



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: PALAZON GARCIA, FRANCISCO DE ASIS

Referencia: RYC2018-024183-I

Área Temática: **Biomedicina**

Correo Electrónico: asispalazon@gmail.com

Título:

Next Generation Immuno-Oncology

Resumen de la Memoria:

I am a pharmacist (2006) and biochemist (2008), degrees obtained at the University of Navarre. I defended my PhD thesis in Cancer Immunology and Immunotherapy in 2012 at CIMA (Pamplona, Spain), supervised by Prof. Ignacio Melero. During this early career stage, I contributed to the understanding of the mechanism of action of anti-CD137 agonist therapeutic antibodies (currently undergoing clinical trials), its combinations with other drugs, and the influence of tumor oxygenation in the efficacy of immunotherapies.

In 2012, I joined Prof. Randall Johnson's lab at the University of Cambridge for a postdoctoral stay supported by a Marie Curie Intra-European fellowship, with the aim of studying the role of hypoxia on immune responses in cancer.

In 2017, I joined the pharmaceutical industry (Medimmune, Cambridge, UK) as a senior scientist, contributing to a range of preclinical activities from target identification to IND-application in the field of immuno-oncology, and supervised two postdoctoral associates.

In early 2019, I joined CICbiogune as a Principal Investigator where I lead the Immuno-oncology lab supported by a highly competitive ERC Starting grant (2M EUR). My lab has a core focus on immuno-oncology, specifically on target discovery and drug development, to exploit several opportunities that the hypoxia pathway in T cells offers for the treatment of cancer. It is well recognised that the clinical response of immunotherapies depends on the ability of T-cells to mount an effective effector response, persist in treated patients and avoid exhaustion and toxicities. Several approaches to immunotherapy have shown promise in clinical trials, especially the use of immune checkpoint inhibitors and, more recently, autologous adoptive T-cell therapies. However, current state-of-the-art immunotherapies are only effective in a small fraction of patients, offering a medical need to be addressed in several cancer types.

Importantly, the tumor microenvironment has specific features that impact the immune response, including decreased oxygenation, aberrant vascularization and altered nutrient availability; all these influence the success of immunotherapies.

During the last 10 years, my research has been focused on elucidating the role of the oxygen sensing machinery in T cell function, and the link of hypoxia-driven metabolism and epigenetic modifications with T cell differentiation into effector and memory T cells within the context of cancer immunotherapy.

My current aims are to exploit these previous findings with a multi-disciplinary strategy, to deliver several early-stage drug discovery outputs. The main objectives are:

1. Development of a novel small molecule inhibitor to modulate the hypoxic response in T cells.
2. Therapeutic target discovery in T cells, focused on hypoxia-driven epigenetic modifications
3. Development of hypoxia-inducible molecular switches for adoptive T cell therapy.

Successful completion of these aims will allow me to further innovate and consolidate my position as a leader in this field, harness this pathway for therapeutic potential and explore potential combinatorial approaches.

Resumen del Currículum Vitae:

h-index: 24. Over 1600 citations. Over 30 original peer-reviewed publications.

- I generated my own line of research (the role of hypoxia in anti-tumor immunity) as shown by a portfolio of high-profile publications in this field, with clear progression on number of citations. These include first author publications in Cancer Cell, Immunity and Cancer Discovery; and an article published in Nature as a second author; all these examples having an impact factor over 20.

- Academic and pharmaceutical industry mixed background. This mixed experience has helped me to develop my expertise in designing hypothesis-driven projects with clear translational, innovative and commercial components.



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AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

- Genuine mobility to accomplish key goals. I have been productive in different international environments, including University of Navarra (Spain), UCSD (US), University of Cambridge (UK) and Medimmune Ltd. (UK)
- Patents and successful technology transfer achievements: I protected my discoveries and raised venture capital funding to further develop and commercialize inventions.
- Successful on highly competitive European funding calls: I was awarded a prestigious ERC Starting grant in 2018, which allowed me to reintegrate in Spain from the UK and become a group leader at the Severo Ochoa excellence center CIC biogune.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: DEOGRACIAS PASTOR, RUBEN
Referencia: RYC2018-025215-I
Área Temática: **Biomedicina**
Correo Electrónico: ruben.deogracias@icloud.com

Título:

Neurobiología del Desarrollo y enfermedades neuronales

Resumen de la Memoria:

Two degrees in Biology (Molecular Biology) and Biochemistry and a PhD in Biochemistry and Biomedicine. Focus on study the molecular mechanisms of neuronal development and neurological disorders due to alterations in the expression of the neurotrophin BDNF and synaptic especification. I carried out my PhD Thesis at the Instituto de Investigaciones Biomedicas Alberto Sols (CSIC-UAM, Madrid) under the main supervisión of Dr. Rodriguez-Pena. I performed my first postdoctoral at the prestigious Biozentrum of the University of Basel under the supervisión of Prof. Yves-Alain Barde. During this period I got numerous publications (3 as first author in PNAS, Stem Cells and J. Neuroscience, and 4 as collaborator) regarding the role of BDNF and MeCP2 during brain development and Rett Syndrome. During this period I use stem cell-derived neurons and human iPSC to conduct all our research. I also contributed as inventor in 5 patents and my research has served to start the first clinical trials for Rett Syndrome.

I did my second postdoctoral as senior research associate at both the Instituto de Neurociencias de Alicante (CSIC-UMH) and King's College London at the group of Prof. Beatriz Rico. During this period I focus on the study of the molecular mechanisms that control inhibitory synapse especification during brain development. My results have been recently published in Science (Deogracias, Favuzzi et al., 2019), where we show that different interneurons express specific genetic programs to control synaptic compartmentalization. I have also contributed as second author in two high impact factor papers in Neuron (Favuzzi et al., 2017) and Cell Reports (Hinojosa et al. 2018), where we also describe molecular mechanisms of synaptic plasticity and specification during development.

I have also contributed in teorical and practical teaching during my two postdoctoral periods and I have been also main supervisor of the thesis of several Master Students and Bachelor Students.

Since August 2017 I am Principal Investigator at ReNeuron and responsible of the Area of Discovery, where I am developing two projects. One is a new research line focused on the generation of new therapeutic products based on genetic modification of human neuronal precursors and the second is focus on the active loading of Extracellular vesicles (EVs) with therapeutic proteins and miRNAs. The use of those therapeutic EVs originated from clinical grade human neurostem cell progenitors opens the possibility of tissue specific targeting and therefore a more direct and efficacious delivery of therapeutic biomolecules. We are currently preparing two patents to cover my inventions as Principal Investigator and investigating new therapeutic approaches based on our genetically modified cells and EVs.

Resumen del Currículum Vitae:

Research Positions

2017-Present. Principal Investigator/Group Leader - Responsible of the Area of Discovery at the Department of Research. ReNeuron LTD, United Kingdom.

Manager of 2 Research projects:

1. Genetic modifications of human neural progenitors to increment their biological activity and potency.

2. Active loading of EVs with therapeutic proteins and nucleid acids using clinical grade human cells.

Currently preparing 2 patents as inventor at ReNeuron.

Line manager of one Research Scientist and PhD-Student

2014-2017. Senior Research Associate at King's College London at the group of Prof. Beatriz Rico (promoted to the Grade 6, spine 10, maximum grade for Research Associates). Manager of 1 Research Assistant. Awarded in 2017 with the Independent Researcher Award from King's College London with the aim to facilitate a streamlined transition into an independent research career. Supervision and mentoring of undergraduate and graduate students.

2013-2014. Senior Post-Doc at Instituto de Neurociencias de Alicante at the group of Prof. Beatriz Rico. Manager of 1 Research Assistant. (Laboratory moved to London in July 2017. Our research was delayed for 6months in order to setup the laboratory and the mouse lines in U.K.).

2007-2013. Research Associate at the Biozentrum of the University of Basel at the group of Prof. Yves-Alain Barde, where I also participated as Co-IP in the grant "Increasing BDNF levels with Fingolimod" successfully obtained (IRSF), and my contribution as Co-Investigator has been aessential in the obtention of the grant "Mouse and human stem cells: control of self-renewal and neural differentiation" (Swiss National Science Foundation). My research has made possible the first clinical trial for Rett Syndrome, actually in Phase II. Inventor of 5 patents related to all my work.

Other Grants and Fellowships:



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Independent Research Grant (April 2017; King's College London) to develop my own project as Independent Researcher entitled "A new tool for gene K.O. to investigate genes involved in neurodevelopmental and neurodegenerative diseases".

Grant from the International Brain Research Organization to present my work at the SfN's 47th Annual Meeting 2017.

Fellowship for Pre-doctoral research training. I3P Program. March 2006 – February 2007. Entity awarding the grant: Spanish National Research Council (CSIC).

Fellowship for Pre-doctoral research training. FPI Program. June 2002 – June 2006. Entity awarding the grant: Spanish Ministry of Science and Technology.

Fellowship for short term stays abroad. July – August 2005. Entity awarding: Spanish Ministry of Science and Technology.

Publications (12)

First author: Science 2019 (IF 2018: 41.058. Q1), PNAS 2012 (IF: 9,737. Q1), Stem Cells 2012 (IF: 7.701. Q1), J Neurosci 2012 (IF:6.908. Q1), Mol Cell Neurosci 2004 (IF:4.17, Q2).

Second, third and other positions: Cell Reports 2018 (IF: 8.032. Q1), Neuron 2017 (IF:14.318 Q1), PNAS 2012 (IF: 9.737. Q1), JCB 2012 (IF: 10.822. Q1), Cell Death & Dis 2012 (IF: 6.044; Q1); J Neurosci 2010 (IF: 7.271. Q1), JCB 2005 (IF:6.16).

Total Number of Citations WoS 767, h-index WoS: 10.

Ad hoc reviewer for peer reviewed international journals.

Member of one Thesis Committee at the Universidad de Salamanca (2015).



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: JANIC , ANA
Referencia: RYC2018-025244-I
Área Temática: **Biomedicina**
Correo Electrónico: ana.janic@upf.edu

Título:

UNDERSTANDING HOW TUMOUR SUPPRESSORS PREVENT THE DEVELOPMENT OF CANCER

Resumen de la Memoria:

Tumour suppressors are proteins that can prevent the development of cancer. My research career has a strong focus on understanding tumour suppressor function in vivo, in the context of the whole organism. During my PhD, in the laboratory of Cayetano Gonzalez at IRB Barcelona, I studied the molecular basis of cancer using *Drosophila* as a model organism. The quality of my PhD research is best demonstrated by my first author publication in *Science* (Janic et al., 2010) and co-authorship on a paper in the equally respected journal *Nature Genetics* (Martinez et al., 2009), and the Special Award for Doctoral Studies from the University of Barcelona in 2011. My first author publication in *Science* has been cited more than 150 times and has attracted editorials in *Science* and *Cell*. Importantly, this work has shown for the first time in vivo that ectopic expression of germ line genes can have a tumour suppressive effect. After my PhD, I joined Professor Andreas Strasser's Laboratory at the Walter and Eliza Hall Institute (WEHI) as a postdoctoral fellow. On joining his laboratory, I changed fields and rapidly integrated my previous knowledge of molecular biology and genomics with mouse genetics and primary cell culture models to study how tumour suppressor p53 protects us from developing cancer. My career has been on a consistently upward trajectory towards independence, with 2 co-senior author publications (Valente et al., 2013, Valente et al., 2016). Most importantly, my work re-shaped the view of the importance of cell death, cell cycle arrest or senescence in p53-mediated tumour suppression (Valente et al., 2013, Valente et al., 2016). My follow up studies were designed to uncover the mysteries of this crucial tumour suppressor, and to get into the heart of its function in preventing the cancerous transformation of the cells. To address this question, I have performed innovative gene-editing screens in pre-clinical mouse models of cancer. In the world's first, I found that the coordination of several DNA repair processes is the most important process by which p53 prevents the development of cancer. My first author publication in *Nature Medicine* (Janic et al., 2018) describing these discoveries has recently been published and it is anticipated that this paper will have a tremendous impact on the p53 field and cancer biology in general. In 2018 I was awarded the Centenary Medical Innovation Prize for my postdoctoral work, the prestigious Australian award to early career scientists judged by the international panel of the reviewers. Furthermore, my increasing recognition in p53 field is demonstrated by selection to speak at 6 international and 5 Australian national conferences, and invitations to give seminars at 5 European institutes. Internationally, I present my work in sessions with leaders in cancer research as Hans Clevers, Tayler Jacks or Laura Attardi. Based on my previous studies, I hypothesise that the coordination of DNA damage repair is the most critical mechanism by which p53 suppresses tumour development. Certainly, my results exclude generalities particularly considering context of accompanying oncogenic lesions and cell type. Over the next 5 years my research efforts will be focused on advancing knowledge in understanding the p53 tumour suppression transcriptional network within different contexts.

Resumen del Currículum Vitae:

I have dedicated my career to using animal models to understand how tumour suppressors are protecting us from developing cancer. I have completed BCs and MSc at the University of Belgrade in 2005 and I obtained a PhD in Biomedicine at IRB Barcelona in 2011. During my PhD I studied the molecular basis of cancer by using *Drosophila* as a model organism. The quality of my PhD research is best demonstrated by a first author publication in *Science*, co-authorship in *Nature Genetics* and the Special Award for Doctoral Studies from the University of Barcelona in 2011. After my PhD a successful Beatriu de Pinós postdoctoral fellowship has allowed me to move to Australia, to not only reinforce the international dimension of my career but also to acquire cross-sector research experience. I moved between substantially different, yet ideally complementary areas in science (*Drosophila* to mouse models to study cancer). The main focus of my research was the identification of the critical mechanisms for p53-mediated tumour suppression. My studies in murine pre-clinical models overturned the dogma that p53 prevents the development of cancer by instructing cells to die, and that DNA repair is a critical process for p53-mediated tumour suppression. My independence as an early-career researcher and further evidence on high regard on the field of cancer is exhibited in my publication record. These include my recent first author paper in *Nature Medicine*, 2 co-senior author publications in *Cell Reports* and *Oncogene*, and invited review in *Cell Death and Differentiation*. This upward trajectory in research output is set to continue underpinned with two postdoctoral fellowships, two Australian young investigator project grants, Craven & Shearer and Page Betheras awards that recognises outstanding female postdoctoral fellows, and highly regarded 2018 Centenary Institute Medical award for the best young biomedical researchers in Australia. Recently I have returned to Spain with the unique set of skills and expertise to build my own independent laboratory in cancer research using *Drosophila* and mouse models.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: SOTOS PRIETO, MERCEDES
Referencia: RYC2018-025069-I
Área Temática: **Biomedicina**
Correo Electrónico: merchesotosprieto@gmail.com

Título:

Epidemiología nutricional y genética, estilos de vida y enfermedad cardiovascular

Resumen de la Memoria:

The overall goal of my research is to improve society's health through better nutrition and lifestyles. My training in nutrition and genetic epidemiology, public health, and clinical research started during my PhD program, I worked on the PREDIMED (Prevention with Mediterranean Diet) trial, which is the largest randomized controlled trial to date, to examine the role of the Mediterranean diet in the prevention of cardiovascular disease among an older population. I sought to understand why some participants responded better than others did to the Mediterranean diet intervention with regard to obesity and related diseases by studying gene-diet interactions. Seeking to enhance my PhD experience, I pursued graduate research visits at Harvard Chan School of Public Health, University College in London, and Cambridge University (UK) to analyze data from complex, observational epidemiologic studies (10 manuscripts, all first author, 3 book chapters, and best doctoral dissertation award).

