



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

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#### Título:

Functional genomics and new therapeutic interventions in Follicular Lymphoma

#### Resumen de la Memoria:

Since my early steps in scientific research, I was very interested in the possible role of tumour suppression genes in longevity and metabolism. To address this question, I joined Manuel Serrano's laboratory at CNIO as a predoctoral fellow. In his lab, I developed a mouse model that overexpressed PTEN, one of the most important tumour suppressor genes. These mice, not only were protected to develop cancer, but also present a significant extension of life span that was independent of their lower cancer incidence. Moreover, these mice, showed increased energy expenditure due to brown adipose tissue hyperactivity, suggesting that a reduction on PI3K signalling could contribute to decrease metabolic damage. My work uncovered unprecedented functions for Pten, and the conclusions were published in Cell Metabolism. This observation led me to test if PI3K inhibitors could be used to ameliorate metabolic syndrome in obese mice. I found that chronic PI3K inhibition resulted in decreased obesity as a result of reduced adiposity and also ameliorated liver steatosis and decreased glucose serum levels, two of the main features associated with metabolic syndrome. These findings suggest that pharmacological inhibition of PI3K is an effective and safe anti-obesity intervention that could reverse the negative effects of metabolic syndrome in humans. The results of this work were reported in Cell Metabolism, and were accompanied by the development of a patent to use PI3K inhibitors for the treatment of obesity, steatosis and ageing of which I am co-inventor.

To further gain expertise in cancer biology, for my postdoctoral studies, I joined the laboratory of Dr. Hans-Guido Wendel at Memorial Sloan Kettering Cancer Center (MSKCC, NYC). There, I became interested in the implementation of functional genomic approaches to understand the functional role of mutations affecting epigenetic regulators in Follicular Lymphoma (FL), and finding new therapeutic targets. Specifically, I characterized the relevance of genetic alterations affecting the epigenetic regulators KMT2D, CREBBP and EP300 using murine models of FL, and dissecting their downstream effects. Specifically, I found that KMT2D and CREBBP function as tumour suppressor genes and their genetic ablation in B cells promote lymphoma development in mice. These results were published in Nature Medicine and Cancer Discovery respectively and we patented the detection of mutations in KMT2D as an indicator of response to therapy in FL.

In 2016, I joined the laboratory of Dr. Alejo Efeyan at CNIO where I am dissecting the role of enhanced nutrient signalling by activating RagC mutations and their impact in FL. During this time, I have shown that RagC mutations exacerbate B cell responses and accelerates lymphomagenesis in mice, while creating a selective vulnerability to pharmacological inhibition of mTORC1. The conclusions of this work were published in Nature Metabolism in 2019. In addition, I am very interested to explore the connection between nutrient sensing signalling pathway, aging and autoimmune disease.

All the aforementioned experience has strengthened my knowledge of scientific research and management, and I am confident that my expertise in FL pathogenesis and mouse models, in addition to knowledge of nutrient sensing and signalling pathways will help to bring this proposal to a successful end.

#### Resumen del Currículum Vitae:

I am an enthusiastic and innovative scientist with research experience in cancer therapeutics, epigenetic, aging, diabetes and metabolic disease areas.

During my PhD (2006-2012), I worked under the supervision of Dr. Serrano at CNIO. My research focused on understanding the role of tumor suppressor gene PTEN in aging and metabolism. PTEN transgenic mice were protected from cancer, presented a significant lifespan extension and showed increased energy expenditure due to brown adipose tissue hyperactivity. My work uncovered unprecedented functions for Pten, and the conclusions were published in Cell Metabolism (2012). These findings suggested that a reduction on PI3K signaling could contribute to decrease metabolic damage. To address this hypothesis, I treated obese mice with PI3K inhibitors and found that chronic PI3K inhibition did not result in treatment refractoriness or toxic side effects, suggesting that pharmacological inhibition of PI3K is a safe anti-obesity intervention that reverse the negative effects of metabolic syndrome. The work was reported in Cell Metabolism (2015) and was accompanied by a patent to use PI3K inhibitors for the treatment of obesity, steatosis and aging.

As a postdoctoral researcher (2012-2015), I worked at MSKCC studying how epigenetic regulators, the most common targets of somatic mutations in lymphoid cancers, contribute to lymphomagenesis. I characterized the relevance of genetic alterations affecting the epigenetic regulators KMT2D, CREBBP and EP300 using murine models of FL, and dissecting their downstream effects. This work was published in Nat Medicine (2015) and Cancer Discovery (2017) and we patented the detection of mutations in KMT2D as an indicator of response to therapy in FL.



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Currently, I am working at CNIO as a staff scientist, dissecting the role of enhanced nutrient signaling by activating RagC mutations and their impact in Follicular Lymphoma (FL). RagC belongs to the Rag family of GTPases, which form a super-complex on the lysosomal surface promoting nutrient-mediated activation of mTORC1. Towards gaining insight on the relevance of RagC mutations for FL development, progression, and treatment, we engineered novel mouse strains that express patient-derived RagC mutations. Oncogenic RagC mutant mice strongly exacerbate B cell responses and accelerate lymphomagenesis, while creating a selective vulnerability to pharmacological inhibition of mTORC1. The conclusions of this work were published in Nature Metabolism (2019). In addition, I am very interested to explore the connection between nutrient sensing signaling pathway, aging and autoimmune disease.

I would like to highlight my capacity to obtain grants and fellowships during my scientific career. I obtained my own funding during my PhD from Regional Government of Madrid to cover the cost of my salary. Moreover, during my postdoctoral stay at MSKCC and at CNIO I was awarded with Leukemia & Lymphoma Society's Career Development Program Fellowship and Banco Santander Foundation Fellowship respectively. In 2017, I was awarded with Miguel Servet Tipo I grant by ISCIII to cover the cost of my salary and part of the cost of the project. Lastly, I have been awarded with the Health Research grant from ISCIII (AES 2018), Fundación Leucemia y Linfoma and L'OREAL-UNESCO For Women in Science 2018 to further support my research on Lymphoma.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

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#### Título:

Tumor stroma as a therapeutic target

#### Resumen de la Memoria:

My work has implications in different contexts. I worked with vascular smooth muscle cells (VSMCs) in the context of hypertension and atherosclerosis, studying mechanisms of fibrosis (Rodríguez-Vita et al. 2005, Rodríguez-Vita et al. 2005, Rodríguez-Vita et al. 2008). I have worked on Macrophages in the context of tumor biology, studying tumor induced immune evasion (Goossens and Rodríguez-Vita et al. 2019). I have worked on endothelial cells (ECs) in the context of endothelial dysfunction studying endothelial oxidation and damage (Ribera and Rodríguez-Vita et al. 2019); or in the context of tumor biology studying their involvement in tumor metastasis (Wieland and Rodríguez-Vita et al. 2017). The behavior of a particular cell depends on the context in which this cell is. This context-dependent behavior is regulated by many different processes, the main one being cell communication, where most of my work has focused. I have described how tumor cells (TCs) alter the membrane composition of the macrophages, inducing a dysregulation in the signaling pathways transducing inflammatory signaling, and eventually leading to immune suppression (Goossens and Rodríguez-Vita et al. 2019). I have also contributed to show how TCs induce EC senescence, rendering the endothelium more permeable and potentiating metastasis (Wieland and Rodríguez-Vita et al. 2017). These two works are the foundation of my line of research.

I am currently focused on two main cancer context, both of them with a very low survival ratio, ovarian and pancreatic cancer. These tumors have proven extremely difficult to treat because of the high drug resistance occurring during their treatment. I am convinced that stroma is a very useful target for therapy in these cancers. I believe that a better understanding of how TCs modify their stroma could lead to the discovery of novel strategies to improve the life expectancy of patients.

In this regard, one of my projects aims at normalizing the desmoplastic extracellular matrix of pancreatic tumors, to improve vessel tone within these tumors and in turn improve drug delivery.

The other project comes from the characterization of tumor associated macrophages (TAM) in metastatic ovarian cancer. As described above, we obtained information that could lead to the identification of an immunosuppressive subtype of macrophages. We will try to re-educate these macrophages to help with the killing of tumor cells induced by chemotherapy.

Another candidates to explore potential as therapies is hyaluronic acid. We discovered that the secretion of this substance by tumor cells induced a pro-tumor phenotype in TAM in metastatic ovarian cancer, but its implications is relevant in both ovarian and pancreatic cancer. I plan to design tools to block the action of this polysaccharide with different hyaluronic binding proteins as well as targeting its receptor in TAM.

Lastly another line of research stems from the knowledge that ECs can control immune recruitment into tumors (Wieland and Rodríguez-Vita et al. 2007), I plan to understand better the mechanisms regulating this process in order to design tools to specifically modify these mechanisms in ECs by the use of monoclonal antibodies and liposomes containing targeting drugs in a similar way as the one published by the group of Toby Lawrence, who is a close collaborator (Etzerodt et al. JEM 2019)

#### Resumen del Currículum Vitae:

During 6 years, first as a PhD student, and later as an early postdoctoral researcher, I worked in the investigation of cardiovascular diseases from a cellular and molecular level, in the Renal and Vascular Research Laboratory, at the Fundación Jimenez-Díaz in Madrid. Among the most prominent achievements that I got it is the determination of a new pathway in the signaling by Angiotensin II, the SMAD pathway, in vascular smooth muscle cells. We also showed that Endothelin-1 increases the connective tissue growth factor, again in vascular smooth muscle cells, through its receptor ETA. Lastly, we showed how statins (HMG-CoA reductase inhibitors) potentiate TGF-beta responses in Vascular Smooth Muscle Cells, being this factor essential for the actions of this drug. It was a very successful PhD, which translated in the extraordinary award from the school of medicine of the UAM.

I also collaborated in several other projects related to chronic inflammatory diseases, so way I decided to dedicate my first postdoctoral period to expand this other aspect of my research. Thanks to a Marie Curie intraeuropean fellowship, I moved to London and then to Marseille to work under the supervision of Dr. Lawrence at the Barts Institute for Cancer and the CIML respectively. In this period I worked in Cancer associated inflammation. This project consisted in the better understanding of the signaling pathways triggered inside tumor associated macrophages (TAMs), in vitro (cell lines and primary culture) and in vivo (transgenic mice). It was a very complicated project that took a long time to finish and led to a very important publication, where we showed that similarly as statins do on macrophages within the atherosclerotic plaques, TCs deplete cholesterol in macrophages to render them tumor promoting.

After this period I moved to Barcelona with a program partially founded by the European Commission s Marie Curie initiative called Biotrack to work at the IDIBAPS. During those years I worked on different novel strategies to improve vascular dysfunction during liver cirrhosis. We discovered how CeO<sub>2</sub> nanoparticles could be employed to reduce oxidative stress in ECs.



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This career trajectory attracted the attention from Prof. Andreas Fischer at the DKFZ in Heidelberg, who recruited me to expand his group by incorporating an immunologist with expertise in vascular biology to investigate the role of ECs in the recruitment of immune cells to tumors. Among other important milestones, we discovered how tumor cells activate Notch1 pathway in tumor vessels as well as in premetastatic niches in order to facilitate metastasis through the recruitment of neutrophils to both locations.

My career shows that I have brought my expertise to each group in which I have worked, contributing to its expansion in new fields of research. And along the way I have accumulated expertise in many different fields and disease contexts.

My research has mostly focused on cell signaling, but with an eye on its potential clinical applications. I always tried to elucidate the mechanisms by which any specific cell behaves as it does, and how this individual behavior could influence the behavior of the whole individual. First, I studied signaling under physiological and pathological conditions; afterwards, in a condition of pharmaceutical modulation; and finally, inside tumor microenvironment.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

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#### Título:

Precision Medicine in Sleep Apnea

#### Resumen de la Memoria:

After obtaining my degree in Biology (University of Jaen) I carried out my Master in Biomedical Sciences and PhD thesis in Genetics with a competitive pre-doctoral fellowship (FI Generalitat-Catalonia). I received postdoctoral training at the University of Chicago, CIBERES, and IRBLleida. I was given a postdoctoral position (AGAUR Program) at the University of Chicago (supervisor Prof. David Gozal). During my postdoctoral training at the University of Chicago, I pioneered the first technology (HIPARCO-score) for personalized management of sleep apnea and resistant hypertension (patent in the process of being licensed, and award-winning; CaixaImpulse Program, EIT MedHealth). I have consecutively received funding as Principal Investigator in competitive calls (a total amount of 662,443 in 12 projects) (i.e. FIS; Spanish Health Ministry) including a very relevant agreement with La Caixa Foundation for HIPARCO-score development (187,000 )(pilot project for CaixaImpulse Consolidate).

My main interest in research is to characterize chronic diseases and the development of precision medicine tools for a cost-effective and personalized management. My research activity has produced 94 publications (14 first author, 20 corresponding author, 1637 Citations. H-Index; 19) (3 The Lancet Respiratory Medicine, 2 JAMA, 3 AJCCM, 1 JACC, 1 EurHeartJ, 9 ERJ, top journals in Medicine, Respiratory Medicine and Cardiology), 3 co-directed Doctoral Theses (4 in progress) and 1526 University teaching hours. I have received 4 awards. I have participated as invited speaker in 19 international (including keynote lectures) and 14 national lectures. I have participated in 3 European Horizon 2020 projects. I am member of 4 international Scientific Boards and 4 at national level. 1 spin-off (Onira Research). I am accredited to the teaching by ANECA (PhD Assistant Lecturer, PhD Lecturer) and AQU (Lecturer and Associate Professor).

Currently, I am Deputy Director at IRBLleida, National Coordinator of the Sleep Research Program, and Principal Investigator of the Precision Medicine in Chronic Diseases research group at IRBLleida (<http://www.irblleida.org/en/research/40/precision-medicine-in-chronic-diseases-group>).

#### Resumen del Currículum Vitae:

Manuel Sánchez (Jaén, 1980) has a degree in Biology from the University of Jaén (2003). He completed his PhD at the University of Lleida in 2007. He has completed postdoctoral training at the University of Chicago, Centro de Investigación Biomédica en Red (CIBERES, Public Research Consortium from Instituto de Salud Carlos III) and Institut de Recerca Biomèdica de Lleida (Biomedical Research Institute, IRBLleida). During his postdoctoral fellowship at the University of Chicago, Manuel Sánchez pioneered the first technology (HIPARCO-score) for personalized management of sleep apnea and resistant hypertension (granted patent and award-winning; with the prestigious program "CaixaImpulse Program for Technology Development" and EIT MedTech). He is cofounder of Onira Research SL (Spin-off IRBLleida). Since 2009 and up to the present, he has accumulated a total of 1526 teaching hours in the Area of Genetics. He is accredited for teaching by the Agencia Nacional de Evaluación y Prospectiva (ANECA; National Agency for the Evaluation of Quality and Accreditation) (PhD assistant Lecturer, PhD Lecturer) and Agència de Qualitat del Sistema Universitari (AQU; Agency for Quality of the University System of Catalonia) (Lecturer and Associate Professor). Manuel Sánchez is the author of 94 original publications (51 in 1st Quartile, 26 in 1st Decile) (14 as First Author. Citations: 1637). His H-Index is 19. He is an independent and consolidated principal investigator (20 publications as Corresponding Author), with several research projects funded in competitive calls (12 as Principal Investigator), with recognition international level (19 conferences by invitation) and at national (17 conferences by invitation). He has co-directed 3 Doctoral Theses and 6 Master Theses. He currently directs 4 Doctoral Theses. He is a research collaborator on 3 projects funded by the European Horizon 2020 program. He has participated in more than 120 communications to congresses and has received 4 awards: "Young Research Award. American Thoracic Society 2016". "Il Astra Zeneca Young Investigators Awards 2016" "Young Award, Sociedad Española de Neumología 2016" "Best Original Publication 2016. Sociedad Española de Sueño". He is Junior Editor of the European Respiratory Journal and ad hoc reviewer of other 22 international journals. He is a scientific reviewer of ANEP (Official agency for evaluation of research projects in Spain), Spanish FIS (Spanish Health Ministry), Fundación Progreso y Salud (Junta Andalucía, Spain), Castilla y León Government (Spain), Sociedad Española de Neumología (SEPAR), Societat Catalana de Neumologia (SOCAP). He is Secretary of the Programa Integrado de Investigación of SEPAR (scientific research program of SEPAR), Program Committee Member of the Publication Policy Committee of the American Thoracic Society (ATS), Program Committee Member of the Assembly on Sleep & Respiratory Neurobiology from ATS, Member of the Continuing Professional Development of the European Respiratory Society, and member of the International Collaboration On Sleep Apnea Cardiovascular Trialists (INCOSACT). He is a member of 8 scientific societies. Manuel Sánchez is the National Coordinator of the Sleep Research Program, Principal Investigator at IRBLleida, and Deputy Director of the IRBLleida (Accredited Institute by the Instituto de Salud Carlos III, Spain).



