, Marín

O, Rico B. Subcellular sorting of neuregulins controls the assembly of excitatory-inhibitory cortical circuits. *Elife*. 2020 Dec 15;9:e57000. doi: 10.7554/eLife.57000. PMID: 33320083; PMCID: PMC7755390.

Dehorter N, Del Pino I. Shifting Developmental Trajectories During Critical Periods of Brain Formation. *Front Cell Neurosci*. 2020 Sep 10;14:283. doi: 10.3389/fncel.2020.00283. PMID: 33132842; PMCID: PMC7513795.

Del Pino I, Tocco C, Magrinelli E, Marcantoni A, Ferraguto C, Tomagra G, Bertacchi M, Alfano C, Leinekugel X, Frick A, Studer M. COUP-TFI/Nr2f1 Orchestrates Intrinsic Neuronal Activity during Development of the Somatosensory Cortex. *Cereb Cortex*. 2020 Oct 1;30(11):5667-5685. doi: 10.1093/cercor/bhaa137. PMID: 32572460.



#### NEW JUNIOR GROUP LEADERS

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## RETINAL DEGENERATION LABORATORY

#### TEAM MEMBERS

Dunja Lukovic Lukovic *Principal investigator*  
Verónica del Buey Furió Technician, Marcos Azpitarte Alabau MSci Student,  
Álvaro Alós Hernández-MSci Student

TOTAL PUBLICATIONS

1

IMPACT FACTOR

4.4

AVERAGE IF

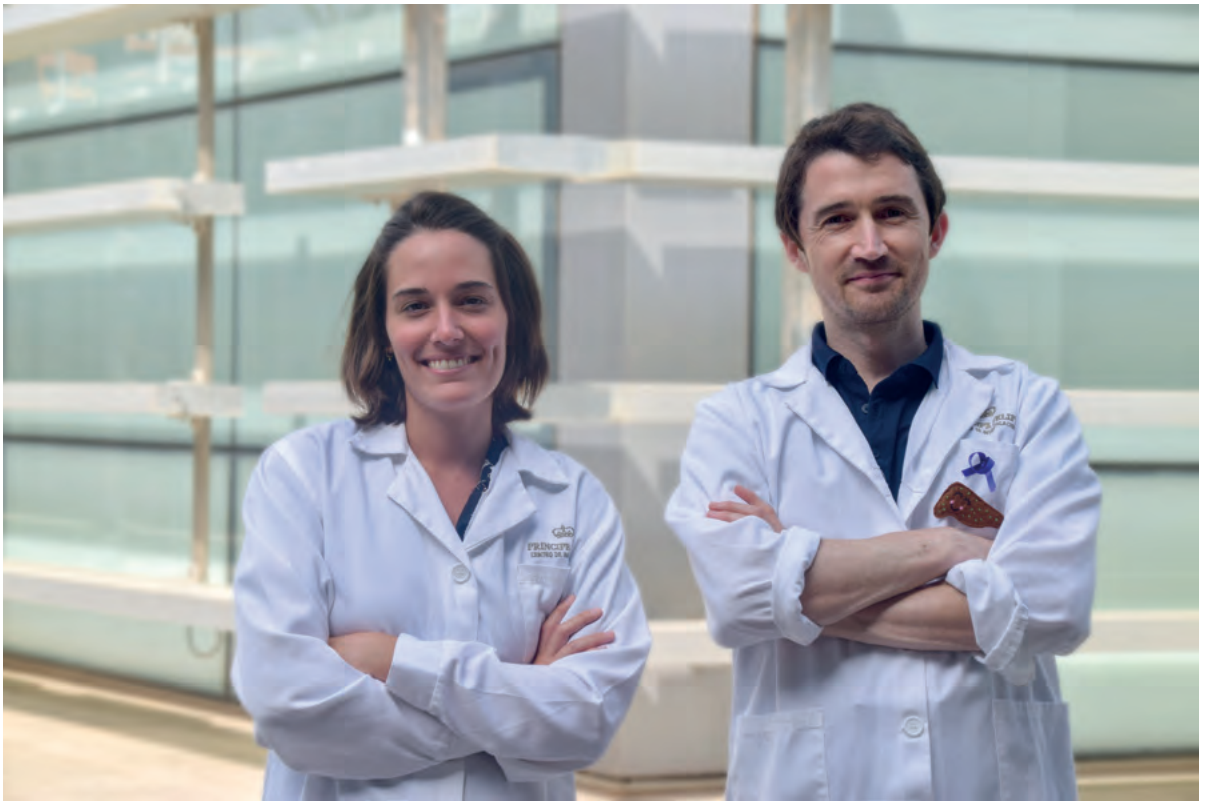
4.4

## OVERVIEW

Vision is the most important sense in humans because the majority of the information in our environment is obtained through sight. Therefore, the loss of vision results in the most debilitating sensorial disorders. Approximately 25% of vision loss is due to retinal dystrophies. The retina is light sensitive tissue that converts light into electrical signals that are sent to the brain for further processing. Retinal dystrophies are progressive disorders that end in blindness and which currently have no cure. Our aim is to understand retinal function in homeostasis and disease by focussing our efforts on the following aims: (1) Understanding hereditary retinal degeneration and correlating patient phenotypes with patient clinical data and animal models with homologous genetic deficiencies. (2) Developing therapeutic strategies based on human pluripotent stem cells. (3) Deciphering the molecular mechanism of retinogenesis, especially photoreceptor specification via the directed differentiation of pluripotent stem cells.

## SELECTED PUBLICATIONS

Lukovic, D, Artero Castro, A, Dogan Kaya, K, Munezero D, Gieser L, Davó Martínez C, Cortón M, Cuenca N, Swaroop A, Ramamurthy V, Ayuso C and Erceg S; *Retinal Organoids derived from hiPSCs of an AIPL1-LCA Patient Maintain Cytoarchitecture despite Reduced levels of Mutant AIPL1*. Sci Rep 2020 Mar 25;10(1):5426.



#### NEW JUNIOR GROUP LEADERS

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## METABOLIC GROWTH FACTORS AND REGENERATIVE MEDICINE

#### TEAM MEMBERS

Luke Noon *Principal investigator*  
María José Anthony Arámbul

TOTAL PUBLICATIONS

1

IMPACT FACTOR

1.16

AVERAGE IF

1.16

## OVERVIEW

In our laboratory, we study the impact of insulin resistance on tissue homeostasis and repair. Our work focuses on the understanding of how insulin signals are integrated by cells within tissues to coordinate the expansion and differentiation of progenitors. We recently showed that insulin directs progenitor cells in the mammalian liver through their stromal microenvironment/niche via stimulation of fibroblast growth factor 7 (FGF7) — a paracrine repair pathway we are referring to as the 'IRS2/FG7-axis'. In 2020, we published our second paper (Manzano et al., JoVE) and presented at "The Liver Meeting" (AASLD). New collaborations were established with: (1) Prof. Angela Valverde (CSIC/UAM) and Dr. Francisco García (CIPF) to investigate potentiation of the IRS2/FGF7-axis, and (2) Prof. Alison Lloyd at the MRC-LMCB (UCL) to investigate peripheral nerves in the hepatic stroma. We coordinated an online workshop for biological imaging in the Comunitat Valenciana and worked with the confocal/electron microscopy units to introduce cutting-edge imaging techniques (CLEM) to the CIPF.

## SELECTED PUBLICATIONS

A High-Throughput In Situ Method for Estimation of Hepatocyte Nuclear Ploidy in Mice F. MANZANO-NUNEZ, R. PETERS, D. BURKS and LA. NOON Jove-Journal of Visualized Experiments, 2020 , Vol. , pag. e60095

Insulin resistance disrupts epithelial repair and niche-progenitor Fgf signaling during chronic liver injury F. MANZANO-NUNEZ, M. ARAMBUL-ANTHONY, A. ALBINANA, A. TASSIAS, C. UMANZOR, I. GASCO, A. HERRERA, J. VILA, D. BURKS and LA. NOON PLOS BIOLOGY, 2019 , Vol. 17, pag. e2006972

Autophagy is a gatekeeper of hepatic differentiation and carcinogenesis by controlling the degradation of Yap Lee YA, Noon LA, Akat KM, Ybanez MD, Lee TF, Berres ML, Fujiwara N, Goossens N, Chou HI, Parvin-Nejad FP, Khambu B, Kramer EGM, Gordon R, Pflieger C, Germain D, John GR, Campbell KN, Yue Z, Yin XM, Cuervo AM, Czaja MJ, Fiel MI, Hoshida Y and Friedman SL Nature Communications, 2018 , Vol. 9, pag. 4962-4962



#### NEW JUNIOR GROUP LEADERS

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## PATHOPHYSIOLOGY AND THERAPIES FOR VISION DISORDERS

#### TEAM MEMBERS

Regina Rodrigo Nicolás *Principal investigator*

Lorena Olivares González, Isabel Campillo Nuevo, Sheyla Campillo Nuevo.

TOTAL PUBLICATIONS

3

IMPACT FACTOR

14.99

AVERAGE IF

4.50

## OVERVIEW

The group of Pathophysiology and Therapies for visual disorders is focused on searching for pharmacological therapies for inherited retinal dystrophies (IRDs). We pay particular attention to cellular processes related to neuroinflammation and oxidative stress that may exacerbate IRD progression. In terms of inflammation, we have described microglia activation, upregulation of tumour necrosis factor alpha (TNF $\alpha$ ), and NLRP3 inflammasome activation, among others, in rd10 mice as a model of IRD. Pharmacological manipulation with anti-TNF $\alpha$  agents downregulates these processes. We are particularly interested in the relationship between inflammation and different cell death mechanisms (e.g., pyroptosis, necroptosis, etc.). In oxidative stress, we evaluated the effect of antioxidant nutraceuticals in rd10 mice and patients with retinitis pigmentosa, the most common form of IRDs. Finally, we are currently analysing the delivery of anti-inflammatory drugs to the retina with nanocarriers.

## SELECTED PUBLICATIONS

Olivares-González L, Velasco S, Millán JM, Rodrigo R. Intravitreal administration of adalimumab delays retinal degeneration in rd10 mice. *FASEB J.* 34(10):13839-13861. 2020 DOI: 10.1096/fj.202000044RR.

Sebastià N, Olivares-González L, Montoro A, Barquinero JF, Canyada-Martínez AJ, Hervás D, Gras P, Villaescusa JI, Martí-Bonmati L, Muresan BT, Soriano JM, Campayo JM, Andani J, Alonso O, Rodrigo R. Redox Status, Dose and Antioxidant Intake in Healthcare Workers Occupationally Exposed to Ionizing Radiation. *Antioxidants (Basel).* 9(9):778. 2020 DOI: 10.3390/antiox9090778

Espinós C, Galindo MI, García-Gimeno MA, Ibáñez-Cabellos JS, Martínez-Rubio D, Millán JM, Rodrigo R, Sanz P, Seco-Cervera M, Sevilla T, Tapia A, Pallardó FV. Oxidative Stress, a Crossroad Between Rare Diseases and Neurodegeneration. *Antioxidants (Basel).* 9(4):313. 2020 DOI: 10.3390/antiox9040313.





## JOINT RESEARCH UNITS

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# FIHGUV-CIPF TRIAL JOINT RESEARCH UNIT

### TEAM MEMBERS

Carlos Camps Herrero *Principal Investigator*, Eloisa Jantus Lewintre and Rafael Sirera Pérez,  
*Co-Principal Investigators*

Silvia Calabuig Fariñas, Macarena Ferrero Gimeno, Elena Duréndez Sáez, Susana Torres Martínez,  
Andrea Moreno Manuel, Eva Escorihuela Alares, José Vicente Bagán Sebastián, Ricardo Guijarro  
Jorge, Miguel Martorell Cebollada, Vega Iranzo González-Cruz, Ana Blasco Cordellat, Alfonso  
Berrocal Jaime (FIHGUV). Enric Esplugues, María Jesús Vicent and Mar Orzáez (CIPF)



TOTAL PUBLICATIONS

8

IMPACT FACTOR

47.01

AVERAGE IF

5.88

## OVERVIEW

The Scientific Collaboration in the field of Biomedicine and Health Sciences between the Prince Felipe Research Center Foundation (FCIPF) and the General University Hospital of Valencia Research Foundation (FIHGUUV) within the framework of the Translational Research Unit in Tumour Oncology and Immunology (TRIAL Mixed Unit) has been in force since 19 July 2019. Currently, we are working on several research lines in our CIPF laboratory and facilities: (1) The search for new molecular biomarkers in cancer. We focus on the early diagnosis and search for prognostic-predictive factors for treatment response through different omic approaches (genomics, transcriptomics, and metabolomics). (2) Immunoregulation, cancer, and tumour microenvironment. Through multidimensional analysis to characterise the immunological status of different types of tumours and the application of this knowledge to discriminate different immunological scenarios.