As a postdoctoral fellow, I continued to study diet and related health behaviors across the life course. First, at the National Center of Cardiovascular Disease (CNIC), I implemented and evaluated a school-based randomized controlled trial in Spain (SI! Program) aiming to enhance a healthy lifestyle in pre-schoolers by targeting parents and the school community in addition to the children. Subsequently, I went to Harvard Chan School of Public Health under a prestigious and competitive fellowship from Spain with funding for two years to study how healthy lifestyles cluster together and influence chronic health outcomes, alone and in combination with genetic risk. For that purpose, I used several large longitudinal epidemiological data (Nurses' Health and Health Professionals Follow-up Studies). After 2-years of postdoc, I took a position at Harvard as a Research Associate within a federally funded grant (\$1,500,000) to conduct a Mediterranean diet-based intervention among U.S. firefighters. My efforts as postdoc and research associate yield success in more than 20 publications in high impact journals, including a first author in the New England Journal of Medicine and Circulation (we evaluated how changes in three different dietary patterns overtime were associated with overall mortality, CVD and cancer). In addition, among others awards I got, the Outstanding Postdoctoral Researcher Award at Harvard, and the prestigious Jeremiah and Rose Stamler Research Award for New Investigators at the American Heart Association.

In 2017, I got a position as an Assistant Professor at Ohio University (teaching load 30%, research 60%, service 10%) while keeping the Visiting Scientist position at Harvard. As I transition to a more independent investigator I got 5 research grants as a PI and 1 as a Co-PI. I am trying to validate different Lifestyle Scores epidemiologically developed in different populations, translate it in the clinical setting, and creating a mobile friendly application. In addition, I am studying temporal changes in metabolome and microbiome in response to Mediterranean Diet as a model system to understand diet-health interactions. I currently teach 3 courses for graduate students and I supervised more than 15 master's dissertations and currently supervising 4 thesis, 2 undergrads, and 1 doctoral student.

Resumen del Currículum Vitae:

EDUCATION

2003-2007 Bachelor of Human Nutrition and Dietetics, and Food Science and Technology (First National Award in both BSC) University of Valencia, Spain

2008-2012 Doctor of Philosophy (Cum laude) Public Health, Concentration: Nutritional and Genetics Epidemiology, University of Valencia, Spain. Mentor: Dolores Corella

POSTDOCTORAL TRAINING

2016-2017 Research Associate, Department Environmental and Occupational Health, Harvard T.H. Chan School of Public Health, Boston,

Mentor: Stefanos Kales, PhD, MD and Frank Hu, MD, PhD, MPH

2014-2016 Postdoctoral Research Fellow, Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston

Mentor: Frank Hu, MD, PhD, MPH and Josiemer Mattei, PhD, MPH

2012-2013 Postdoctoral Research Fellow, National Center of Cardiovascular Diseases (CNIC), Madrid, Spain. Department of Epidemiology and Population Genetics

Mentor: Valentin Fuster, PhD, MD

FACULTY POSITIONS

2017 present Assistant Professor, Department of Food and Nutrition Science, School of Applied Science and Professions, Ohio University, Athens, OH, USA

2017 present Visiting Scientist, Department of Nutrition & Environmental and Occupational Health, Harvard T.H. Chan School of Public Health, Boston, MA, USA



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

TEACHING EXPERIENCE AND MENTORING

Spring 17-19 Advance seminar in Food Sciences and Nutrition and Research Methods in Nutrition (Graduate Students), 120 hours each year. Ohio University

Spring 14 Nano-course Instructor, Nutritional Epidemiology (Graduate students) Harvard T.H. Chan School of Public Health, Boston
2012-2014 Adjunct Faculty, Promotion of Health in School and Didactics of Experimental Science (Graduate students), University of Camilo José Cela, Madrid, Spain (650 hours)

Mentor 18 Master's thesis, currently advising 3 and co-advising 5, 2 honors students, 1 doctoral student

SCIENTIFIC ACTIVITY

External competitive grants as PI: 7, as Co-PI: 1, Participation and collaboration in projects I+D+I (>15)

Scientific publications: 37- As first/corresponding author or senior author: 22. In the first Quartile: 15. H-Index 9 (JCR) or 13 (google scholar), sum of times cited 310 or 558. Best 5 scientific publication

- New England Journal of Medicine 2017, 377(2):143-153. IF:72.4 (1/155) D1 (cites:75)
- Circulation. 2015;132(23):2212-2219. IF 18.9 (2/124) D1
- J Am Coll Cardiol. 2015;66(14):1525-34. IF 14.9 (1/125) IF D1
- J Am Heart Assoc. 2016;5(12). IF 5.17 (18/124) D2/Q1
- J Nutr. 2015;145(7):1531-40. IF 4.4 (16/81) D2/Q1

Participation in conferences: 11 invited talks, 8 oral presentations, 25 posters as main author

Honors and Awards: 18. (First National Award in the BSc, dissertation, Outstanding postdoc award (Harvard), Jeremiah and Rose Stamler Research Award for New Investigators, American Heart Association, Early Career Travel Award, Finalist for the American Society Nutrition Emerging Leaders)

Competitive scholarships: Doctoral Formación Personal Universitario, MICIN, Alfonso Martín Escudero Foundation Postdoctoral Research Fellowship, Dannon Institution Research Grant for graduates in Nutrition

Research stays: Postdoctoral: 3 years at Harvard School of Public Health, USA. Predoctoral: 7 months (University College of London, Cambridge University, Harvard School of Public Health).

Scientific reviewer for journals, abstracts, and grants

Honorary Academy member of the Nutrition and Dietetic Association.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: SANCHEZ MUT, JOSE VICENTE
Referencia: RYC2018-025298-I
Área Temática: Biomedicina
Correo Electrónico: SANCHEZMUT@GMAIL.COM

Título:

Genetic and epigenetic underpinnings of brain function in health and neurodegenerative diseases: Alzheimer's Disease

Resumen de la Memoria:

My scientific career has focused on the genetic-epigenetic underpinnings of brain function in physiological and pathological conditions, with a special emphasis on Alzheimer's (AD) and Parkinson's disease (PD). Early on, during my undergraduate training, I got expertise in bioinformatics (Dpt. Genetics, University of Valencia, Spain, 2003) and showed interest in the epigenetics field developing a series of new epigenetic panels for genetic consulting (Genetic Analysis ANCOR, Spain, 2004). I moved to the laboratory of Prof. Perez-Tur at Biomedicine Institute of Valencia (IBV-CSIC, Spain, 2005) and investigated the genetic underpinnings of PD, contributing to the characterization of the prevalence of Leucine-rich repeat kinase 2 (LRRK2) mutations (Mov Disord, 2006) and other frequent polymorphisms in the Basque population (Mov Disord, 2009). There, I further developed my bioinformatic skills and in silico predicted the functional consequences of disease-causing mutations of PD associated genes (Hum Mutat, 2011). As a demonstration of my early maturity as independent researcher, I also developed and got funding for a totally new line of research, investigating the relationship between genetics, epigenetics and AD (Young research project awarded by Fundación Bienvenida-Navarro, Spain, 2006). Immediately after, I was awarded with a training scholarship for Epigenetics (UIMP, Spain, 2006), and conducted a research stay in the Cancer Epigenetics Group lead by Prof. Manel Esteller at the Spanish National Cancer Research Centre (CNIO, Spain, 2008). The same year, I was awarded with a Research Staff Training (FPI) Fellowship (2008), and joined Esteller's lab to investigate epigenetic alterations AD hypothesis. During this time, I developed a new array for investigating DNA methylation in mice. I contributed to the identification of the epigenetic specificity of different brain regions in physiological conditions, and to the alteration of those regions in AD e.g., hypermethylation of the Axonal Initial Segment (AIS) gene SPTBN4, which has been shown to accelerate AD pathology (Brain, 2013). Of note, during my PhD, I compiled the most comprehensive DNA methylation catalogue of neurodegenerative diseases done so far including AD and PD among others (Transl Psychiatry, 2016) and was the first one demonstrating the functional relevance of DNA methylation alterations in AD pathophysiology i.e., hypermethylation of DUSP22 and TAU hyperphosphorylation (Hippocampus, 2014). After my PhD, I moved to the laboratory of Prof. Johannes Gräff at École Polytechnique Fédérale de Lausanne (EPFL, Switzerland, 2014) as a postdoctoral researcher. There, I gave another twist to the field and took an important step forward by integrating genetic, epigenetic, and RNA expression in silico and experimental analysis the biggest ensemble of samples investigated so far in these type of studies. I identified the first methylation/expression quantitative trait locus for AD, and the mechanism by which it confers a risk for AD. Namely, by forming a chromatin loop with a hitherto not well-characterized metalloproteinase, Peptidase M20 Domain Containing 1 (PM20D1), which protects against Aβ₄₂; accumulation and cognitive impairment in AD (Nat Med, 2018). This type of study is the first of its kind, and opens a new avenues for AD research. These results have been presented in s

Resumen del Currículum Vitae:

Since 2014, I am working as scientific collaborator in the Laboratory of Neuroepigenetics of Prof. Johannes Gräff at the École Polytechnique Fédérale de Lausanne (EPFL, Switzerland). I have received a BS in Biology from the University of Valencia (UV, Spain, 2005) and a PhD in Neurosciences from the Autonomous University of Barcelona (UAB, Spain, 2014). I have authored 26 research papers in high impact scientific journals (24 in Q1), and more than 20 communications in national and international conferences. I accumulate more than 2200 citations (h-index of 17), have written several high profile review articles (e.g., Lancet Neurol), and have served as reviewer for prestigious journals (e.g., Acta Neuropathol) and funding agencies (e.g., Alzheimer Association, UK). My scientific career has focused on the genetic and epigenetic underpinnings of brain function in health and disease. My research combines in vitro and in vivo experiments with the analysis of human postmortem samples, plus a rare combination of wet and dry lab approaches. I have developed new arrays for DNA methylation, contributed to the identification of the epigenetic specificity of different brain regions (Brain, 2013) and cell types (Synapse, 2017), and highlighted genetic (Mov Dis, 2006 and 2009; Hum Mutat, 2011) and epigenetic alterations (Brain, 2013; Hippocampus, 2014; 2016 Transl Psychiatry, 2016) underlying neurodegenerative processes such as Alzheimer's and Parkinson's disease. In my most recent publication, I have developed an innovative approach combining human genome-wide association studies with whole genome gene expression and epigenetic studies, compiling the biggest ensemble of samples investigated so far in these type of studies (Nat Med, 2018). This study the first of its kind has paved the way to re-assess and re-evaluate previous investigations. With this pioneering approach, I have been able to identified a new risk factor for AD, outside of the box of the canonical theories: a new AD-associated locus that displays enhancer-like characteristics, contacts the promoter of a previously unknown gene, PM20D1, via a CTCF-mediated chromatin loop, and regulates its expression by DNA methylation. Using an elegant approach, I have also bidirectionally



MINISTERIO
DE CIENCIA, INNOVACIÓN
Y UNIVERSIDADES



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

increased and decreased the expression of PM20D1, showing a reduction and impairment in AD-related pathologies and cognitive performance, respectively, further supporting the functional relevance of identified alterations. These results hold a patent for AD diagnosis and substantiate a new potential treatment for AD that is currently under evaluation.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: VALDEARCOS CONTRERAS, MARTIN

Referencia: RYC2018-025757-I

Área Temática: Biomedicina

Correo Electrónico: marvalcon@gmail.com

Título:

Targeting hypothalamic microglia to regulate energy and glucose homeostasis

Resumen de la Memoria:

The prevalence of obesity has reached epidemic proportions worldwide and current preventive strategies and medical interventions have not limited this upsurge, underscoring the need for new and effective ways to mitigate metabolic diseases. Recent studies implicate glial cells as physiological regulators of the hypothalamic control over energy balance and highlight the potential benefit of exploring how such non-neuronal cells contribute to the pathogenesis of obesity.

My research interests are focused on the emerging field of neuroimmunology, in particular how immunological and metabolic responses within the hypothalamus regulate homeostasis and contribute to disease pathogenesis. I have a special interest in exploring the role of microglia, resident macrophages of the CNS, in the hypothalamic control of energy and glucose homeostasis. We have shown that microglia in the mediobasal hypothalamus (MBH) can sense rising levels of saturated fats, and transduce this sensory capacity to instruct local neurons to regulate energy balance (Cell Reports, 2014). Moreover, using innovative genetic mouse models combined with bone marrow lineage tracing, we showed that diet-induced microgliosis is heterogeneous, and involves both resident and bone marrow-derived cells that acquire microglial morphology. Also, we found that mice can be protected from diet-induced weight gain by controlling microglial inflammatory signaling, and that spontaneously forcing microglial inflammatory signaling is sufficient to increase both food intake and weight gain, even in the absence of an obesity-promoting diet (Cell Metabolism, 2017). These exciting findings define microglia as approachable targets that can be harnessed to manipulate hypothalamic function.

The role of hypothalamic immune signaling in response to nutrient excess is a novel interdisciplinary field which sits at the intersection of immunology, neuroscience and metabolism. This project has the potential to gain an unprecedented view of the neuroimmune communication in hypothalamic physiology, and uncover new therapeutic targets to control metabolic function, obesity and its consequences.

Resumen del Currículum Vitae:

I completed my degree in Biology at the University of Granada in 2005. After my graduation, I joined the Department of Innate Immunity and Inflammation at the Institute of Molecular Biology and Genetics, part of CSIC and University of Valladolid, Spain. I was awarded a predoctoral fellowship from the Junta de Castilla y Leon to carry out a research project focused on lipid signaling in immune cells. In 2011, I obtained my Ph.D. under the supervision of Drs. Jesús Balsinde and María Balboa, well-recognized scientists in the field of inflammation, and its regulation by cellular lipid metabolism. This work resulted in two impactful first-authored publications (Valdearcos M, et al., J Immunol., 2011; Valdearcos M, et al., J Biol Chem., 2012) among other publications. The first described how lipin-1 participates in the biogenesis of lipid droplets in human macrophages. The second defined a protective role for lipin-2 against saturated fat-induced macrophage activation, a finding relevant for the development of new pharmacologic targets to treat metabolic diseases. During my Ph.D., I performed an internship for 3 months at the Gladstone Institutes (San Francisco, USA) under the supervision of the investigator Dr. Robert Farese Jr., an internationally recognized expert in lipid metabolism and mouse physiology.