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

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#### Título:

Cancer immunogenomics

#### Resumen de la Memoria:

I did my PhD in Bioinformatics in Barcelona (2013), with Ana Maria Rojas, where I worked on how mutations associated to different diseases also have different molecular properties. Then, I moved to San Diego, USA, to join Adam Godzik's laboratory (2013-2017). There, I focused my initial research on the identification of cancer driver protein regions. I developed e-Driver, an algorithm that finds protein regions (domains or interaction interfaces) enriched in cancer somatic mutations. Using data from The Cancer Genome Atlas I found novel regions that had not been previously linked to cancer. My results have also given novel insights into well-established cancer-driver genes, such as TP53 or EGFR.

We also applied this sub-gene analysis to identify novel drug biomarkers. I analyzed data from the Cancer Cell Line Encyclopedia (CCLE), a database with the genomic data of 500 cancer cell lines and their sensitivity to 24 drugs. My domain-centric analysis found 405 protein domains associated with differences in drug sensitivity. As a result, we created a spin-off company, Genrix, that aimed to help drug companies find biomarkers for their drugs.

I have also worked in cancer immunology. It is now clear that cancer cells need to avoid the immune system in order to survive, and therapies aimed at restoring the immune response against cancer cells are transforming cancer care in a way that was unimaginable only a few years ago. I discovered over 100 protein regions that, when mutated, correlate with the presence of lymphocytes in the tumor micro-environment.

This last example highlights the core values of my research: ethical and scientific integrity, maximize its impact in society and collaborate with others to achieve a greater goal. For example, to ensure the transparency and reproducibility of my research, all the algorithms that I created are posted on my Github account. This also helps to maximize their impact, since they can be used by other researchers for their own projects.

Another example is my recent role as lead analyst of the TCGA PanCancer Atlas project. This consortium put together over 1000 scientists in more than 20 countries to jointly analyze the entire TCGA dataset. As a member of the oncogenic processes, driver genes and pan-immunity analysis working groups, I have had the opportunity and privilege to contribute my expertise to this community and help to discover new subtypes of cancer immune responses, expand the catalogue of cancer driver genes and how germline variations predispose to different cancer types.

During the last two years I have been working with Alfonso Valencia at the Barcelona Supercomputing Center. There, I focused my efforts on the integration of multiple types of omics data to understand how they contribute to oncogenesis together, instead of individually. I also obtained a La Caixa Junior Leader Fellowship that funded me and a PhD student.

Finally, since November 2019, I have accepted a position as Junior Group Leader of the Cancer Immunogenomics Group. This group will be a joint project between the Josep Carreras Leukaemia Research Institute and the Barcelona Supercomputing Center. It will focus on the integration of germline genetics, somatic mutations and the immune response against tumors, to understand cancer predisposition and oncogenic processes driving the development of this disease.

#### Resumen del Currículum Vitae:

I obtained my PhD in Biomedicine in 2013 at Universitat de Barcelona. Immediately after, I joined Adam Godzik's Laboratory at SBP Medical Discovery (San Diego, USA), where I was tasked with establishing a completely new research line at the interface between cancer genomics and structural biology. As a result of this new research line, during my four years in his laboratory I:

- Published 7 papers as first / co-first author in journals focused either on bioinformatics (Nature Methods, PLoS Computational Biology, Bioinformatics), genomics (Nucleic Acids Research) or cancer (Cancer Immunology Research)
- Published a patent (Application number 15029676)
- Created a company, Genrix, to exploit such patent
- Supervised one college student and one high-school student ([https://hsrc.himmelfarb.gwu.edu/gw\\_research\\_days/2017/SMHS/81/](https://hsrc.himmelfarb.gwu.edu/gw_research_days/2017/SMHS/81/))



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- Joined The Cancer Genome Atlas PanCanAtlas project

After these four years in the USA, I joined Alfonso Valencia's laboratory at the Barcelona Supercomputing Center (Barcelona, Spain) in May 2017 to lead the line research in cancer genomics. There, over the last two and a half years, I have:

- Obtained a Beatriu de Pinos postdoctoral fellowship with a project that I wrote on my own (96.000 euros)
- Obtained a La Caixa Junior Leader fellowship with a project that I wrote on my own (295.200 euros)
- Published 2 papers as co-first author in Cell (one of them was the cover)
- Published 3 papers as contributing author in Immunity, Nucleic Acids Research and Cell Reports
- Supervised two PhD students
- Been invited by The Society of Immunotherapy of Cancer (SITC) to present my work at their last Cancer Immune Responsiveness Workshop in Houston (September 4-5, 2019)

Finally, since November 2019, I have accepted a position as Junior Group Leader of the Cancer Immunogenomics Group. This group will be a joint project between the Josep Carreras Leukaemia Research Institute and the Barcelona Supercomputing Center.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

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#### Título:

Dissecting epigenetic and epitranscriptomic regulation of ageing and age-associated disorders

#### Resumen de la Memoria:

Throughout my career I have been interested in understanding how transcriptional and epigenetic networks collaborate in cell fate decisions, and their critical relevance both in mammalian development and in age-related disorders. During my PhD I investigated how the protein Zfp42/Rex1 contributes to pluripotent cell identity. This allowed me to discover a novel function for this transcription factor in regulating endogenous retroviruses (ERVs) whose deregulation has been linked to cancer and ageing. As a result of my PhD, I published 4 papers, including a first author paper in the prestigious journal *Nucleic Acids Research*.

Afterwards, I was committed to pursue a successful research career in the Stem Cell field, where the pluripotent cells represent the paradigm of a youthful cellular age. Thus, I joined the laboratory of Dr. Wang, at Mount Sinai where I was able to use and develop cut-edge proteomic and epitranscriptomic technologies. Significantly, I uncovered an unexpected new mode of action of the DNA epigenetic modifier TET2, showing that this enzyme also participates in RNA epigenetics through m5C oxidation. Given that TET2 is widely known for its function not only in pluripotency but also in hematopoietic diseases, this novel finding opens new avenues for revisiting the molecular mechanisms and potential treatments in several age-related disorders (e.g. cancer) where aberrant TET2 function has been established. Besides of being published in a top ranked journal (Guallar et al, *Nature Genetics* 2018), this work has already granted me several awards and invitations as a speaker in prestigious international conferences.

In 2017, I was able to come back to Spain to the Center for Research in Molecular Medicine and Chronic Diseases (CiMUS) at the University of Santiago de Compostela (USC) thanks to a competitive Campus Vida s International Postdoctoral Program Award. Hosted at the laboratory of Dr. Miguel González-Blanco, with wide expertise in DNA damage repair in *S. cerevisiae*, I consolidated my training and started my emancipation by establishing a new research line on DNA/RNA epigenetics implication in several age-related hallmarks (i.e. DNA damage, DNA methylation) in mammalian cells. The resulting paper will be submitted for publication soon. In parallel, I continued my work on RNA A-to-I editing during iPSC generation by somatic cell reprogramming in collaboration with Dr. Wang and Dr. Fidalgo (CiMUS). As a result, we have a manuscript where I am the co-first and co-corresponding author, under 2nd revision in *Cell Stem Cell*. Since 2019, I obtained a RETOS-JIN grant as a Principal Investigator. Now, taking advantage of my previous experience, my work is focussed in studying the implications of Epitranscriptomics in Ageing and cellular rejuvenation by somatic cell reprogramming.

In summary, during these years I have secured my own funding, including the 2018 RETOS-JIN grant awarded as a Principal Investigator, I have led research lines and projects and gained experience in mentoring MSc, BSc and now also PhD students. I am convinced that been awarded with a Ramón y Cajal grant will be the crucial for continuing my independent scientific career in Epitranscriptomics, Pluripotency and Ageing and putting myself at the forefront of this exciting field of knowledge.

#### Resumen del Currículum Vitae:

I became passionate about scientific research while in my BSc in Biochemistry, when I had the opportunity to spend time in different laboratories both at Universities (BIFI and Univ. of Zaragoza, and Gelsenkirchen Fachhochschule) and public research centres (Cajal Institute, CSIC). Then, I decided to start my PhD in embryonic stem cells, in the laboratory of Dr. Schoorlemmer (Univ. of Zaragoza), where I was able to dissect novel players involved in the regulation of endogenous retroviruses, whose expression is deregulated during ageing. This resulted in the publication of 4 papers, including a first author paper in *Nucleic Acids Research*. Afterwards, I joined the newly created laboratory of Dr. Wang, at Mount Sinai Hospital, in New York to expand my expertise in epigenetic and proteomic approaches to study cell fate specification in pluripotent cells and during somatic cell reprogramming. There, I set up a new research line in RNA-binding proteins and RNA modifications which has now been followed up by several PhD students in Dr. Wang's lab. During this time, I used and developed cut-edge proteomic and epitranscriptomic technologies and I uncovered an unexpected new mode of action of the DNA epigenetic modifier TET2 on RNA epigenetics through m5C oxidation (Guallar et al., *Nature Genetics* 2018). This work has already granted me several awards (e.g. Young Investigator Competition Award, MINDICH Inst., NY; Best Poster Award, Hydra) and invitations as a speaker in prestigious conferences (e.g. ISSCR 2017, EMBO RNA meeting 2018). Moreover, not only have these findings granted my mentor with competitive grants from the NIH, but also has allowed me to recently start close collaborations with the top experts in the RNA epitranscriptomic field as a part of the European Epitranscriptomic (Epitrans) COST Action.

In 2017 I decided to return to Spain after being awarded with a competitive Campus Vida s International Postdoctoral Program, where I consolidated my training and started my emancipation by establishing a new research line on DNA/RNA epigenetics implication in several age-related hallmarks (i.e. DNA damage) in mammal cells, at the laboratory of Dr. González-Blanco (CiMUS). The resulting paper will be submitted for publication soon. In parallel, I continued in collaboration with Dr. Wang and Dr. Fidalgo (CiMUS) the study of RNA A-to-I editing implications in pluripotency acquisition by somatic cell reprogramming. As a result, we have a manuscript under 2nd revision in *Cell*





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Stem Cell, where I am the co-first and co-corresponding author.

Last year I was able to obtain one of the few RETOS-JIN grants as a Principal Investigator to lead my own project in hm5C modification of RNA during ageing. In the frame of this project, I am supervising a team which includes two PhD students and three undergraduate students (two BSc and one MSc students). Up to date, I have published 17 articles, most of them in the best top-ranked journals (Nature Genetics, Cell Stem Cell, Cell Reports, eLife, Nucleic Acids Research, ) both as first author and co-author, and two papers as co-corresponding which are currently under 2nd revision (Cell Stem Cell and Life Science Alliance). In summary, my research has contributed to moving forward the current knowledge on transcriptional and post-transcriptional regulation of cellular identity and plasticity in mammalian cells.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

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**Título:**

Computational analysis of chromatin regulatory genes role in cancer

**Resumen de la Memoria:**

Chromatin regulatory genes, including chromatin and histone modifiers, are key players in cancer development. As an example, members of SWI/SNF complex have a mutation frequency (as a complex) ~20%, similar to TP53. My main research topic is to investigate the role of chromatin regulatory genes in cancer progression, invasion and drug resistance using computational approaches, by integrating several layers of (epi) genetic data. I have extensive experience in developing algorithms of data integration and analyzing different multi-omic datasets.

During my postdoc at Stanford University I lead the discovery of how chromatin regulatory genes modify the sensitivity to anthracyclines in early stage breast cancer, by modifying the accessibility of TOP2A to the DNA (recently published in Nature Medicine). The development of a gene expression signature using this set of genes will allow to identify which woman will benefit of this therapy. This has very important implications: first, 6 months of adjuvant anthracycline-based chemotherapy reduces the annual breast cancer death rate by 38% for women younger than 50 years and 20% for women aged 50 to 69 years, so the identification of the woman resistant to this therapy could improve these percentages, and second, anthracyclines are highly toxic (related with cardiotoxicity and risk of secondary malignancies), so the identification of resistant women will avoid to expose these women to serious secondary effects.

**Resumen del Currículum Vitae:**

I was originally trained as computer scientist (BSc, MSc) and in 2012 I obtained my PhD in Computer Science from the University of A Coruña, which was awarded as Special Award in the categories for Computer Science and Mathematics from the Universidade da Coruña. After that I moved to University of Bristol in UK in order to improve my international experience and to acquire new skills in bioinformatics, genetics, genomic, epidemiology and systems biology. The focus of my research was the development of biomedical data integration strategies in order to correlate omics data and phenotypes. During this postdoc, I publish as first author my results in the two most important bioinformatics journals, Bioinformatics and PLoS Computational Biology. During this stage I got interested in cancer biology and epigenetics, so in 2014 I moved to US for a second postdoc at Stanford University. In my second postdoc my research topic was to investigate the role of chromatin regulatory genes in cancer progression, invasion and drug resistance combining different layers of (epi) genetic data. I was funded by the Susan G. Komen Foundation to find the role of chromatin regulatory genes in anthracycline resistance. The results of this project are reflected in my first author paper recently published Nature Medicine. I was also part of The Cancer Genomic Atlas analyst for the esophageal, gastrointestinal and ATAC-Seq working groups. My publication record during my second postdoc includes papers in Nature (x3), Science, Cancer Cell (x2), Nature Genetics (x2) or JAMA Oncology.

Total journal publications with Impact Factor: 30, 22 in Q1 (73%), 14 in D1 (46%). 24 conference papers, 9 book chapter and one technical report.

Accumulated impact factor 392.672. Total citations 1321 according Google Scholar, 1044 according Scopus. H-Index of 19 (Google Scholar), 15 (Scopus)

Participated in a total of 25 research grants or fellowships, 3 of them as PI. 12 patents or software registries, one of them licensed



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** BRAMINI , MATTIA  
**Referencia:** RYC2019-027692-I  
**Área Temática:** **Biomedicina**  
**Correo Electrónico:** mbramini@ugr.es

#### Título:

Micro-CAST: nano-magnetic tools to foster and guide neural regeneration

#### Resumen de la Memoria:

Material Science researchers are increasingly getting involved in biomedical research and interdisciplinary skills are becoming a real need and an asset for scientists who want to work in the evolving field of biomedicine. Starting with my PhD training and then as a post-doctoral researcher I had the major opportunity to merge material science, and in particular nanotechnology, with biological sciences, focusing on neuro-nanotechnological applications for brain disorders. I have an extremely interdisciplinary background that range from chemical biology to molecular and cellular biology, physical chemistry and tissue engineering. I was able to exploit these subjects to focus on the application and characterization of innovative smart-material neuronal interfaces. In particular, during my PhD studies, I explored the biological effects of a variety of nanoparticles with a human in vitro model of blood-brain barrier (BBB). I focused on: (i) developing the blood brain barrier model and (ii) use it to assess whether engineered nanoparticles could cross the BBB and potentially reach the brain. In this project, I developed advanced live fluorescence microscopy methods to determine the mechanism of nanoparticle crossing the BBB in order to engineer innovative drug-delivery nanotools to tackle neurodegenerative pathologies. During the post-doctoral experience I then focused my attention to nanotechnological strategies for neuronal regeneration within the central nervous system (CNS). I have been working with graphene-related materials, 2D and 3D conductive scaffolds and photosensitive polymeric nanoparticles exposed to primary neurons and astrocytes, as well as brain slices and in vivo animal models. The main goal of my research has always been direct toward the application of new technologies for neurodegenerative disorder treatments, including the restoration of neuronal communication upon lesion/damage. By exploiting the conductive properties of graphene, I managed to describe and characterize the altered synaptic activity in neuron-astrocyte co-cultures and promisingly adopt such material for the treatment of focal epilepsy. From the 2D and 3D scaffold research, neuronal signaling was enhanced and amplified, making these tools of extreme interest in case of compromised neuronal network signalling. Finally, the use of photosensitive molecules as well as polymeric nanoparticles has been successfully investigated in the field of retina disorders (Retinitis Pigmentosa and Age-Related macular Degeneration) both in vitro and in vivo. This latest work has been of great success since we were able to restore vision in blind animals. I am now working on a new project based on ferro-fluid solutions for axonal regeneration. The idea is to create an injectable liquid prosthesis and by the use of an external magnetic field trigger the axonal re-growth. In summary, my research had been focused on exploring new approaches to improve the current state-of-the art biomedical devices for neuronal/cellular regeneration and drug-delivery to the CNS by minimizing the invasiveness of the medical procedures and increase the efficacy of the treatments.