## SELECTED PUBLICATIONS

Prognostic impact of KRAS G12C mutation in patients with NSCLC: results from the ETOP Lungscape Project. Finn SP, Addeo A, Dafni U, Thunnissen E, Bubendorf L, Madsen LB, Biernat W, Verbeken E, Hernandez-Losa J, Marchetti A, Cheney R, Warth A, Speel EM, Quinn AM, Monkhurst K, Jantus-Lewintre E, Tischler V, Marti N, Dimopoulou G, Molina-Vila MA, Kammler R, Kerr KM, Peters S, Stahel RA; ETOP Lungscape investigators. *J Thorac Oncol*. 2021 Feb 26;S1556-0864(21)01734-2. doi: 10.1016/j.jtho.2021.02.016. Online ahead of print. PMID: 33647504 IF: 13.357; D1

3D printing novel in vitro cancer cell culture model systems for lung cancer stem cell study. Herreros-Pomares A, Zhou X, Calabuig-Fariñas S, Lee SJ, Torres S, Esworthy T, Hann SY, Jantus-Lewintre E, Camps C\*, Zhang LG\*. *Mater Sci Eng C Mater Biol Appl*. 2021 Mar; 122:111914. doi: 10.1016/j.msec.2021.111914. Epub 2021 Jan 29. PMID: 33641907 IF: 5.880; D1 (\*co-corresponding authors)

CD5 and CD6 as immunoregulatory biomarkers in non-small cell lung cancer. Moreno-Manuel A, Jantus-Lewintre E, Simões I, Aranda F, Calabuig-Fariñas S, Carreras E, Zúñiga S, Saenger Y, Rosell R, Camps C, Lozano F, Sirera R. *Transl Lung Cancer Res*. 2020 Aug;9(4):1074-1083. doi: 10.21037/tlcr-19-445. PMID: 32953486 Free PMC article. IF: 5.132 Q1



## JOINT RESEARCH UNITS

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# FISABIO-CIPF BIOMEDICAL IMAGING JOINT RESEARCH UNIT

### TEAM MEMBERS

Mariam de la Iglesia *Principal Investigator* (FISABIO), Vicente Felipo,  
Francisco García (CIPF), *coIPs*

Marta R. Hidalgo García, Rubén Sánchez García (CIPF), Irene Pérez  
Díez, José Manuel Saborit Torres, Joaquim Montell Serrano, Adolfo López  
Cerdán, Jhon J. Saenz Gamboa, Elena Oliver García, Marisa Caparrós  
Redondo, Julio Doménech Fernández.

TOTAL PUBLICATIONS

6

IMPACT FACTOR

28.56

AVERAGE IF

4.76

## OVERVIEW

The FISABIO-CIPF Joint Unit of Biomedical Imaging is expert in the anonymisation, curation, and processing of medical image data through the application of artificial intelligence and radiomics techniques. Our work involves the creation of medical imaging datalakes, and application of anonymisation, segmentation, and data curation techniques for medical images. We also study sex differences in neurodegenerative diseases, including Alzheimer and Parkinson disease and multiple sclerosis, through massive analysis and integration of omic data and biomedical imaging. In 2020 we have also been working on the diagnosis, prognosis prediction, and triage of COVID-19 patients and in the development and application of new computational methods for the characterisation of pancreatic, lung, and breast cancer. As a result of our work in 2020, we made the BIMCV-COVID19 dataset, a large, widely accepted, annotated set of RX and CT images of COVID19 patients, available to the international scientific community.

## SELECTED PUBLICATIONS

J. M. Saborit-Torres, J. J. Saenz-Gamboa, J. À. Montell, J. M. Salinas, J. A. Gómez, I. Stefan, M. Caparrós, F. García-García, J. Domenech, J. V. Manjón, G. Rojas, A. Pertusa, A. Bustos, G. González, J. Galant, M. de la Iglesia-Vayá. 2020. Medical imaging data structure extended to multiple modalities and anatomical regions arXiv:2010.00434

Aurelia Bustos, Antonio Pertusa, Jose-Maria Salinas, Maria de la Iglesia-Vayá, PadChest: A large chest x-ray image dataset with multi-label annotated reports, Medical Image Analysis, Volume 66, 2020, 101797, ISSN 1361-8415, <https://doi.org/10.1016/j.media.2020.101797>. (<https://www.sciencedirect.com/science/article/pii/S1361841520301614>)

Germán González, Aurelia Bustos, José María Salinas, María de la Iglesia-Vaya, Joaquín Galant, Carlos Cano-Espinosa, Xavier Barber, Domingo Orozco-Beltrán, Miguel Cazorla, Antonio Pertusa. 2020. UMLS-ChestNet: A deep convolutional neural network for radiological findings, differential diagnoses and localizations of COVID-19 in chest x-rays ArXiv.4



#### JOINT RESEARCH UNITS

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## CIPF-UPV DISEASE MECHANISMS AND NANOMEDICINE JOINT RESEARCH UNIT

Developmental Biology and Disease Mechanisms

#### TEAM MEMBERS

Máximo Ibo Galindo *Principal Investigator*  
Andrea Tapia Gonzalez, Maria del Carmen Martín Carrascosa, and  
Desamparados Andrés Bordería.

TOTAL PUBLICATIONS

1

IMPACT FACTOR

5.01

AVERAGE IF

5.01

## OVERVIEW

The group is part of the UPV-CIPF joint unit which was established in 2016 to promote scientific collaborations between researchers in both institutions in the fields of pathophysiology and nanomedicine. We use *Drosophila melanogaster* to study the basic biological mechanisms underlying development and disease, and to model rare diseases. We are especially interested in inherited peripheral neuropathies and Dravet syndrome as well as other rare epileptic encephalopathies. Our ultimate goals are to understand the disease mechanisms involved and to generate new tools for the discovery of biomarkers and drug targets. To achieve this, we collaborate with a network of researchers including groups working in *Drosophila* genetics, physiology, and rare diseases; we are also starting collaborations with clinical groups and patient associations. Moreover, our work uses genome editing techniques with the aim of uncovering disease mechanisms that can then be used in the discovery of new biomarkers and treatments for rare diseases. In these cases, our objective is to replace the *Drosophila* gene with the equivalent human gene carrying clinical mutations found in patients in order to help us develop treatment strategies for personalised and precision medicine in these patients.

## SELECTED PUBLICATIONS

Oxidative Stress, a Crossroad Between Rare Diseases and Neurodegeneration. Espinós C, Galindo MI, García-Gimeno MA, Ibáñez-Cabellos JS, Martínez-Rubio D, Millán JM, Rodrigo R, Sanz P, Seco-Cervera M, Sevilla T, Tapia A and Pallardó FV *Antioxidants*, 2020 , Vol. 9, pag. 313



## JOINT RESEARCH UNITS

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# IBV-CIPF BIOLOGICAL NOISE AND CELL PLASTICITY JOINT RESEARCH UNIT

### TEAM MEMBERS

Francisco José Iborra Rodríguez *Principal Investigator*  
María Cristina Martí Ibañez

TOTAL PUBLICATIONS

1

IMPACT FACTOR

10.80

AVERAGE IF

10.80

## OVERVIEW

The Príncipe Felipe Research Centre Foundation (FCIPF) and the Institute of Biomedicine of Valencia (IBV) have been collaborating for many decades on different biomedicine projects. Currently, we are working on several research projects, for example, in tumour cellular heterogeneity. We are studying how the tumour microenvironment contributes to cellular variability. Interestingly, partial chemotherapy resistance results in cancer relapse. We are exploring the contribution of cellular energy metabolism to this phenomenon, addressing our objectives using cell biology, systems biology, and different omic approaches (transcriptomics, proteomics, and metabolomics).

## SELECTED PUBLICATIONS

de la Fuente L, Arzalluz-Luque Á, Tardáguila M, Del Risco H, Martí C, Tarazona S, Salguero P, Scott R, Lerma A, Alastrue-Agudo A, Bonilla P, Newman JRB, Kosugi S, McIntyre LM, Moreno-Manzano V, Conesa A. tappAS: a comprehensive computational framework for the analysis of the functional impact of differential splicing. *Genome Biol.* 2020 May 18;21(1):119. doi: 10.1186/s13059-020-02028-w. PMID: 32423416; PMCID: PMC7236505. IF: 10.8; D1



## JOINT RESEARCH UNITS

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# IVO-CIPF JOINT RESEARCH UNIT IN CANCER

### TEAM MEMBERS

José Antonio López Guerrero (IVO), M<sup>a</sup> Jesús Vicent Docón (CIPF), Mar Orzáez Calatayud (CIPF) *Principal Investigators*

Francisco García García (UBB-CIPF), María de la Iglesia Vayá María (FISABIO-CIPF), María García Flores, Antonio Fernández Serra, Raquel López Reig, Ángel Guerrero Zotano, Belén Pastor Navarro (IVO).



TOTAL PUBLICATIONS

4

IMPACT FACTOR

14.59

AVERAGE IF

3.65

## OVERVIEW

The mission of the Joint Research Unit in Cancer IVO-CIPF is to translate the basic research performed at the CIPF into clinical scenarios and vice versa. We mainly focus on the discovery of new molecules that could play a role as prognostic or predictive biomarkers. In addition, we explore the design of new drugs as well as new therapeutic combinations which we test in appropriate cell and animal models. One of our tasks is also to develop new diagnostic tools based on next generation sequencing.

## SELECTED PUBLICATIONS

Poveda A, Oaknin A, Romero I, Guerrero-Zotano A, Fariñas-Madrid L, Rodríguez-Freixinos V, Mallol P, Lopez-Reig R, Lopez-Guerrero JA. A phase I dose-finding, pharmacokinetics and genotyping study of olaparib and lurbinectedin in patients with advanced solid tumours. *Sci Rep.* 2021 Feb 24;11(1):4433. doi:10.1038/s41598-021-82671-w. PMID: 33627685; PMCID: PMC7904806.

Gómez-Cebrián N, García-Flores M, Rubio-Briones J, López-Guerrero JA, Pineda-Lucena A, Puchades-Carrasco L. Targeted Metabolomics Analyses Reveal Specific Metabolic Alterations in High-Grade Prostate Cancer Patients. *J Proteome Res.* 2020 Oct 2;19(10):4082-4092. doi: 10.1021/acs.jproteome.0c00493. Epub 2020 Sep 23. PMID: 32924497.

Pastor-Navarro B, García-Flores M, Fernández-Serra A, Blanch-Tormo S, Martínez de Juan F, Martínez-Lapiedra C, Maia de Alcantara F, Peñalver JC, Cervera-Deval J, Rubio-Briones J, García-Rupérez J, López-Guerrero JA. A Tetra-Panel of Serum Circulating miRNAs for the Diagnosis of the Four Most Prevalent Tumour Types. *Int J Mol Sci.* 2020 Apr 16;21(8):2783. doi: 10.3390/ijms21082783. PMID: 32316350; PMCID: PMC7215589.



## JOINT RESEARCH UNITS

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# CIPF-UPV DISEASE MECHANISMS AND NANOMEDICINE JOINT RESEARCH UNIT

### Nanomedicine

#### TEAM MEMBERS

Ramón Martínez Máñez *Principal Investigator*

Félix Sancenón Galarza, María Dolores Marcos Martínez, José Ramón Murguía Ibáñez, Andrea Bernardos Bau, Elena Aznar Gimeno, María del Carmen Martínez Bisbal, Alba García Fernández, Juan Francisco Blández Barradas, Paula Díez Sánchez, Alejandra Estepa Fernández, Araceli Lérida Viso, Elena Lucena Sánchez, Blanca Escriche Navarro, Beatriz Lozano Torres, Vicente Candela Noguera, Andrea Escudero Noguera, Javier Martínez Latorre, Angela Morella Aucejo.

TOTAL PUBLICATIONS

29

IMPACT FACTOR

162.91

AVERAGE IF

5.82

## OVERVIEW

Our group (IDM-UPV) works on the development of new treatments from a multidisciplinary point of view and applied the latest advances in nanomedicine to solve health problems. This multidisciplinary research includes the synthesis of molecular probes and nanoparticles, their physico-chemical characterisation, and their in vitro and in vivo evaluation in preclinical models of cancer and senescence, among other areas. During 2020, the group continued its intense scientific activity, publishing 29 articles in international journals where we described the development of different systems applied both to diagnosis and therapy in different diseases. In the context of the joint research unit, we would like to especially highlight our work related to the development of nanoparticles and molecules for the detection and specific elimination of senescent cells as well as the development of new nanosystems for cancer therapy.

## SELECTED PUBLICATIONS

Lozano-Torres, B., Blandez, J. F., Galiana, I., Garcia-Fernandez, A., Alfonso, M., Marcos, M. D., Orzaez, M., Sancenon, F., & Martinez-Manez, R. Real-Time In Vivo Detection of Cellular Senescence through the Controlled Release of the NIR Fluorescent Dye Nile Blue. *Angewandte Chemie-International Edition*, 2020, 59(35), 15152-15156.

Gonzalez-Gualda, E., Paez-Ribes, M., Lozano-Torres, B., Macias, D., Wilson, J. R., III, Gonzalez-Lopez, C., Ou, H.-L., Miron-Barroso, S., Zhang, Z., Lerida-Viso, A., Blandez, J. F., Bernardos, A., Sancenon, F., Rovira, M., Fruk, L., Martins, C. P., Serrano, M., Doherty, G. J., Martinez-Manez, R., & Munoz-Espin, D. Galacto-conjugation of Navitoclax as an efficient strategy to increase senolytic specificity and reduce platelet toxicity. *Aging Cell*, 2020, 19(4).

Galiana, I., Lozano-Torres, B., Sancho, M., Alfonso, M., Bernardos, A., Bisbal, V., Serrano, M., Martinez-Manez, R., & Orzaez, M. Preclinical antitumour efficacy of senescence -inducing chemotherapy combined with a nanoSenolytic. *Journal of Controlled Release*, 2020, 323, 624-634.