In 2011, I was recruited as a postdoctoral researcher by the laboratory of Suneil Koliwad, MD, Ph.D., in the University of California San Francisco (UCSF) Diabetes Center. In this exceptional environment, I expanded my research interests to focus on understanding the role of immune cells in the mediobasal hypothalamus, a brain area controlling food intake, energy metabolism, and body weight. Switching from the periphery to the CNS was challenging, but I received additional mentorship from experts in hypothalamic physiology at UCSF to develop innovative mouse models and genetic tools. This work led to a seminal paper (Valdearcos M. et al., Cell Reports, 2014; 155 citations) in the nascent area of microglial nutrient sensing. This finding was recognized in the field and I was awarded a scholarship to present my work at the Keystone symposia (Snow Bird, USA, 2015). This work was followed by a more comprehensive study (Valdearcos M. et al., Cell Metabolism, 2017) in which we show that hypothalamic microglia orchestrate a multicellular response to instruct the neuronal control of energy balance, providing a mechanistic framework to develop cell-specific therapeutic targets to treat obesity and its consequences.

During my postdoctoral training I received a 2- year award from QB3 (Quantitative Biosciences Consortium: UCSF, Berkeley, Santa Cruz) and Calico, a biotechnology company focused on aging and related diseases, including metabolic aspects. These funds allowed me to



MINISTERIO
DE CIENCIA, INNOVACIÓN
Y UNIVERSIDADES



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

investigate the role of microglia in postoperative hippocampal inflammation and cognitive decline in mice (Feng X*, Valdearcos M*, et al., JCI Insight, 2017, *Co-first author).

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In 2017, I was awarded a highly competitive K01 career development award, as principal investigator, from the National Institute of Health (NIH) with an application that received an exceptionally good score. The goal of these awards is to promote the transition to be an independent investigator. In 2018, I was promoted to Assistant Professor in the Department of Medicine at UCSF, a faculty position that allowed me to establish an independent line of



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: MELGAR LESMES, PEDRO
Referencia: RYC2018-023971-I
Área Temática: Biomedicina
Correo Electrónico: melgarpedro@yahoo.com

Título:

Translational research in new therapeutic and diagnostic strategies in liver diseases

Resumen de la Memoria:

After completing a degree in Pharmacy, and a second degree in Biochemistry, I joined a research group specialized in translational research in liver disease at the Hospital Clinic of Barcelona to complete a PhD in Biomedicine. My research investigations uncovered how dysfunctional angiogenesis is responsible for vascular and tissue damage leading to fibrosis and ascites in liver cirrhosis. We discovered that VEGF-A, Angiopoietin-2 and Apelin are pro-angiogenic factors that can mediate pathological angiogenesis and fibrosis in liver disease, and interfere with fibrosis resolution and hepatic regeneration. During my PhD I also had the opportunity to join a group specialized in hepatocellular carcinoma at the Mount Sinai Medical Center in New York City to investigate new pharmacological treatments for liver cancer.

After completing my PhD and with the objective of investigating new therapeutic approaches to treat liver diseases, I joined a scientific group at the Institute of Advanced Chemistry of Catalonia/Faculty of Pharmacy in Barcelona. I applied my knowledge and skills in biomedical sciences to the design of new therapeutic tools at the nanoscale to target diseased hepatic cells. During this postdoctoral fellowship we successfully designed multifunctional polymeric nanoparticles able to target, tag and treat dysfunctional endothelial cells or liver cancer cells, working towards detecting these diseased cells and arresting angiogenesis and cancer cell growth.

Based on my work in Barcelona I was invited to pursue a second postdoctoral fellowship with the Edelman group at the Massachusetts Institute of Technology in Cambridge, MA. This research group is specialized in cell therapy, dysfunctional angiogenesis in injury and cancer, and Biomedical Engineering. During my almost four years of work, we identified how circulating monocytes can interact with endothelium to select sprouting points and drive angiogenesis, and also how engineered implants of healthy matrix-embedded endothelial cells can help dysfunctional endothelium to reduce injury and boost angiogenesis and hepatic regeneration.

I am now back in Barcelona with lab space at the Faculty of Medicine, University of Barcelona. I am a Group leader taking part in a multidisciplinary consolidated group recognized by the Generalitat of Catalunya since 2017. This team includes different experts in liver diseases from Hospital Clinic of Barcelona. I obtained in 2016 a Research Grant from Generalitat of Catalunya to carry out a project to modulate macrophages for boosting liver regeneration using functionalized carbon nanoparticles. I am a coordinator PI in a coordinated project submitted to the Plan Nacional 2018 in collaboration with a PI from Institut Químic de Sarrià. I have supervised two students of Master degree and I am supervising two PhD students. My line of research will continue aimed at investigating molecular mechanisms involved in hepatic injury and finding new diagnostic and therapeutic strategies for liver disease. My extensive training and experience (more than 14 years) in a variety of scientific settings and disciplines will allow my research to focus not only on new solutions to diagnose and treat major global health problems such as liver disease, but also on developing technological tools to address broader scientific, medical and industrial questions.

Resumen del Currículum Vitae:

I graduated with a Bachelor's degrees in Pharmacy in 2001 and in Biochemistry in 2003, and completed a PhD in Biomedicine from the University of Barcelona in 2010 working at Hospital Clinic of Barcelona. My PhD investigations earned me the Extraordinary Doctorate award in 2010. Following my PhD studies, I completed a two-year postdoc at the Chemical and Biomolecular Nanotechnology Department of IQAC-CSIC/Faculty of Pharmacy in Barcelona (2011-2012). Based on my work in Barcelona I was invited to pursue a second postdoctoral fellowship with the Edelman group at the Institute for Medical Engineering and Science of the Massachusetts Institute of Technology in Cambridge, MA in 2013. Then, I received a postdoctoral fellowship from the European Association for the Study of Liver (EASL) to return to Barcelona (Fundació Clinic) in 2016 and a Beatriu de Pinós contract in 2018 at IDIBAPS.

To date, my experience in biomedical research extends over 14 years. I have published 1 book chapter and 28 original articles (16 in first decile, 12 in first quartile) in high-impact international journals (4 in Gut IF= 17.016; 5 in J Hepatol IF=15.040; 1 in Hepatology IF= 14.079; 1 in Nano Letters IF=12.080, etc) with a total number of 501 citations, a personal h-index of 14 in google scholar, and a personal h-index of 11 in researcherID. I have been corresponding author in 6 of these articles.

I am an Expert Evaluator of R&D projects for the Spanish National Research Agency since 2018.

I am a coordinator PI in a project submitted to the Plan Nacional 2018 (Ministry of Science, Spain) coordinated with a PI from Institut Químic de Sarrià. I am Group leader in a consolidated group recognized by the Generalitat of Catalunya and I am PI of a project funded by that public entity. I have participated in 8 projects funded by public Institutions and 2 funded by industry (3 ongoing). I have been invited to present my work at the Brigham Research Institute in 2015 and at the Koch Institute for Integrative Cancer Research in 2016.

I am author of one patent for liver transplantation.

I am an invited peer-reviewer in Gut, Journal of Hepatology and PLOS ONE among others.



MINISTERIO
DE CIENCIA, INNOVACIÓN
Y UNIVERSIDADES



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

I am member of different scientific societies:

-As from 2010: Member of the Colegio Oficial de Farmacéuticos de Barcelona. (Official Association of Pharmacists of Barcelona).

-As from 2015: Member of the Sociedad Española de Bioquímica y Biología Molecular (Spanish Society of Biochemistry and Molecular Biology).

-As from 2015: Member of the European Association for the Study of the Liver (EASL).

I am accredited as Lecturer and Aggregated teacher by the Agencia de Qualitat Universitaria from the Catalanian Government and I teach some subjects at the Faculty of Medicine, University of Barcelona. I have supervised two Master Degree thesis (TFM) and I am supervising two PhD students, one at MIT and one in Barcelona

I was granted by the FPI program from the Spanish Ministry of Science to carry out my thesis on biomedicine. Since then I have been granted by different public and private institutions: Spanish Association for the Study of Liver; Biomedical Foundation Alfonso Martin Escudero; Program Beatriu de Pinos from Generalitat de Catalunya (2013 and 2016); EASL; and Plan estratégico de investigación e innovación en salud (PERIS) 2016-2020 from Departament de Salut de la Generalitat de Catalunya.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: TOMA , CLAUDIO
Referencia: RYC2018-024106-I
Área Temática: **Biomedicina**
Correo Electrónico: c.toma@neura.edu.au

Título:

Combining genomic approaches to identify genes implicated across major psychiatric disorders

Resumen de la Memoria:

Therapeutic interventions in autism, schizophrenia and bipolar disorder first depend on identifying the underlying genes, which are mostly unknown. My scientific career has focused on understanding the genetic contributions to a range of complex psychiatric disorders across multiple prestigious institutions.

My research started at WTCHG, University of Oxford (UK), where I characterized the biological function of the dyslexia-associated KIAA0319 gene (2004-2005). I obtained my Ph.D. from the University of Bologna (Italy) in 2009, where I focused on autism susceptibility genes in the context of the main international consortia in the genetics of autism (IMGSAC and AGP).

I then started postdoctoral research at the University of Barcelona (Spain). In 2010, I was a CIBERER fellow transferring methodologies from research to clinical genetic testing in rare diseases. Afterwards, under a Marie Curie fellowship (European Commission), and funded as PI (Marató-TV3) I performed the first exome sequencing in multiplex autism families that led to the identification of novel genes for the disorder.

Since 2014, I have been a Senior Researcher at Neuroscience Research Australia (Sydney, Australia) where I have: i) identified novel genes for bipolar disorder; ii) associated the burden of truncating gene variants with psychiatric symptom severity; iii) and combined linkage studies with next-generation sequencing as a novel approach in psychiatric genetics.

My vision in the next few years is to combine high-throughput genetic analyses with molecular biology approaches to understand the biological role for genes that I have implicated in psychiatry in previous genetic studies, and to extend my expertise in disease gene discovery.

Resumen del Currículum Vitae:

My scientific career has focused on understanding the genetic contributions to a range of complex psychiatric disorders across multiple prestigious institutions in Europe and Australia. I joined the group of Prof. Anthony Monaco at WTCHG, University of Oxford (UK), to study functional aspects of the dyslexia-associated KIAA0319 gene (2004-2005). I obtained my Ph.D. from the University of Bologna (Italy) in 2009 under the supervision of Prof. Elena Maestrini (University of Bologna) and Prof. Anthony Monaco (University of Oxford), where I focused on autism susceptibility genes in the context of the main international consortia in genetics of autism (IMGSAC and AGP).

I then started postdoctoral research in the group of Prof. Bru Cormand at University of Barcelona (Spain) focused on psychiatric diseases and rare Mendelian diseases (2009-2014). In 2010 I received a Marie Curie European fellowship and funding as Principal Investigator to perform the first exome sequencing in multiplex autism families that led the identification of novel candidate genes for the disorder. In 2014, I joined the group of Dr Fullerton at Neuroscience Research Australia (NeuRA) in Sydney investigating the genetics of bipolar disorder by whole-exome/genome sequencing, linkage studies, structural variant analysis and genome-wide association studies.

During my career I have received 15,000 in research prizes from national or international funding bodies. I have authored 33 research articles (58% as 1st, 2nd or last author) in top ranked journals, including Nature Genetics, Molecular Psychiatry (x3), Science, with >2,300 citations (70 citation/paper; H-index of 19), and have attracted 2.4 million as chief Investigator (A-E). I have peer reviewed 40 articles from 22 journals, including the top journals in psychiatry (Molecular Psychiatry x2, or Acta Psychiatrica Scandinavica x3). I am member of 3 editorial board journals. Currently, I lead projects on novel candidate genes implicated in multiple psychiatric phenotypes.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: MARTIN GAYO, ENRIQUE
Referencia: RYC2018-024374-I
Área Temática: Biomedicina
Correo Electrónico: enrique.martin@uam.es

Título:

Nuevas terapias celulares para tratar enfermedades infecciosas y autoinmunes

Resumen de la Memoria:

My scientific career started upon initiation of my Ph.D. studies, under the great mentoring of Dra. Maria Luisa Toribio, who introduced me to immunology by studying the ontogeny and contribution of intrathymic dendritic cells to the development of T regulatory cells. These studies allowed me to understand how the activation of key cell types such as DCs determines polarization of T cells and therefore, orchestrate immune responses. This was a very productive period that produced two first-authored scientific articles and several collaborative publications and allowed me to build a strong background as a basic immunologist. Thanks to the remarkable mentoring of Dra. Toribio I established multiple collaborations that greatly expanded my knowledge and expanded my productivity. In addition, already as a predoctoral fellow I was invited to attend to several national and international scientific meetings where I was able to present my work and I was awarded with competitive funding program that allowed me to work in the Institut Curie as a visiting Ph.D student in the laboratory of Sebastian Amigorena.

After my PhD I continued my education in Immunology in the context of infectious diseases at Harvard University in Boston USA, where I joined Dr. Xu Yu's group at the Ragon Institute. As a postdoctoral fellow I focused on the role of conventional dendritic cells in HIV-1 immuno-pathology. During this time, I quickly acquired new knowledge in virology and translational research, which in combination with my previous expertise in immunology, has allowed me to address fundamental questions regarding the contribution of human dendritic cells to the spontaneous immune control of HIV-1 infection. These studies produced 6 first author publications and a patent. During this period I secured funding as a principal investigator from very competitive grant programs from Harvard University and Massachusetts General Hospital. In addition, I have been invited to give oral presentations in the most prestigious meetings from the field and to externally review scientific manuscript for top scientific journals. I also have been successful in expanding my network of collaborators, key for my subsequent studies. My next scientific interest is to manipulate innate cells to treat infectious and autoimmune diseases. I was recruited back to Spain 8 months ago through the competitive attraction of talent program (modality 1) from the Comunidad de Madrid. This program allowed me to create my own research group at the Hospital Universitario de la Princesa in Madrid and provided funding to start studying of the role of dendritic cells in inflammatory autoimmune disorders such as Rheumatoid arthritis and Sjögren's syndrome. In addition, I was able to recruit an R21 grant from the NIH and transfer it to Spain to continue investigating in the field of HIV vaccines. Importantly, I have successfully established collaborations with Dr. Isidoro Sanchez from the Rheumatology service and Dr Ignacio de los Santos from the Infectious Disease division from our hospital, who are providing samples from their patients for the two mentioned research lines. Therefore, I have already been recognized by the DC biology and HIV immunopathology fields and obtained scientific independence. My next goal is to transition into a recognized tenure track position to secure my group and research.