#### Resumen del Currículum Vitae:

##### EDUCATION

2010-2014: PhD in Bionanointeractions, University College Dublin, Ireland  
2007-2009: MSc in Medical and Pharmaceutical Biotechnology, University of Modena and Reggio Emilia, Italy  
2004-2007: BSc in Biotechnology, University of Modena and Reggio Emilia, Italy

##### RESEARCH EXPERIENCE

2019-present: MSCA-COFUND Athenea3i Researcher, University of Granada, Spain  
2016-2019: Post-Doctoral Researcher, Center for Synaptic Neuroscience and Technology, Istituto Italiano di Tecnologia (IIT), Genova, Italy  
2014-2016: Post-Doctoral Researcher, Neuroscience and Brain Technologies Dept., IIT, Genova, Italy

##### MAIN RESEARCH ACTIVITIES:

23 publications in peer-reviewed journals, including 1 Nature Nanotechnology (IF: 33.4), 2 ACS Nano (1st author, IF: 13.9), 1 Nano Letters (1st and corresponding author, IF: 12.3), 1 Small (1st and corresponding author, IF: 10.9); total time cited > 550 (no self-citations)

h-index: 12 (from WoS); i10-index: 14

Total IF: 157.63 &#61664; IF per document on journals: 7.51

2 book chapters

Oral Contributions: (i) 5 invited seminars; (ii) 4 invited talks at international conferences; (iii) 7 selected talks after peer-review at international conferences

Projects: Direct involvement in 6 European Projects (NeuroNano, NanoTransKinetics and NeuroScaffold (FP7), Graphene Flagship (H2020); Graphtivity (ERA-NET H2020) and EuroNanoMedIII (ERA-NET H2020 COFUND)); 2 Italian projects (Spinal injury: towards the development of cell-instructive scaffolds for nerve tissue repair (PRIN-MIUR) and NANOSPARKS)



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

Grants: (i) MSCA-COFUND Athenea3i - 2019 (no. 754446): MAG-NEUROREG, Universidad de Granada); (ii) EuroNanoMedIII (no. 723770) ERA-NET Cofund scheme of H2020: collaborator (2019); (iii) Joint International Projects of Particular Interests (Italy-Korea; no. PGR00820): collaborator 2018; (iv) EpitopeMap (no. 2828), European Science Foundation (ESF) 2010 12 weeks

Awards: (i) European Materials Research Society Young Scientist Award in recognition of the outstanding oral contribution, E-Mrs Spring Meeting (Nice, France, 2011); (ii) Best oral presentation award at the Irish Cytometry Society meeting (Galway, Ireland, 2012); (iii) Best oral presentation at the Dublin Chemistry Graduate Programme (Dublin, Ireland, 2013); (iv) 9th Nanotox 2018 outstanding oral contribution (Neuss, Germany, 2018)

#### EDITORIAL and REFEREE ACTIVITIES

Editorial Board Member: The Graphene Technology journal (Springer Nature); Biology (MDPI)

Reviewer for: ACS Nano, ACS Omega; 2D Materials, Biomedical Physics & Engineering Express; Nanoscale, RCS Advances; Carbon, Chemosphere, Synthetic Metals; Nanomedicine

#### TEACHING and SUPERVISION

Supervision: 2 Bachelor students (Giulia Borgonovo, Omar Varvicchio); 2 Master students (Alice Podestà, Emanuele Giordano); 2 PhD students (Martina Chiacchiaretta, Eleonora Centonze),

Teaching: (i) PhD-course of 3 CFU for the Doctoral School in Neuroscience, University of Genova, Italy (2016-2019); (ii) Class for the Bachelor Degree in Biomedical Sciences (IANUA-ISSUGE, University of Genova, Italy) (2019); (iii) Class for the Degree in Medicine (University of Genova, Italy) (2019); (iv) Lecturer at the Core Technology Summer School 2013, (Flow-Cytometry: Principles and Practice), University College Dublin, Ireland, (2013); (v) 284 hours of tutoring in Experimental Chemistry, University College of Dublin, Ireland (2010-2013)



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** MERINO RIBAS, JORDI  
**Referencia:** RYC2019-028423-I  
**Área Temática:** **Biomedicina**  
**Correo Electrónico:** jmerino@mgh.harvard.edu

#### Título:

Towards precision approaches for the prevention and treatment of obesity and diabetes

#### Resumen de la Memoria:

**Personal Statement:** I am a Research Associate at the Center for Genomic Medicine, Massachusetts General Hospital and Instructor in Medicine at Harvard Medical School. My research interests span nutrition, metabolism, and genomics, all aimed at elucidating molecular mechanisms underlying the development of obesity, type 2 diabetes and related metabolic complications to drive innovation in clinical care and improve public health

**Contributions to Science:** My initial studies as a Ph.D. student, corroborated the hypothesis that atherosclerosis progression can be delayed by implementing healthy lifestyle behaviors and identified oxidative stress and inflammation markers as key molecular features linking endothelial dysfunction and healthy lifestyle. Upon completing my PhD and clinical training, I was fascinated by the potential of genomics to improve our understanding of the mechanisms responsible for metabolic diseases, and to use this knowledge to develop more effective clinical strategies. I have applied advanced computational methods to quantify the interplay between environmental and genetic factors on the risk of diabetes and related metabolic complications, and to identify molecular mechanisms underlying how people interact with and respond to foods.

**Career Goal:** My career goal is to lead an innovative translational research program dedicated to unravel mechanisms underlying variable progression to obesity and type 2 diabetes. In doing so, I expect to integrate a wealth of high-throughput molecular and environmental data using state-of-the-art computational methods to: a) help provide a more refined understanding of dysglycemia, both by dissecting its heterogeneity and by illuminating mechanistic pathways to identify susceptible individuals; b) contribute to advance the era of precision medicine in which the integration of multiple data points across orthogonal axes of biological and environmental information will guide actionable preventive and therapeutic strategies that benefit subpopulations more efficiently; and c) combine core quantitative disciplines and health-related behaviors with the goal of leveraging data and methods that will inform practice and policy.

My multidisciplinary background and knowledge-base will be crucial when applying for international projects and will position me well for my path towards independence in the near future. My PhD training with well-known endocrinologists and cardiologists in Spain and my five years of postdoctoral training in the outstanding environment of Massachusetts General Hospital and Harvard University, make the applicant an excellent candidate to lead the future generation of research leaders in Spain.

#### Resumen del Currículum Vitae:

**Education and current position:** I obtained my bachelor's and Master's degrees in Nutrition and Metabolism from the Rovira i Virgili University (2005-2008) and Barcelona University (2008-2010), where I placed in the top 5% of my class. I completed productive Ph.D. training with Prof. Masana at Rovira i Virgili University (2010-2013). My doctoral dissertation on the effect of lifestyle interventions on subclinical atherosclerosis earned the top grade (Excellent cum laude) and led to the publication of seven first-authored publications in top-ranked journals from the Q1. Following my Ph.D., I completed clinical training at Sant Joan Hospital, Reus (2013-2015). Since 2015, I have been conducting my postdoctoral research on genomics and diabetes at the Center for Genomic Medicine, Massachusetts General Hospital under the supervision of Dr. Florez. In 2018 I was promoted to Research Associate at Massachusetts General Hospital, a position I currently hold. I also hold a position of Instructor in Medicine at Harvard Medical School.

**Research and leadership:** My research activities have resulted in a total of 42 peer-reviewed articles (94% of them published in top-ranked journals from the Q1). I am the first author of 22 peer-reviewed articles and the senior author of 4 publications, and my work has been cited ~600 times (h-index = 14). My publications have been published in prestigious journals of high impact factor including: Nature Medicine, The British Medical Journal, Diabetes Care, or Molecular Psychiatry among others. I have also co-authored 2 book chapters and presented my research at >20 national and international conferences and research seminars. My diligence, collegial work ethic and initiative has earned me a very active leadership role in the CHARGE Consortium (Cohorts for Heart and Aging Research in Genomic Epidemiology), where I co-lead the Nutrition Working Group. I have shown myself capable of securing extramural funding from a diverse and rich portfolio of funding agencies, including funding from the European Commission through the prestigious Marie Skłodowska-Curie Fellowship. I am now the PI of a recall-by-genotype study to better understand molecular mechanisms leading to higher food reward stimulation or impaired satiety perception with the support of a joint award from NORCH (Nutrition and Obesity Research Center in Harvard) and BADERC (Boston Area Diabetes Endocrinology Research Center). In addition, I am one of the recipients of the Funds for



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## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

Medical Discovery, a highly competitive funding mechanism at Massachusetts General Hospital designed to conduct research on a problem of direct clinical relevance across all medical domains.

Teaching experience: I have been actively involved in teaching, training, and mentoring activities both in Spain and the United States, including lecturing in the Rovira i Virgili University (2011-2015) and Harvard University since 2015. I have supervised several master theses and co-supervised the scientific work of two Ph.D. students and one clinical fellow. I am currently the co-director of a doctoral thesis.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** MARTINS DA ROSA, JULIANA  
**Referencia:** RYC2019-026870-I  
**Área Temática:** Biomedicina  
**Correo Electrónico:** juli.martins.rosa@gmail.com

#### Título:

Neuronal circuits and Neuron-glia interaction

#### Resumen de la Memoria:

My scientific training has been multidisciplinary and has helped to gain expertise in distinct aspects within the field of the neurobiology. As a Bachelor and Master student in my home country, Brazil, I was trained in pharmacology and neuroscience; wherein I studied the mechanisms of depression and pain. In this period, I published 1 first author and 3 co-author papers. I then moved to Spain to take my PhD at the Universidad Autónoma de Madrid (supervisors: Dr. Antonio G. Garcia and Dr. Luis Gandía), by which I was the recipient of a FPU fellowship. By studying the cellular mechanisms related to changes in neurotransmission I accomplished my 1st major scientific achievement. I demonstrated, for the first time, a functional coupling between endocytosis and L-type calcium channels, leading to 5 papers as 1st author and 2 prizes in Scientific Meetings. This coupling had crucial implications in neurodegenerative diseases in which endocytosis is seen to be enhanced as Alzheimer (Rosa et al., 2010). I then moved forward with my scientific interest and obtained from the EU the prestigious Marie Curie Fellowship to join Dr. Leon Lagnado's lab at the University of Cambridge (UK, 2011-13). The Marie-Curie grant shows that I belong to a chosen group of scientists whose potential has been recognized early on by the EU. I then got my second major achievement studying the basis of neuronal circuitry by which different frequency channels are generated in the retina. For that, I first authored a Neuron paper (Rosa et al., 2016) and co-authored another Neuron (Esposti et al 2013). Then, I decided to move to the University of California, Berkeley (2014-16) to join Dr. Feller's lab to increase my expertise in neural circuitry. I then achieved my 3rd major achievement: the discovery of a neuron-glia interaction mediated by glutamate during development, which to a 1st author eLIFE paper (Rosa et al., 2015). My fourth major achievement was also at Berkeley: I revealed the mechanism by which distinct neuronal pathways in the retina interact to modulate motion detection. For that, I authored a J Neuroscience (Rosa et al., 2016). I then had to stop for a while (18 months) my career due to maternal/medical care of my newborn son. After this, I returned to Spain with a Stop Fuga de Cerebros Fellowship to carry out my research at the IIS La Princesa. I then started my own research line focused on the study of microglia-astrocyte interaction in the control of neural circuits and synaptic plasticity in health and disease. As a result, I am have co-authored one paper, I am corresponding/first author on a bioRxiv and have a patent under evaluation. At the beginning of 2018, I was then awarded for the 2nd time with a Marie-Curie Grant. Since August 2018 I am a Principal Investigator at the Hospital Nacional de Paraplégicos (2nd maternal leave from Sep 2018 to Feb 2019). I also obtained in 2018 from a competitive call a grant as Principal Investigator from the Junta de Comunidades de Castilla-La Mancha (Proyectos de Investigación Científica y Transferencia de Tecnología, Convocatoria 2018-2021) and I am on a second phase of evaluation of a Wings for Life Individual Grant as principal investigator.

#### Resumen del Currículum Vitae:

Pharmacy Degree 2002 Universidade do Sul de Santa Catarina, Master Degree 2003-05 Universidade Federal de Santa Catarina (Brazil) studying endogenous modulators of depression 4 papers  
PhD 2005-11 Universidad Autonoma de Madrid FPU fellow. Supervisors: Antonio Garcia, Luis Gandia, studying the biophysical properties of Calcium channels in the regulation of neurotransmission. 7 papers, 1 invited review  
Visiting Scientist 09-12/08 Neuroscience Institute Alicante. FM1-43 dyes for studying endocytosis at neuroendocrine cells. 2 papers, one in Neuron  
Marie Curie Fellow 2011-13 and Research Associate 2013 LMB-MRC, University of Cambridge, UK. Supervisor: Leon Lagnado. Projects: Synaptic transmission at the retina. 2 Neuron papers  
Postdoctoral Researcher 2014-16 University of California, Berkeley, USA Supervisor Marla Feller, studying neuron-glia interaction and direction selectivity in the developing retina. 3 papers J Neurosci 2016, eLife 2015, 1 review Cur Biology 2015  
Principal Investigator 2017-18 IIS La Princesa, Madrid. Homeostatic role of astrocytes in neural circuits and synaptic plasticity after brain injuries. 2 papers (1 as corresponding bioRxiv)  
Principal Investigator (Marie Curie Researcher) 2019- Hospital Nacional de Paraplégicos (HNP). My own line studying 1) cortical synaptic signalling changes associated with astrocytes-microglia interaction after CNS injuries and 2) astrocyte manipulation to restore locomotion and neural function after spinal cord injury.

I am 1st or 2nd author in 15 out of 20 papers in journals like Neuron, J Neurosci, eLife, Cur Biology. My contributions have determined several aspects of neural circuits such as generation of frequency channels (Neuron 2016), synaptic mechanisms for gain control (Neuron 2013), synaptic interactions in motion detection (J Neurosci 2016), mechanisms of neuron-glia interaction during development (eLife 2015) and synaptic cycle (several articles).



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

Since my return to Spain with my own funds, first at the IIS La Princesa and now at the HNP by which I obtained for the SECOND time a Marie Curie Grant, I lead my own line studying the changes that neuronal circuits undergo to burst plasticity after CNS injuries. For that I study how astrocyte and microglia, interact to control neuronal transmission and synaptic plasticity. To undergo my research independently, I obtained in less than two years 3 projects as PI from competitive calls (Horizon2020 MSCA, Junta de Comunidades de Castilla-La Mancha and RochePharma) summing up ~400.000,00 (and with two maternal leaves in between). I am also in a 2nd phase of evaluation of an international 180.000,00 Wings for Life Grant (only ~15% of the applications passed to the 2nd phase). The first results from my independent research line are available on bioRxiv. In addition, I have two more papers from my research at the HNP in preparation to be submitted soon, one as first and corresponding and another as co-first.

In the last RyC call 2018, I was ranked 2nd on the final Reserve List. Given my high-quality publication record, strong sign of independence and leadership and international mobility/network, I do believe I have the perfect profile to be a RyC grantee and to excel in science.

Miscellaneous:

09/18-02/19: Maternal leave

02/16-10/17: Break for maternal and medical care towards my newborn son.





## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** BONAVENTURA MORERA, JORDI

**Referencia:** RYC2019-027371-I

**Área Temática:** Biomedicina

**Correo Electrónico:** jorgh82@gmail.com

**Título:**

Hijacking the brain receptor systems to treat neurological disorders

**Resumen de la Memoria:**

My research spans the areas of molecular pharmacology, molecular imaging, chemical biology, and behavioral and circuit neuroscience. Within these areas, a large portion of my training has been centered around in vitro to in vivo drug target discovery and drug development, including PET radiopharmaceutical development. My current contributions to these areas include the development of novel genetic neurotechnologies, developing PET imaging reporter systems for extending chemogenetic and optogenetic methods to encompass a therapeutic component. The other big focus of my research has been the deconvolution of the precise mechanism of action of psychoactive drugs from a global and integrative perspective (from multiple and complex sites of action to metabolism and pharmacokinetics).

After obtaining my degrees in chemistry (2005) and biochemistry (2006), I carried out my PhD tesis with an FPI predoctoral fellowship (Spanish Ministerio de Educación y Ciencia) in the Molecular Neurobiology lab in the University of Barcelona. My PhD thesis was focused on the role that GPCR dimerization plays in the modulation of dopamine signaling. After finishing my PhD, I joined Dr. Ferré's lab (2013) at the National Institute on Drug Abuse (National Institutes of Health, United States) to continue exploring the effects of receptor dimerization and its relevance in neurobiological disease. During this postdoctoral training I developed new tools to translate the in vitro findings obtained during my PhD to in vivo animal models.

In 2017, I joined Dr. Michaelides lab as a senior postdoc initially and later as a Research Fellow (2019) where I combined behavioral neuroscience and molecular neuroimaging to identify the precise mechanism of action of drugs targeting the nervous system. During this time, I have been leading several projects in order to advance vast the current knowledge of circuit neuroscience and precise novel tools to manipulate it into transformative clinical applications. Since longitudinal imaging is a key step for the clinical use of gene therapy one of my main goals has been to develop methods that allow non-invasive tracking of several widely used genetic technologies such as chemogenetics (DREADD, PSAM) and optogenetics (ChannelRhodopsins and others). Some of the methods and drugs developed are patented and being commercialized and used worldwide in rodents and non-human primate models. Although my institute is funded from government intramural funds and hence we are not allowed to obtain public funding through the regular academic sources (NIH, ERC,...) my work advancing chemogenetics and optogenetics supposed the award of several CRADA agreements with companies such as Redpin Therapeutics (a preclinical stage gene therapy company) and Atomwise (an artificial intelligence company).