## JOINT RESEARCH UNITS

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# IIS LA FE-CIPF JOINT RESEARCH UNIT FOR RARE DISEASES

### TEAM MEMBERS

José María Millán (IIS La Fe) and Carmen Espinós (CIPF)  
*Principal Investigators*

TOTAL PUBLICATIONS

11

IMPACT FACTOR

49.10

AVERAGE IF

4.46

## OVERVIEW

The Research Group on Molecular, Cellular, and Genomic Biomedicine (BMCG) was accredited in 2010 and comprises a total of 21 researchers, 10 of them belonging to the joint Unit for Rare Diseases CIPF-IIS La Fe led by Dr. José M. Millán. This multidisciplinary group includes ophthalmologists, ENT doctors, geneticists, molecular biologists, and biochemists, and participates as a member in the Centre of Networked Biomedical Research (CIBER) of Rare Diseases. Its objective is to deepen our knowledge of the physiology, genetics, and clinical picture of diseases that fundamentally affect the organs of vision and hearing, but also neuromuscular and neurodegenerative disease that affect these organs. We aim to find immediate applications for the results of this research in clinical practice to benefit patients.

## SELECTED PUBLICATIONS

Gómez-Escribano AP, Bono-Yagüe J, García-Gimeno MA, Sequedo MD, Hervás D, Fornés-Ferrer V, Torres-Sánchez SC, Millán JM, Sanz P, Vázquez-Manrique RP. Synergistic activation of AMPK prevents from polyglutamine-induced toxicity in *Caenorhabditis elegans*. *Pharmacological Res.* 30:105105 (2020). 1º decil

Rodríguez-Muñoz A, Aller E, Jaijo T, González-García E, Cabrera-Peset A, Gallego-Pinazo R, Salom D, García-García G, Millán JM. Expanding the clinical and molecular heterogeneity of nonsyndromic inherited retinal dystrophies. *J Molecular Diagnostics*. pii: S1525-1578(20)30008-8 (2020). 1º decil

Espinós C, Galindo MI, García-Gimeno MA, Ibáñez-Cabellos JS, Martínez-Rubio D, Millán JM, Rodrigo R, Sanz P, Seco-Cervera M, Sevilla T, Tapia A, Pallardó FV. Oxidative stress, a crossroad between rare diseases and Neurodegeneration. *Antioxidants*. 9: 313 (2020). 1º decil.



## JOINT RESEARCH UNITS

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# CIPF-INCLIVA NEUROLOGICAL IMPAIRMENT JOINT RESEARCH UNIT

## TEAM MEMBERS

Carmina Montoliu, Vicente Felipo, *Principal Investigators*

Andrea Cabrera, Maria Pilar Ballester, Juan José Gallego, Franc Casanova, Alessandra Fiorillo, Dalia Rega, Critina Ipiens, Mika Aiko, Amparo Escudero, Paloma Lluch, Joan Tosca, Cristina Montón, José Ballester, José Luis León, Roberto Aliaga, Paula Cases, Rut Vitorio, Nicolas Peñaranda, Alberto Sabio, Clara Barbera, Fermín Ordoño, María Pilar Ríos, Lucia Durban, Salvador Benlloch (INCLIVA)

Marta Llansola, Amparo Urios, Carla Giménez Garzó, Tiziano Balzano, María Sancho, Paula Izquierdo, Paola Leone, Yaiza Arenas, Gergana Ivaylova, Mar Martínez, Mari Carmen Castro, Alejandra Hernández (CIPF)

TOTAL PUBLICATIONS

9

IMPACT FACTOR

54.10

AVERAGE IF

6.76

## OVERVIEW

The CIPF-INCLIVA Joint Unit for Neurological Impairment performs basic and translational research on cognitive, motor, sleep, and circadian rhythm alterations in different pathological situations, including minimal and clinical hepatic encephalopathy (HE), hyperammonemia, and developmental exposure to food and environmental contaminants. We also apply our wide range of methodologies to other pathological situations with the following aims: In animal models (1) unveil the molecular mechanisms leading to neurological impairment; (2) identify new therapeutic targets for its treatment; (3) design and assess new therapeutic procedures to reverse neurological impairment. In patients (4) study the mechanisms, diagnosis, and treatment of neurological impairment; (5) identify early diagnostic procedures for neurological impairment; (6) bring the diagnostic procedures identified to the clinic.

## SELECTED PUBLICATIONS

Balzano T, Dadsetan S, Forteza J, Cabrera-Pastor A, Taoro-Gonzalez L, Malaguarnera M, Gil-Perotin S, Cubas-Núñez L, Casanova B, Castro-Quintas A, Ponce-Mora A, Arenas YM, Leone P, Erceg S, Llansola M, Felipe V. Chronic hyperammonemia induces peripheral inflammation that leads to cognitive impairment in rats: Reversed by anti-TNF- $\alpha$  treatment. *J Hepatol.* 2020; 73(3):582-592. doi: 10.1016/j.jhep.2019.01.008. Epub 2019 Jan 14. PMID:30654069 Cuartil: Q1 (DECIL 1) F.I.: 14,679

Balzano T, Arenas YM, Dadsetan S, Forteza J, Gil-Perotin S, Cubas-Núñez L, Casanova B, Gracià F, Varela-Andrés N, Montoliu C, Llansola M, Felipe V. Sustained hyperammonemia induces TNF- $\alpha$  IN Purkinje neurons by activating the TNFR1-NF- $\kappa$ B pathway. *J Neuroinflammation.* 2020; 17(1):70. doi: 10.1186/s12974-020-01746-z. PMID: 32087723; PMCID: PMC7035786. Cuartil: Q1 F.I.: 5,793

Arenas YM, Cabrera-Pastor A, Juciute N, Mora-Navarro E, Felipe V. Blocking glycine receptors reduces neuroinflammation and restores neurotransmission in cerebellum through ADAM17-TNFR1-NF- $\kappa$ B pathway. *J Neuroinflammation.* 2020; 17(1):269. doi: 10.1186/s12974-020-01941-y. PMID: 32917219; PMCID: PMC7488331. Cuartil: Q1 F.I.: 5,793





## JOINT RESEARCH UNITS

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# INCLIVA-CIPF RARE DISEASES JOINT RESEARCH UNIT

## TEAM MEMBERS

Carmen Espinós (CIPF) Federico V. Pallardó (INCLIVA) *Principal Investigators*



TOTAL PUBLICATIONS

18

IMPACT FACTOR

83.04

AVERAGE IF

4.61

## OVERVIEW

The scientific collaboration in the fields of biomedicine and health sciences between the Principe Felipe Research Center Foundation (FCIPF) and the INCLIVA IIS-Carlos III, within the framework of the Translational Research Unit for research in Rare Diseases, has been active since 2016. We are currently working on several research lines including (1) the search for new molecular biomarkers in rare diseases for early diagnosis; (2) the search for prognostic-predictive factors of treatment response through different omic approaches (genomics, transcriptomics, and metabolomics); (3) study of the physiopathology of inherited neurodegenerative diseases using human samples and different animal and cellular models of these diseases.

## SELECTED PUBLICATIONS

Rodríguez LR, Calap-Quintana P, Lapeña-Luzón T, Pallardó FV, Schneuwly S, Navarro JA, Gonzalez-Cabo P. Oxidative stress modulates rearrangement of endoplasmic reticulum-mitochondria contacts and calcium dysregulation in a Friedreich's ataxia model. *Redox Biol.* 2020 Oct;37:101762. doi: 10.1016/j.redox.2020.101762. Epub 2020 Oct 16. PMID: 33128998; PMCID: PMC7585950. IF: 9.986

Espinós C, Galindo MI, García-Gimeno MA, Ibáñez-Cabellos JS, Martínez-Rubio D, Millán JM, Rodrigo R, Sanz P, Seco-Cervera M, Sevilla T, Tapia A, Pallardó FV. Oxidative Stress, a Crossroad Between Rare Diseases and Neurodegeneration. *Antioxidants (Basel)*. 2020 Apr 15;9(4):313. doi: 10.3390/antiox9040313. PMID:32326494; PMCID: PMC7222183. IF:5.014

Muñoz-Lasso DC, Romá-Mateo C, Pallardó FV, Gonzalez-Cabo P. Much More Than a Scaffold: Cytoskeletal Proteins in Neurological Disorders. *Cells*. 2020 Feb 4;9(2):358. doi: 10.3390/cells9020358. PMID: 32033020; PMCID: PMC7072452. IF: 4.366



## JOINT RESEARCH UNITS

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# CYTOMICS RESEARCH UNIT

### TEAM MEMBERS

José Enrique O'Connor University of Valencia  
Alicia Martínez CIPF

TOTAL PUBLICATIONS

1

IMPACT FACTOR

4.83

AVERAGE IF

4.83

## OVERVIEW

We work on the biomedical applications of cytomics and, in particular, the development of in vitro cytomic tests that predict acute and chronic toxicity in humans and animals and the application of cytomics to the functional study of cells in immunopathology and regenerative medicine. Our main research lines are the flow cytometric study of immunological alterations in patients with Idic-15 syndrome and the use of flow cytometry to study cell function: autophagy, apoptosis, regulation of intracellular pH, and oxidative stress in human cells and bacteria.

## SELECTED PUBLICATIONS

Sala de Oyanguren FJ, Rainey NE, Moustapha A, Saric A, Sureau F, O'Connor J-E, Petit PX. Highlighting Curcumin-Induced Crosstalk between Autophagy and Apoptosis as Supported by Its Specific Subcellular Localization. *Cells*. 2020; 9 (2): 361. <https://doi.org/10.3390/cells9020361>







## CIPF\_ Dissemination and outreach events

Before the confinement due to the COVID-19 pandemic, we organised and hosted several conferences, seminars, and events, while in the months subsequent to the lockdown we moved all of these activities online. We were able to adapt to the situation very quickly thanks to our IT team and the technology available at the CIPF, allowing our scientists to carry on with this important aspect of their careers: collaborating, networking, and sharing knowledge. Nonetheless, we recognize that although technologies represent interesting tools for scientific events, in-person meetings create so many other opportunities that virtual meetings cannot replicate.

### EVENTS

26

### PRESS RELEASES

15

### CIPF IN THE MEDIA

44

## CIPF\_ in the media

### SOCIAL MEDIA FOLLOWERS



Twitter\_ 4,681



Facebook\_ 2,203



LinkedIn\_ 4,851



Youtube Views\_ 25,344

New website [www.cipf.es](http://www.cipf.es)





Lucas Cervantes, Jhosland Maestre and Vicent Francès\_ CIPF TI team

On 27 November 2020, the CIPF launched its new fast and intuitive website using WordPress as a user-friendly platform to allow us to update information and adapt the design as needed.

Throughout the year we have had the following traffic to the site:

Visits to the old website\_ **39,028**

Visits to the new website\_ **12,437**

Total visits [www.cipf.es](http://www.cipf.es)\_ **51,465**

## Seminars

MOLECULAR PERSPECTIVES ON SHORT-TERM  
FASTING AS A NUTRITIONAL STRATEGY AGAINST  
AGING-RELATED DISEASES

Pablo J. Fernández-Marcos

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ARTIFICIAL INTELLIGENCE AND SOCIETY:  
CHALLENGES AND OPPORTUNITIES

Nuria Oliver

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UNDERSTANDING THE PLACENTA IN HEALTH AND  
DISEASE: IMPLICATIONS FOR CANCER (ONLINE)

Vicente Pérez García

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THE PROCESS OF PUBLISHING SCIENTIFIC PAPERS  
(ONLINE)

Juan Bisquert

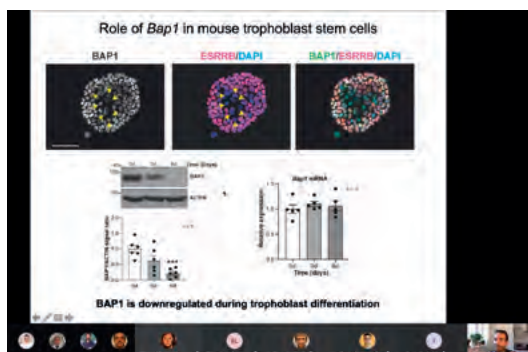
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LIPOTOXICITY AND OBESITY-ASSOCIATED  
METABOLIC COMPLICATIONS: A STEM CELL-  
BASED STRATEGY (ONLINE)

Stefania Carobbio



Pablo J. Fernández-Marcos\_ Seminar



Vicente Pérez García\_ Seminar



Juan Bisquert\_ Seminar

## FBR Lecture Series Conferences

INTEGRATED OMICS TO UNDERSTAND  
MISSING HERITABILITY IN INHERITED RETINAL  
DISEASES THAT CAUSE BLINDNESS

Elfride de Baere

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GENETICS, ACTIVITY, AND PATTERNING  
IN A MOUSE MODEL OF A RECENTLY DESCRIBED  
NEURODEVELOPMENTAL BRAIN DISORDER

Michèle Studer



Elfride de Baere\_ *FBR Lecture*



Michèle Studer\_ *FBR Lecture*

## Scientific and Dissemination Conferences

INFORMATIVE SESSION OF THE PROGRAMS AND  
SCHOLARSHIPS FOR RESEARCH OFFERED BY "LA CAIXA"

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IS IT POSSIBLE TO REPAIR THE BRAIN? ORGANIZED IN  
COLLABORATION WITH THE CIPF AND HELD AT THE  
SCIENCE MUSEUM