Resumen del Currículum Vitae:

I obtained my PhD. in the Universidad Autonoma de Madrid in 2010, at the laboratory of Maria Luisa Toribio where I studied several aspects of the tolerogenic function of intrathymic DCs. My first article as a first author in Blood identified the physiologic progenitor of human nTreg cells and demonstrated that pDCs can instruct these precursors to develop into a unique IL-10 producing Treg subset. Also during my Ph.D. period I characterized the intrathymic CD123+ myeloid precursor of pDCs that is generated in situ in the human thymus in response to permissive Notch signals in the medulla and published the study in the Journal of Experimental Medicine. I was invited to present both of these works in national and international scientific meeting. Importantly, I obtained Formacion de Profesorado Universitario (FPU) grant and the Contrato de Investigador de apoyo (CAM) that supported these studies. In addition, I established several national and international collaborations with different groups that led to the publication of articles in top journals. In these collaborations I contributed to understand of how Notch signaling regulates the differentiation of human T cells and the development of leukemia, the functional diversity of thymic monocytes and the role of CD69 in the development of Treg.

After graduating from my Ph.D., I continued my postdoctoral training in the context of infectious diseases in the laboratory of Dr. Xu Yu at the Ragon Institute of MGH, MIT and Harvard in Boston, USA, where I studied the contribution of human DCs to spontaneous control of HIV-1 infection. In a collaborative study with Dr. Mary Carrington's laboratory published in PLoS Genetics, I demonstrated that affinity of LILRB2 to HLA-B alleles affected the antigen presenting function of DCs. My subsequent studies published in PLoS Pathogens, investigated how DC directly interact with HIV-1 and participate in effective immune responses against the virus in elite controllers. These studies led to a collaboration with Dr. Alex Shalek from the MIT to further dissect the molecular mechanisms responsible for different functional subsets of DC responses in HIV-1 elite controllers, which was published in Genome Biology. More recently, in studies published in JCI Insight, we evaluated the role of DCs facilitating effective humoral immune responses against HIV-1 in controllers.



MINISTERIO
DE CIENCIA, INNOVACIÓN
Y UNIVERSIDADES



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

In addition, to my scientific productivity, during the postdoctoral period I recruited competitive funding as a principal investigator from Harvard University CFAR and the MGH ECOR programs that funded my research. I have been invited to present my postdoctoral projects as oral presentations in the most prestigious conferences (CROI, HIVR4P) and awarded early career and junior investigator awards from the Gates Foundation.

Finally, I recently started my research group as a Principal Investigator thanks to the Attraction of Talent program from the CAM and funded a project to perform phenotypical, transcriptional and functional characterization of different dendritic cell subsets from primary samples from patients suffering inflammatory autoimmune disorders in collaboration with Dr. Isidoro Gonzalez from the Rheumatology Service. In addition, in collaboration with Massachusetts General Hospital and UAM, I have obtained a NIH R21 grant that will test a dendritic cell-based HIV-1 vaccine.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: ORDOÑEZ MORAN, PALOMA
Referencia: RYC2018-025627-I
Área Temática: **Biomedicina**
Correo Electrónico: pomordonezmoran@yahoo.com

Título:

Stem Cell Plasticity in Cancer

Resumen de la Memoria:

My experience along with novel concepts emerging in biology have led me to identify an innovative and translational line of research focused on gene regulatory mechanisms which control tumour-initiating cells. I also study tissue regeneration that is mainly due to stem cell's ability to replenish itself and, in parallel, produce differentiated progeny. My aim is to understand how extrinsic and intrinsic signals regulate stem cell behaviour and how the balance between self-renewal and differentiation maintains homeostasis. Loss of this balance tends to lead to uncontrolled cell growth which results in tumours that are heterogeneous. Cancer stem cells have been put forward to be one of the determining factors that contribute to intra-tumour heterogeneity, however, recent findings have shown that the stem-like state in a given tumour cell is a plastic quality. For all these reasons, my goal is to study the factors that contribute to stem cell plasticity, cancer stem cell heterogeneity and the potential implications for cancer therapy. My long-term aim will be to develop novel therapeutic approaches to successfully treat cancer patients.

Resumen del Currículum Vitae:

Mobility has provided me an excellent background in different fields. First, I obtained my PhD (Autónoma University of Madrid-CSIC) where I studied Nuclear Receptors Biology in Cancer. During this period I did several short-term visits to top-research Institutes (The Netherlands, Vall d'Hebron Institute of Oncology). My interests on stem cells led me to conduct a postdoc at EPFL where I was granted with an EMBO long-term fellowship. There, I acquired valuable knowledge in stem cell and tumour biology, a high expertise in in vivo models and 3D-organoid culture. After, I worked for two years at the University of Geneva as Senior Postdoc and later on, I went back to EPFL as Researcher Scientist (I am running my own projects). Recently, I have been appointed Assistant Professor at the University of Nottingham (UK) where I will begin in July 2019. Throughout my career I have established a wide range of national/international collaborations, I have ran many interdisciplinary projects and I have taught students and researchers at all levels.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: SANCHEZ DANES, ADRIANA
Referencia: RYC2018-024827-I
Área Temática: Biomedicina
Correo Electrónico: adrianasanchezdanes@yahoo.es

Título:

Descripción de las poblaciones celulares responsables de la iniciación y recaídas en el cáncer de piel más común

Resumen de la Memoria:

Mi trayectoria investigadora se ha centrado en estudiar enfermedades muy frecuentes en nuestra sociedad: las enfermedades neurodegenerativas (concretamente la enfermedad de Parkinson) y el cáncer. Durante mi doctorado generé el primer modelo celular in vitro de la enfermedad de Parkinson a partir de células de pacientes. El modelo generado recapitula las características clave de esta enfermedad y representa un buen modelo para investigar los mecanismos celulares y moleculares implicados en esta patología (EMBO Molecular Medicine 2012, primera autora, citado en más de 100 publicaciones).

La identificación del tipo de célula a partir de la cual se origina el cáncer y la población de células tumorales que resiste a la terapia y conduce a la recaída del tumor constituyen la base de mi investigación postdoctoral desarrollada en el laboratorio del Prof. Cédric Blanpain en Bruselas. He utilizado el carcinoma de células basales (BCC), el cáncer de piel que resulta de la activación constitutiva de la vía de señalización de Hedgehog y que constituye el cáncer más frecuente en los seres humanos, como modelo de cáncer para mis estudios.

Usando modelos genéticos de ratón que permiten estudiar la progenie de las células que expresan oncogenes (lineage tracing), en combinación con análisis clonal, pude contestar una pregunta clave en el campo del cáncer: la identificación de la célula a partir de la cual se originan los tumores (célula madre o célula progenitoras) y también identificamos cómo la activación de un oncogén altera la dinámica clonal de una célula conduciendo a la formación de un cáncer. Descubrimos que solo las células madre, y no las progenitoras, eran competentes para iniciar la formación de tumores después de la activación del oncogén. Este estudio demuestra que la capacidad de las células que expresan oncogenes para inducir la formación de tumores depende de la dinámica clonal específica de la célula de origen de cáncer (Nature 2016, primera autora). Precisamente, la célula en el origen de los diferentes tipos de carcinomas de células escamosas es el tema de la revisión que escribí junto con el Prof. Blanpain en Nature Reviews Cancer 2018. Durante mi postdoc también he contribuido a la comprensión de los mecanismos moleculares implicados en la iniciación del BCC. Demostramos que YAP y TAZ son esenciales para la iniciación de BCC (EMBO Journal 2018, co-primer autora) y que Sox9 es necesario para la formación del BCC (Cell Stem Cell 2015).

Recientemente, he descubierto la población de células tumorales responsables de la recaída en el BCC y he identificado un nuevo mecanismo de resistencia a la terapia en este tipo de cáncer de piel. Un proyecto más mecanístico que me ha permitido ampliar mi dominio a nuevas técnicas: ablación de linaje genético, FACS sorting, transcriptómica, secuenciación y tecnología RNAscope. Usando estas técnicas, identificamos una población de células tumorales resistentes que expresan Lgr5 y activación de la vía Wnt en ratones y humanos. Esta población de células tumorales resistentes es responsable de la recaída tras la finalización del tratamiento. Finalmente, demostramos que la inhibición combinada de las vías Hedgehog y Wnt conduce a la erradicación de BCC, constituyendo un tratamiento prometedor para evitar la recaída en pacientes con BCC (Nature 2018, primera autora).

Resumen del Currículum Vitae:

EDUCACIÓN

Investigación Postdoctoral. Agosto 2012- Actualidad
Université Libre de Bruxelles, Brussels (Bélgica)
Professor. Cédric Blanpain Lab, Stem Cells and Cancer Laboratory

Doctorado en Biomedicina (distinción cum laude). Junio 2008- Julio 2012
Universitat Pompeu Fabra, Barcelona (España)
Supervisores: Dr Antonella Consiglio y Professor Ángel Raya.

Master in Biomedical Research. Septiembre 2007- Junio 2008
Universitat Pompeu Fabra, Barcelona (España)

Grado en Biotecnología Septiembre 2003 Junio 2007
Facultad de Biosciencias, Universitat Autònoma de Barcelona, Bellaterra (España)
Nota: 3.4/4 (primera de la promoción)



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

PREMIOS Y BECAS

- 2013 2016 Postdoctoral fellowship, Fonds de la Recherche Scientifique, Bélgica
2008 2012 Beca FPU para desarrollar un doctorado, Ministerio Español de Ciencia y Educación
2006 2007 Beca de colaboración en un Departamento Universitario, Ministerio Español de Ciencia y Educación

- 2012 Distinción Cum laude doctorado, Universitat Pompeu Fabra, Barcelona
2007 Premio primera de la promoción 2003-2007 en Biotecnología por la Universitat Autònoma de Barcelona
2007 Premio Extraordinario Nacional de Excelencia en el campo de la Biotecnología, Ministerio Español de Ciencia y Educación

PONENCIAS EN CONGRESOS (más relevantes)

- 2018 -Invited speaker, Gene2Skin Final Conference, Guimaraes, Portugal
2018 -Selected oral presentation. 25th Biennial Congress of the European Association for Cancer Research (EACR), Amsterdam, Netherlands
2016-Selected oral presentation, Beyond Cancer Genomes- Barcelona conference on Epigenetics and Cancer, Barcelona, Spain
2015 -Invited speaker, Targeting Hedgehog Signalling in Cancer Stem Cells Meeting, Barcelona, Spain
2015 -Invited speaker, XXIII Porto Cancer Meeting - Stem Cells and Cancer, Porto, Portugal
2015 -Invited speaker, I Norwegian meeting on WNT/SHH signaling, Henningsvær, Norway
2014 -Selected to represent Belgium, 64th Lindau Nobel laureate meeting : Physiology and Medicine, Lindau & Mainau Island, Germany

PUBLICACIONES MÁS RELEVANTES

(*co-primeros)

- 1.Sanchez-Danes, A., et al., A slow-cycling LGR5 tumour population mediates basal cell carcinoma relapse after therapy. *Nature*, 2018.
- 2.Debaugnies, M*., Sanchez-Danes, A*., et al., YAP and TAZ are essential for basal and squamous cell carcinoma initiation. *EMBO Rep*, 2018. 19(7).
- 3.Sanchez-Danes, A. and C. Blanpain, Deciphering the cells of origin of squamous cell carcinomas. *Nat Rev Cancer*, 2018. 18(9): p. 549-561.
- 4.Sanchez-Danes, A*., Hannezo, E*., et al., Defining the clonal dynamics leading to mouse skin tumour initiation. *Nature*, 2016. 536(7616): p. 298-303.
- 5.Sanchez-Danes, A. and C. Blanpain, Maintaining hair follicle stem cell identity in a dish. *EMBO J*, 2017. 36(2): p. 132-134.
- 6.Larsimont, J.C., et al., Sox9 Controls Self-Renewal of Oncogene Targeted Cells and Links Tumor Initiation and Invasion. *Cell Stem Cell*, 2015. 17(1): p. 60-73.
- 7.Sanchez-Danes, A., et al., Efficient generation of A9 midbrain dopaminergic neurons by lentiviral delivery of LMX1A in human embryonic stem cells and induced pluripotent stem cells. *Hum Gene Ther*, 2012. 23(1): p. 56-69.
- 8.Sanchez-Danes, A., et al., Disease-specific phenotypes in dopamine neurons from human iPS-based models of genetic and sporadic Parkinson's disease. *EMBO Mol Med*, 2012. 4(5): p. 380-95.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: FERNANDEZ SANTIAGO, RUBEN
Referencia: RYC2018-024532-I
Área Temática: Biomedicina
Correo Electrónico: ruben.fernandez.santiago@gmail.com

Título:

'Tackling prodromal Parkinson disease: from early pathophysiology to disease progression biomarkers'

Resumen de la Memoria:

Since 2003 my research focus is dedicated to investigating the molecular basis of neurodegeneration from a genetics perspective. My major research interest is Parkinson disease (PD) and more specifically the prodromal stage of disease. The main goal of my research is to stop PD before it starts. I tackle this objective by using two complementary approaches: (i) elucidating the largely unknown early pathophysiological mechanisms of prodromal PD before manifestation of the motor symptoms, mainly by studying subjects at-high-risk of PD incl. non-affected carriers of the PD pathogenic LRRK2 p.G2019S mutation, among other at-risk populations, and (ii) identifying early progression biomarkers informative of disease status before motor pheno-conversion and PD diagnosis when neuroprotective clinical intervention could modify disease course, ultimately to be available for assessing drug response in clinical trials. Overall, my research is highly multidisciplinary, translational, and close to the patient. Some three selected key achievements of my career include: (1) the first description that aberrant epigenetic DNA methylation changes, along with related transcriptomic and microRNA alterations, are involved in PD using iPSC-derived dopaminergic neurons from PD patients; (2) the identification of genetic risk polymorphisms in the alpha-synuclein (SNCA) gene which are strongly associated with higher disease penetrance and earlier age-at-onset in LRRK2-associated PD patients (up to 11 years); (3) the identification of specific microRNA as early pheno-conversion candidate biomarkers in prodromal PD years before motor manifestation and disease diagnosis (up to 5 years). I have co-authored a total of 43 publications (23 D1; 13 Q1). As main author I have published the results of my studies in top journals within my research area incl. EMBO Mol Med (1), Ann Neurol (2), Neurology (2), or Mov Disord (1). In future appointments as independent investigator I expect to consolidate and expand this research line which is entitled to halt or prevent PD and genuinely in line with potential benefits for the patients, the public health systems, and the society.