Additionally, I have been working on elucidating the precise in vivo pharmacology of drugs of abuse, including ketamine, a drug used for several indications including anesthesia, pain, and more recently, depression.

**Resumen del Currículum Vitae:**

After graduating in chemistry (2005) and biochemistry (2006) at the University of Barcelona, I carried out my PhD thesis with an FPI predoctoral fellowship (Spanish Ministerio de Educación y Ciencia) in the University of Barcelona. My PhD thesis was focused on the role that GPCR heteromerization plays in the modulation of dopamine signaling. I published several papers demonstrating the dynamic role of receptor complexes involving the dopamine D2 receptors in the pathology of Parkinson's disease. After finishing my PhD in 2012 I joined Dr. Ferré's lab at the National Institute on Drug Abuse (National Institutes of Health, United States) to continue exploring the effects of receptor dimerization and its relevance in neurobiological disease. I developed new tools (combining microdialysis and optogenetics) to translate the in vitro findings obtained during my PhD to in vivo animal models. This work led to two major publications in PNAS (IF: 9.24 - Bonaventura et al., 2015 -the discovery of the quaternary structure and function of the adenosine A2a-dopamine D2 receptor complex) and Science Advances (IF: 11.51 - Bonaventura et al., 2017 -demonstrating a key role of the dopamine D4 receptor and its polymorphic variants in corticostriatal neurotransmission).

In 2017, I joined Dr. Michaelides lab at NIDA where I combined behavioral neuroscience and molecular neuroimaging to identify the precise mechanism of action of drugs targeting the nervous system. We published a transformative paper on chemogenetics, showing how the effects of the prototypical chemogenetic actuator CNO were actually mediated by converted clozapine (Gomez and Bonaventura et al., Science 2017, IF: 37.2). After identifying this problem, I evolved the chemogenetic field with the generation of better ligands and new imaging tools to non-invasively identify transgene expression (DREADD, PSAM, opsins) in living animals, a key step in non-human primate



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

research and in future therapeutic applications. This work is partially published in two major publications: Bonaventura et al. (Nature Communications 2019, IF: 11.88) and Magnus et al, (Science 2019, IF: 37.2). There are two companies (HelloBio, Tocris) that licensed the patent for the compounds that we created and they are currently commercialized and used world-wide. In addition, I am currently working with other companies through CRADA agreements (Redpin Therapeutics, Atomwise) to bridge the gap between basic science and clinical therapy.

While at NIDA I am also leading a project to create ChRERa (a new opsin that can be tracked using PET), the manuscript is currently in preparation and a patent is being filed, however the presentation of this work in conferences generated such interest that I am starting collaborations with several international non-human primate laboratories to adapt the technology to their needs.

Finally, my broad interest is to understand the mechanism of action of drugs from a global perspective (multiple sites of action, the role of kinetics, state-dependent actions...). My recent work on ketamine (a dissociative anesthetic being used as antidepressant) led to the identification of a novel mechanism of action of ketamine through the opioid system and that allows to separate the antidepressant vs the rewarding effects of the drug opening the door for safer and more effective treatment.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** VILLA BELLOSTA, RICARDO  
**Referencia:** RYC2019-027920-I  
**Área Temática:** Biomedicina  
**Correo Electrónico:** metabol@hotmail.com

#### Título:

Vascular calcification associated with diseases of aging

#### Resumen de la Memoria:

I started my career at the University Zaragoza with a Beca de Colaboración (MINECO, 2005) and a predoctoral grant (Government of Aragon, 2007). My doctoral thesis focused on the role of phosphate transporters in vascular calcification, renal physiology, and toxicokinetics of arsenic. I became a researcher at Emory University School of Medicine in Atlanta (USA), where I studied extracellular pyrophosphate (a potent endogenous inhibitor of calcification) in the aortic wall. In 2012, I joined the Spanish Center for Cardiovascular Research (CNIC, Spain) as a Juan de la Cierva postdoctoral researcher. My work focused on the role of extracellular pyrophosphate metabolism in both atheroma plaque calcification and medial calcification in Hutchinson-Gilford Progeria Syndrome (HGPS) mice. In 2015, I moved to the Fundación Jiménez Díaz University Hospital Health Research Institute (Spain) with an I+D+I Young Researchers fellowship by MINECO as a principal investigator to study the role of extracellular pyrophosphate metabolism on vascular calcification in chronic kidney disease and diabetes. In December 2016, the Progeria Research Foundation (USA) awarded me a grant for a project entitled Therapeutic strategies to recover the normal pyrophosphate homeostasis in HGPS. Finally, in December 2017, the Madrid Community awarded me a predoctoral contract, enabling me to hire a student to perform research in my team.

Overall, pathologic cardiovascular calcification is a frequent complication of aging and of diseases characterized by accelerated aging, such as diabetes and chronic kidney disease. My financed research line focuses on the role of phosphate and pyrophosphate homeostasis in vascular calcification associated with these diseases of aging. I have received grants from MINECO, which supports my studies in diabetes and hemodialysis; and from the Progeria Research Foundation (USA), which supports my studies in a mouse model of accelerated aging.

#### Resumen del Currículum Vitae:

I have a degree in Biochemistry (2005) and PhD (2010) by Zaragoza University (Spain). According with my scientific evaluation from the ISI web of knowledge I have been cited 1013 times by 664 documents with an H-index of 15. During my scientific research career since a PhD student (2007-present), I have co-authored a total of 51 scientific publications mainly related to phosphate and pyrophosphate homeostasis in vascular calcification, including the following: a) 8 as only author (including PNAS, A.T.V.B, Aging and Kidney International). b) 12 as first and corresponding author, c) 14 as first author, and d) 6 as corresponding author.

I have presented my work at multiple national and international meetings (>40), obtaining a prize For an outstanding poster representing innovative basic science and an important contribution to the field of progeria research (PRF meeting, 2013). I have been an invited speaker in prestigious institutions and meeting including Karolinska Intitutet (2016), 8 European Crystal Network (2017), 6 Symposium Updates in Dialysis (2018), 9 Progeria Research Foundation Meeting (2018) and FIIS-FJS (2015, 2016, 2017, 2018). I have worker as researcher in several different I+D+I research laboratories. My research work as PI is funded by a Progeria Research Foundation (USA) project grant, by an I+D+I Younger Research (MINECO, Spain) project grant and by a Madrid community predoctoral contract. During my scientific career I have also been involved in 11 competitive projects.

I have received several competitive fellowships, including Beca de Colaboración from MINECO (2005), Predoctoral fellowships from the government of Aragon (2007-2010), Juan de la Cierva postdoctoral contract from MINECO (2012-2014), and I+D+I Jovenes Investigadores sin vinculación postdoctoral contract (2015-2018). Also, I have received several awards, including the Enrique Coris Research Award (2009), the Spanish Royal Academy of Doctors Award (2011), and the Extraordinary Doctoral Award (2012). As a teaching experience I taught practical classes (240 hours) and I have accumulated more than 1513 hours as supervisor of students and technicians. Moreover, I was accredited by ANECA as assistant professor (2011), professor contratado doctor (2019) and private university professor (2019). I also do work as reviewer for the Agencia Nacional de Evaluación y Prospectiva (ANEP, Spain) and for several biomedical journals.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** ROCA SOLER, FRANCISCO JOSE  
**Referencia:** RYC2019-027799-I  
**Área Temática:** Biomedicina  
**Correo Electrónico:** aq.dreammaster2012@gmail.com

#### Título:

Cell Death at the interface of host-intracellular bacterial pathogens

#### Resumen de la Memoria:

My entire research career has focused on understanding the molecular and cellular logic of infection and inflammation *in vivo*, particularly using the zebrafish model. During my PhD, I worked with marine farmed fish to study immune responses to be used to improve fish farming and then started working with the zebrafish. I focused mainly on the pro-inflammatory cytokine TNF. I identified and cloned gilthead seabream colony-stimulating factor-1 receptor (CSF1R) and Interleukin-8. Subsequently, CSF1R sequence was used to generate an antibody recognizing seabream macrophages, a tool of vital importance for further studies of the immune response in seabream. I also characterized the biological activity of TNF in gilthead seabream and zebrafish, and found that the role of TNF in endothelium pro-inflammatory activation is conserved in fish. Finally, I showed that TNFR1 triggers caspase-8/p53-dependent endothelial cell death in the zebrafish when TNFR2 is downregulated or non-functional. The zebrafish was a model that fascinated me and, during my postdoc, I turned my interests into biomedical research.

I joined the Ramakrishnan lab in Seattle, where I planned to dissect the mechanisms underlying TNF-mediated protection against tuberculosis. Instead, and to my surprise, I found that TNF, when in excess, triggered a highly pathogenic programmed necrosis pathway, so, over the course of three papers published in *Cell*, I went on to determine the mechanism of this susceptibility. After being recruited to Cambridge, I showed that TNF mediates necrosis through a previously undescribed circuit, and this understanding has led me to identify inexpensive, oral drugs that are already used for other conditions. In my next phase, I want to explore the mechanism of select new findings from my pathway, based on what I think are the most important and interesting findings that will truly move the fields of tuberculosis pathogenesis and cell death forward.

Overtime, I have acquired extreme fascination for the complexity of host-pathogen interactions at a molecular level and this disease took me to study cell death. As I was discovering cell death pathways manipulated by mycobacteria, I became broadly interested in how other bacterial pathogens manipulate these pathways to cause disease, including *Salmonella* and *Listeria*.

My research has been delineated over these years and it could be described as focused on cell death and immunometabolism in the context of intracellular bacterial pathogens.

I have built a deep and unparalleled array of zebrafish lines deficient in important effectors of cell death, and engineered transgenic lines expressing genetically encoded fluorescent sensors and reporters to study cell death in real time in live animals. I have thus already established the zebrafish tools and resources I will need during the next stage of my career. I am confident that my research will thrive and that my ambitious goals to significantly advance the fields of cell death and bacterial pathogenesis will be achieved.

#### Resumen del Currículum Vitae:

After graduating in Biology, I did my PhD under the supervision of Dr Victoriano Mulero in the University of Murcia. During my PhD, I focused on the role of the pro-inflammatory cytokine TNF in the immune response of farmed marine fish. I identified/cloned sequences of proteins in animal models whose genome was not sequenced, which helped develop antibodies as important tools to detect different immune factors by IHC and WB. I detailed the role of TNF signaling *in vitro* in fish primary endothelial cells, and *in vivo* in animals challenged with viral and bacterial pathogens. One important discovery from my PhD is under the patent Orally administrable immunostimulant product for aquaculture (co-inventor). After my PhD I was awarded with a Postdoctoral Fellowship to join the laboratory of Lallita Ramakrishnan (University of Washington) and also with the Juan de la Cierva Postdoctoral Fellowship (MICINN) and the XXII Nature Science Postdoctoral Award (Ramon Areces). When my fellowship ended, I was invited to stay in the lab for two more years (48 months total). I found that excess inflammation, in concrete excess TNF, is extremely detrimental for the host in tuberculosis, a disease long thought to be caused by lack of inflammation. As a result, I must highlight that I published a second author *Cell* paper in my second year in the lab, followed by a first author *Cell* paper a year later. After this postdoctoral stay in the US, I was recruited by the Department of Medicine (University of Cambridge) to work in the Molecular Immunity Unit as a Senior Research Associate (60 months total). Working in Cambridge, I have dissected the molecular mechanisms of excess TNF susceptibility in tuberculosis, and have discovered a new programmed necrosis pathway that results from a mitochondrial-lysosomal-endoplasmic reticulum pathogenic circuit. This work resulted in another first/corresponding author *Cell* paper. In addition, I have 1 co-first author paper in *Plos Pathogens*, 1 second author in *Plos One* and 1 second author review in *Immunological Reviews*, plus the publications derived from my PhD: 3 first author papers, 6 collaborative papers and 2 book chapters. H Index: 15; 1446 total citations by 1180 documents (Scopus).

As a consequence of my discoveries, I have been invited to deliver 3 keynote speaker talks at prestigious international meetings and 7 seminars at important Universities and Research Centers. I have presented 12 oral presentations (chosen among submitted abstracts) and



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## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

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18 poster presentations in relevant international meetings. I have participated in 9 research projects/grants. Importantly, I have acquired supervisory/mentoring skills as I have supervised two Erasmus Scholarship students, a student for his M. Phil research project, a medical student research rotation, a Graduation Project and co-supervised two Undergraduate Honors Thesis. I have mentored students for a Bachelor Thesis of Applied Sciences, a MSci in Biochemistry, a Master Thesis in Biology and 2 Mini-project Rotations. I directly trained these students in their lab work, oral presentations and written reports. I am currently co-supervisor for a PhD student (thesis will be defended in 2020). Finally, I have been internal examiner for 1 MRes in Medical Sciences (Infection, Immunity and Inflammation) and external international examiner in the evaluating committee of 3 PhD Thesis.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** DOMINGO CALAP, PILAR  
**Referencia:** RYC2019-028015-I  
**Área Temática:** **Biomedicina**  
**Correo Electrónico:** domingocalap@gmail.com

#### Título:

Phage discovery: Towards new therapies against multidrug-resistant bacteria

#### Resumen de la Memoria:

I am a biologist working in the field of virology from different, complementary approaches, including viral genetics, evolutionary biology, and the biomedical applications of viruses. I obtained my master and PhD degrees from the Universitat de València (UV), both with honors. During my PhD (2008-2012), I investigated the fitness effects of mutations in bacteriophages (the most abundant biological entities on Earth) and the implications for phage evolution. My PhD training was supplemented with internships (2011, 2012) at the CNRS (France), where I studied how HIV-1 produces spontaneous mutations in vitro. I then moved to the Université de Strasbourg for a postdoctoral stay (2013-2016), where I investigated the genetic diversity of human BK polyomavirus in vivo and how this diversity correlates with clinically relevant processes such as viral reactivation and immune escape in patients. After obtaining a permanent position in France (declined), in 2016 I moved back to Spain with a Juan de la Cierva-Incorporación contract at the Instituto de Biología Integrativa de Sistemas (UV-CSIC, 2016-2018), where I further worked on viral immune evasion. There, I started my own research line in the field of phage therapy, a promising treatment strategy against antibiotic-resistant bacteria. This allowed me to combine my expertise in phage biology, evolutionary biology, and biomedicine. My goal is to isolate new phages from the environment and use them to treat pathogenic bacteria. For this, I am establishing new collaborations with medical doctors, which allows me to get direct access to clinical isolates. Currently, I am hired as a senior postdoc contract funded by a European Research Council grant but, in order to secure my own funding, I am applying to several calls for young researchers. As of today, I have published 30 articles, 20 of which as first or last author and 10 as corresponding author.

#### Resumen del Currículum Vitae:

I am a biologist interested in the biomedical implications of viruses. I obtained my biology degree and master in biodiversity at the Universitat de València (UV), both with honors. During my PhD (supervised by Dr. Sanjuán, defended in 2012 at UV with honors), I investigated the fitness effects of mutations in phages, as well as their influence on phage evolution. This work was published in PLoS Genetics, Mol Biol Evol, and J Virol, among other Q1 journals. My PhD training was extended with two internships at the Institut de Biologie Moléculaire et Cellulaire (CNRS, France), where I studied the mutation rate of HIV-1 co-funded by a European Research Council (ERC) Starting Grant (PI: Dr. Sanjuán). This resulted in a co-first authorship in a Nature Comms article. During my PhD (2008-2012), I published nine scientific articles in total, five as first author.

Whereas my PhD was mainly focused on fundamental research topics, my interests shifted towards biomedicine during my postdoc. In 2013, I joined a Laboratoire d'Excellence from the Institut National de la Santé et de la Recherche Médicale (INSERM) at the Centre de Recherche d'Immunologie et Hématologie (Université de Strasbourg). Under the supervision of Dr. Bahram, I started a new research line aimed at characterizing BK polyomavirus genetic diversity and immune escape in kidney transplant recipients, using next-generation sequencing and epitope analysis. During this period, I also established several collaborations with medical doctors and clinical virologists to study polyomavirus genetics and immunity. Overall, this work resulted in 10 publications, most in Q1 journals within the areas of virology, clinical microbiology and biomedicine (PLoS Pathogens, J Am Soc Nephrol, J Clin Microbiol, etc). I was first author in three of these articles, and corresponding author in two.