---

1-DAY COMMUNICATIONS WORKSHOP, OPEN SCIENCE,  
AND EUROPEAN HORIZONS, FUNDACIÓN FECYT

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V NATIONAL CONFERENCE OF WOMEN RESEARCHERS  
IN RARE DISEASES

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EUROPEAN RESEARCHERS NIGHT (ONLINE)

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BIOLOGICAL IMAGING IN THE COMUNITAT VALENCIANA,  
1ST WORKSHOP (ONLINE)

---

2ND CONFERENCE ON THE MANAGEMENT OF PRECISION  
ONCOLOGY IN THE VALENCIAN COMMUNITY

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CYCLE OF RETINAL DYSTROPHIES, DIET, ANTIOXIDANTS,  
AND RETINITIS PIGMENTOSA (ONLINE)



1-day communications workshop by Fundación FECYT



Informative session offered by "La Caixa"

## Doctoral Thesis

20/01/2020

ROLE OF IRS2 IN REPAIRING LIVER DAMAGE AND CANCER

Fátima Manzano Núñez\_ *Doctoral Student*  
Luke Noon\_ *Director*

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15/07/2020

DEVELOPMENT OF POLYMER-BASED THERAPEUTICS FOR THE  
TREATMENT OF CASTRATION RESISTANT PROSTATE CANCER

Sonia Vicente Ruiz Salvador\_ *Doctoral Student*  
M<sup>a</sup> Jesús Vicent\_ *Director*

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14/10/2020

UNDERSTANDING AND DRUGGING THE BCL-2 TRANSMEMBRANE  
DOMAIN INTERACTOME FOR TUMOUR TREATMENT

Estefanía Lucendo Gutiérrez\_ *Doctoral Student*  
Mar Orzáez\_ *Director*

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12/11/2020

ROLE OF PERIPHERAL INFLAMMATION AND  
NEUROINFLAMMATION IN COGNITIVE AND MOTOR  
DETERIORATION IN RATS WITH DIFFERENT DEGREES OF LIVER  
DAMAGE. EFFECTS OF RIFAXIMIN TREATMENT

Paola Leone\_ *Doctoral Student*  
Vicent Felipo, Marta Llansola\_ *Directors*

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30/11/2020

EVALUATION OF THERAPEUTIC STRATEGIES BASED ON  
ANTI-INFLAMMATORY SUBSTANCES AND ANTIOXIDANTS IN  
RETINITIS PIGMENTOSA

Lorena Olivares González\_ *Doctoral Student*  
Regina Rodrigo\_ *Director*





Fátima Manzano Núñez\_ *Doctoral Thesis*



Sonia Vicente Ruiz Salvador\_ *Doctoral Thesis*



Estefanía Lucendo Gutiérrez\_ *Doctoral Thesis*



Paola Leone\_ *Doctoral Thesis*

## UCC+I Unit

Since 6 October 2020, the CIPF has belonged to the Unit of Scientific Culture and Innovation (UCC+i) as a member accredited by the FECYT in recognition of our activities in scientific dissemination, communication, outreach, and training.



## CIPF\_ Visits

- Students of the UPV Master's course in Radiological Protection in Radioactive and Nuclear Facilities.
- INDACEA Association
- Jesús y María School Valencia
- Caxton College

## CIPF\_ Outreach activities

- Collection for the Food Bank of Valencia
- Toy collections (Fundación Colegios Siglo XXI)



## CIPF\_ Events

ARTIFICIAL INTELLIGENCE AND SOCIETY:  
CHALLENGES AND OPPORTUNITIES, 6<sup>TH</sup>  
OF FEBRUARY

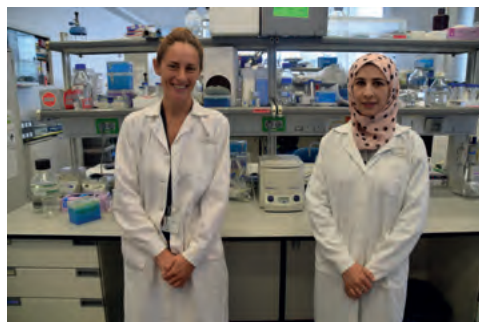


TRIBUTE TO MARGARITA SALAS  
HELD AT THE CONSELL VALENCIÀ  
DE CULTURA ON 10 FEBRUARY 2020,  
WITH BROAD ATTENDANCE BY  
SEVERAL ADMINISTRATIONS AND  
REPRESENTATIVES OF THE VALENCIAN  
SCIENTIFIC COMMUNITY.



DR. HODA ELKHENANY, FROM THE  
SURGERY DEPARTMENT IN THE  
FACULTY OF VETERINARY MEDICINE AT  
ALEXANDRIA UNIVERSITY.

Thanks to the collaboration agreement  
between the CIPF and the Women for  
Africa Foundation, Dr. Elkhennany was  
selected among the final candidates  
in the 5th Edition of Science by Women  
grants. She collaborated with Dr. Victoria  
Moreno from CIPF Neuronal and Tissue  
Regeneration Laboratory.





#### 4<sup>TH</sup> HEALTHCARE RESEARCH CONFERENCE WITH GENDER PERSPECTIVES HELD AT INCLIVA 11<sup>TH</sup> FEBRUARY 2020

Concha Andrés Sanchis, regional secretary for Health Efficiency and Technology, delivered awards recognising health research projects incorporating gender perspectives. The CIPF obtained three recognitions: 'Metafun', coordinated by Francisco García; 'Sex differences in lung adenocarcinoma', coordinated by Rosa Farras and Francisco García; and 'Meta-analysis of sex differences in the effects of alcoholism', directed by Consuelo Guerri and Francisco García.



V NATIONAL CONFERENCE OF  
WOMEN RESEARCHERS IN RARE  
DISEASES, CELEBRATED THE  
21<sup>ST</sup> OF FEBRUARY 2020 AT THE  
CIPF, WE WERE HONOURED OF  
HAVING TERESA NAVARRO AND  
CUCA PAULO AS MODERATORS  
AND CARMEN AGUSTI, BERTA  
FUSTÉ, INMACULADA PITARCH,  
SILVIA CASTILLO, EVA FAGES,  
FIDE MIRÓN AND JAVIER S. BURGOS  
AS SPEAKERS.



CONFERENCE HELD AS PART OF THE COLLABORATION AGREEMENT WE HAVE SIGNED WITH MUSEU DE LES CIÈNCIES, CACSA TO PROMOTE AND DISSEMINATE SCIENTIFIC RESULTS.



6<sup>TH</sup> MARCH 2020. THE WOMEN WHO PROPEL US FORWARD COLLOQUIUM, 4<sup>TH</sup> WOMEN IN SCIENCE AND BUSINESS MEETING, AN EVENT PROMOTED BY THE FVEA AND PREMIOS REI JAUME I FOUNDATION.



## Press releases

FECYT CONFERENCE "COMMUNICATION, OPEN SCIENCE,  
AND EUROPEAN HORIZONS"

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THE BANKIA SANEC CALL IS OPEN TO PROMOTE MEDICAL  
RESEARCH AMONG FP DUAL STUDENTS

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4TH CONFERENCE ON HEALTH RESEARCH WITH  
A GENDER PERSPECTIVE

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RESEARCHERS AND PATIENTS MAKE VISIBLE THE LATEST ADVANCES  
IN RARE DISEASES

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CIPF RESEARCHERS STUDY THE RELATIONSHIP OF  
NEUROLOGICAL FAILURES WITH MUTATIONS IN PATIENTS  
WITH CHILDHOOD EPILEPSY

---

CIPF RESEARCHERS DISCOVER A NEW MECHANISM  
THAT REGULATES THE CORRECT DISTRIBUTION OF NEURONS  
IN THE BRAIN

---

NEW TOOL FOR THE GENETIC DIAGNOSIS  
OF WILSON'S DISEASE

---

THE CIPF ADVANCES IN A NEW MOLECULAR AND CELLULAR  
APPROACH TO GLAUCOMA

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BIOLOGICAL TREATMENT FOR RETINAL DEGENERATION  
SUCCESSFULLY TESTED IN ANIMAL MODELS

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CIPF AND FIHGUV IMPLEMENT  
CIRCULATING TUMOUR DNA ANALYSIS

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EARLY ALTERATIONS IN THE BRAIN ASSOCIATED WITH  
NEUROLOGICAL DISEASES ARE IDENTIFIED

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AN INTERNATIONAL TEAM LED BY THE CIPF DISCOVERS AN  
INNOVATIVE ANTITUMOUR TREATMENT STRATEGY

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THE CIPF COLLABORATES WITH THE ONCE FOUNDATION IN A  
PROJECT TO DELAY VISION LOSS IN INHERITED RETINAL DYSTROPHIES

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THE CIPF DEVELOPS A METHOD FOR DETECTING SARS-COV-2  
IN SALIVA SAMPLES

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TRIPLE NEGATIVE BREAST CANCER THERAPY  
SUCCESSFULLY TESTED

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## News Highlights

We had two radio interviews on the Spanish National Radio (RNE), two televised interviews (one on *À punt* and the other on *La Sexta*), and many videos from the CIPF were uploaded by the CIPF and Generalitat Valenciana on their YouTube channels.

The CIPF in Valencia develops a saliva test to detect SARS-CoV-2.  
31/12/2020, **Diario Médico**

Researchers will use artificial intelligence to detect coronavirus in x-rays.  
10/12/2020, **Información**

Faster, cheaper, and as effective as a PCR: this is how the saliva test works.  
05/12/2020, **La Sexta**

The CIPF develops a method for detecting Sars-CoV-2 in saliva samples.  
28/11/2020, **Valenciaplaza**

The Príncipe Felipe Research Center develops a method for detecting coronavirus in saliva samples.  
28/11/2020, **Vilaweb**

The Príncipe Felipe Research Center in Valencia develop a method to detect the virus in saliva.  
28/11/2020, **El País**

The Príncipe Felipe Research Center develops a test for Covid-19 from saliva samples.  
28/11/2020, **El Mundo**

ONCE and the Príncipe Felipe Research Center in Valencia collaborate on a project to delay vision loss in retinitis pigmentosa.  
13/11/2020, **Servimedia**

The CIPF collaborates with ONCE on a therapy for retinitis pigmentosa.  
13/11/2020, **La Vanguardia**

The UCV participates in an international study on the SARS-CoV-2 virus genome.  
12/11/2020, **La Vanguardia**

Discovery of an innovative strategy to kill tumour cells.  
10/11/2020, **Levante-EMV**

An international team discovers an innovative antitumour treatment strategy.  
02/11/2020, **El económico**

Investigation of two proteins involved in programmed cell death to treat skin and lung cancers.

26/10/2020, **20 Minutos**

An international team led by the CIPF discovers an innovative anti-tumour treatment strategy.

26/10/2020, **elperiòdic.com**

The Príncipe Felipe Research Center makes advances in improving antitumour treatments.

27/10/2020, **Acta Sanitaria**

A CIPF researcher has identified early brain disorders associated with neurological diseases.

15/10/2020, **20 Minutos**

A CIPF researcher identifies early brain disorders associated with neurological diseases.

15/10/2020, **La Vanguardia**

A CIPF researcher identifies early brain disorders associated with neurological diseases.

15/10/2020, **Infosalus**

Maria Burgal Martí: making visible what nobody could see.

13/10/2020, **Levante-EMV**

The Provincial Hospital Foundation and the UJI define alliances in biomedical research.

02/10/2020, **Castellón Plaza**

Researchers from the CIPF and the FIHGUV General Hospital Foundation implement analysis of circulating tumour DNA.

24/09/2020, **Infosalus**

The Provincial Hospital Foundation lays the foundations for the future Health Research Institute that will put Castellon at the biomedical forefront.

10/09/2020, **elperiòdic.com**

38 Valencian FP Dual students selected for the Bankia Foundation SANEC health research program.

01/09/2020, **elEconomista.es**

CIPF advances in a new molecular and cellular approach to glaucoma.

25/08/2020, **ConSalud.es**

New advances in glaucoma research at the CIPF .

25/08/2020, **Las Provincias**

Researchers from the CIPF make advances in a new molecular and cellular approach to glaucoma.

24/08/2020, **Infosalus**

Researchers from the CIPF make advances in a new molecular and cellular approach to glaucoma.

24/08/2020, **Europa Press**

A new method for diagnosing Wilson's disease has been developed.

10/08/2020, **Levante-EMV**

CIPF researchers discover a new mechanism that regulates the correct distribution of neurons in the brain.

22/07/2020, **Informa Valencia**

A mechanism controlling the distribution of neurons in the brain is discovered.

22/07/2020, **La Vanguardia**

A new therapy for triple negative breast cancer is successfully tested.

02/06/2020, **Agencia Sinc**

New therapy from the Príncipe Felipe Research Centre for negative triple breast cancer.

25/05/2020, **Las Provincias**

A new therapy for triple negative breast cancer is successfully tested.

22/05/2020, **La Vanguardia**

A new therapy for triple negative breast cancer is successfully tested.

22/05/2020, **Heraldo**

CIPF researchers successfully test a new therapy for triple negative breast cancer.

22/05/2020, **InformaValencia**

Researchers successfully test a new therapy for triple negative breast cancer in animal models.

22/05/2020, **20 minutos**

Valencian healthcare has tested 42.21% of patients with symptoms.