Resumen del Currículum Vitae:

I earned an undergraduate degree in Biology from the University of Oviedo (Spain) in 2003 and a PhD in Neuroscience from the Eberhard Karls Universität Tübingen (Germany) in 2009. During my thesis dissertation at the lab of Prof. Thomas Gasser (6 years), I investigated the genetics of amyotrophic lateral sclerosis (ALS). As a postdoctoral investigator, in 2009 I joined the lab of Prof. Eduardo Tolosa / Prof. María-José Martí at IDIBAPS / Hospital Clínic de Barcelona (Spain). Since then, I investigate the genetics and epigenetics of Parkinson's disease (PD), by using both classical and OMICs approaches, and with a special interest in the prodromal stage of PD before motor manifestation and diagnosis of the disease. Using iPSC-derived dopaminergic neurons (DAn) from PD patients visited at our centre, I have been first reporting that epigenetic deregulation encompassing aberrant DNA methylation profiles and deficiency of specific transcription factors (TFs) relevant to DAn occur in PD, and that PD-associated epigenetic changes are similar in the sporadic and the familial LRRK2 PD forms of disease. More recently I am exploring whether these epigenetic changes also occur early in prodromal PD by studying asymptomatic carriers of the PD pathogenic LRRK2 G2019S mutations who are at-high-risk of disease. Currently my h-index is of 17. I have been awarded a Marie Skłodowska-Curie grant from the European Commission, a Juan-de-la-Cierva grant from the Ministry of Economy and Competitiveness (MINECO), and three research grants from the prestigious Michael J. Fox Foundation for Parkinson's Research (MJFF) as principal investigator (PI). Between 2011 and 2013 I have been project coordinator of the LRRK2 Cohort Consortium initiative from the MJFF at the Barcelona site. In 2015, the patient-supported Federación Española de Parkinson has recognized my microRNA work as publication of the year in PD for the identification of phenoconversion microRNA biomarkers in the prodromes of disease years before disease diagnosis. In 2016, I have been awarded a Jóvenes Investigadores (JIN) grant from the MINECO / Agencia Estatal de Investigación (AEI) (SAF2015-73508-JIN) which currently supports the development of my own research lines as junior PI. In 2017 I have generated a patent (EP17382248.7) consisting of a novel method for stratification of PD patients treated with levodopa. Recently, in 2018, I have been accredited by the AQU as Associate Professor.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: RODILLA , VERONICA
Referencia: RYC2018-024099-I
Área Temática: **Biomedicina**
Correo Electrónico: veronicarodilla@gmail.com

Título:

In vivo models to study cellular hierarchies and cancer

Resumen de la Memoria:

Después de licenciarme en Biología (2015), realicé el Máster en Ciencias Biomédicas de la Universidad de Barcelona. Durante las prácticas del máster empecé a investigar el papel de las vías de Notch y Wnt en el cáncer de colon, convirtiéndose en el principio mi tesis doctoral. Combinando técnicas de biología celular y molecular con modelos transgénicos de ratón, descubrimos que Jagged1 (ligando de Notch) es un gen diana de Wnt explicando por qué Notch está activo en tumores colorrectales, y también que esta vía es crucial durante la iniciación tumoral. Este trabajo fue publicado en PNAS, y su relevancia se refleja en el número de citas acumulado hasta la fecha (220).

En colaboración con el Prof. Radtke (Suiza), mostramos que el programa génico observado en tumores es extremadamente parecido al de las células madre intestinales. Demostramos que mientras algunos ligandos de Notch son críticos para mantener la homeostasis intestinal (ligandos Delta), otros son dispensables (ligandos Jagged). En colaboración con Genentech Inc realizamos el primer estudio preclínico utilizando anticuerpos bloqueantes de Jagged1 para el tratamiento del cáncer colorrectal, proponiendo el bloqueo de ligandos específicos como tratamiento para el cáncer de colon sin afectar el funcionamiento del intestino sano.

Algunas claves para entender el cáncer pueden obtenerse de estudiar las células madre de esos mismos tejidos. Con esta idea en la cabeza, me incorporé a la Unidad de Genética y Biología del Desarrollo del Instituto Curie. Gracias al soporte incondicional de mi supervisora, la excitante atmosfera científica del instituto y mi fascinación por el proyecto, me hice experta en el estudio in vivo de células madres basado en el seguimiento de linaje (lineage tracing). Mi objetivo principal consistía en estudiar el papel de Notch en el desarrollo mamario y para ello, utilicé una serie única de ratones transgénicos. Estos animales permiten marcar genéticamente con una proteína fluorescente, las células que expresan estos receptores y analizar su progenie. En mis investigaciones, descubrí que cada subpoblación de la glándula mamaria es capaz de perpetuar sólo su propio linaje. Fue entonces cuando decidí indagar en la existencia de una célula madre multipotente (que genere todos los subtipos celulares de la mama) y con capacidad de auto-renovación (que pueda mantener su existencia sin extinguirse) en algún periodo del desarrollo embrionario. Combinando técnicas de imagen con modelos computacionales concluimos que la pluripotencia es una cualidad que se pierde muy tempranamente durante el desarrollo (E15.5 del embrión), y que a partir de ese momento las células mamarias sólo producirán un subtipo celular. Este trabajo fue publicado en NCB ocupando la portada y recibiendo un comentario en el News and views del mes de su publicación.

Para mi segundo postdoc, me pareció estimulante destinar mis conocimientos a una investigación más aplicada. Por esta razón, me uní al laboratorio del Prof. Arribas. En esta etapa, he diseñado y generado nuevos modelos transgénicos que revolucionarán el campo de la senescencia. El uso de éstos, junto a tumores de pacientes implantados en ratones inmunodeprimidos (PDXs), ha sido mi pilar para unir investigación básica y clínica, abordando cuestiones relacionadas con la progresión tumoral y respuesta a quimioterapia.

Resumen del Currículum Vitae:

Education

2007-2011 PhD in Biomedicine. Universitat de Barcelona (Spain)
2006-2007 Master in Biomedicine. Universitat de Barcelona (Spain)
2000-2005 Degree in Biology. Universitat Pompeu Fabra, Barcelona (Spain)

Research Experience

2015-Today Postdoctoral Researcher. VHIO, Barcelona (Spain)
2011-2015 Postdoctoral Researcher. Institut Curie, Paris (France)
2007-2011 PhD Student. IDIBELL-IMIM, Barcelona - IDIBELL, Hospitalet del Llobregat (Spain)

Fellowships & Awards

2019-2021 Postdoctoral Fellowship Stop-Fuga-de-Cerebros de Roche Farma- Generalitat de Catalunya
2015-2017 Postdoctoral Fellowship Beatriu de Pinós (AGAUR)
2012-2015 Postdoctoral Fellowship ARC (Fondation ARC pour la Recherche sur le cancer)
2011 Extraordinary Doctorate Award (Universitat de Barcelona)
2010 EMBO Short-Term Fellowship (EMBO)
2006-2008 Predoctoral IDIBELL Fellowship (IDIBELL)

Training & Mentoring



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

2018 Junjie Zhang, PhD Student (UAB). Role: Thesis co-director
2018 Marta Lalinde, Master Student (UAB). Role: Supervisor
2018 Irene Garcés, Master Student (Pompeu Fabra). Role: Supervisor
2016-2017 Rita Casa. Master Student (UAB). Role: Supervisor
2014-2015 Laura Barnabei. Undergraduate Student (Leonardo European Programme). Role: Co-supervisor
2013-2014 Alessandro Dasti. Undergraduate Student (Leonardo European Programme). Role: Co-supervisor

Publications

Scientific articles: 12

Reviews: 2

Articles as first author: 7

Articles as co-corresponding author: 2

Total citations: 760

1. Could JAG1 protein inhibition prevent colorectal cancer?. *Future Oncol.* 2019 Jan.
2. Cellular Plasticity of Mammary Epithelial Cells Underlies Heterogeneity of Breast Cancer. *Biomedicines.* 2018 Nov.
3. Manic Fringe deficiency imposes Jagged1 addiction to intestinal tumor cells. *Nat Commun.* 2018 Jul.
4. Clonal analysis of Notch1-expressing cells reveals the existence of unipotent stem cells that retain long-term plasticity in the embryonic mammary gland. *Nat Cell Biol.* 2018 Jun.
5. Impaired PRC2 activity promotes transcriptional instability and favors breast tumorigenesis. *Genes Dev.* 2015 Dec.
6. Luminal progenitors restrict their lineage potential during mammary gland development. *PLoS Biol.* 2015 Feb.
7. Bmi1 regulates murine intestinal stem cell proliferation and self-renewal downstream of Notch. *Development.* 2015 Jan.
8. Notch3 marks clonogenic mammary luminal progenitor cells in vivo. *J Cell Biol.* 2013 Oct.
9. Long range epigenetic silencing is a trans-species mechanism that results in cancer specific deregulation by overriding the chromatin domains of normal cells. *Mol Oncol.* 2013 Dec.
10. Chromatin-bound β -catenin; regulates a subset of polycomb target genes in differentiation and cancer. *Cancer Cell.* 2013 Aug.
11. Dll1- and dll4-mediated notch signaling are required for homeostasis of intestinal stem cells. *Gastroenterology.* 2011 Apr.
12. The Notch/Hes1 pathway sustains NF- κ B activation through CYLD repression in T cell leukemia. *Cancer Cell.* 2010 Sep.
13. Jagged1 is the pathological link between Wnt and Notch pathways in colorectal cancer. *Proc Natl Acad Sci U S A.* 2009 Apr.
14. Efficient nuclear export of p65- κ B complexes requires 14-3-3 proteins. *J Cell Sci.* 2006 Sep.

Other merits

- Benchstorming Seminars: informal seminars for undergraduates, PhD students and postdocs. Role: Co-founder, organizer and moderator.
- Volunteer in



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: TRABA DOMINGUEZ, JAVIER
Referencia: RYC2018-026050-I
Área Temática: **Biomedicina**
Correo Electrónico: javimelose@hotmail.com

Título:

Papel de los nutrientes en la función mitocondrial y su efecto en la inmunidad innata.

Resumen de la Memoria:

Mi interés se centra en el papel que juega la mitocondria en procesos patológicos y enfermedades asociadas con el envejecimiento. Mi trabajo predoctoral en el laboratorio de la profesora Jorgin Satrustegui (Centro de Biología Molecular Severo Ochoa, CSIC/UAM, Madrid) trata sobre la caracterización funcional de los transportadores mitocondriales de ATP-Mg/Pi en levaduras y mamíferos, y sobre su implicación en la señalización mitocondrial por calcio. Obtuve mi doctorado en 2009, con una calificación de sobresaliente cum laude y premio extraordinario de doctorado. Desde 2011 trabajo en el laboratorio del doctor Michael Sack, en el National Heart, Lung and Blood Institute del NIH, Bethesda, Maryland (Estados Unidos de America), donde estudio el papel de la mitocondria y su disfunción en procesos de inmunidad innata, como el inflamasoma NLRP3.

Resumen del Currículum Vitae:

Durante mi carrera investigadora he publicado 20 artículos en revistas científicas (12 de ellos como primer autor), y he obtenido dos proyectos de investigación en Estados Unidos como investigador principal.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: GARCIA FERNANDEZ DE BARRENA, MAITE

Referencia: RYC2018-024475-I

Área Temática: Biomedicina

Correo Electrónico: magarifer@unav.es

Título:

Study of the Mechanisms Involved in Chronic Hepatopathies and Carcinogenesis

Resumen de la Memoria:

My main field of research over the past 15 years has been the study of the cellular and molecular mechanisms involved in the progression of Chronic Liver Diseases and in Hepatic and Pancreatic tumor development.

After an intensive scientific education and training in prestigious National (Universities of La Rioja, Oviedo and Navarra) and International Institutions (Mayo Clinic, Rochester, MN, USA), I joined the Hepatology Department of the Center for Applied Medical Research-University of Navarra (CIMA, Pamplona) to lead a research group in liver pathophysiology.

After graduating in Chemistry with Honors and Summa Cum Laude in 2003, I began my doctoral training in Biological Sciences in the University of Oviedo (Spain) where I earned an F.P.U. Scholarship. I completed my Ph.D. in 2010 at the University of Navarra (Spain), being hired as junior investigator by CIBERehd. During that time, I focused on the analysis of molecular and cellular mechanisms of liver disease progression. From May 2011 until May 2014 I was a postdoctoral fellow in Dr. Fernandez-Zapico's laboratory at Mayo Clinic, Rochester, USA, working on the characterization of epigenetic mechanisms regulating hepatic and pancreatic carcinogenesis. I was appointed Assistant Professor of Medicine, Mayo Clinic College of Medicine in March 2014.

On May 2014, I returned to the Hepatology Department of CIMA, directed by Prof. Matías A. Ávila. I was awarded a Marie Skłodowska-Curie Individual Fellowship Contract from the EU, and a MINECO-RETOS Project (SAF2014-54191-R) including an F.P.I. student, who has already defended her doctoral Thesis with Cum Laude and International Mention. This initial funding allowed me to start a new line of research as Principal Investigator based on the study of Epigenetic Mechanisms of liver disease. I got a second MINECO-RETOS Project (SAF2017-88933-R), and subsequent grants as PI and as participant in other collaborative projects which are allowing me to reinforce and expand my research career.

I have published 41 manuscripts in top international journals (32 original articles, 5 reviews, 3 editorials and a book chapter) that accumulate a JCR IF of 317,499, 2.755 citations and a Hirsch Index of 16. I have supervised several TFG students (final graduation Project), one doctoral thesis and another that is in progress. I have presented numerous works in national and international congresses and participated in dissemination activities as well as in innovative teaching projects. I am Academic Editor of PLoS One Editorial Board and a member of the Management Committee in the COST Action European Cholangiocarcinoma Network CA18122.

Resumen del Currículum Vitae:

My main field of research over the past 15 years has been the study of the cellular and molecular mechanisms involved in the progression of Chronic Liver Diseases and in Hepatic and Pancreatic tumor development.

After an intensive scientific education and training in prestigious National (Universities of La Rioja, Oviedo and Navarra) and International Institutions (Mayo Clinic, Rochester, MN), I joined the Hepatology Department of FIMA, Pamplona to lead a research group in liver pathophysiology.

After graduating in Chemistry with Honours and Summa Cum Laude in 2003, I began my doctoral training in Biological Sciences in the University of Oviedo (Spain) where I won an F.P.U. Scholarship. I completed my Ph.D. in 2010 in the University of Navarra (Spain), being hired as junior investigator by CIBERehd. During that time, I was focused on the analysis of molecular and cellular mechanisms of liver disease progression. From May 2011 until May 2014 I was a postdoctoral fellow in Dr. Fernandez-Zapico's laboratory at Mayo Clinic, Rochester, USA, focusing on the characterization of epigenetic pathways regulating hepatic and pancreatic carcinogenesis. I was appointed Assistant Professor of Medicine, Mayo Clinic College of Medicine in March 2014.