In 2016, I obtained an INSERM permanent position as Ingénieur de Recherche, but I declined this position to come back to Spain with a Juan de la Cierva Incorporación contract under the supervision of Dr. Sanjuán at the Instituto de Biología Integrativa de Sistemas (UV-CSIC). There, I extended my work on viral pathogenesis and immunity. Using a model rhabdovirus, we showed how virus-virus interactions determine immune evasion both in vitro and in vivo (first-author article in Nature Microbiol, also highlighted in Nature). Currently, I am hired as a senior postdoc funded by an ERC Consolidator Grant.

Recently, I have initiated my own research line on phage therapy, a promising treatment strategy against multi-drug-resistant bacteria. This allows me to combine my expertise in phage biology and biomedicine. Phages are ubiquitous in the environment and immensely diverse, thus making phage discovery a powerful source of new therapies against pathogenic bacteria. Over the last three years, I have published three original research articles, four reviews, and two book chapters on this subject, all as corresponding author. Most of these works are co-authored with my master and degree students. I have recently applied to two grant calls for junior investigators to fund this research line. I am also a member of the Spanish phage network (FAGOMA). Additionally, I have signed transfer agreements and established collaborations with local hospitals, which will allow me to directly explore phage therapy in the clinical setting.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** CEPERUELO MALLAFRE, VICTORIA

**Referencia:** RYC2019-026490-I

**Área Temática:** Biomedicina

**Correo Electrónico:** vceperuelo@gmail.com

#### Título:

Metabolic derangements associated to T2D and obesity. Role of the succinate/SUCNR1 axis in NAFLD.

#### Resumen de la Memoria:

Currently I am a senior researcher working in my own research line on the filed metabolic derangements associated to type 2 diabetes (T2D) and obesity. During my all career, I have performed translational studies, combining clinical and basic research. I have developed a broad skill-set in human, murine and in vitro studies regarding mechanistic pathways involved in adipose tissue metabolism.

In my pre-doctoral period I studied the role of several proteins in metabolic homeostasis both, in peripheral blood and also in adipose tissue, in the context of obesity and T2D.

Later, in my track as junior researcher I take advantage from mechanistic studies by using cellular models of human adipose-derived stem cells, macrophages and adipocytes which improved my skills on mechanistic pathways involved in adipose tissue metabolism. In 2010, I received the Spanish competitive Juan de la Cierva post-doctoral grant (Málaga). In 2014 I was granted with a post-doctoral fellowship from Rovira i Virgili University to work in the Molecular Basis of Obesity and Insulin Resistance Group (Tarragona) that led me to gain advantage in the study of the insulin signalling pathway deepening on molecular mechanisms involved in insulin resistance (IR) and adipocyte metabolism. Later, I obtained a post-doctoral position for a one-year stay funded by Harvard Medical School in Boston. I was working in the same line, focusing on understanding the mechanisms linking obesity with IR and the development of T2D, expanding in other tissues and cell types, such as liver, muscle and immune cells. Furthermore, I started using animal studies as a step in the design of my experimental models. During my all post-doctoral periods I established collaborations with clinical groups to combine basic with clinical research trying to arise and answer relevant questions that impact in the welfare of population.

In December 2016 I was granted as a senior researcher position from CIBERDEM to work in the Diabetes and metabolic associated diseases research group. For the last four years, my responsibilities as a young senior investigator, afford me a great experience to develop and advance an independent research line in the role of the succinate/SUCNR1 axis in the setting of obesity, inflammation and T2D. In this line my recent contributions in the field as a lead author, in three high IF journals, opens a new perspective of succinate as a key player in the active resolution of inflammation associated to obesity (published at The ISME journal 2018 and Nature Immunology 2019) and a biomarker of the T2D remission after bariatric surgery (published at Diabetes Care). Currently, I am PI of an innovative project funded by CIBERDEM and ISCIII, titled Role of the succinate / SUCNR1 axis in the physiopathology of NAFLD. In addition, I am assistant professor at Rovira i Virgili University.

In spite of a career break (maternity leaves in 2017), I have accumulated outstanding scientific records: 36 scientific publications (72.2% Q1, 46.2% D1), 39 works submitted to national or international conferences, Work package leader in national and international projects, teaching, supervision, member of research groups/teams, 4 grants as a post-doctoral or senior researcher, international research stay, 2 patents and reviewer for scientific journals.

#### Resumen del Currículum Vitae:

During my all career, I have been very active researcher publishing several scientific articles. I have 36 publications (72.2% Q1, 46.2% D1), 35 original articles (12 as first author, 33.3% D1, 41.7% Q1 and 25% Q2) and one review article. My average impact factor is 6.2 and my h-index in Web of Science is 19 (average citations per item=16.02; times cited without self citations=814 and citing articles without self citations=736). In addition, scientific dissemination of my research has been presented in several national and international Conferences and Congresses: 17 oral presentations and 22 poster presentations. I have received 4 grants as a post-doctoral and senior researcher (Juan de la Cierva, grant from Rovira i Virgili University and grant from Harvard Medical School as a Post-doctoral Researcher and grant from CIBERDEM as a senior researcher).

Since 2015 I am a Senior Researcher at IISPV, in the Diabetes and metabolic associated diseases research group (DIAMET). It is a remarkable achievement that in these last 5 years I have published 12 original articles, more importantly I have been actively involved as designing, performing, supervising, leading and main author in 6 of them (50%) belong to the Q1 in the field (four of them in the first Decile). I would like to highlight the work that published in a major journal (Nature Immunology). The quality of my publications has grown up remarkably, from an average impact factor of 5.4 in my pre-doctoral and post-doctoral period to 9.2 in my senior researcher period.

Regarding my experience in the project design and management, I contributed as associated investigator in my pre-doctoral period in several national competitive projects funded by Institute of Health Carlos III. In my second post-doctoral position I was work package leader in a project from the Plan Nacional. And I also collaborated in several international competitive projects. Currently, I am PI of an innovative project funded by CIBERDEM and ISCIII and I lead several Work Packages in two national and one international -competitive projects.



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Regarding my teaching/supervision experience, since 2013 I am involved in teaching activities, I have supervised three students, 2 end-of course projects and 1 minor thesis. Currently I am the co-director of a thesis and I am assistant professor at Rovira i Virgili University. In addition, I have established strong and enduring collaborations with several groups from national and international centers. To highlight, I have also experience in generation of industrial and intellectual property (PCT/EP2019/051157, EPO 19382564.3).





## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** TEIJEIRA SANCHEZ, ALVARO

**Referencia:** RYC2019-026406-I

**Área Temática:** Biomedicina

**Correo Electrónico:** ateijeiras@unav.es

#### Título:

Dissecting the spatio temporal dynamics of the immune response to cancer for the identification of new therapeutic approaches

#### Resumen de la Memoria:

My scientific career has been focused in the study of immune cell biology and cancer immunotherapy with a particular focus on the mechanisms of immune cell migration and the use of live-imaging approaches to understand the spatio-temporal dynamics of the immune responses.

I did my PhD work under Drs Rouzaut and Melero supervision on describing mechanisms governing dendritic cell through lymphatic vessels. During my PhD I progressively gained interest in the use of microscopic analysis, which I applied in several collaborations within the lab of Dr Melero.

I performed a 2-year and a half first post doc in ETH in Zurich with Professor Halin where I continued studying leukocyte migration via LVs, but with the use of advanced microscopy techniques as intravital imaging. By direct intravital visualization of LVs, T and dendritic cells we identified new mechanisms governing immune cell migration from the periphery to lymph nodes.

I came back to Spain to Professor Melero's group with two main objectives: first, help in the coordination of PROCROP H2020 european project and second, to progressively start my own line of research focused on the study of mechanisms of immune evasion and the effects immunotherapy by the use of live imaging approaches.

For this purpose, I have developed a unique structure in Spain, gathering experimental tools and models to perform live microscopy analysis in living mice and in human cancer patient's derived material to analyze immune responses to cancer. In pursuing this line of research I recently got a first funded project as a PI from La Caixa Foundation (La Caixa Junior Leader 2018, 300K). The results of the setup of this research structure are starting to get published (First author, Immunity, in press; Senior Co-author, Cancer Cell). During these years I have also authored two publications as correspondent, co-correspondent author (which highlights my leadership position in these projects (CIR 2018,2019) in prof Melero's group studying immunometabolic effects of CD137 activation.

My goal as an independent researcher can be summarized in two-specific aims. First, to apply 4D imaging approaches to further investigate the mechanisms of action of current immunotherapeutic strategies, with the aim of developing new combination therapies, identifying biomarkers and describing undiscovered new mechanisms of co-option of immunity by tumors. My second objective is to design new therapeutic approaches for cancer based on modulation of immune cell migration.

#### Resumen del Currículum Vitae:

Scientific production: 36 indexed publications (plus 5 editorials). 6 as first-/co-first author (Faseb J, JID, Front Immunol, Semin. Immunopath. Cell Rep), 3 as first corresponding/co-corresponding author, (CIR and Immunity(in press)), 1 as co-senior author (Cancer Cell, 2019). 12 papers as second/third author. Co-author in high impact journals (Nature, Cancer discovery, Annals of Oncology, ). General bibliometric indicators: H index 19, 833 citations, 138 citations per year (last 5 years).

Funding and I+D projects:

-Grants: FPU predoctoral fellowship (2009-2012), Swiss federal scholarship for postdoctoral students (2013-2014), Juan de la Cierva Incorporación (2017-2018)

-Projects as PI: La Caixa Junior Leader (2018-now)

-Public funded projects as research team: SAF2017-83267-C2-1-R (2018-now); PROCROP, H2020- 635122(2016-now); CB16/12/00364. (CRI: 2017-2019); PI10/02131 (2011-2013).

-Projects with industrial partners: Experience in supervising research sponsored by the industry (PI, Ignacio Melero). Two projects with Roche Genentech (2017-18, 2017-now), two project with Bristol Myers Squibb (2017-18, 2019-now) and a project with Astra Zeneca (2019-now).

-Teaching and mentoring:

- Co-supervising a PhD Student under an european commission funded ITN consortium (2019-on) a Master student (year 2019) and supervising the bachelor research work of a graduate student.

- Past supervisor of Master student (2014) and undergraduate student (2016)

-Teaching. Assistant in biochemistry grade, UN (240 hour, 2008-12); assistant in medical chemistry, ETH (25 hours, 2015), invited lecturer in Methods in Biochemistry , UN (9 hours, 2019)and Immunoncology Postgrade (UN, 3 hours, 2019).

Others

- 11 abstracts accepted in international conferences and 3 travel grants to attend these meetings.

- Peer reviewer in Immunology/Oncology journals (7 times <https://publons.com/researcher/2102489/alvaro-teijeira/>) and grants



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**AYUDAS RAMÓN Y CAJAL  
CONVOCATORIA 2019**

**Turno de acceso general**

(Foncyt/Argentina).



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** PIVA, MARCO  
**Referencia:** RYC2019-027726-I  
**Área Temática:** Biomedicina  
**Correo Electrónico:** pivamarc1@gmail.com

#### Título:

Mechanisms of cancer progression and therapy resistance at the single cell level

#### Resumen de la Memoria:

I have devoted my scientific career to cancer research and in particular to understand the mechanisms of resistance to treatment. My career has progressed from the study of essential molecular and cellular mechanisms (PhD), up to the integrative analysis of genomic, transcriptomics, cancer biology, and complex cancer models (Postdocs in Spain and USA). Now, as an Assistant Project Scientist I have built logically and coherently on my previous work and expanded into relevant areas of cancer research by incorporating clinical settings in my studies. I am a dynamic scientist that has established long-lasting and successful collaborations in the broad field of cancer research, which will be key for my next scientific endeavor. All these features were essential to build a solid base for my development as an independent researcher.

At this early stage of my career I have a remarkable publication record with a total of 12 research articles (5 as first or co-first author) and one additional article that is under review. My work has 507 citations and has been presented in international meetings. I participated in 7 national & international projects. As a proof of the relevance and recognition of my independent research lines, I am PI in two grants and I was an invited speaker by one research institution.

Importantly, my research expertise would be a great asset for Spanish Research, since I master cutting-edge technologies that are yet to be implemented in the majority of Spanish Research centres. I strongly believe that a 5-year contract will ensure the fulfillment of my long-term research aims and give me the opportunity to continue contributing to scientific excellence in Spain as an independent and mature group leader.

#### Resumen del Currículum Vitae:

During my PhD training (2006-2011) and brief postdoc under the supervision of Dr MdM Vivanco in CicBiogune, Bilbao, Spain, I set out to understand the clinical implications of breast cancer-initiating cells and of resistance mechanisms to tamoxifen treatment. In these 5 years I published two papers as first and co-first author (Piva M, 2014; Gonzalez E., 2014) and other 2 paper as co-author. After I joined Dr Carracedo in CicBiogune and I showed that cancer stem cells (CSC) are responsible of breast cancer initiation and progression and we propose different therapeutic strategy to target CSC in estrogen receptor negative breast cancer subtype (1 paper as first co-author, Martin-Martin N et al, 2016, and 1 paper as co-author). In Dr Carracedo's lab, I also contributed to show role of metabolic rewiring in prostate cancer (2 papers as co-author). This training prompted me to seek postdoctoral training in Dr. Roger Lo's lab at UCLA, as his lab at the time had already made seminal contributions to the development of targeted therapy against melanoma. Training in the Lo Lab and the broader UCLA Melanoma Program has been transformational. Scientifically, I have been productive, being the co-first author on two publications. In my recent publications as co-first author in Cell (2015) and Cancer Discovery (2017) I showed the transcriptomic epigenomic and immune evolution in MAPKi treated melanoma, early on treatment and with acquired resistance. These studies contributed to rationalize combination of MAPKi and checkpoint inhibitors treatment. As a proof of the relevance and recognition of my independent research lines, I am principal investigator in 2 grants. I was also an invited speaker at PICI Center UCLA Annual Meeting.

During my postdoctoral training in UCLA I got to master single cell sequencing strategies, which provides me with a unique set of skills as a cancer researcher that would represent critical added value upon my return to the Spanish research system. My research plan revolves around the capacity to study molecular alterations in tumor cell and in the tumor microenvironment at the single cell level taking advantage of the most cutting-edge technologies.

Over these years, my postdoctoral training in different labs has provided me with the laboratory tools, scientific judgment, a set of PI skills, and professional connections to launch the next phase of my career. Leading these studies, I gained substantial first-hand knowledge of multi-disciplinary (technologist, bioinformatics, animal modeling, clinical sample analysis, etc.) research, which is required to address complex medical problems and derive clinically relevant knowledge.

I plan to join Dr Carracedo lab next year and I intend to progressively establish my independent line of research throughout the 5-year period of the RyC program, in line with my agreement with Dr Carracedo. Importantly, Dr Carracedo will be my mentor to help me gain visibility in the Spanish and European Research network, and to establish local collaborations with clinicians in Basurto, Cruces and Donostia hospitals.

I believe that the next five years as RyC researcher in Dr Carracedo's lab will provide me with the experimental techniques, scientific acumen, collaborative and leadership skills, and professional connections to address this goal and launch the next phase of my career.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** GUIU SAGARRA, JORDI  
**Referencia:** RYC2019-026908-I  
**Área Temática:** **Biomedicina**  
**Correo Electrónico:** jordi.guiu@hotmail.com

#### Título:

Regulation of stemness

#### Resumen de la Memoria:

I have been always interested to understand how tissues are formed and maintained. I believe that unraveling the mechanisms that govern the ability to transition reversibly between cellular states will impact our understanding of tissue homeostasis and empower us with new and exciting opportunities to develop cell-based regenerative medicine treatments. For this reason I decided to study Biology and Biochemistry in Autonomous University of Barcelona. Then, in order to get a more practical and translational view I decided to study a Master in Molecular Biotechnology (University of Barcelona). My scientific interest and commitment to improve quality of life of chronic patients pushed me to start my PhD at IMIM-Hospital del mar in Dr. Anna Bigas and Dr. Lluís Espinosa laboratory.

During my PhD I investigated the role of Notch in embryonic hematopoiesis. Hematopoietic Stem Cells (HSC) emerge from arteries during development. Because Notch is crucial to generate arteries it was unclear whether Notch had a direct role in HSC generation or whether hematopoietic defects in Notch mutants were a secondary effect of impaired arterial development. My work demonstrated that the roles of Notch in arterial and hematopoietic programs are uncoupled and therefore we changed the existing paradigm. Altogether resulted in three first-author publications (1x EMBO J 2008 and 2x Journal of Experimental medicine 2013 and 2014) and I received the award of Best Thesis 2012 by Pompeu Fabra University. This basic research is crucial to develop iPSC/ESC based therapies.