11/05/2020, **Levante-EMV**

The numbers required to pass Phase 1 in the Valencian Community.

07/05/2020, **El Mundo CV**

A drug that reduces toxicity in cancer treatment is tested.

06/05/2020, **El Heraldo**

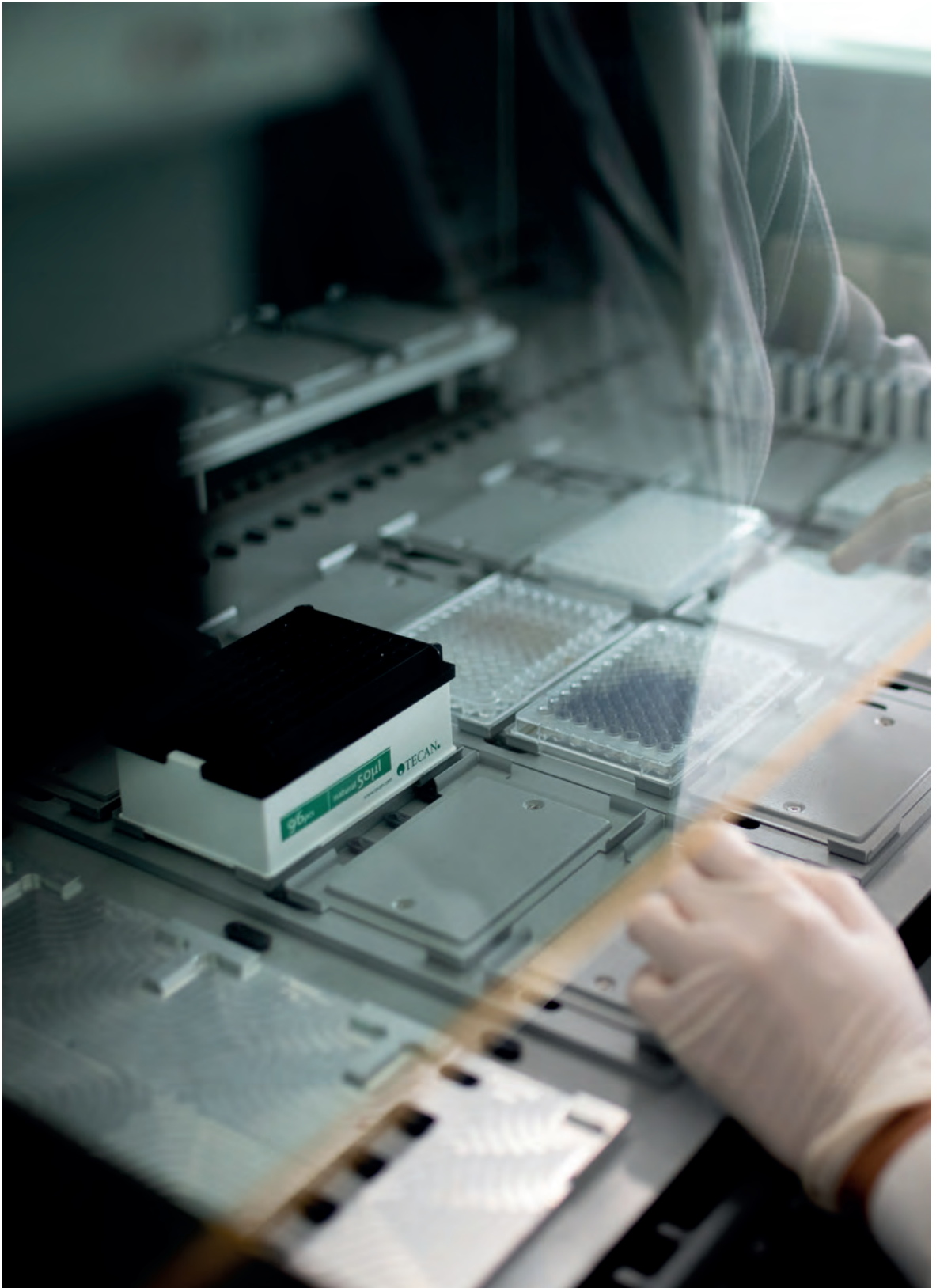
Artificial Intelligence for the early detection of COVID-19 pneumonia with a simple x-ray.

31/03/2020, **ABC Comunidad Valenciana**











# NUCLEAR MAGNETIC RESONANCE

## UNIT MEMBERS

Martina Palomino- Schätzlein





## OVERVIEW

The Nuclear Magnetic Resonance (NMR) Unit provides advanced applications for the identification, characterisation, and quantification of small molecules and macromolecules, offering tools to elucidate the molecular mechanisms underlying their biological activity. The Unit offers access to three NMR spectrometers with different field strengths (300, 500, and 600 MHz), equipped with a variety of probes and automation systems, including a probe for intact tissue analysis (HRMAS), a cold probe with enhanced sensitivity, and a *SampleJet* robot system for up to 500 samples. As support to its users, the Unit offers its extensive experience to help in the interpretation of NMR spectra and the characterisation and structural analysis of different chemical compounds and macromolecules. Furthermore, the Unit can perform metabolic profiling of a broad range of biofluid samples, including plasma, serum, urine, amniotic fluid, cerebrospinal fluid, or tear fluid.

The quantification of metabolites in different tissue and organ samples from patients and model animals, as well as in cellular models, can also be carried out. As a result, NMR technology has been applied to study the alterations of the metabolic profiles associated with different biochemical, pharmacological, or pathological process, including cancer, diabetes, Alzheimer, or rare diseases. The Unit has worked in close partnership with research groups and hospitals on several of these projects. On the other hand, the NMR Unit also provides its equipment and experience for screening drug libraries to search for hits for specific protein targets, as well as to characterise the geometry of the interaction between drug molecules and protein or RNA macromolecules.

## HIGHLIGHTS

The NMR Unit has recently optimised a protocol for the metabolomics profiling of blood cells, which has been successfully applied for the identification of metabolic alterations in red blood cells of diabetic patients, and leucocytes in obese patients. A study of the impact of COVID-19 on the metabolism of red blood cells in patients is in progress. Furthermore, the Unit is also working to provide a methodology to determine the metabolic profile of specific organelles such as mitochondria or nuclei.

## SELECTED ARTICLES

Becerra JE, Rodríguez-Díaz J, Gozalbo-Rovira R, Palomino-Schätzlein M, Zúñiga M, Monedero V, Yebra MJ. Unique Microbial Catabolic Pathway for the Human Core N-Glycan Constituent Fucosyl- $\alpha$ -1,6-N-Acetylglucosamine-Asparagine.

Neira JL, Palomino-Schätzlein M, Ricci C, Ortore MG, Rizzuti B, Iovanna JL. Dynamics of the intrinsically disordered protein NUPR1 in isolation and in its fuzzy complexes with DNA and prothymosin  $\alpha$ . *Biochim Biophys Acta Proteins Proteom*. 2019 Nov;1867(11):140252.

Palomino-Schätzlein M, Lamas-Domingo R, Ciudin A, Gutiérrez-Carcedo P, Marés R, Aparicio-Gómez C, Hernández C, Simó R, Herance JR. A Translational In Vivo and In Vitro Metabolomic Study Reveals Altered Metabolic Pathways in Red Blood Cells of Type 2 Diabetes. *J Clin Med*. 2020 May 27;9(6):1619.

# FLOW CYTOMETRY AND CYTOMICS

## TEAM MEMBERS

Alicia Martínez-Romero and Domingo Gil Casanova



## OVERVIEW

The CIPF Cytomics Facility provides technological solutions for high-speed polychromatic analysis, fluorescence activated cell sorting (FACS), and high-content screening (HCS) assays. It offers high-quality experimental support applied to biomedicine, biotechnology, translational medicine, microbiology, and environmental sciences.

## HIGHLIGHTS

In 2020, the Facility participated in different research projects related to immunological studies in marine mammals and the environmental toxicology of pinene aerosols on human lung cells resulting in a scientific publication (\*). A PhD student is finishing this work, which will be defended next year in 2021, about the effect of environmental pollutants on the immunology of marine mammals.

This year we also installed a new SONY cell sorter and set up a new high-content screening system with a robotic arm and an independent incubator in the Facility. This system allows us to perform long-term multi-user time-lapse experiments under controlled cell culture conditions.

## SELECTED ARTICLES

"Toxicological Responses of  $\alpha$ -Pinene-Derived Secondary Organic Aerosol and its Molecular Tracers in Human Lung Cell Lines". Chemical Research in Toxicology. Faria Khan, Karina Kwapiszewska, Yue Zhang, Yuzhi Chen, Andrew T. Lambe, Agata Kołodziejczyk, Nasir Jalal, Krzysztof Rudzinski, Alicia Martinez-Romero, Rebecca C.Fry, Jason D. Surratt, Rafal Szmigielski (in press).

# TRANSMISSION ELECTRON MICROSCOPY

## TEAM MEMBERS

Mario Soriano Navarro



## OVERVIEW

Electron microscopy uses an accelerated electron beam which, upon impacting the sample, generates different signals that provide information about its atomic structure. In Transmission Electron Microscopy (TEM), transmitted electrons are detected to generate conventional, dark-field, and high-resolution transmission images. Due to its high-resolution power, TEM has several useful applications in the fields of biomedical research, biotechnology, and diagnostics.

The Electron Microscopy Unit at the CIPF collaborates with internal and external research groups offering invaluable tools to address certain scientific questions. The Unit also provides technological support to pathology services for the diagnosis of some renal diseases.

## HIGHLIGHTS

In recent years there has been a significant increase in the number of studies related to the extracellular vesicles and exosomes, which is 'in vogue'. Due to their size and composition, electron microscopy is one of the main tools that allows the morphological characterisation of these particles.

One remarkable technique in the Unit is Cryo-TEM because it is not currently available in any other institute in the Comunidad Valenciana. In Cryo-TEM, vitrified fluid samples are prepared and analysed by cryogenic electron microscopy, preserving their native biological structures for observation.

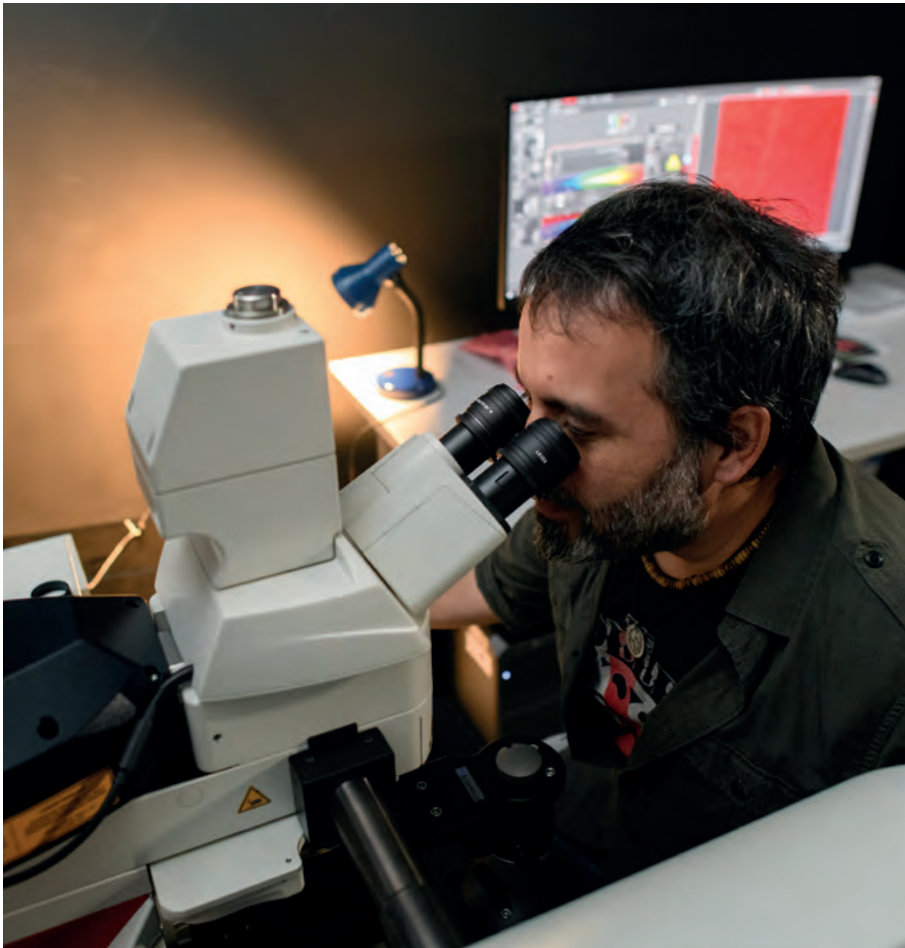
In 2020, in view of the increasing demand for new approaches related to electron microscopy, the Unit developed new techniques such as pre- and post-immunogold staining for histological tissues, collaborating closely with CIPF researchers.

Also in this line of developing new techniques, we started working jointly with the Advanced Light Microscopy Unit on the implementation of Correlative Light and Electron microscopy techniques (CLEMs). We developed correlation techniques in both cell culture and histological tissues. In addition, in order to raise awareness of CLEM, the unit participated in the first Biological Imaging Workshop in the Comunidad Valenciana in order to provide a simple forum for communication between institutes and to encourage discussions between the many imaging experts and services in our community.