On May 2014, I returned to the Hepatology Department of FIMA, directed by Prof. Matías A. Ávila. I was awarded a Marie Skłodowska-Curie Individual Fellowship Contract from the EU,



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

and a MINECO-RETOS Project (SAF2014-54191-R) including an F.P.I. student. This funding has allowed me to start a new line of research as Principal Investigator based on the study of Epigenetic Mechanisms of liver disease. Recently, I got a second MINECO-RETOS Project (SAF2017-88933-R), which will allow me to reinforce and expand my research career. Member of the European Network for the Study of Cholangiocarcinoma (ENSCCA) and recently granted with a COST Action CA18122 (HORIZON2020) EUROPEAN CHOLANGIOCARCINOMA NETWORK (EURO-CHOLANGIO-NET) being designed with a position within the Management Committee (MC).

I have published 41 manuscripts in top international journals (32 original articles, 5 reviews, 3 editorials and a book chapter) that accumulate a JCR IF of 317,49, 2734 citations and a Hirsch Index of 16. I have supervised several TFG students (final graduation Project) and directed one doctoral thesis and another is in progress. I have presented numerous works in national and international congresses and participated in dissemination activities as well as in innovative teaching projects.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: BLAZQUEZ GARCIA, LOREA
Referencia: RYC2018-024397-I
Área Temática: **Biomedicina**
Correo Electrónico: lorebg@gmail.com

Título:

CRISPR-Cas13 delivered antisense RNA molecules for research and therapeutics of splicing-related disorders

Resumen de la Memoria:

Post-transcriptional modification of precursor RNA is a fundamental mechanism that strongly influences gene expression and contributes to disease. My scientific career has focus on this field, where I have studied molecular mechanisms of splicing and their deregulation in different diseases. I have also developed therapeutic strategies, based on the use of antisense RNA molecules, to correct several disorders.

My research experience already started as an undergraduate student with rewarding research placements from 2000 to 2002. In 2003, as soon as I graduated in Biology, I joined Lopez de Munain lab, first as a MSc student (2003-2005) and later for my PhD studies (2005-2009). In my thesis, I characterized CAPN3 expression at RNA and protein level in different tissues and I took advantage of my results to develop a new diagnostic approach for LGMD2A. Using this technique, I identified and characterized splicing mutations in a cohort of patients (Neurogenetics, 2008). My PhD studies were complemented with internships in additional labs in Spain and abroad. These include Juan Valcarcel lab (CRG, Barcelona), and Luis Garcia lab (CNRS, Paris), where I applied the exon-skipping approach to successfully correct the first deep intronic mutation in CAPN3 (Hum Mut 2013).

In October 2009, I joined Puri Fortes lab at CIMA (Pamplona), where I employed RNA-based gene-silencing methods (RNAi and U1i) in vitro and in vivo (2009- 2014). This approach was successfully applied to tackle HBV infection, as published (NAR 2012) and patented (WO 2012/045894 A1). In 2014, I joined Jernej Ule lab (UCL, London), as a Marie Curie fellow. Here, I have deeply characterized recursive splicing (RS), a two-step splicing mechanism. In 2015, we proved the existence of RS in vertebrates as a mechanism that regulates gene expression in the brain (Nature 2015). Although I joined late in the project, my initiative and leadership merited a second authorship. Also, I was invited to review non-canonical splicing mechanisms in Nature Reviews Genetics as co-first author. In 2016, the lab moved to The Crick Institute, the biggest single biomedical research institute in Europe, where I have experimentally and computationally characterized RS regulation by RNA-binding proteins. My latest results demonstrate that 4% of all canonical exons in the transcriptome can be alternatively spliced via recursive splicing, but this mechanism is repressed by the Exon Junction Complex (EJC). These results have been published in Molecular Cell, where I am first and co-corresponding author due to my independency while leading the project. In 2017, I was promoted to Senior Research Associate and I have recently secured competitive funding as lead applicant to explore CRISPR-Cas13 technology for therapeutics. This project is supported by the Translation Team in The Crick and involves training in Life-Science Entrepreneurship. So far, I have 9 years of postdoctoral experience but noteworthy, my research has been interrupted due to 3 maternity leaves.

In the future I will continue the study of RNA-processing in health and disease, by deciphering the role of EJC-mediated regulation of RS in neurogenesis and in brain disorders. Moreover, modulation of RNA-processing has proven a therapeutic strategy in many diseases and I plan to exploit RNA-targeting CRISPR-Cas systems for a therapeutic benefit.

Resumen del Currículum Vitae:

I have over 15 years of research experience (2003-present) in 7 different labs, only interrupted 3 times due to maternity leaves (2010, 2012 and 2018). Overall, I have 16 peer-reviewed publications, which include 12 research articles (6 as first author; 5 as co-corresponding author), 3 reviews and 1 book chapter (all as first author). So far, my work has been cited 471 times and my h-index is 10.

Selected publications as first/second author (*co-first/CAco-corresponding author/NS:without PhD supervisor):

- 1- Blazquez LCA et al. Mol Cell. 2018. NS.
- 2- Sibley C*, Blazquez L*, Ule J. Nat Rev Gen. 2016. NS. Review.
- 3- Sibley C*, Emmett W*, Blazquez L et al. Nature. 2015. NS.
- 4- Blazquez L, Fortes P. Adv Exp Med Biol. 2015. NS. Review.
- 5- Blazquez L, Fortes P. Applied RNAi. 2014. NS. Book chapter.
- 6- Blazquez LCA et al. Human Mutation. 2013.
- 7- Blazquez L, Fortes P. Current Molecular Medicine. 2013. NS. Review.
- 8- Blazquez L*, Gonzalez-Rojas SJ* et al. Nucleic Acids Research. 2012. NS.
- 9- Blazquez LCA et al. Neurogenetics. 2008.
- 10- Blazquez L*, CA, De Juan D* et al. Neurobiology of Aging. 2007.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

11- Blazquez LCA et al. Neuroscience Letters. 2006.

Patents: Blazquez L, et al. Components and compositions for treatment of diseases caused by HBV. WO 2012/045894 A1.

Competitive funding and awards:

Awards: Premio extraordinario Fin de Carrera . Universidad de Oviedo. 2003.

Competitive Fellowships: (1) PhD fellowship. Basque Government, 2005-2009; (2) Torres Quevedo fellowship, 2010-2012; (3) Marie Curie Intra-European fellowship, 2014-2016.

Research projects as lead applicant: Idea to Innovation (i2i) grant. The Crick Institute. £74400. 2018.

Travel grants: Marie Curie Alumni Association (2017), the RNA society (2017), Universidad Internacional de Andalucía (2013), ESF-EMBO (2010) and the Spanish Society of Microbiology (2003).

Invited talks and Selected abstracts

Invited Speaker:

- Systems Biology Program, CRG, Barcelona. 2017.
- Royal Society - IBS Bilateral Meeting. South Korea. 2017.
- 1st International Splicing Meeting. Portugal. 2016.

Selected abstracts as oral presentations:

- Crick Genome editing Symposium. UK. 2017.
- 5th UK RNA Splicing Workshop. UK. 2017.
- EMBO/EMBL The Complex Life of mRNA. Heidelberg. 2016.
- Post-EURASNET RNA Alternative Splicing. Italy. 2015.
- Gene expression as a circular process. Universidad Internacional de Andalucía. 2013.
- VI Meeting of the Spanish Society of Gene and Cell Therapy, Zaragoza. 2011.
- ESF-EMBO Antiviral applications of RNAi. Spain. 2010.
- LIX Meeting of Spanish Society of Neurology (SEN). Barcelona, 2007.

Research supervision:

- PhD rotation students: (1) Pablo Izquierdo, July-Sept 2017; (2) Rupert Faraway, Feb-June 2017; (3) Andrea Elser, Feb-June 2016.
- Graduate students: Mary Bronks (June 2016-June 2017).
- Undergraduate students: (1) Iñaki Etxeberria (July-Aug 2012), (2) Eduardo Castañeda (July-Aug 2011), (3) Marina Barriocanal (July-Aug 2010).

Other remarkable activities and courses:

- Lecturer in CRISPR mechanisms (MSc Functional Omics. Imperial College. Nov 2017 & 2018), RNA-mediated mechanisms of neurodegeneration (MSc Neuroscience. UCL, London. Oct 2015 & 2016).
- Peer reviewer in Cell, Nat Comms and NSMB. publons.com/a/1548488/.
- EMBO 3-day Lab Management Course. UK. March 2017.
- Bioinformatics courses in Unix, High Performance computing, R and Python. UCL and The Crick Institute.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: LIESA ROIG, MARC
Referencia: RYC2018-024389-I
Área Temática: Biomedicina
Correo Electrónico: marcliesa@gmail.com

Título:

El papel de la mitocondria en salud y enfermedad

Resumen de la Memoria:

My research interests are focused on defining and understanding the mechanisms by which mitochondria adapt to different metabolic demands and pathogenic states. The ultimate goal is to use these mechanisms as a therapeutic point of intervention to treat metabolic and age-related diseases. More specifically, we are focused on:

- 1) Defining mechanisms by which mitochondrial functional heterogeneity is generated intracellularly in liver, beta cells and adipose tissue and how these mechanisms can be used to prevent lipotoxicity, senescence and oxidative stress.
- 2) Define the mechanisms by which mitochondria adapt to redox changes related to heme homeostasis in these same tissues, which are largely unknown.

Resumen del Currículum Vitae:

I participated in seminal findings linking mitochondrial function, dynamics and metabolic diseases during my PhD. I identified that a mitochondrial pro-fusion protein Mfn2, decreased in type 2 diabetic muscles, is regulated by the nuclear coactivators PGC-1alpha and PGC-1beta. These results provided a plausible molecular mechanism by which Mfn2 expression is decreased in obesity with type 2 diabetes.

My post-doctoral research led to the discovery of a novel mechanism protecting the mitochondria from heme-related redox stress, constituted by the transporter ABCB10. This research received distinctions by the organizing committee of an international conference and by the editorial board of the journal *Circulation*. My studies constitute the identification of a potential therapeutic target for alterations related to mitochondrial oxidative stress, which plays a key role in metabolic and age-related diseases. Furthermore, I have been co-leading a project that developed a methodology to determine ABCB10 regulators and potential substrates, identifying for the first time its regulation by the glutathione redox state, in collaboration with Dr. Liz Carpenter at Oxford.

My knowledge and expertise on mitochondrial biology was essential to complete two projects related with telomere biology related to cancer progression and ageing in collaboration with Dr. DePinho at Harvard.

My extensive knowledge and technical expertise on mitochondrial dynamics led to the description of the biophysical properties that 2 individual mitochondria show before engaging a fusion event. I had an essential contribution, both conceptually and experimentally, to the demonstration that Drp1-mediated fission is required for mitochondrial uncoupling and thermogenesis during brown adipocytes activation.

As a new independent investigator, I co-directed a study identifying mitochondrial heterogeneity within brown adipocytes in lipid metabolism and being the first demonstration that mitochondria bound to the lipid droplet are located there to support lipid accumulation. Finally, I identified that mitochondrial fragmentation in Brown adipose tissue mediated by Mfn2 deletion improves insulin sensitivity in the obese, but causes cold intolerance. These findings constitute the identification of a novel pathway to manipulate brown adipocytes and thus its potential use to improve glucose tolerance in obese subjects and related metabolic alterations.

I developed both technical and conceptual knowledge in autophagy, as this is one of the main mechanisms of mitochondrial quality control, with an intimate relationship with mitochondrial dynamics and bioenergetics. My expertise in these processes led to collaborations describing that pancreatic cancers require autophagy for tumor growth, likely providing substrates for mitochondrial respiration, and that these type of cancers could be treated with chloroquine, an autophagy inhibitor. As a new independent investigator, my expertise in mitochondrial quality control and regulation was essential for the identification of one of the first mediators of mitochondrial retrograde signaling, namely GPS2, in collaboration with Dr. Perissi.

Finally, I am a co-founder in a novel biotech company at UCLA, Enspire Bio. I received the Alumni of Excellence award from the IRB, Barcelona.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: ROTINEN DIAZ, MIRJA SOFIA
Referencia: RYC2018-023874-I
Área Temática: **Biomedicina**
Correo Electrónico: mirjarotinen@gmail.com

Título:

The journey towards the discovery of a new strategy for treating lethal prostate cancer.

Resumen de la Memoria:

My scientific focus has been on investigating how transcription factor networks regulate gene expression in cancer. During my PhD training I studied the transcriptional regulation of the human 17beta-hydroxysteroid dehydrogenases (HSD17Bs), a family of enzymes involved in the synthesis and metabolism of sex steroids (estrogens and androgens) in gonads and peripheral tissues. I demonstrated that canonical DNA sequences, known as CCAAT boxes, are a common regulatory motif in some of these genes, and that they participate in their regulation by hormones. These findings are particularly relevant in the context of hormone-dependent tumors, such as breast or prostate cancer, where altered expression of these enzymes provides a positive balance of active steroids that ultimately stimulate cell proliferation. During my postdoc I acquired new expertise in prostate cancer biology. My main project led us to the discovery that a developmental transcription factor, ONECUT2 (OC2), is a master regulator of aggressive variants of metastatic castration-resistant prostate cancer. I also demonstrated that OC2 acts as a survival factor, suppresses the androgen receptor (AR) transcriptional program and activates genes associated with neural differentiation and progression to lethal disease. Importantly, I further showed that OC2 can be targeted with a series of small molecule inhibitors, providing a novel strategy for prostate cancer treatment. As a project scientist, I have continued deepening my understanding of how OC2 networks with other well-known oncogenes in prostate cancer to regulate gene expression programs. I have made a series of discoveries that strongly suggest that OC2 is also a viable drug target in other types of cancer. In the project that I have been leading as an independent investigator, I have compiled evidence that targeting OC2 can suppress the major driver of the classic form of small cell lung cancer (SCLC). Moreover, throughout my career, I have had the opportunity of contributing to several relevant projects linked to prostate cancer biology, cancer metabolism, and mechanisms of disease progression to metastasis.

Resumen del Currículum Vitae:

I earned my Bachelor Degrees in Pharmacy (2004) and Biochemistry (2006) at the University of Navarre in Spain. My doctoral studies were undertaken at the Public University of Navarre in Spain, under the supervision of Dr. Ignacio Encío Martínez. During my PhD, I studied the transcriptional regulation of human 17beta-hydroxysteroid dehydrogenases (HSD17Bs), a group of enzymes that control intracellular availability of active sex steroids in gonads and peripheral tissues. My work resulted in five publications, four as a first author, in journals including the Journal of Endocrinology, Journal of Steroid Biochemistry and Molecular Biology, and Molecular and Cellular Endocrinology. I was also the recipient of numerous predoctoral fellowships and travel support to attend international workshops and meetings.