Then I decided to challenge my career shifting to a different research topic, which is the study of the intestinal stem cells (ISC). I performed my postdoctoral training in Dr. Kim B. Jensen laboratory (Copenhagen University) funded by a Marie Curie fellowship (MSCA-IF-2014-EF-656099). I believe that this resolution represented an essential step towards the enhancement of my scientific knowledge, training and professional maturity. For many years, there was the inferred notion that designated fetal cells were destined to become ISCs, using multidisciplinary approaches I demonstrated that prior to birth all intestinal cells (regardless of the cell phenotype and marker expression) are equal and certain cells by serendipity are chosen to become adult stem cells if they are in the right place at the right time. These findings provide a direct link between the observed plasticity of differentiated cells in adult tissue following damage, revealing that stem cell identity is an induced rather than a hardwired property. This work resulted in a first author publication in Nature (2019).

In addition to my research activities, I have actively participated in international meetings invited as speaker, thus establishing an extensive network of collaborators. Moreover, I have participated in a plethora of outreach activities including workshops for high school students and teachers.

#### Resumen del Currículum Vitae:

I am an ambitious and enthusiastic scientist, who wishes to establish my own independent research group in order to pursue a research program that aims to understand the regulation of intestinal cellular plasticity and to facilitate pioneer treatments for intestinal chronic patients. Thus pushing regenerative medicine beyond the actual borders. Ramon y Cajal aids would allow me to establish the appropriate framework to achieve these goals.

I did my Biology Bachelor degree in Autonomous University of Barcelona. Since I have been always interested in both cellular biology and the chemical aspects that drives basic processes I decided to simultaneously study Biochemistry. Thereafter to get an industrial point of view I did a Master in Molecular Biotechnology that I combined with the beginning of my PhD in Anna Bigas laboratory where I worked in hematopoietic development. Altogether let me to publish three first author publications (one EMBO J 2008 and two Journal of Experimental Medicine 2013-2014), as well as several coauthor publications (Cancer Cell, Nature communications, Journal of Experimental Medicine, Blood, Development and Blood cells, molecules & diseases). Furthermore, I received the Extraordinaire award by Pompeu Fabra University given to the best thesis defended during the year 2012/2013. I subsequently joined the team of Kim Jensen (Copenhagen University) in order apply my knowledge to a different stem cell system, the intestine, funded by a Marie Curie fellowship (IF-EF). Here my research has focused on the specification of intestinal stem cells using fate mapping technologies, state of the art imaging, biophysical modeling and a plethora of sequencing techniques including scRNAseq, CAGE-seq, Hi-C, ATAC-seq. The first part of this work has been recently published in Nature. Additionally during my postdoctoral training I publish as a coauthor in Cell Stem Cell and EMBO J. Altogether allowed me to become Assistant Professor in Copenhagen University. Currently I am working in three manuscripts that will be submitted within the near future.



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The results of my recent work showing that differentiated-like intestinal cells are extremely plastic and able to de novo generate stem cells have inspired me in order to develop an innovative research program that aims to exploit this knowledge to develop therapies. This will allow me to tackle radiation-induced enteritis by boosting intestinal epithelial tissue regeneration and reeducating immune cells to facilitate anti-fibrotic treatments. I am convinced that with my work I will contribute to accelerate the translation of stem cell-based regenerative medicine strategies in into clinical practice.

In summary during my career I achieved some remarkable milestones that might be of your interest:

- Non-stop high impact publications track (including a Nature recently published).
- Successful in attracting funding (Including postdoctoral Marie Curie fellowship and participation in European Research Council grants among others).
- Trained as supervisor: Supervision of six master students, a PhD student and participation in EMBO leadership course and Pedagogic Certificate.
- International background: I worked in five different countries (Spain, Denmark, Netherlands, Japan, UK).
- Several prizes and awards including best PhD thesis and BRIC young investigator award .



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** VALDOR ALONSO, RUT  
**Referencia:** RYC2019-027520-I  
**Área Temática:** **Biomedicina**  
**Correo Electrónico:** rut.valdor@um.es

#### Título:

Molecular mechanisms of the activator and/or suppressive immune response: A possible key target for blocking glioblastoma progression ¿Chaperone-mediated autophagy in pericytes¿.

#### Resumen de la Memoria:

Since I was young researcher, I have been focused on the molecular mechanisms that regulate the immune response, activation and tolerance. I got the European PhD tittle, studying the poly(ADP)ribose-polymerase-1 function in T cell activation and tolerance.

During my postdoctoral training of five years in Albert Einstein College Medicine, (New York), I continued working on the regulation of an activated or suppressive immune response. My main contributions were focused on the study of autophagy, showing the role of Macroautophagy in T cell activation and the mechanism of how Chaperone mediated autophagy regulate immune responses through negative regulators of T cell activation (Nature Immunology).

In 2017, I got my own funding with a JIN-MINECO fellowship (SAF2014-61233-JIN). My research career has provided me, the knowledge and expertise to carry out my main research line and start my transition as group leader in Murcia University-IMIB-Arrixaca, establishing national and international collaborations.

My main interest is the study of Autophagy in pericytes functions during Glioblastoma progression. I have described that glioblastoma tumor cells ablate the anti-tumor immune function of pericytes, through aberrant upregulation of the protein degradation by chaperone-mediated autophagy. The work was accepted in PNAS.

I am also directing one project to find an effective therapy to treat glioblastoma through autophagy inhibition. I supervised 4 undergraduate students, 2 technicians, 3 postdocs, and 1 PhD student. I am a member of the european Cost-BiONECA action (Stem cells and Neurology), organizer committee of junior researchers (TERCEL-ISCIH). My interest in science is not only based in the generation of knowledge but also in communicating to society the importance of it (news in press, radio and tv; research revisions, chapters, formative talks, invited research communications).

I think that I am a well-suited candidate for Ramon y Cajal Program with: (1) a significant track record of publications in high impact journals, including several articles as Corresponding Author, (2) international scientific recognition exemplified by invitations to conferences, to write reviews and book chapters, and to participate in the peer-review process of scientific articles; (3) capacity to obtain funds independently as PI; (4) strong international and national collaborations; and, (5) proven leadership capacity to coordinate different research groups, recruit, supervise and train junior researches and technicians. Overall, I believe that I have acquired the professional maturity to warrant for a successful independent scientific career.

Therefore, my next goal is to get the transition into a recognized tenure track position to secure my group and research.

#### Resumen del Currículum Vitae:

##### EDUCATION

2010 Degree in Biochemistry. University of Murcia (UMU), Spain.  
2008 European PhD thesis. (UMU). Sup: J. Yélamos and P. Ramirez.  
2008 Master in Teacher training (C.A.P), UMU.  
2004 PhD Master in Molecular Biology and biotechnology (UMU).  
2002 Degree in Biology. UMU.  
2000 Internal student in Cell biology Depart.: TFG

##### POSITIONS

2017 Principal Investigator. College of Medicine. Internal Medicine Department. UMU.  
2014 Assoc. Researcher of Brain and development gene Unit, Biomedical Research Instit. Murcia (IMIB-Arrixaca).

##### FELLOWSHIPS, AWARDS and PRIZES

2018, 2019 Best communication prize (Covidien). III/IV Research Conference of IMIB-Arrixaca  
2017- MINECO-JIN fellowship, Internal Medicine Depart. UMU,  
2015- Travel award ¿Jimenez de la Espada¿, Seneca Foundation; for USA (6 months).  
2015-2017 Postdoc. fellowship. Anatomy and Psychobiology Department. UMU.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

2014-2015 Postdoc. Award. FFIS foundation (IMIB)-Virgen de la Arrixaca. Spain.  
2009-2014 NIH Postdoc. fellowship. Pathology Depart., Albert Einstein College of Medicine, NY, USA;  
2012 Daniel Shields travel award, Albert Einstein College of Medicine, USA  
2011 Keystone symposium autophagy postdoc. award. British Columbia, Canada.  
2008-2009 Postdoc. fellowship, Seneca Foundation. Experimental surgery Unit. Hospital Virgen de la Arrixaca.  
TEACHING, ORGANIZATION ACTIVITIES  
2019 Organizer Committee member of Junior researcher (TERCEL-ISCIII).  
2016 Professor with *¿venia docendi¿* (80 hours/year), Immunology Department, UMU.  
2016-2019 Supervision: 2 Postdocs/ 1 PhD (currently)/ 3 TFG students/2 technicians/1 curricular practice student 2014-2016 Master degree professor -Inflammation molecular pathologies. Catholic University (UCAM).  
2009-2014 Collaborator Professor Immunology, Albert Einstein College of Medicine, NY, USA.  
2009-2014 Organizer Committee Member of internal seminars. Insti. of Aging Studies, Albert Einstein College, USA.  
REVIEWING, OUTREACH, INTERNATIONAL ACTIVITIES; MEMBERSHIPS  
2010-2019 Peer-Reviewer, *¿Aging cell¿* (Q1) journal and Autophagy journal (decil).  
2019- Research results diffusion by radio, press and T.V.  
2019- Member of European-Cost BIONECA action-Stem cells and Neurology.  
2015-2019 Memberships in SEFAGIA, TERCEL, NEAR networks  
GRANTS (as P.I.)  
-Seneca Foundation 20840/PI/18. Study of the genetic and pharmacological inhibition of Chaperone- mediated autophagy in the immunosuppressive function of pericytes during Glioblastoma. 79.200 , 05/01/2019-05/01/2022.  
-JIN- MINECO/AE/FEDER- SAF2015-73923. Role of autophagy in the immune function of pericytes during Glioblastoma multiforme. 02/01/2017- 04/30/2020. 170.000 .  
-I also participated in other 16 research projects  
PUBLICATIONS  
I have published 15 articles in high impact journals (PNAS, Nature Immunol, Cancers, Molecul. Immunology, BMC genomics, Toxicol, Seminars Immunol., MCB, JImmunology, Cell reports, Pharmaceutical research, Biogerontology, Oncotarget, Biology J Leukoc journal, Autophagy). - Number of publications in Q1(9); 1D(4); as only or last corresponding author = 2; Sum of citations = 6616; - Average citations last 5 years= 989; - hindex = 10; - i10 index = 11; Source: Google scholar; 6 book chapters.  
CONFERENCES I have participated in more than 25 national and international meetings (presenting author 21) and I have been invited s



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** MATAS RICO, ELISA  
**Referencia:** RYC2019-027950-I  
**Área Temática:** **Biomedicina**  
**Correo Electrónico:** elimatas@gmail.com

#### Título:

Cancer and Neural Cell regulators

#### Resumen de la Memoria:

During my scientific career I have been greatly interested in cell signaling and its clinical impact. My main research line has focused on the involvement of lysophosphatic acid (LPA) signaling in central nervous system, and tumor progression. I started my career as associated researcher in University of Malaga (Cell Biology Department) to investigate cortical development and patterning of the mouse brain. Due to my interest in neuroscience and experience, I obtained a PhD fellowship to carry out my doctoral thesis in the group of Neuropharmacology of Lipid Transmitters, at Research Foundation (FIMABIS), Málaga. During my PhD I studied the role of Lysophosphatidic acid receptor 1 (LPA1) signalling pathways on neurogenesis in adult and developing brain using a LPA1 knockout mice model. Findings from my PhD demonstrated, for the first time, a role for LPA signaling in adult neurogenesis, and they highlight the LPA1 receptor as a key regulator of neurogenesis and structural plasticity and as a potential target in neurodegenerative diseases. In addition, I participated in the study of the LPA1 knockout mice as a model for the study of myelinating diseases. Results showed a key role of LPA1 in cortical myelination and it implied a significant relevance for therapies of neuroinflammatory and demyelinating diseases such as multiple sclerosis. After my PhD, I joined to the Cell Biology Division at the Netherlands Cancer Institute (Amsterdam) as a Postdoctoral researcher to develop a broader knowledge of LPA signaling pathways involved in tumor formation and progression and in its clinical implications. I initially focused on LPA signaling and its relation with cancer progression and metastasis. My results revealed a new mechanism of LPA-induced chemorepulsion through LPA5 receptor with potential therapeutic relevance for cancer. Later on, I established and leading a novel line of research focusing in the mode of action of transmembrane ecto-glicerophosphodiesterases enzymes (GDEs) as key regulators of cancer malignancy. Results with GDEs are published in high-impact factor journals and have laid the foundation of a new project funded by KWF (Dutch Cancer Society). Moreover, my findings highlighted GDEs as novel player in cell differentiation and cancer biology that influence the malignant phenotype and are markers of clinical outcome. During that time, I have supervised two PhD students Michiel van Veen (thesis defended in 2018, <https://openaccess.leidenuniv.nl/handle/1887/65601>), and Fernando Salgado Polo, which thesis will be defended in 2021. Currently, my research focused in the study of LPA and LPA-producing enzyme Autotaxin in tumor immunology and as a potential drug target in cancer immunotherapy. Results from this project were awarded with the International Journal of Molecular Sciences Award from Federation of American Societies for Experimental Biology (FASEB), 2019, and a manuscript reporting these results will be submitted next month to a high impact factor Journal.

#### Resumen del Currículum Vitae:

I studied Biology at University of Malaga graduating in 2001. Immediately after I joined to Cell Biology Department as an associated researcher to work in a project focussed on cortical development and patterning of mouse brain. In February 2004, I joined to the group of Neuropharmacology of Lipid Transmitters at Research Foundation FIMABIS, to carry out a PhD project focused on the study of the role of Lysophosphatidic acid receptor 1 (LPA1) signaling pathways on neurogenesis in adult and developing brain, as well as a key regulator of myelination and neuroinflammation process. After obtained my PhD (2009), to gain experience in clinical translation, I continued working in the same group participating in projects together with the Clinical Management Unit of Neurology, directed by Dr. Oscar Fernández Fernández. During this whole period, I developed a remarkable expertise and knowledge about LPA1 signaling, neural proliferation, differentiation, myelination and how neural cell processes correlate with cognition and function. In November of 2009, I visited the labs of Prof Wouter Moolenaar at the Cell Biology Department of The Netherlands Cancer Institute (NKI), (overall 10 months). His group discovered LPA as a lipid growth factor and has made major contributions to elucidating the biological actions and signaling mechanism of LPA. During that period, I opportunity to acquired knowledge and expertise in LPA signaling and its relation with cancer progression and metastasis. In 2010, I acquired a postdoctoral position at the same group at the NKI. I focused on LPA signaling and LPA-producing enzyme and their relation with cancer progression, metastasis and tumor immunology. During that period, I established and led a new research line, focusing in the mode of action of transmembrane ecto-glicerophosphodiesterases enzymes (GDEs) as novel player in cell differentiation and cancer biology that influence the malignant phenotype and are markers of clinical outcome. Working at the NKI, offered me the opportunity to work as an independent researcher in different projects, opening a novel line of research, making important decisions in the course of the projects, collaborate with national and international groups, and writing manuscripts that have been published in high-impact journals. Moreover, I improved my leadership qualities by the co-supervision of two PhD students; Michiel van Veen (Thesis defended in 2018, Leiden University, Netherlands), and Fernando Salgado Polo (which thesis is expected to be defended in 2021). As a result of my scientific career, I have published 14 research articles in peer-reviewed journals with high impact factors (Q1:13, D1:3). My papers have received more than 377 citations and his h-index is 8 (source: Publons, January 13th 2020. Since 2008). My work has been presented in several conferences (27 oral and poster presentation). I have participated in more than 10 research National and





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European projects. I have a solid multinational network of co-authors. I was awarded with International Journal of Molecular Sciences Award from Federation of American Societies for Experimental Biology (FASEB), July 2019.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** COLL LOPERENA, MAR  
**Referencia:** RYC2019-026662-I  
**Área Temática:** **Biomedicina**  
**Correo Electrónico:** mariuscoll@gmail.com

#### Título:

molecular mechanisms underlying liver chornic diseases

#### Resumen de la Memoria:

My translational research has focused over the years on the study of the pathogenic basis of liver injury to develop new therapeutic strategies to target liver diseases. During my PhD I developed a new research line that investigated the molecular pathways involved in liver cirrhosis. My PhD research gave rise to 7 publications, 3 of them as a first author (Coll.M, J Hepatol 2008, IF: 19; Coll.M, Liver Int 2010 IF: 5.5 and Coll.M, Hepatology 2012, IF: 14.1). I started my post-doc at Pau Sancho-Bru laboratory as a responsible of an EU project (FP7-HEALTH 2010) aimed at generating a hepatic microfluidic device comprising liver cells derived from induced pluripotent stem cells (iPSC). In this project context I moved to Dr. Verfaillie laboratory (Leuven Stem Cell Institute, Belgium) to learn the iPSC technology. As a result of this collaboration we described for the first time a protocol for differentiating iPSC towards hepatic stellate cells (Coll.M, Cell stem cell 2018, IF: 21.46, patent WO/2017/093418). Moving forward, I was awarded with the post-doctoral grant Sara Borrell (ISCIII) and I focused my research on regenerative mechanisms underlying chronic liver diseases (Coll. M, Scientific Reports, IF: 5.5). Next, I started as a senior post-doctoral investigator at Dr. Pere Ginès group (IDIBAPS) and I centred my investigation on inflammatory cells in chronic liver disease. I participated in the LiverHope project (H2020-SC1-2016-RTD) in which I led a translational study regarding systemic inflammation and microbiome of patients with advanced chronic disease. To further increase my expertise on liver inflammation I stayed at Dr. Paul Kubes lab (Calgary, Canada) who is one of the worlds leading experts on immune cell imaging. Thanks to this collaboration we have recently submitted a paper in which I am the corresponding author (assessing the revisions, Hepatology, IF: 14.1). Currently, I have established my independent translational research. The overall objective of my research line is to describe the adipose tissue-liver axis during the progression of Non-alcoholic fatty liver liver disease (NAFLD). NAFLD is the most common chronic liver disease worldwide with a prevalence of 25-30% in the general population and it is expected to become an epidemic in the 21st century. The main goal of my research line is to characterize the pro-inflammatory subset of macrophages infiltrating the adipose tissue in patients with NAFLD and to identify new mediators secreted by these macrophages that might be worsening liver function. My translational research line is funded by a competitive grant from Instituto de Salud Carlos III (PI18/00862, totalling 86.515 ) in which I am the PI. I am leading a multidisciplinary team composed by a Hepatologist who is the responsible of the area of NAFLD in Hospital Clínic, a resident in hepatology in the Hospital Clínic and a biologist who is developing her PhD project. During my scientific career, including 3 maternity leaves (2011, 2013 and 2019), I have produced 22 high impact factor original publications (5 as a first author) with an average citation per year of 48.3.