# ADVANCED LIGHT MICROSCOPY

## TEAM MEMBERS

Alberto Hernández Cano



## OVERVIEW

Advanced microscopy provides users with a wide range of techniques and key tools in the field of biomedical research, but also in other scientific areas such as nanoscience and nanotechnology, new materials, QC and QA, etc. Amongst all available technologies, confocal microscopy is probably one of the most relevant to biomedical research. Not only because of its great resolution power, but also because of a greater sample penetration capacity. Confocal microscopy allows the capture of images in different focal planes that can be processed to generate three-dimensional reconstructions of structures. The CIPF Advanced Light Microscopy Unit offers a wide range of applications in microscopy techniques and data analysis, including conventional optical microscopy, fluorescence, in vivo imaging, confocal techniques, super-resolution, multiphoton, etc.

## HIGHLIGHTS

In 2020, the Unit incorporated a new intravital multiphoton microscope. Intravital microscopy (IVM) is a live imaging technique that allows researchers to study dynamic processes at cellular and subcellular resolutions in their natural environment. In particular, long-term IVM can be applied to visualise migration and proliferation over days to months within the same animal without recurrent surgeries. IVM has also played a key role in studies of tumour angiogenesis. This equipment was funded with ERDF Funds.



## SCREENING FACILITY AT CIPF

### TEAM MEMBERS

Scientist in Charge: Dr Maria J. Vicent

Technician in charge: Esther Masiá

ERIC-EU-OpenScreen Specialist Site CIPF also with Dr Mar Orzáez and David Charbonnier





## OVERVIEW

The CIPF Screening Platform supports the evaluation of biological and pharmacological compound libraries, including in-house libraries and those from external agencies such as EU-OpenScreen once the CIPF became a specialist site for complex cellular assays. We aim to identify and characterise novel bioactive agents in areas including cancer treatment, regenerative medicine, and infectious diseases.

## HIGHLIGHTS

We have validated our HTS approach for identifying exosome biogenesis/release inhibitors through AlphaScreen™, also allowing us to understand the origin of exosomes in patient samples (i.e., blood), which may improve diagnostic and therapeutic approaches in cancer, neuroinflammation, and other diseases. Oncology represents an important area at our site, for example within the ERCCoG-MyNano project, we performed screenings comparing 2D vs. 3D breast cancer models to develop personalised combination therapies for breast cancer subtypes, at the same time as trying to identify functional biomarkers (by means of proteomics) to better design subtype-specific nanotherapies. With Tübingen University, we developed a screening assay to identify modulators of intracellular interactions in the H2020-DRIVE project coordinated by the EU-OpenScreen. Other projects used massive screening approaches for the identification of activators of caspase 9, skin permeation enhancers, and psoriasis treatments or the identification of novel FXN-modifying genes in drosophila cell lines looking at novel therapeutic approaches for Parkinson's disease. Finally, we collaborated with the cytomics and confocal services at the CIPF as well as with the Bioimaging CIPF-Fisabio Joint Unit, towards the implementation of High Content Screening (HCS) approaches, in particular, looking at cell morphology by means of cell painting assays in 2D and 3D cell models. The unit participates in: ERIC-EU-Openscreen, SDDN, Geivex, and networks of excellence (REDEFAR, ES-OpenScreen or Tentacles).

## PUBLICATIONS AND COMMUNICATIONS

Silvestri A., Vicente F, Vicent M.J., Stechmann B., Fecke W. Academic collaborative models fostering the translation of physiological in vitro systems from basic research into drug discovery. *Drug Discovery Today* 2021. <https://doi.org/10.1016/j.drudis.2021.02.024>

Dolz-Pérez, et al. Polypeptide-corticosteroid conjugates as a topical treatment approach to psoriasis. *J Control Rel*, 2020(318):210-222.

Andreu Z., Masiá E., Charbonnier D., Vicent MJ. Importancia de los ensayos fenotípicos en descubrimiento de fármacos. Dossier SEBBM, Revista nº 205, 2020

Andreu Z., Hidalgo M, Masiá E., García-García F., Vicent MJ. Proteomic Signatures in Breast Cancer Exosomes and Cell Lines. GEIVEX/TeNTaCLES Minisymposium. Virtual Dec. 2020

Andreu Z., Hidalgo M, Masiá E., García-García F., Vicent MJ. Proteomic Signatures in BCa Exosomes and Cell Lines. Annual Meeting ISEV. Virtual Conference 20-22 July 2020.

## ANIMAL MODELS PLATFORM

### TEAM MEMBERS

Viviana Bisbal, Begoña Laínez, Amparo Moragón, Nerea Marín



## OVERVIEW

Advances in biomedical research often require the use of in vivo models and the consistency and reproducibility of data can only be achieved with high-quality standardised models, facilities, and procedures. At the CIPF, we are committed to the highest standard of animal welfare. The Animal Facility provides CIPF scientists with high-quality animal care services and facilities to improve animal research and ensure the health, well-being, and humane treatment of animals used in research and teaching.

## HIGHLIGHTS

In 2020, the Unit was involved in multiple projects about breast cancer, different PDX orthotopic models of cancer, regeneration of the central and peripheral nervous system, and the use of nanoparticles in the senescence of cancer cells, among others. On the other hand, the Animal Models Platform worked to provide scientists with high-quality and efficient transgenic services.

This pandemic year has highlighted the excellence of the Animal Facility team, thanks to which it was possible to maintain all the transgenic lines and to finish ongoing experiments. The Animal Facility did not stop working during the state of alarm so that it could ensure the well-being and health of the animals. It was a challenge successfully overcome. Thank you so much, colleagues!

## PUBLICATIONS AND COMMUNICATIONS

Galiana I, Lozano-Torres B, Sancho M, Alfonso M, Bernardos A, Bisbal V, Serrano M, Martínez-Mañez R, Orzáez M. Preclinical antitumor efficacy of senescence-inducing chemotherapy combined with a nanoSenolytic. *J Control Release*. 2020 Jul 10;323:624-634. doi: 10.1016/j.jconrel.2020.04.045. Epub 2020 May 4. PMID: 32376460.

Moreno-Manzano V, Mellado-López M, Morera-Esteve MJ, Alastrue-Agudo A, Bisbal-Velasco V, Forteza-Vila J, Serrano-Aroca A, Vera-Donoso CD. Human adipose-derived mesenchymal stem cells accelerate decellularized neobladder regeneration. *Regen Biomater*. 2020 Mar;7(2):161-169. doi: 10.1093/rb/rbz049. Epub 2019 Dec 22. PMID: 32296535; PMCID: PMC7147364.

# GENOMICS AND TRANSLATIONAL GENETICS

## TEAM MEMBERS

Scientist in Charge: Carmen Espinós

Laura Ramírez, Eloisa Barber, Vincenzo Lupo, Virginia Rejas



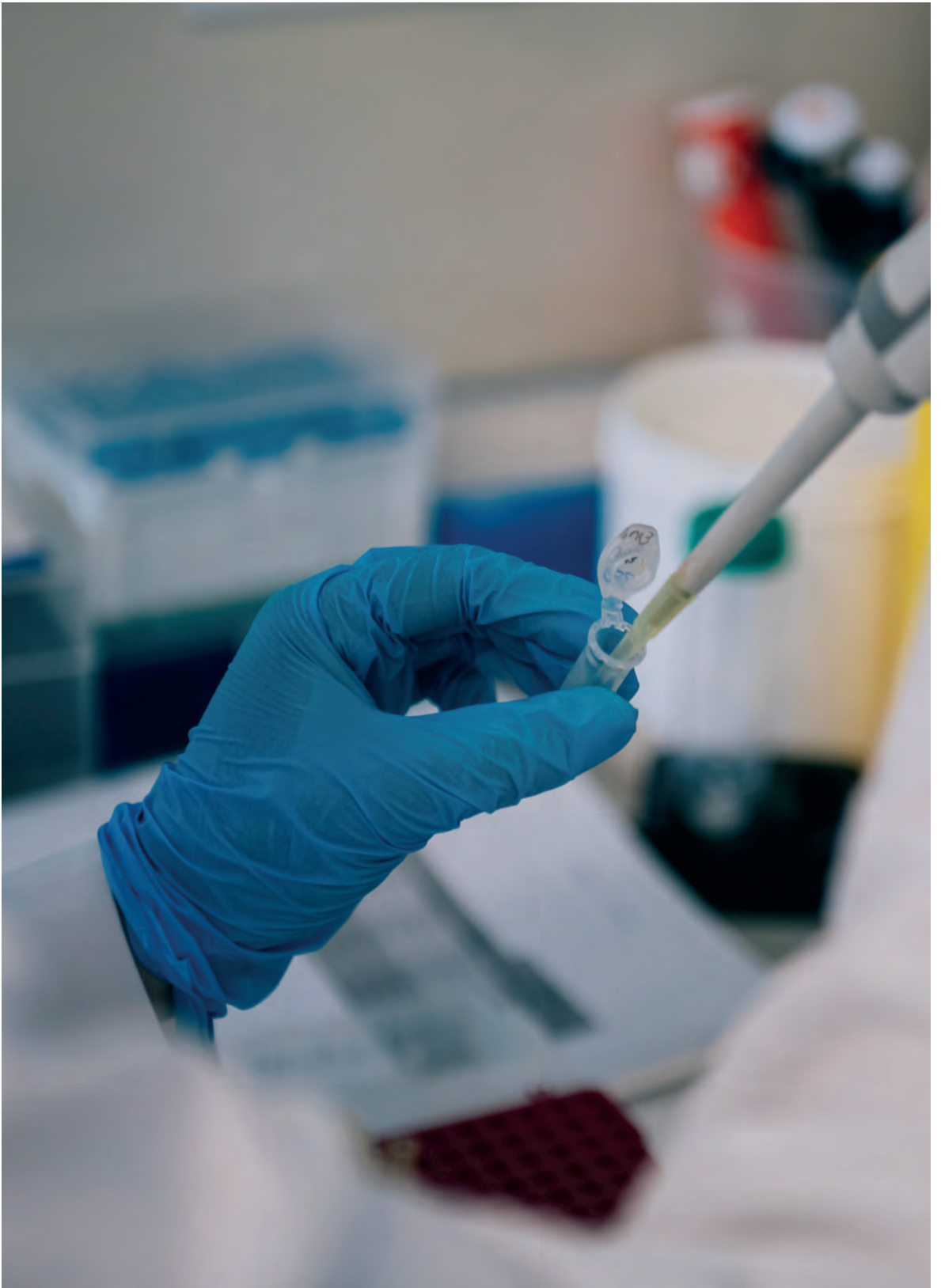
## OVERVIEW

The Genomics and Translational Genetics Service offers advanced genetic analysis and genomics applications. To achieve its main goal, the service integrates scientific advances from the CIPF in the fields of human genetics, genomics, and bioinformatics, with the knowledge generated through different collaboration projects and their experience in genetic diagnosis. This goal is to provide genetic information and tools to health professionals interested in the diagnosis and prognosis of hereditary pathologies. In particular, at the CIPF we focus on the study of hereditary peripheral neuropathies, hereditary ataxia/spastic paraparesis, neurodegenerative diseases related to iron accumulation in the brain, among other motion disorders. Using our growing scientific know-how and in collaboration with clinicians, we have designed custom gene panels for the diagnosis of some of these neurological disorders.

## HIGHLIGHTS

In the area of genomics, we focussed on supporting users in their next-generation sequencing (NGS), qPCR, Sanger, and microarray experiments. Some of the most commonly used applications were targeted resequencing, small genome sequencing, metagenomics, targeted gene expression profiling, miRNAs, aCGH, differential expression, inter-individual genetic variation, and epigenetic profiling, among others.

In the area of translational genetics, we designed and validated diagnostic panels for peripheral hereditary neuropathies, in particular for distal spinal atrophy (AED), spinal muscular atrophy (SMA), Charcot-Marie-Tooth (CMT) disease, and amyotrophic lateral sclerosis (ALS).