In December 2011, I joined the Division of Cancer Biology and Therapeutics Research, at Cedars-Sinai Medical Center, Los Angeles, USA. During my postdoctoral studies in Dr. Michael Freeman's laboratory I developed a project defining ONECUT2 (OC2), a transcription factor largely unstudied in prostate cancer, as a master regulator of aggressive variants of prostate cancer. I have been able to demonstrate that OC2 can be targeted with a series of small molecule inhibitors, providing a novel therapeutic strategy for lethal prostate cancer. I am the first author on the paper describing these results that has been published in Nature Medicine (33.409 impact factor). The drugs discovered in this study led to two international patents (PCT/US2017/034768 and PCT/US2018/047569). In addition I received the American Urological Association Research Scholar Award (2016-2018), a prestigious competitive award directed to foster the career of outstanding young investigators into urologic research. As a result, in May 2016 I was promoted to the position of Project Scientist. I have also received multiple travel awards and I have been selected and invited to present my work at national and international meetings and conferences. Recently I have obtained the 2018 Donna and Jesse Garber Award for Cancer Research, earning competitive funding as a principal investigator to develop my independent research career.

My record also includes publications in Cancer Research, American Journal of Pathology, PLoS ONE and Clinical & Experimental Metastasis. I have a strong background in cancer biology, computational biology and grant-writing obtained in institutions of the height of Georgetown University, UCLA (University of California, Los Angeles) or the American Urological Association. My teaching experience includes classes and seminars at the at PhD program of Cedars-Sinai Medical Center. I have trained several technicians, master and graduate students. I am also an active member of the Cedars-Sinai Medical Center community where I have participated giving lectures and at outreach activities.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: ABARRATEGI LOPEZ, ANDER
Referencia: RYC2018-025502-I
Área Temática: **Biomedicina**
Correo Electrónico: anderabarrategi@gmail.com

Título:

Development of in vivo implantable experimental approaches for Regenerative Medicine, Stem Cell Biology and Disease Modelling purposes.

Resumen de la Memoria:

1- Research field and career path:

My fields of interest are Biomaterials, Tissue Engineering and Stem Cell Biology, always applied to mesenchymal tissues. As PhD. student I developed clinically relevant implantable devices for Regenerative Medicine purposes. Then, I moved to industry (4 years) and worked in translational research in the same field. Eventually, I became postdoc head of R&D laboratory (2 years). In this role, I gained seniority and experience at management of budget and staff, setting-up research labs and training, supervising and coordinating the technician staff.

Back to academia as postdoc, I applied my know-how in Tissue Engineering to basic Stem Cell Biology and Disease Modelling studies. Specifically, I have developed implantable approaches to define the cell-of-origin of sarcoma tumors, and the role of microenvironment in Acute Myeloid Leukemia (AML). That has been done under personal fellowships and in national (3 years) and international (5 years in UK) stays in internationally-renowned institutions.

2- Outcome and Achievements:

During my career, I obtained 5 different competitive personal fellowships with independent projects, including a Junior PI fellowship cofunded by EU and with grant support. Also, I have worked as researcher in national and international (EU-FP7) externally funded and core-funded projects.

My work has been presented in multiple international congresses and published in 29 indexed journals, including 17 publications as main author and 2 as corresponding author. My work has been rewarded with 2 awards and multiple invitations to paper review processes.

I have done technology transfer activities related to the generation of preclinical data for potentially clinically relevant therapeutic approaches in Spain and in UK, under two different University-Industry partnerships (2007-2010 Complutense-Noricum and 2018-2019 UCL-Apollo Therapeutics). I have leaded research projects and staff, including technicians and MSc. and PhD. students, in academia and industry. Due to it, I have experience in R&D management, with 2 corresponding authorships and a thesis advisor role as the outcome.

3- Future goals:

Recently, I have obtained a tenure-track position at CICbiomaGUNE and I am about to stablish an independent and brand-new research group: "Tissue Engineering and Stem Cells". Broadly, my group will use biomaterials-based approaches as tool to solve biological scientific questions. Specifically, we will start studying the physiological mesenchymal cell dynamics in bone tissue, aiming to elucidate any role of these processes in leading or promoting bone pathologies.

At medium-term, the goal is to secure external funding for the research lab and gain experience as PI. At long-term, the aim is to consolidate as research group and regularly deliver translational science, including bone implantable products potentially useful in clinical settings.

Resumen del Currículum Vitae:

1- Positions:

- 2003-2006: PhD. Student at Complutense University and Hospital Clinico San Carlos.
- 2007: Research Technician at Noricum SL (Biotech company).
- 2008-2010: Head of R&D Laboratory at Noricum SL (Biotech company).
- 2011-2013: Postdoc. Instituto de Salud Carlos III.
- 2014-2018: Postdoc. London Research Institute - The Francis Crick Institute.
- 2018-2019: Postdoc. University College London.
- 2019-2024: Junior PI. CICbiomaGUNE.

2- Productivity and Publications in indexed journals:

- Number of publications = 29
- Number of publications in Q1 = 19
- Number of publications as first author = 17. Examples: IF 12 J.Clin.Invest.; IF 10 J.Exp.Med.; IF 6 Biomaterials and Acta Biomater.; IF 5 Stem Cells (x2).
- Number of publications as last corresponding author = 2



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

- Number of congresses as presenting author = 17
 - Technology transfer activities in 2 University-Industry partnerships (Complutense-Noricum and UCL-Apollo/therapeutics).
- 3- Metrics (Relevance of publications):
- Sum of citations = 1189
 - Average citations last 5 years (775/5) = 155
 - h index = 19
 - i10 index = 21
- Source: Google scholar. Author number Cb61FSEAAAAJ
- 4- International activities:
- 5 years as postdoc in London(UK) under personal postdoc fellowships.
 - 4 years in a FP7-EURONANOMED project with coordination and administrative roles.
 - A competitive fellowship with grant, cofounded by the EU (FP7-PEOPLE-COFUND-Marie-Curie Action-WOLFRAM-600380).
- 5- Other activities:
- 4 years at industry.
 - Teaching experience at University (ANECA certifications).
 - R&D management experience, including: Coordination of research and staff, administrative duties, advisory boards for industry, and organization of research meeting.
 - Experience as reviewer in 10 different indexed-journals and as referee for grants.
 - Best European Thesis Prize and also "Extraordinary thesis" award.
- 6- Independence:
- 5 different competitive personal fellowships with independent projects, including postdoctoral "Sara-Borrell" and "Juan de la Cierva", and Ikerbasque-fellowship as PI with entailed funding support.
- 7- Leadership:
- Head of R&D laboratory at a biotech company: Coordination of research and technical staff.
 - In charge of undergraduate, master and PhD. students in different academic institutions.
 - Research leader role: thesis advisor once and corresponding author twice.
 - Recruited as PI to stablish an independent and brand-new research group "Tissue Engineering and Stem Cells" at CICbiomaGUNE.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: GUEDAN CARRIO, SONIA
Referencia: RYC2018-024442-I
Área Temática: Biomedicina
Correo Electrónico: sguedan@clinic.cat

Título:

Chimeric Antigen Receptor (CAR)-modified T cells for the treatment of cancer

Resumen de la Memoria:

As a classically trained pharmacist, the major objective of my research is to develop novel therapies to address unmet medical needs. Since my early career, I have focused on developing effective gene and cell-based therapies for the treatment of cancer. During my PhD, I generated and conducted the preclinical development of two different oncolytic viruses for the treatment of epithelial tumours: (a) an adenovirus armed to express fusogenic glycoproteins (Guedan et al. *Gene Ther*, 2008 and Guedan et al. *Gene Ther*, 2014) and (b) an adenovirus expressing a hyaluronidase able to disrupt the extracellular matrix of tumours (Guedan, *Mol Ther*, 2010). These strategies were designed to address some of the challenges that novel targeted therapies find in solid tumours, and both of them resulted in an improvement of the therapeutic potential of oncolytic viruses. In 2010, I moved to the University of Pennsylvania to generate new CAR-T cell treatments under the supervision of Dr. Carl June. I studied how signalling through different CAR endodomains may affect the polarisation, differentiation, and metabolism of CAR-T cells. I showed that small modifications on the CAR construct, including the promoter, transmembrane domains and intracellular domains, can have major consequences on the effector functions of T cells. Choosing the right endodomain for each condition or T cell subset is important to enhance therapeutic outcomes (Guedan et al. *Blood* 2014, Guedan et al. *JCI Insight*, 2018, Kawalekar et al. *Immunity* 2016). These pioneering results are highly relevant as they provide a better understanding on CAR engineering and its role in the persistence and anti-tumour effect of CAR-T cells. Moreover, I generated new CAR-T cell therapies with enhanced therapeutic potential, and I provided the rationale to test them in human clinical trials. On a different approach, I also investigated the possible role of oncolytic adenoviruses as CAR-T cell partners. I showed that tumours can escape CAR-T cell therapy by losing the expression of the CAR targeted-antigen. Tumour pre-treatment with oncolytic adenoviruses engineered to express immunostimulatory molecules resulted in better T cell accumulation and activation in the tumour, and reduced tumour escape. Overall, the combination therapy resulted in enhanced animal survival, and is an innovative solution to an important problem in cancer immunotherapy (Wing et al, 2018, *Cancer Immunol Res* and Watanabe et al, 2018, *JCI Insight*). I recently moved to IDIBAPS (Barcelona) to lead a new program on CAR-T cells for solid tumours. Given the clinical impact of solid tumours in the society and the promise of CAR-T therapies in blood cancers, optimising CAR-T cell therapy for solid tumours is of paramount importance. My current research is focused on understanding the obstacles that lead to CAR-T treatment failure (including T cell exhaustion and tumour escape due to loss of antigen expression) and developing novel strategies to overcome these hurdles. My ultimate goal is to move CAR-T cells for solid tumours into the clinic.

Resumen del Currículum Vitae:

I obtained my Pharmacy degree from the University of Barcelona in 2003, and my PhD degree in Biotechnology in 2009. In order to pursue my PhD studies in the Virotherapy group, lead by Dr. Alemany (IDIBELL), I received a competitive grant from the Generalitat de Catalunya (FI 2005). During my PhD, I published three articles as first author and four articles as coauthor, all of them in first quartile journals. My biggest contribution during this early stage was the development of an oncolytic virus able to degrade the extracellular matrix of solid tumours. The results from this work led to a well-cited publication in the field of virotherapy (Guedan, *Molecular therapy*, 2010. IF: 7.008. Citations: 73), and to the filing of a patent that was used to create a spin-off, VCN Biosciences. Their first clinical candidate was based on the results generated during my PhD and is now being tested in three clinical trials for the treatment of cancer (NCT02045602, NCT02045589, NCT03284268). I next moved to the University of Pennsylvania to develop new CAR-T cell therapies for the treatment of solid tumours, under the supervision of Dr. Carl June. In 2011, I was awarded with a Marie Curie fellowship to conduct my postdoctoral research. A few years later (end 2015), I was offered a leading position to supervise and manage a big part of Dr. June team, an offer that I was honoured to accept. My motivation and initiative working in the June laboratory led to the publication of two articles as first author (Guedan 2014, *Blood*; Guedan 2018, *JCI Insight*), another manuscript that is under-preparation, one manuscript as senior author (Wing 2018, *Cancer Immunol Res*), and five manuscripts as co-author. The article published in *Blood* (IF:15.132), in which I am first and corresponding author, has received close to 100 citations since its publication in 2014. This was the first demonstration of the role of CAR endodomains in T cell differentiation fates. I have also published three review articles in the CAR-T cell field as main author in high-impact journals. This includes a review I recently published as first and corresponding author in *Annual Review of Immunology* (IF:22.714). My leadership in these projects justified my signature as corresponding author in five of the articles published after my PhD studies. I am also an inventor in four patents developed at the University of Pennsylvania and licensed to Novartis, which indicates my contribution in the conception of the inventions. I have more than 20 abstracts accepted at peer-reviewed, internationally established conferences and I have received a total of 4 meritorious abstract travel awards. Because of my achievements, I have been invited to present at various national and international conferences and research centres, to teach at Universities, to review articles for journals (see publons.com/a/1550931/),



MINISTERIO
DE CIENCIA, INNOVACIÓN
Y UNIVERSIDADES



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

and to participate in the review process of grants (CWCUK PhD scheme 2018), abstracts (ESGCT 2018) and posters (ASGCT 2017 and 2018) at international conferences. On 2018, I was recruited by IDIBAPS to lead a CAR-T cell program for the treatment of solid tumours. Here, I supervise a postdoctoral researcher, a PhD student and a master student. I have an h-index of 12 and a total of 573 citation (198 citation in 2018). This numbers should increase soon, as I published seven articles in 2018.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: HERNANDEZ ALVAREZ, MARIA ISABEL
Referencia: RYC2018-024345-I
Área Temática: **Biomedicina**
Correo Electrónico: misabel.hernandez.alvarez@gmail.com

Título:

Mitochondrial dynamics and lipid biology

Resumen de la Memoria:

Mi formación científica consiste en una licenciatura en ingeniería bioquímica (1998-2003) en el "Instituto Tecnológico de Celaya" México, Master en Biología Molecular (2003-2006) "Instituto de Investigación Científica y Tecnológica (IPICYT) México, PhD en Fisiología (2006-2011) por la Universidad de Barcelona (España), 1ª estancia posdoctoral (2011-2016) en el IRB Barcelona (España), y 2ª posición posdoctoral "Juan de la Cierva-Incorporación" en el "Institut d'Investigació Sanitària Pere Virgili" (2017-2019) Tarragona (España).

Durante mi doctorado (2006-2011), me centré en la investigación de enfermedades metabólicas relacionadas con la obesidad como la diabetes tipo 2 (T2D). Mis logros más importantes de este período son el hallazgo de que la deficiencia de la proteína mitocondrial mitofusina 2 (Mfn2) en el músculo esquelético y el hígado causa disfunción mitocondrial y estrés en el retículo endoplásmico, lo que lleva a la resistencia a la insulina y la intolerancia a la glucosa (Sebastian *, Hernández-Alvarez *, Segalès *, et al. PNAS 2012) y que en los músculos esqueléticos de pacientes con formas extremas de T2D después del ejercicio, los niveles de Mfn2 se redujeron, en contraposición al grupo control (Hernández-Alvarez, et al. Diabetes Care 2010).