#### Resumen del Currículum Vitae:

I graduated in Chemistry in 2004 by the University of Barcelona. In 2005 I was awarded with a competitive grant from Vall d'Hebron Research Institute (VHIR) to carry out my PhD project focused on molecular mechanisms underlying liver cirrhosis supervised by Dr. Joan Genescà. I completed my PhD in Biochemistry and Molecular Biology (Universitat Autònoma de Barcelona) with a scientific output of 7 publications, 3 of them as a first author (Coll.M, J Hepatol 2008, IF: 19; Coll.M, Liver Int 2010, IF: 5.5 and Coll.M, Hepatology 2012, IF: 14.1). Afterwards, I moved to the laboratory of Pau Sancho-Bru at IDIBAPS as a post-doctoral investigator responsible of an European grant (FP7-HEALTH -2010) aiming at generating a Microfluidic Bioreactor comprising hepatic cells differentiated from induced Pluripotent Stem Cells (iPSC). In this context, I stayed at the laboratory of Catherine Verfaillie (Leuven Stem Cell Institut, Belgium) where I established the basis for the generation of a protocol that efficiently differentiates hepatic stellate like cells from iPSC. This technology gave rise to a high impact factor publication (Coll, M; Cell Stem Cell 2018, IF: 21.46), the development of a patent (WO/2017/093418) and attract the interest of multiple companies of the biotechnology sector. In 2014 I was awarded with a Sara Borrell grant (ISCIII) in order to continue my post-doctoral research focused on the study of molecular mechanisms involving liver regeneration. In 2016 I joined CIBERehd (ISCIII) as a senior post-doctoral researcher in the research group of Dr. Pere Ginès. During this period my post-doctoral research was centred on the dysfunction of immune cells in chronic liver injury. I participated in the LiverHope project (H2020-SC1-2016-RTD) in which I led a translational study regarding systemic inflammation and microbiome of patients with advanced chronic disease. To further increase my understanding on liver inflammation I moved to the laboratory of Dr. Paul Kubes at the University of Calgary (Canada). As a result of this collaboration we have recently submitted a paper in which I am the corresponding author (assessing the revisions, Hepatology, IF: 14.1). Overall, during my postdoc, I have produced 15 high impact factor original publications, two of them as a first author (Scientific Report, 2015, IF:4.1; Cell Stem cell, 2018, IF:21.4) and 4 of them as a second co-author (Scientific report,2017, IF:4.1; Hepatology, 2017, IF:14.1 and Gut, 2016, IF:17.9). Also, I have participated in the elaboration of three book chapters (one of them as a first and another as a senior author). I have been invited to participate in international workshops organized by European Association for the Study of the Liver (EASL).



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## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

Recently, I funded my independent research group focus on understanding molecular mechanisms responsible for the progression of Non-alcoholic Fatty Liver Diseases. This research line is being funded by Instituto Carlos III by a FIS grant (PI18/00862) in which I am the PI. During my scientific career, including 3 maternity leaves (2011, 2013, and 2019), I have produced 22 high impact factor original publications with an average citation per year of 48.3. Moreover, I have disseminated my research in national and international conferences. As a lecturer, I have participated in Master in Translational Research (UB) and Master in Clinical Investigation (UB) and in the International Liver School (EASL).



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** AVGUSTINOVA , ALEXANDRA  
**Referencia:** RYC2019-027738-I  
**Área Temática:** **Biomedicina**  
**Correo Electrónico:** alexandra.avgustinova@irbbarcelona.org

#### Título:

Chromatin in cancer evolution

#### Resumen de la Memoria:

My scientific career has been driven by my interest in the mechanisms of cancer progression in search of novel therapeutic strategies to enhance patient survival. Two principal factors worsen cancer patient prognosis and survival: metastatic dissemination and (acquired) resistance to therapy. During my PhD and the first years of my postdoctoral studies I focused on the mechanisms of metastatic dissemination. More recently my research has centered on the molecular mechanisms that determine the evolutionary potential of tumours, and with it their adaptability to different selection pressures, e.g. cytotoxic chemotherapy. As an independent investigator I propose to continue this line of research and functionally identify the true determinants of mutation rate variability within cancer genomes. My principal aim is to develop clinical therapies that reduce the adaptive potential of tumours and hence improve patient survival. Trimethylation of lysine 36 (H3K36me3) has emerged as the most likely mutation rate determinant within cancer genomes, and patients with H3K36me3-low tumours have particularly poor prognosis. I plan to model H3K36me3-low tumours, assess their mutability and seek synthetic lethality pathways in order to identify targeted clinical therapies.

As an independent investigator will research the following key biological questions:

- 1) Is H3K36me3 a determining factor of the mutation rate across the genome?
- 2) Are evolutionary fitness and resistance to chemotherapy of tumour cells enhanced upon H3K36me3 loss?
- 3) Which molecular pathways are H3K36me3-low tumour cells sensitized to? Can they be utilized as a novel clinical intervention point through synthetic lethality?

To do so I will establish two different models H3K36me3-low lung adenocarcinoma tumours:

- 1) CRISPR/Cas9-based deletion of SETD2, the only H3K36 trimethylase in the human genome; in human lung adenocarcinoma cells, generating isogenic cell line pairs to be used for in vivo assays;
- 2) A syngeneic, immunocompetent mouse model by crossing Setd2<sup>fl/fl</sup> mice to oncogenic Kras<sup>G12D</sup> knock-in mice; Setd2 deletion and oncogenic Kras<sup>G12D</sup> expression are triggered by intranasal viral Cre delivery.

Using these models, I will generate individually dissectible and clonally traceable lung adenocarcinoma tumours. Tumour cells will be isolated using FACS-based cell separation and subject to whole genome sequencing. Using the computational approaches established in my recent Nature Cell Biology publication, I will assess different mutability and aggressiveness parameters. In later stages of the project, the findings will be compared to data obtained using the same approach but under chemical chemotherapy (cisplatin) to determine the resilience of H3K36me3-low tumour cells under cytotoxic stress, as well as whether different mutational processes (purely replicative vs. mutagenic chemotherapy) trigger differential responses in H3K36me3-low tumours. Finally, using the same in vivo models, I will conduct a large-scale CRISPR/Cas9-based screen to identify synthetic lethality pathways that H3K36me3-low tumours are sensitised to. Thus I will identify new intervention strategies to improve the prognosis of patients with H3K36me-low tumours.

Due to my experience with mouse models, hospital collaborations, epigenomics and cancer genomics, I am uniquely suited to direct this project.

#### Resumen del Currículum Vitae:

My publication record is a testament to my scientific excellence. I have authored publications in a number of high-impact scientific journals including Nature, Nature Cell Biology and Cell Stem Cell. My high-impact review articles (Nature Reviews Molecular Cell Biology 2016; Current Opinion in Genetics and Development 2016) are evidence of my standing as an expert of epigenetics in the scientific community. Indeed, all of my publications to date have been in journals of the first quartile (7 out of 8 also being in the first decile); and although very recent (all since 2016), have already been cited extensively (total of 484 citations), generating an H index of 7. In addition to my published scientific articles, I am currently preparing the manuscript for a further first and corresponding author publication, to be submitted in February to Cell Stem Cell.

My ability to conceptually develop and lead a project is demonstrated by publications as corresponding author (Nature Cell Biology 2018;



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

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Nature Reviews Molecular Cell Biology 2016). Additionally, I have formally mentored two highly successful Master's students who are both currently undertaking their PhDs internationally.

As a testament to my scientific excellence, I have been awarded prestigious fellowships at every stage of my career, allowing me to conduct my research internationally:

- a) Sainsbury Undergraduate Studentship to conduct a 8-week research placement at the Rowland Institute, Harvard University, MA, USA;
- b) Cancer Research UK-funded PhD Studentship at the Institute of Cancer Research, London, UK;
- c) Marie-Sklodowska-Curie Actions Postdoctoral Fellowship to fund part of my postdoctoral stay in the laboratory of Prof. Aznar Benitah at the Institute for Research in Biomedicine Barcelona, Spain.

I put great emphasis on collaborative endeavors in science. Therefore I have disseminated my work at a multitude of international conferences both in the form of award-winning poster and oral presentations (Best Poster Prize, 2016; Proffered Abstract oral presentations at "10th International Behr Symposium", Heidelberg 2018 and "EACR Conference on Basic Epigenetics", Berlin 2015; 1st Prize in MedImmune European Cancer Competition 2011). The result of my scientific dissemination efforts are a number of national and international collaborations (Ben Lehner, Barcelona, Spain; Fran Supek, Barcelona, Spain; Cedric Blanpain, Brussels, Belgium; Cord Brakebusch, Copenhagen, Denmark; Erik Sahai, London, UK).



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** CASTELLANO RODRIGUEZ, JUAN MANUEL

**Referencia:** RYC2019-027938-I

**Área Temática:** Biomedicina

**Correo Electrónico:** b82caroj@uco.es

#### Título:

Novel regulatory pathways linking metabolism and reproductive function.

#### Resumen de la Memoria:

My Ph.D. studies at the group of Dr. Tena-Sempere (University of Cordoba) were focused on understanding the roles of a family of neuropeptides, termed kisspeptins, in the central control of puberty and reproduction, with special emphasis to its involvement in linking metabolism and reproductive function. During that time, I contributed to: (i) characterize the role of kisspeptin system in the central regulation of puberty and reproduction (Endocrinology, 2004; 145(10):4565-74; Citations: 539); (ii) identify the novel role of locally produced kisspeptin in the control of ovarian function (Endocrinology, 2006; 147(10):4852-62; Citations: 179); (iii) identify and characterize the novel role of kisspeptin in the metabolic control of puberty (Endocrinology, 2005 146(9):3917-25; Citations: 357); and (iv) unravel the physiopathological implication of kisspeptins in altered reproductive function linked to type 1 diabetes (Diabetes, 2006. 55(9):2602-10; Citations: 176). I was the first author in all these publications.

During my postdoctoral stage at Dr. Ojeda's group (Neuroscience Division, Oregon National Primate Research Center, Beaverton, USA), my work was focused on the study of the potential roles of epigenetic regulatory mechanisms in the central control of puberty. By that time, I contributed to unravel the key roles of two novel epigenetic mechanisms of transcriptional repression in the central control of puberty, involving different members of the family of transcriptional repressors Polycomb genes: CBX7/EED (Nature Neurosci, 2013; 16(3):281-9; Castellano JM: Third author), and Zinc Finger genes: GATAD1/ZNF573 (Nature Commun, 2015; 6:10195; Castellano JM: First author).

As an emerging scientist in Tena-Sempere's group, I have developed two lines of research: (i) the role of epigenetic mechanisms linking metabolic stress and altered reproductive function and (ii) the involvement of novel regulatory pathways in the central control of puberty. During this time I has contributed to: (i) unveil the novel role of SIRT-1 as a central hub of a novel epigenetic mechanism mediating the effect of nutritional cues on female puberty (Nature Commun, 2018. 9(1):4194. Castellano JM: Second author); (ii) characterize the impact of early exposure to bisphenol A on pubertal maturation and its influence on the development of hypothalamic Kiss1/NKB neurons (Environ Health Perspect, 2019. 127(10):107011; Castellano JM: Corresponding author); and (iii) identify and characterize the novel role of the hypothalamic miR-30/Mkrn3 pathway in the central control of puberty (PLoS Biol, 2019. 17(11):e3000532; Castellano JM: Corresponding author).

#### Resumen del Currículum Vitae:

I obtained my Ph.D. degree under the supervision of Drs. Manuel Tena-Sempere and Leonor Pinilla at the University of Cordoba. My Ph.D. project was focused on the characterization of the physiological roles of kisspeptins and GPR54 in the central control of puberty and reproduction, with special attention to its involvement in linking metabolism and reproductive function. During that time, I contributed to: (i) characterize the role of kisspeptin system in the central regulation of puberty and reproduction (Navarro VM\*, Castellano JM\*, et al. 2004. Endocrinology. 145(10):4565-74. \*: First author; Citations: 539); (ii) identify the novel role of locally produced kisspeptin in the control of ovarian function (Castellano JM et al. 2006. Endocrinology. 147(10):4852-62; Citations: 179); (iii) identify and characterize the novel role of kisspeptin in the metabolic control of puberty (Castellano JM et al. 2005. Endocrinology. 146(9):3917-25; Citations: 357); and (iv) unravel the physiopathological implication of kisspeptin system in altered reproductive function linked to type 1 diabetes (Castellano JM et al. 2006. Diabetes. 55(9):2602-10; Citations: 176). During my postdoctoral period, I was awarded a Marie Curie Fellowship (PIOF-GA-2010-273034) that allowed me to join Dr. Ojeda's group (Oregon Health & Science University, USA). By that time, I contributed unravelling the key roles of two novel epigenetic mechanisms of transcriptional repression in the central control of puberty, involving Polycomb genes: CBX7/EED (Lomniczi A, Loche A, Castellano JM\* et al. 2013. Nature Neurosci. 16(3):281-9; \*: Third author), and Zinc Finger genes: GATAD1/ZNF573 (Lomniczi A\*, Wright H\*, Castellano JM\* et al. Nature Commun. 2015.6:10195; \*First author). In 2013 I re-joined Tena-Sempere's group, and two years later, I was awarded a new Postdoctoral Marie-Sklodowska Curie fellowship (GAP-2014-655232; 2016-2018) and I obtained a research project as a Principal Investigator focused on the role of epigenetic mechanisms in the overweight-induced hypogonadism (SAF2014-56995-JIN;2015-2018). During that time, I have contributed to: (i) unveil the novel role of SIRT-1 as a central hub of a novel epigenetic mechanism mediating the effect of nutritional cues on female puberty (Vazquez MJ1, Toro CA1, Castellano JM\* et al. Nature Commun. 2018.9(1):4194. \*: Second author); (ii) characterize the impact of early exposure to bisphenol A on pubertal maturation and its influence on the development of hypothalamic Kiss1/NKB neurons (Environ Health Perspect. 2019. 127(10):107011; Corresponding author); and (iii) identify and characterize the novel role of the hypothalamic miR-30/Mkrn3 pathway in the central control of puberty (PLoS Biol. 2019. 17(11):e3000532; Corresponding author). Recently, I have obtained a new research project as a Principal Investigator to explore the role of lipid sensing in the central control of puberty (UCO-1258369; 2020-2021). Overall, my research work has resulted in: (i)



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## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

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77 scientific congress contributions; (ii) 69 publications, including top journals, such as Nat Neurosci, Nat Commun, PNAS, Diabetes, PLoS Biol, and Endocrinology, with 22 first authorships and 4 corresponding authorships, H-index: 37 (WoS); (iii) 15 participations in research projects, two of them as a PI and two of them as a Postdoctoral Marie Curie Fellow; and (iv) 2 Thesis supervised.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2019

### Turno de acceso general

**Nombre:** DIAZ ALONSO, JAVIER  
**Referencia:** RYC2019-026889-I  
**Área Temática:** Biomedicina  
**Correo Electrónico:** javi.diazalon@gmail.com

#### Título:

Molecular mechanisms of pyramidal neuron development and synaptic plasticity.

#### Resumen de la Memoria:

Throughout my training as a scientist in the field of neurobiology, I have studied CNS development, synaptic transmission and plasticity and neurodevelopmental and neurodegenerative disease. In addition to my research training, I have developed my teaching and mentoring skills during my PhD and postdoc. Furthermore, I have had multiple chances to develop my grantsmanship skills and have been able to fund my training and research with prestigious international fellowships and awards. I have presented my work at numerous domestic and international meetings.