## CIPF\_ Economic Figures

FUNDS WITH A  
COMPETITIVE ORIGIN

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1,732,495 €

FUNDS WITH A  
NON-COMPETITIVE ORIGIN

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403,385 €

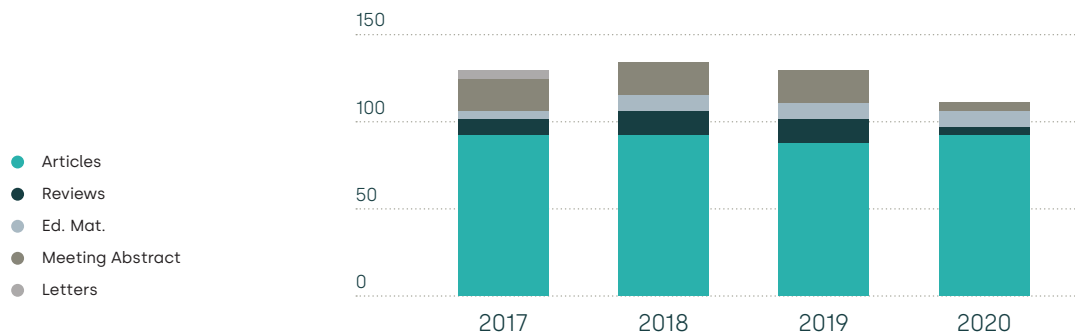
DIRECT FUNDS  
FROM GENERALITAT VALENCIANA

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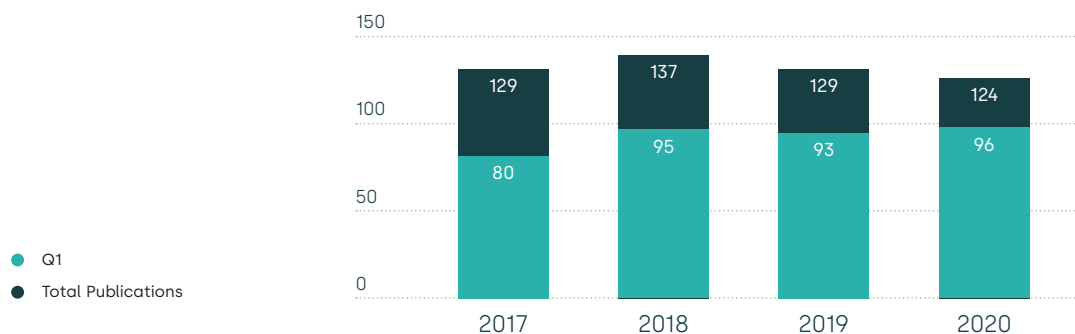
4,714,000 €



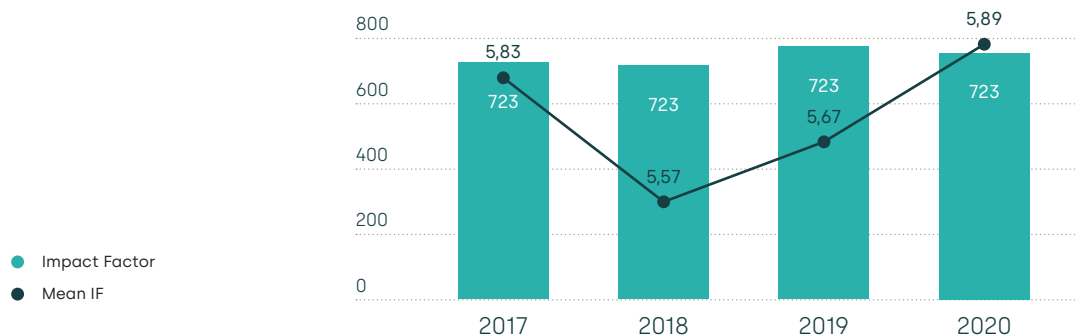
## NUMBER OF PUBLICATIONS



## PUBLICATIONS IN 1ST QUARTILE



## IMPACT FACTOR



## CIPF\_ Human Resources

In 2020, the CIPF implemented the European Commission's Human Resources Strategy for Researchers (HRS4R) to promote research careers in accordance with the principles established by the European Charter for Researchers and the Code of Conduct.

## CIPF\_ Staff



- Women\_ 99
- Men\_ 51



- Staff\_ 150
- Students\_ 61
- Collaborators\_ 62

### CIPF Research Personnel

	NUMBER	%	MEN	WOMEN
PRINCIPAL RESEARCHERS / PLATFORM MANAGERS	17	11	7	10
POSTDOCTORAL RESEARCHERS	26	17	15	11
PHD RESEARCHERS	24	16	3	21
TECHNICAL	33	22	6	27
TECHNICAL CORE FACILITIES	11	7	3	8

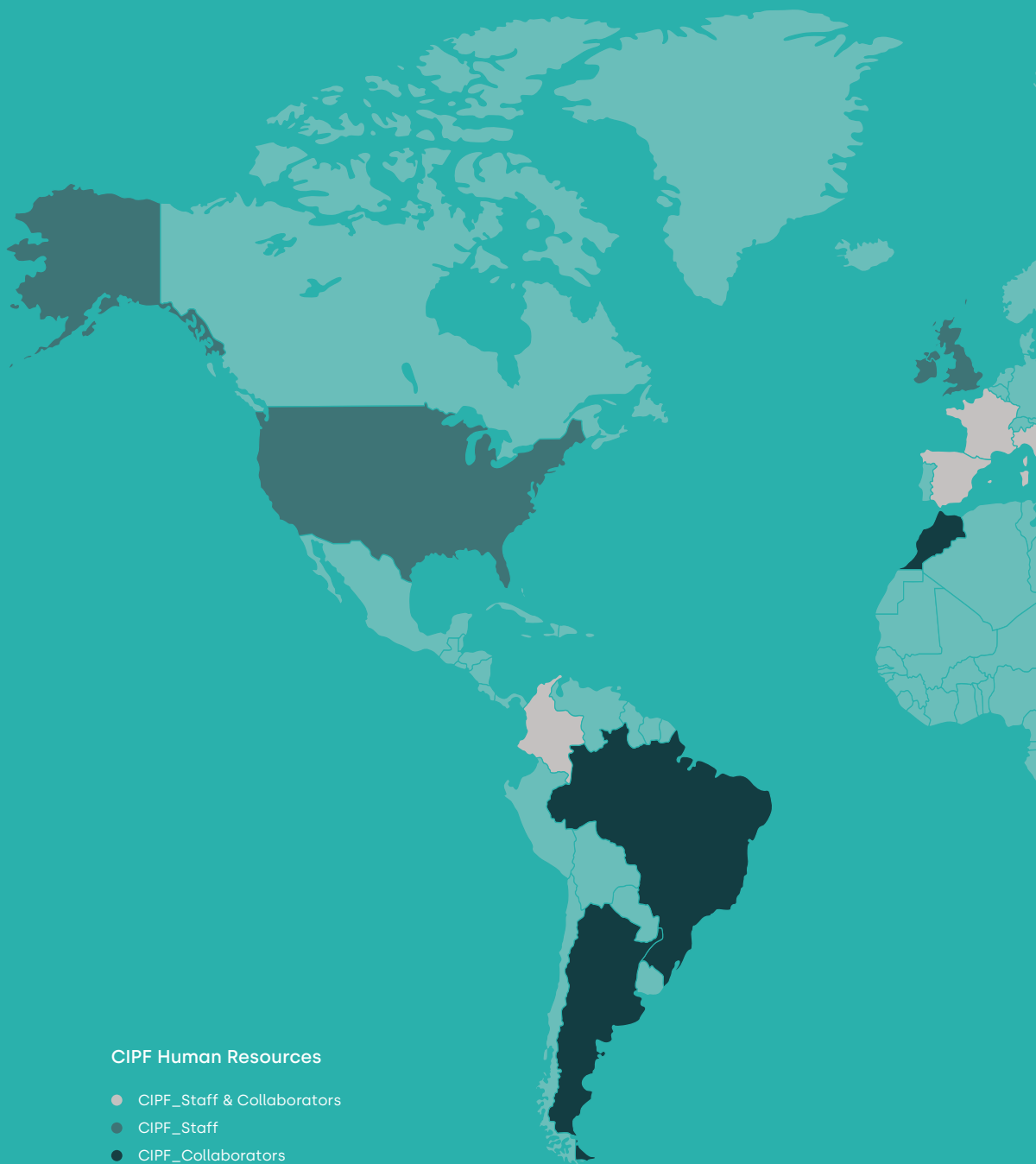
## CIPF Staff

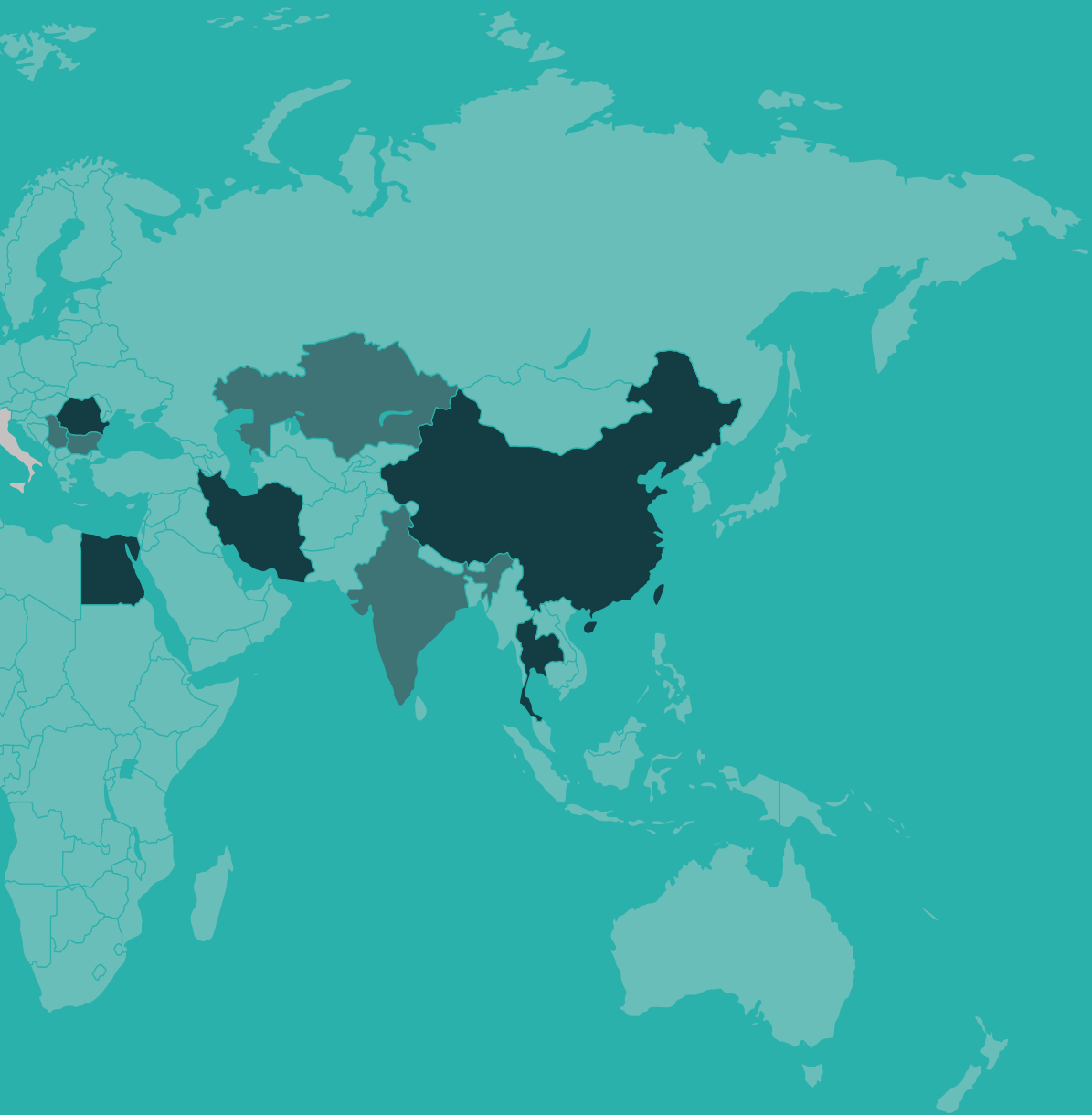
NATIONALITIES	MEN	WOMEN	TOTAL
<b>RESEARCHERS</b>	<b>51</b>	<b>99</b>	<b>150</b>
SPANISH	42	91	133
BULGARIAN	0	1	1
INDIAN	0	1	1
SERBIAN	1	2	3
COLOMBIAN	1	0	1
NORTH AMERICAN	0	1	1
ITALIAN	4	2	6
UKRAINIAN	0	1	1
BRITISH	2	0	2
FRENCH	1	0	1

## CIPF Collaborators

NATIONALITIES	MEN	WOMEN	TOTAL
<b>RESEARCHERS</b>	<b>18</b>	<b>44</b>	<b>62</b>
SPANISH	12	35	47
THAI	0	1	1
MOROCCAN	1	2	3
ARGENTINIAN	0	2	2
BRAZILIAN	0	1	1
COLOMBIAN	2	0	2
IRANIAN	0	1	1
CHINESE	1	0	1
EGYPTIAN	0	1	1
FRENCH	1	0	1
ITALIAN	0	1	1
ROMANIAN	1	0	1

	MEN	WOMEN	TOTAL
<b>STUDENTS</b>	<b>24</b>	<b>37</b>	<b>61</b>
SPANISH UNIVERSITIES	20	32	52
EUROPEAN UNIVERSITIES	1	2	3
VOCATIONAL TRAINING	3	3	6











**Horizon 2020 - EU Research and Innovation Programme**

GRANT TYPE	TITLE	INVESTIGATOR
H2020-MSCA-ITN-2019	Molecular Machines Functioning in Cells. BIOMOLMACS	M <sup>a</sup> Jesús Vicent
H2020-INFRADEV-03-2018-2019	Ensuring long-term sustainability of excellence in chemical biology within Europe and beyond. EU-OPENSREEN-DRIVE	M <sup>a</sup> Jesús Vicent Mar Orzáez
H2020-ERC-Proof of Concept	Off the self polypeptide-based immunotherapy for Advanced Melanoma Treatment. POLYMMUNE	M <sup>a</sup> Jesús Vicent
H2020-ERC-2014-Consolidator Grant	MyNano: Towards the design of Personalised Polymer-based Combination Nanomedicines for Advanced Stage Breast Cancer Patients. MyNano	M <sup>a</sup> Jesús Vicent

**ISCIII - ES Instituto de Salud Carlos III**

GRANT TYPE	TITLE	INVESTIGATOR
Research Platform	Proteomics platform, genotyping, and cell lines	Slaven Erceg
Research Platform	Bioinformatics platform	Francisco García
CIBER	Diabetes and associated metabolic diseases (Ciberdem)	Deborah J. Burks
FIS Project	3D retinas derived from iPS cells as a tool to find effective therapies for inherited diseases of the retina	Dunja Lukovic
FIS Project	Patient specific disease models as a tool toward effective therapies for hereditary retinal dystrophies	Dunja Lukovic
FIS Project	Clinical studies, genetic bases, and prognostic biomarkers in rare neurodegenerative diseases	Carmen Espinós
FIS Project	Preclinical study of the regenerative powers of stem cell-derived astrocytes in the treatment of mouse spinal injury	Slaven Erceg
FIS Project	Characterisation of new genes and protein biomarkers to advance the diagnosis, prognosis, and therapy of hereditary axonal neuropathy (CMT2)	Vincenzo Lupo
FIS Project	Development of anti-inflammatory nanotherapies in retinitis pigmentosa	Regina Rodrigo

FIS Project	Personalised therapy targeting the activated AP-1 pathway in lung and breast cancer	Rosa Farràs
RETICS	Addictive Disorders Network	Consuelo Guerri
Miguel Servet Programme	Hiring doctors with an accredited research career in centres in the National Health System	Dunja Lukovic
Miguel Servet Programme	Hiring doctors with an accredited research career in centres in the National Health System	Alfonso Benítez
PFIS Predoctoral Training Contract	Isabel Hinarejos Predoctoral Molecular bases and prognostic biomarkers for neurodegenerative diseases with cerebral accumulation of iron, and related movement disorders	Carmen Espinós

### MSCBS - ES Ministry of Health

GRANT TYPE	TITLE	INVESTIGATOR
National Drug Plan	Neuroinflammation and alterations in brain plasticity in adolescents with alcohol abuse: Gender differences, biomarkers, and therapies	Consuelo Guerri

### MCINN- ES Ministry of Science and Innovation

GRANT TYPE	TITLE	INVESTIGATOR
Excellent Networks	Spanish network for ion channels	Victoria Moreno
Excellent Networks	Translational Network for the clinical application of Extracellular Vesicles	M <sup>a</sup> Jesús Vicent
Excellent Networks	Consolidation and strategic positioning of the Spanish node in the ERIC EU-OPENSREEN network	Mar Orzáez
Excellence Networks	Role of ubiquitin family proteins in signalling, proliferation, and cancer	Rosa Farràs
Research Challenges Collaboration Grant	RTC-2017-6600-1 Development of a gene therapy platform for kidney genetic diseases	M <sup>a</sup> Jesús Vicent
Research Challenges Collaboration Grant	Development of topical therapies based on polypeptide transport systems	M <sup>a</sup> Jesús Vicent
Dynamization Actions	Intranasal polypeptide carrier for the treatment of CNS pathologies. Dynamization Actions "Europe Research 2019"	M <sup>a</sup> Jesús Vicent

R&D+i Projects Research Challenges	Phenotypic variability: origins and consequences	Francisco Iborra
R&D+i Projects Research Challenges	New bio-active biomaterial for the regeneration of spinal cord injuries	Victoria Moreno
R&D+i Projects Research Challenges	Synergistic approach for metastatic tumour and neurodegenerative disorder treatments using versatile SynVerPPC polypeptide-based conjugates	M <sup>a</sup> Jesús Vicent
R&D+i Projects Research Challenges	Targeting Nuclear Receptor REV-ERV-alpha in Inflammatory Bowel Disease	Enric Esplugues
R&D+i Projects Research Challenges	Channelopathies underlying prefrontal cortex dysfunction in Alzheimer's disease	Isabel del Pino
R&D+i Projects Research Challenges	Molecular bases of neurological disorders (cognitive and motor) in hyperammonemia and hepatic encephalopathy. Therapeutic implications	Vicente Felipo
R&D+i Projects Research Challenges	Deciphering and modulating the transmembrane interactome of Bcl-2 proteins as an antitumour target	Mar Orzáez
R&D+i Projects Research Challenges	Regulation of the adaptation and proliferation of beta cells by Insulin Receptor Substrate 2	Deborah Burks
R&D+i Projects Research Challenges	NRG1 signalling in cortical circuits: information on the molecular bases of schizophrenia	Pietro Fazzari
Ramón y Cajal Programme	Incorporation of national and foreign researchers with an outstanding career trajectory into R&D centres	Pietro Fazzari
Ramón y Cajal Programme	Incorporation of national and foreign researchers with an outstanding career trajectory into R&D centres	Martin Valdearcos
Researchers Training	Yaiza Arenas Molecular bases of neurological disorders (cognitive and motor) in hyperammonemia and hepatic encephalopathy. Therapeutic implications	Vicente Felipo
Researchers Training	Ángela Rodríguez NRG1 signalling in cortical circuits: information on the molecular bases of schizophrenia	Pietro Fazzari
Researchers Training	M <sup>a</sup> del Mar Sánchez New Bio-Active biomaterial for the regeneration of spinal cord injuries	Victoria Moreno

### MEyFP - ES Ministry of Education and Vocational Training

GRANT TYPE	TITLE	INVESTIGATOR
FPU	Inés Domingo Development of new procedures to characterise biochemical routes altered in breast cancer in vitro and in vivo using metabolomic profiles obtained by NMR spectroscopy	M <sup>a</sup> Jesús Vicent

FPU	Paz Boix Development of polymeric combination therapy for the treatment of triple- negative metastatic breast tumours	M <sup>a</sup> Jesús Vicent
FPU	Paula Izquierdo Molecular mechanisms of cognitive and motor disorders in hyperammonemia and hepatic encephalopathy. Therapeutic implications	Vicente Felipo
FPU	Gergana Yvaylova Molecular mechanisms of cognitive and motor disorders in hepatic encephalopathy. Therapeutic implications	Vicente Felipo

### CIUCiSD - GVA Valencia Regional Innovation, University, Science and Digital Society Ministry

GRANT TYPE	TITLE	INVESTIGATOR
PROMETEO Programme	MEMBDEATH: Cell death and membranes: a new niche in the fight against cancer	Mar Orzáez
PROMETEO Programme	Regenerative medicine of the human uterus: From cell therapy to organ creation through bioengineering	Deborah J Burks
PROMETEO Programme	From genes to therapy in neurodegenerative and neuromuscular diseases	Carmen Espinós Máximo Ibo Galindo
PROMETEO Programme	Molecular and cerebral mechanisms of cognitive and motor disorders in hyperammonemia and hepatic encephalopathy. Therapeutic and diagnostic implications	Vicente Felipo
Emerging Groups - GV	Identification of new genetic causes in patients with hereditary peripheral neuropathies and difficult genetic diagnosis	Vincenzo Lupo
Emerging Groups - GV	Mitochondrial tRNA fragments: biomarkers and new therapeutic targets in mitochondrial diseases	Salvador Meseguer
Emerging Groups - GV	Design of theranostic polymeric systems for the treatment of breast cancer	María Medel
Emerging Groups - GV	DifGenOmics. The study of sex and gender differences in health with omic approaches	Francisco García
Plan GenT	Channelopathies underlying prefrontal cortex dysfunction and cognitive deficits in Alzheimer's disease	Isabel del Pino
GRISOLIA Programme	Paola Leone The role of peripheral inflammation and neuroinflammation in cognitive and motor deterioration in hepatic encephalopathy	Vicente Felipo
GRISOLIA Programme	Sonia Prakash – Neural stem cells from inducible-pluripotent stem-cells and PA-Curcumin combinatory treatment for spinal cord injury regeneration	Victoria Moreno
Predocctoral - ACIF	Antonio Serrano [Identification of new biomarkers and development of combination polymeric conjugates in metastatic prostate cancer]	M <sup>a</sup> Jesús Vicent Ana Armiñán

Predoctoral - ACIF	Ana González- Nrg1: neuronal protection and recovery from stroke in cortical neurons	Pietro Fazzari
Predoctoral - ACIF	Beatriz Martínez Optogenetic and pharmacological stimulation of neural stem cells for the treatment of spinal cord injuries	Victoria Moreno
Predoctoral - ACIF	Maria Sancho Alonso [Mechanisms by which cyclic GMP and neuroinflammation modulate neurotransmission and cognitive and motor function	Vicente Felipo Marta Llansola
Predoctoral - ACIF	M <sup>a</sup> José Arámbul Reversible control of autophagy by Insulin / IGF1 signalling and its involvement in hepatogenesis	Luke Noon
APOSTD	Role of neuroinflammation in cognitive and motor impairment in hepatic encephalopathy and Parkinson's disease. Molecular mechanisms. Therapeutic implications	Vicente Felipo

### CSUISP - GVA Valencia Regional Health Ministry

GRANT TYPE	TITLE	INVESTIGATOR
Plan GenT	Local insulin-induced paracrine signalling ("LiiPS") in regenerative medicine and cancer	Luke Noon
Internationalization - AFI	Actions aimed at promoting and managing participation in international research programs in biomedicine, healthcare, and public health	Francisca Gómez
Amper	Grants to finance human resources activities to promote research and training in healthcare, biomedical, and public health research	Francisca Gómez

### AVI - GVA Innovation Agency for the Valencian Region

GRANT TYPE	TITLE	INVESTIGATOR
Results Transfer to Business- INNVAl	In vivo pharmacological validation of ROCK2 inhibitor nanopharmaceuticals in metastatic breast cancer and spinal cord injury	M <sup>a</sup> Jesús Vicent Victoria Moreno

### FOUNDATIONS & OTHER PRIVATE ENTITIES

GRANT TYPE	TITLE	INVESTIGATOR
La Caixa Foundation	Sensitizing pancreatic cancer to immunotherapy with multimodal precision nanomedicines	M <sup>a</sup> Jesús Vicent
La Marató de TV3	Combinatory treatment of Neural precursor cells and a new nanoconjugate of fasudil for clinical application in Acute Spinal Cord Injury	M <sup>a</sup> Jesús Vicent Victoria Moreno

La Marató de TV3	Transplant of combined cell therapy from clinical grade iPSC-derived cells with neuroprotective small chemicals in a SCI rat model for central regeneration of spinal pathways	Victoria Moreno
IDIBAPS	Implication of the specific cutaneous immune profile determined in peripheral blood in the prognosis and responsiveness to immunotherapy in melanoma	Francisco García
EASI- Genomics	Molecular basis of NBIA and NBIA-mimics	Carmen Espinós
Fundació per Amor a l'Art	Genetic bases and prognostic biomarkers for Wilson and Wilson-like disease	Carmen Espinós
EMBO Short-Term Fellowships	Presynaptic mechanisms involved in synaptic transmission. Underlying molecular and electrophysiological components of glutamatergic and GABAergic neurotransmission in adult brain. Effect of cGMP. Maria Sancho.	Vicente Felipe
EMBO Short-Term Fellowships	Evaluation of neuroinflammation and glial activation induced by extracellular vesicles from hyperammonemic rat in adult brain organotypic cultures. Paula Izquierdo	Vicente Felipe
International Brain Research Organization, IBRO	International collaboration between Del Pino Lab in Spain and Di Cristo Lab in Canada	Isabel del Pino Pariente
ASSOCIATION FRANÇAISE CONTRE LES MYOPATHIES	An integrative approach to develop cellular models and characterize disease mechanisms implicated in CMT2Z, a newly described axonal form of neuropathy	Carmen Espinós
ONCE	Development and optimisation of anti-inflammatory nanotherapies in hereditary retinal dystrophies	Regina Rodrigo
ASEICA	Identification of new biomarkers and development of combination nanoconjugates for metastatic prostate cancer treatment	M <sup>a</sup> Jesús Vicent
INDACEA	Precision medicine in Dravet syndrome	Máximo Ibo Galindo
PROYECTO DRAVET	Generation of models in Drosophila melanogaster by knock-in of patient mutations	Máximo Ibo Galindo
AECC - Predoctoral	Fernanda Rodríguez Design of novel targeted Polymer Therapeutics as combination therapy for the treatment of Brain Metastasis – Overcoming the Blood Brain Barrier	M <sup>a</sup> Jesús Vicent
AECC - Predoctoral	Tetiana Melnyk Brain Drug Delivery using polymer therapeutics as an intranasal platform towards paediatric glioma treatment	M <sup>a</sup> Jesús Vicent
AECC - Predoctoral	Arantxa Martínez New therapeutic strategies against lung cancer based on the control of protein synthesis mediated by polyamines	Rosa Farràs
Fundación Ramón Areces	Identification and modelling of molecular and cellular events of the immune response associated to the appearance of minimal hepatic encephalopathy in cirrhotic patients	Vicente Felipe

## RESEARCH CONTRACTS

ENTITY	TITLE	INVESTIGATOR
IMEGEN	New comprehensive tool for the identification of precision immunotherapy biomarkers	Francisco García
POPLIPEPTIDE THERAPEUTIC SOLUTIONS	Proof of Concept for Liver-targeted Gene Delivery	M <sup>a</sup> Jesús Vicent
IIS LA FE	Generation of miRNA recognition probes	M <sup>a</sup> Jesús Vicent
BIOMAR	Advice and Technological Support	Máximo Ibo Galindo
SPIRAL THERAPEUTICS	Characterization of Apoptosome Inhibitors	Mar Orzáez
ESTEVE	Study of the response of individual or combinatory treatments of Esteve compounds with neural precursor cell transplantation in a rodent model of traumatic spinal cord injury to test neurological neuro-protection and neuro-regeneration	Victoria Moreno







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