During my Ph.D. work under the mentorship of Dr. Ismael Galve-Roperh and Dr. Manuel Guzmán at the Complutense University of Madrid, I explored the role of the cannabinoid CB1 receptor (CB1R) throughout cortical pyramidal neuron development, and how deregulation of cannabinoid signaling underlies neurodevelopmental diseases such as epilepsy. During my predoctoral period, funded by a PFIS fellowship, I greatly benefited from a collaboration with Dr. Francois Guillemot, whose lab at the MRC in London, UK, I visited 3 times, aided by a FEBS short-term fellowship. My Thesis work resulted in 5 first author papers (one as co-corresponding author) and 8 other papers (2 of which are reviews). All of them published in the first decile in their respective fields. Also, directly stemming from my thesis work, is one patent (EP2733205).

I decided to pursue training in neurophysiology and synaptic plasticity during my postdoc in Dr. Roger Nicoll's laboratory at the University of California, San Francisco, where I expanded my background and toolbox with diverse techniques in electrophysiology and molecular biology. My postdoc work resulted in 2 first author papers (one as co-corresponding author) and 4 other papers (3 of them as second author). All of them in the first decile in their respective fields.

In 2018 I was awarded a K99/R00 Pathway to Independence Award from the National Institute of Mental Health. This prestigious grant currently funds my research in the Nicoll laboratory using biochemistry, proteomics, electrophysiology, molecular biology and behavior to elucidate fundamental aspects of AMPA receptor (AMPA) synaptic trafficking. This research has direct implications in multiple forms of synaptic plasticity, including long-term potentiation (LTP), widely regarded as the molecular and cellular substrate of learning and memory.

My long-term goal is to pursue an academic career in neurobiology, studying the mechanisms governing synapse formation, transmission and plasticity. The multidisciplinary approach that I will use in my laboratory, combining genetic, proteomic, molecular, electrophysiological and behavioral techniques will allow the dissection of the complex processes in brain development and synaptic transmission that underlie neurological disease, with the goal of contributing to the improvement of current treatments.

#### Resumen del Currículum Vitae:

I received my Ph.D. in the Biochemistry and Molecular Biology program at the Complutense University of Madrid in 2014. My Thesis received the European mention and an Extraordinary Doctorate Award. My Ph.D. work, supervised by Dr. Manuel Guzman and Dr. Ismael Galve Roperh, focused on the role of the CB1 cannabinoid receptor (CB1R) during brain development. In summary, we showed that i) CB1R signaling controls the self-renewal of cortical precursor cells (Diaz-Alonso et al., *Cereb. Cortex*, 2015), ii) Loss of CB1R results in reduced generation of corticospinal motor neurons, resulting in impaired fine motor control (Diaz-Alonso et al., *J. Neurosci.* 2012), iii) Mice exposed to THC, the main active ingredient of marijuana, during prenatal development, develop cellular and behavioral traits reminiscent of CB1R KO and show increased susceptibility to epileptogenesis (de Salas-Quiroga\*, Diaz-Alonso\* et al., *Proc. Natl. Acad. Sci. USA*, 2015), iv) CB1R signaling promotes neuronal migration, and its loss of function results in cortical layering defects and increased seizure susceptibility (Diaz-Alonso\*#, de Salas-Quiroga\* et al., *Cereb. Cortex*, 2017) and v) Non-psychoactive cannabigerol derivatives are neuroprotective in a mouse model of Huntington's disease (Diaz-Alonso\*, Paraiso-Luna\*, Navarrete\* et al., *Sci. Rep.*, 2016).

During my Ph.D. I greatly benefited from a collaboration with Dr. Francois Guillemot, in whose laboratory at the MRC National Institute for Medical Research in London, UK, I spent a total of 5 months.

Then I pursued postdoctoral training at the University of California, San Francisco, with Dr. Roger Nicoll, focusing on elucidating the molecular underpinnings of AMPA receptor (AMPA) synaptic trafficking and synaptic plasticity. We demonstrated that i) the amino-terminal domain is the master gatekeeper of AMPAR trafficking and long-term potentiation (LTP) (Diaz-Alonso\*#, Sun\*, Granger\* et al.,





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Proc. Natl. Acad. Sci. USA, 2017) and ii) the entire cytoplasmic tail of the AMPAR auxiliary subunits TARPs is required for binding to the postsynaptic scaffolding protein PSD-95. This multivalent interaction controls both constitutive and activity-dependent AMPAR synaptic trafficking (Zheng\*, Diaz-Alonso\* et al., Neuron, 2019).

I am currently the PI of a K99/R00 Pathway to Independence Award, a prestigious grant from the NIH that provides additional funding - totaling \$989,460 in 5 years- for the transition to an independent-tenure-track position in a US academic institution. The first work derived directly from this grant, where the role of the cytoplasmic C-tail of AMPAR is explored, is currently in preparation for publication.

I currently have an h-index of 13 (Google Scholar). I have published a total of 17 peer-reviewed original research papers and 2 reviews, all of them in journals in the first decile in their respective fields, 7 as first or co-first author and 2 as co-corresponding author. I am also inventor in one patent.

I have a substantial teaching experience. During my Ph.D., I contributed to teaching lab courses in biochemistry, clinical biochemistry and genetic engineering. During 2017-2019 I was appointed as associate professor at the University of San Francisco, where I taught 2 entire courses of Survey in Human Physiology Lab.



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### Turno de acceso general

**Nombre:** SANZ BARTOLOME, ANA BELEN

**Referencia:** RYC2019-026916-I

**Área Temática:** Biomedicina

**Correo Electrónico:** asanz@fjd.es

#### Título:

Molecular mechanisms of kidney disease: in search of new therapeutic approaches

#### Resumen de la Memoria:

Kidney disease is predicted to become the fifth cause of death by 2040. I have focused my research on understanding the cellular and molecular mechanisms of kidney disease to develop novel therapeutic approaches:

In my PhD training at Fundación Jimenez Diaz, I studied the role of the cytokine TWEAK in kidney diseases, and this research had a direct translational impact since the first clinical trial of blocking anti-TWEAK antibodies addressed a kidney disease.

During my postdoctoral period at IdiPAZ, I deepened on the study of new pathogenic mechanisms of TWEAK in kidney injury. Moreover, I described the inflammatory role of TWEAK during peritoneal inflammation and its potential as target in prostate cancer. As part of my postdoctoral training, I moved to the Institute Gustave Roussy, Unit 848 INSERM (France) under supervision of Dr. Guido Kroemer, where expanded my knowledge on the study of cell death mechanism.

In 2013 I returned to the IIS-FJD as group leader with a Miguel Servet contract and set the knowledge base, both published and unpublished, to develop the line research of her group: a clear understanding of the mechanisms of kidney disease and the molecular mechanisms that regulate cell death and inflammation, the setup of the required techniques and the generation of preliminary data. The kidney research experience is reflected in 114 publications, 49 Q1 and 36 D1 publications, an h-index of 33 (WOS)/38 (Google Scholar), and publications in top journal as: J Am Soc Nephrol (n=10, IF 8.54, top nephrology research journal), Kidney Int (n=7, IF 8.3, second top nephrology research journal) and PNAS USA (n=2, IF 9.4) including 4 as corresponding author (JASN 2011, Kidney Int 2016, JASN 2017, PNAS 2018). I have directed 4 doctoral thesis, 3 final master projects, and 5 end-of-degree studies projects. I have been PI for 3 Spain National Research Plan projects, an International joint program (ERAPERMED) project, and 4 competitive projects from private foundations. Moreover, I am a member of the RETIC REDINREN (FIS) and of the research consortium on AKI (CIFRA-CM2, Comunidad de Madrid). The international projection is reflected on publications with international authors (4 JASN, 2 PNAS, 1 Cell Death Dis and others), invited reviews and conferences in international Congresses (e.g. ESAO 2018) and to review for high ranking journals (e.g. Nature Commun y Nat Rev Nephrol).

#### Resumen del Currículum Vitae:

##### Education:

2007- PhD Biochemistry, Autonoma University of Madrid

2001- BSc Biochemistry, Autonoma University of Madrid

##### Fellowships and funding:

Aug. 2018 Miguel Servet II (highest category), IIS-FJD, Madrid

2013- Aug. 2018, Miguel Servet, IIS-FJD, Madrid

2009-12, Sara Borrell, IdiPAZ, Madrid

2008, post-doctoral contract of CAM; IIS-FJD, Madrid

2004-07, PhD student (PFIS, ISCIII), Jimenez Diaz Foundation

2001-03, PhD student, predocotral grant, Conchita RabagoFoundation - Jimenez Diaz Foundation

##### International stay

2010, Laboratory of Dr. Guido Kroemer (Unit 848 INSERM, Institute Gustave Roussy, Villejuif, France as part of the Sara Borrell program

##### Scientific contribution

h-index: 33(WOS) / 38 (GS)

i-10 index: 85

Citations: 3827/5396

Accumulated impact factor: 530

Publications: 113 publications, : J Am Soc Nephrol (n=15, IF 8.54, top nephrology research journal), Kidney Int (n=9, IF 8.3, second top nephrology research journal) and PNAS USA (n=2, IF 9.58) including 4 as corresponding author (JASN 2011, Kidney Int 2016, JASN 2017,



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PNAS 2018).

Total Corresp. Author : 13 (5 in D1 and 6 in Q1)

Book Chapters: 6

Supervised PhD Thesis: 4

Contribution to scientific meetings and invited talks:

5 invited talks in national and international meetings

16 contributions (10 poster and 6 oral communications) in national and international meetings

Awards

2019, Young Investigator Award (sponsored by IBUB), SEBBM

2012, XXII Basic Research Award in Nephrology JANSSEN-CILAG, SENEFRO

2011, VII Translational Medicine Award, Hospital Madrid Foundation

2010, XX Basic Research Award in Nephrology JANSSEN-CILAG, SENEFRO

2009, XXI Basic Research Award in Nephrology, Iñigo Alvarez de Toledo Renal Foundation (the most prestigious Spanish nephrology Award)

2002, XII Basic Research Award in Nephrology JANSSEN-CILAG, SENEFRO

Peer reviewer:

Projects: FWF Austrian Science Fund

Journals: Nature Commun, Nature Reviews in Nephrology, JASN, Redox biology, Antioxidants, British Journal of Pharmacology among others.

Additional teaching activities:

Clinical teaching collaborator, Medicine Department, School of Medicine, UAM, 2017-today

Supervisor 3 master thesis

Supervisor 5 end-of-degree studies projects



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### Turno de acceso general

**Nombre:** LAX PEREZ, ANTONIO MANUEL

**Referencia:** RYC2019-027635-I

**Área Temática:** Biomedicina

**Correo Electrónico:** alax@um.es

#### Título:

Myocardial Remodeling and Heart Failure: Novel treatments and therapies

#### Resumen de la Memoria:

Through his career, he has been interested in research related to biomedicine and cell biology, with a special emphasis in cardiac diseases. After completing a BSc in BioChemistry at the University of Murcia in 2000, he was granted an FPU fellowship for a PhD focused on the characterization of the cell death mechanisms induced by Ca<sup>2+</sup> after myocardial infarction (MI) at the same University. His contributing in the identification of the mitochondrial Na<sup>+</sup>/Ca<sup>2+</sup> exchanger as a novel therapeutic opportunity was very important at scientific and technical level. In this period, he joined the lab of Prof. Inesi (California, USA), 3 months overall. In 2009, he received his PhD with Honors (Award to The Best PhD Thesis, UMU) and moved to Virgen de la Arrixaca Hospital (Murcia, Spain) to perform his postdoct. In 2010 he obtained a Juan de la Cierva post-doctoral scholarship; had the opportunity to take the lead and developed his own research line. In collaboration with Prof. Januzzi (stay of 3 months; USA), he contributed to the understanding of novel cardiac biomarker testing (Gal-3, TnT-T, ...); his studies have set international action standards. Furthermore, he demonstrated that pharmacological activation of FHC/NF-kB axis prevents cardiotoxicity in oncological patients. In 2014, he was awarded a Sara Borrell contract, which allowed him to continue with his independent research at the IMIB Institute (Murcia, Spain). In 2016, he joined the lab of Prof. Roger Hajjar (stay of 2 years, Mt. Sinai Hospital; USA) where he pioneered the identification of two trans-elements involved in the overexpression of poor prognostic marker sST2; data which has contributed to the design of novel treatments and therapies specifically aimed at silencing their expression in infarcted myocardium. In 2018, he was awarded a Research contract for access to the Spanish System of Science, Technology and Innovation and returned to IMIB-Arrixaca Institute to continue with his independent research career and projects as PI. In the last two years, he has defined new concepts as "extra-cardiac sST2 production" and discovered non-described molecular mechanisms of different factors as Yin-yang 1 or HDAC4 as well as the molecular hierarchy of AMPK/PKC/NOX4/Gal-3 axis and its relationship with adverse fibrosis. Dr. Lax has published 35 original articles, all of them in first-quartile/decil journals. It has obtained 899 citations according to Google Scholar yielding an h-index of 17 and an i10 of 23. He has 88 conference papers; 1 patent (+1 in elaboration), 3 monographs presenting the results of his research and participation in 24 research projects. He has opened independent collaborations with other groups in USA and London, which he has obtained two collaborative competitive projects as PI. Recently, he has created a Technology Based Company entitled Biocardio SL. Finally, he is reviewer for 7 high impact JCR journals in the areas of Cardiology, member of two prestigious Editorial-teams in their area and since 2015 he has acted as scientific evaluator of the GRIS European program (Czech). At present, he is Associate Professor-Cardiology, University of Murcia/Faculty of Medicine, where he has supervised 2 Ph.D. theses, three master thesis and several undergraduate students projects. Additionally, he has the "Profesor contratado doctor" certificate by the ANECA.

#### Resumen del Currículum Vitae:

Since my Degree in Biochemistry at the University of Murcia (UMU) (2000) my scientific career has gone through the completion of my doctoral thesis (2003-2009) in the laboratory of Prof. Fernandez-Belda at the same University. I obtained my PhD in 2009 with a Spanish FPU fellowship focused on the characterization of the cell death mechanisms induced by calcium following myocardial infarction. In 2009, I received my PhD with Honors (Award to The Best PhD Thesis, UMU). In the same year, I join to Prof. Pascual-Figal's lab at the Clinical and Experimental Cardiology Research Group at the Hospital Virgen de la Arrixaca as post-doctoral fellow supported by a Regional fellowship by Comunidad Autonoma de la Región de Murcia. In 2010 I was awarded a Juan de la Cierva Research Fellow from the Ministry of Science in Spain (MEC) within the area of Biomedicine. In this period, he joined the lab of Prof. Bayes-Genis (Barcelona, Spain), 7 months overall. Thank to my first project as PI (FFIS/CM10/011), aimed at identifying procedures that reduce the cardiotoxicity and myocardial remodeling and heart failure associated with the use of anthracyclines, I was able to set up my laboratory and directed my own line of research "Myocardial Remodeling and Heat Failure". In 2014, I was awarded a Sara Borrell contract, and continued with my main research line. Later in 2015, with the second project as IP, I was able to form my own research group by being able to hire and directing the thesis of my first PhD student: Maria del Carmen Asensio López. In 2016, I carried out a stay at the Cardiovascular Research Center (New York, USA) (2 years), in collaboration with the research group of Roger Hajjar, partially funded by a Jose Castillejo Fellowship (CAS16/00111). I pioneered the identification of two key elements involved in the overexpression of sST2; these results have recently been patented (ES2637032). In 2018, I was awarded a Research contract for access to the Spanish System of Science, Technology and Innovation and returned to IMIB-Arrixaca Institute (Murcia, Spain) to continue with my independent research career and projects as PI. Indeed, in October 2018 I was awarded with my third project as PI (20652/JLI/18) as PI as a junior Group leader from Seneca Foundation (Spain). Moreover, in 2019 I have been aware with a new project as PI (PI19/00519) from ISCIII. I have published 35 original articles in major international journals (Q1/D1) and I am first, senior or corresponding author of 33 of these publication. The indicated publications have obtained 897 citations according to Google Scholar yielding an h-index of 17 and an i10 of 23. I have participated in 21 research project, one international project



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funding by Novartis and 20 national projects. I have been PI in 4 projects (2 of them in collaboration with international Research Centers). I am reviewer for 7 high impact JCR journals and I am member of the editorial board of leading international journals such as Journal of Heart and Cardiovascular Medicine and Arrhythmia: Open Access. Moreover, since 2015 I have acted as Scientific Evaluator of the GRIS European program (Czech). Since 2018, I am Associate Professor-Cardiology (ANECA certified) (Faculty of Medicine, UMU, Spain). I would like to highlight among other supervisory actions that I am the director of two PhD thesis and co-director of another one. Recently, I have created a Technology Based Company entitled Biocardio.