En mi primera posición posdoctoral (2012-2016), me uní al consorcio europeo DEXLIFE, donde participé en muchas reuniones internacionales y adquirí el conocimiento de la gestión de datos "ómicos". De esta investigación colaborativa, publiqué la existencia de un defecto en el catabolismo de aminoácidos de cadena ramificada en el músculo esquelético cuando progresan de resistentes a la insulina a T2D (Hernández-Alvarez et al. Scientific Reports 2017). Además, durante este período, investigué las implicaciones metabólicas de Mfn2 en el metabolismo hepático. Dirijí completamente la fenotipación metabólica de ratones Mfn2 KO específicos del hígado y descubrí que Mfn2 se une a la fosfatidilserina (PS) y participa en la transferencia de PS de ER a mitocondrias. Este trabajo se ha publicado en una revista de muy alto factor de impacto, donde soy el primer autor y coautor del artículo (Hernández-Alvarez et al, Cell, en la edición de 2019).

Para mi segundo post doctorado (2017-2019), quería profundizar mi conocimiento en la correlación entre el sistema inmunológico y la obesidad. Por esa razón me trasladé como "Juan de la Cierva-Incorporación" al laboratorio del Dr. Joan Vendrell y la Dra. Sonia Fernández-Veledo, donde estudiamos cómo la inflamación está relacionada con la respuesta metabólica en la obesidad en el tejido adiposo. De esta estancia, soy coautor de un artículo en el que mostramos que el receptor de succinato controla la activación alternativa de macrófagos y regula las respuestas metabólicas inmunes en la obesidad (Keiran *, Ceperuelo-Mallafré *, Calvo, Hernández-Alvarez et al. Nature Immunology, 2019).

En resumen, las habilidades que he desarrollado en el banco, junto con mis responsabilidades como investigador principal, me dieron la experiencia de desarrollar y avanzar una línea de investigación que investiga una función novedosa de las proteínas dinámicas mitocondriales en el mantenimiento de los componentes de la membrana lipídica y su relación con los síndromes metabólicos.

Resumen del Currículum Vitae:

My scientific training consists of a degree in Biochemical engineering (1998-2003) at the Instituto Tecnológico de Celaya México, Master in Molecular Biology (2003-2006) Instituto de Investigación Científica y Tecnológica (IPICYT) México, PhD in Physiology (2006-2011) by the University of Barcelona (Spain), 1st Postdoctoral stay (2011-2016) at IRB Barcelona (Spain), and 2nd Postdoctoral position Juan de la Cierva-Incorporación at the Institut d'Investigació Sanitària Pere Virgili (2017-2019) Tarragona (Spain).

During my PhD (2006-2011), I focused on the investigation of obesity related metabolic diseases like type 2 diabetes (T2D). My most important achievements of this period are the finding that deficiency of mitochondrial protein mitofusin 2 (Mfn2) in skeletal muscle and liver causes mitochondrial dysfunction and endoplasmic reticulum stress, leading to insulin resistance and glucose intolerance (Sebastian*, Hernández-Alvarez*, Segalès*, et. al. PNAS 2012) and that in skeletal muscles of patients with extreme forms of T2D after exercise the levels of Mfn2 were reduced, in contrary to control group (Hernández-Alvarez, et. al. Diabetes Care 2010).

In my first postdoctoral position (2012-2016), I joined the European consortium DEXLIFE, where I participated in many international meetings and acquired the knowledge of omics data management. From this collaborative research, I published the existence of a deficient catabolism of branched chain amino acids in skeletal muscle in the progression of insulin resistance to T2D (Hernández-Alvarez et. al. Scientific Reports 2017). In addition during this period, I further investigated the metabolic implications of Mfn2 in liver metabolism. I entirely lead the metabolic phenotyping of liver-specific Mfn2 KO mice and discovered that Mfn2 binds to phosphatidylserine (PS) and participates in the transfer of PS from ER to mitochondria. This work is published in a high impact factor journal, where I am first and co-corresponding author (Hernández-Alvarez et al, Cell, in press 2019).



MINISTERIO
DE CIENCIA, INNOVACIÓN
Y UNIVERSIDADES



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

For my second post doctorate (2017-2019), I wanted to deepen my knowledge in the correlation between immune system and obesity. For that reason I moved as Juan de la Cierva-Incorporación to the laboratory of Dr.Joan Vendrell and Dra. Sonia Fernández-Veledo where we studied how inflammation is connected to metabolic response in obesity in adipose tissue. From this stay, I co-authored the paper where we report that the succinate receptor controls macrophage alternative activation and regulates immune metabolic responses in obesity, also in a high impact factor journal (Keiran*,Ceperuelo-Mallafre*, Calvo, Hernández-Alvarez et. al. Nature Immunology, 2019).

In addition, I supervised master and students in their final-year projects and I am co-director of a PhD student from University of Barcelona.

In summary, the skills I have developed at the bench, together with my responsibilities as a lead investigator, gave me the experience to develop and advance a research line investigating a novel function of the mitochondrial dynamic proteins in the maintenance of lipid membrane components and their relation with metabolic syndromes.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: ROJAS EXPOSITO, JUAN JOSE
Referencia: RYC2018-025425-I
Área Temática: **Biomedicina**
Correo Electrónico: juan.rojas@micro.vetmed.uni-muenchen.de

Título:

Potencial inmunoterapéutico de virus oncolíticos

Resumen de la Memoria:

My research career has been dedicated to develop therapies able to induce antitumor immune responses (cancer immunotherapies). For this activation of an effective antitumor immune response, viruses that replicate selectively in cancer cells are a very interesting tool, and my research is focused on the improvement of these agents and on their combination with other cancer immunotherapies. Replication of the virus in the tumor acts as a danger signal for the immune system and is able to overcome tumor immunosuppression; at the same time, lysis of cancer cells driven by virus replication releases significant tumor antigens that can be uptake by immune cells for initiating an adaptive immune response. These immune-oncolytic agents have already demonstrated their potential to produce clinically effective cancer treatments, with data from several recent trials resulting in impressive response rates. In 2015 T-VEC (Imlygic) became the first oncolytic virus approved by FDA. In addition, recent studies demonstrated the impressive synergistic effect that these agents can have with other modalities of cancer immunotherapies. However, these agents can still be highly optimized, and my research is currently focused on improving the mechanisms that allow the establishment of a robust antitumor immune response in order to construct more effective oncolytic clinical candidates.

Firstly, during my PhD project and first postdoc experience at the Catalan Institute of Oncology (Spain, 2004-2010), my research focused on improving the selectivity of oncolytic Adenoviruses through the modification of promoters controlling E1A protein (Mol Ther 2007; 15:1607-15, Gene Ther 2009; 16:1441-51, Mol Ther 2010; 18:1960-71, Clin Cancer Res 2010; 16:3035-43) and through the improvement of the infectivity to cancer cells (Gene Ther 2012; 19:453-7; Clin Cancer Res 2015; 21:1406-18). In addition, expression of transgenes (Mol Ther 2010; 18:1275-83; Gene Ther 2012; 19:1048-57), combination with drugs (Mol Ther 2010; 18:903-11) and usage of cells as carriers (Cancer Gene Ther 2010; 17:792-802) were also evaluated to improve the capacity of the oncolytic agent to destroy the tumor. Afterwards, at the University of Pittsburgh (USA, 2010-2014), my research interest turned to exploiting the immunotherapeutic potential of oncolytic Vaccinia viruses. My projects focused on improving the antitumor immune response through the cloning of immune-activating transgenes (Cancer Cell 2016; 30:108-19, Cell Rep 2016; 15:264-73). In addition, the combination with novel cancer immunotherapies such as anti-CTLA4 antibodies was also explored with impressive results (Clin Cancer Res 2015; 21:5543-51). I also explored different technics for imaging small animals (J Clin Invest 2015; 125:3915-27). In 2015 I began my third postdoc at the Ludwig-Maximilians-University (Munich, Germany), where my research interest remained in improving the capacity of oncolytic Vaccinia viruses to elicit antitumor immune responses. The projects were then focused on developing novel strains with the capacity to induce immunogenic tumor cell death (manuscripts in preparation). In May 2017 I was promoted to Junior Principal Investigator thanks to the project granted by the German Cancer Foundation (Deutsche Krebs Hilfe) for developing clinical oncolytic candidates with increased immunotherapeutic potential.

Resumen del Currículum Vitae:

I am currently a Junior Principal Investigator at the Ludwig-Maximilians University in Munich (Germany) and I am an expert in novel therapies able to induce an antitumor immune response (cancer immunotherapies) and in the modification of viruses to be used as weapons against cancer. I obtained my PhD in Molecular Biology and Biochemistry at the Catalan Institute of Oncology-IDIBELL (Spain, year 2010) working on the improvement of the selectivity of oncolytic adenoviruses. Later, during my postdoctoral experience at The University of Pittsburgh (USA, 2010-2014), my research turned to exploiting the immunotherapeutic potential of oncolytic Vaccinia viruses. My projects focused on improving the antitumor immune response through the cloning of transgenes and the combination with novel cancer immunotherapies such as anti-CTLA4 antibodies. In 2015 I accepted an offer at the Ludwig-Maximilians University (Munich, Germany), where my research interest remained in boosting the immunotherapeutic aspects of oncolytic Vaccinia viruses. The projects were then focused on developing novel strains with the capacity to induce immunogenic tumor cell death. In May 2017 I was honored with a Junior PI project from the German Cancer Foundation (Deutsche Krebs Hilfe) for developing clinical candidates with increased capacity to elicit potent antitumor immune responses.

In my research career I have published 16 articles in peer-reviewed journals, all of them journals from the first quartile (Q1) and including some of the most important journals in biomedicine and oncology, such as Cancer Cell, Cell Reports, Clinical Cancer Research, International Journal of Cancer, or Molecular Therapy. These papers have a total number of citations of 439, and an annual average of 59.2 citations per year in the last 5 years. My h-Index is 13 and I am also the author of one book chapter. In addition, I am an inventor in 2 international patents; thanks to these patents, oncolytic viruses design and constructed by me are currently being tested in clinical trials: one of the viruses developed during my PhD (VCN-01) is being tested in Phase I clinical trials. In addition, the technology I developed during my post-doc experience at the University of Pittsburgh is currently being translated to the clinic thanks to Western Oncolytics.

As a Junior PI, I am currently directing the work of my first PhD student. In addition, I have plenty of experience in the mentoring of PhD (4



MINISTERIO
DE CIENCIA, INNOVACIÓN
Y UNIVERSIDADES



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

students), Master (5 students), and summer students (7 students). As a member of the Chair of Virology at the Ludwig-Maximilians-University, I am involved since 2015 in teaching virology classes to veterinary medicine students. In addition, I have been invited to give master classes to students both at the Universidad Autonoma de Madrid (Spain) and at the Tzu Chi University (Taiwan). I have also experience in the educational training of medical doctors and relatives of patients suffering from cancer.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: GONZALEZ AGUILERA, CRISTINA
Referencia: RYC2018-025485-I
Área Temática: **Biomedicina**
Correo Electrónico: crisgacgo@gmail.com

Título:

Regulation of nuclear dynamics as a barrier for human diseases

Resumen de la Memoria:

My line of research has been focused on the study of the interconnection of nuclear processes and its relevance on human diseases such as cancer, neuromuscular dystrophies and developmental alterations. My career started in 2003 in the laboratory of Dr. A. Aguilera at University of Seville with a Collaboration fellowship followed by two PhD fellowships (FPU and Junta de Andalucía fellowship). My work revealed the links between the mRNA metabolism and genetic instability. During that time, I mastered on molecular biology techniques and I published 2 articles as first author (MBoC 2008, 2011) that have accumulated more than 118 cites in high-impact journals. The latest one involved collaborations started by my own initiative. I also participated in several collaborations and wrote reviews (PloS Genet. 2009, JCB 2009, MCB 2011, EMBO 2011, NAR 2014).

In 2009, during my postdoc in the laboratory of Dr. P. Askjaer, at CABD, Seville, I established the DamID technique for the first time in *C. elegans*. Combining DamID with high-density microarrays analysis, I contributed to the discovery of the molecular mechanisms responsible for the anchoring and silencing of heterochromatin at the nuclear envelope (Cell 2012). This project was part of a collaboration with the laboratory of Dr. S. Gasser at FMI, Basel, where I spent a month learning the bioinformatics tools necessary for the analysis of both microarray and high-throughput sequencing results. In parallel, in another DamID study, I demonstrated the role of Emerin in the regulation of the neuromuscular synapses (Genom. Biol 2014). Moreover, I also supervised the work of students and from this supervision we discovered a new interaction between the nucleoporin Nup107 and the mitotic spindle assembly checkpoint protein MAD1 (MBoC 2012).

In 2012, given my expertise in bioinformatics tools, my work with Dr. JR Martínez-Morales at CABD, analysing ChIPseq and RNAseq data identified key regulatory regions for the control of the gene networks that sustain the vertebrate body plan (Genome Res 2014).

In 2013, I moved to the laboratory of Anja Groth at BRIC, University of Copenhagen, to study how the epigenetic information is maintained during chromatin replication. With the support of a grant from Lundbeck Foundation (281.441) where I was the PI, I developed a new technology called ChORseq that, for the first time, has allowed to monitoring the epigenetic mark restoration during cell division in a genome-wide manner (Mol Cell 2018 F1000Prime recommendation). Showing the relevance of the work, I was invited to give seminars at international congresses and research institutes. In parallel, I contributed to other projects (EMBOJ 2016, NSMB 2015). In this period, I also performed tasks of more responsibility since I was invited to evaluate articles from high-impact scientific journals and scientific projects from international organizations.

Based on the potential of ChORseq to understand the etiology of important human diseases linked to epigenetics alteration such as cancer, in 2016, I came back to Spain with the intention of developing my own lines of research based on the this technology. While I find funding, I have collaborated with Dr. F. Cortés-Ledesma in the context of an ERC project studying the role of topoisomerase during DNA replication.

Resumen del Currículum Vitae:

ACADEMIC DEGREE
2004 Bachelor in Biology
2009 PhD in genetics

RESEARCH ACTIVITY
06/2016-12/2018 Postdoc. CABIMER (F. Cortés lab)
05/2013-04/2016 Postdoc. BRIC (A. Groth lab)
10/2012-04/2013 Postdoc. CABD (JR Martínez Morales lab)
09/2009-08/2012 Postdoc. CABD (P Askjaer lab)
10/2004-07/2009 PhD student. University of Sevilla (A. Aguilera lab)

FELLOWSHIPS
2011 EMBO Short-term fellowship. FMI Institute, Basel, Switzerland (S. Gasser lab)
2005-2008 FPU PhD Fellowship. (Spanish Ministry of Education)



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

2004-2005 PhD Fellowship (Andalusian government)

2003-2004 Undergraduate Collaboration fellowship. Spanish Ministry of Education (A. Aguilera lab)

GRANTS

ncChIP-seq: A novel technology for the analysis of epigenome maintenance in proliferating cells. Lundbeck Foundation. 01/08/2014 - 30/08/2016, 281.441 , PI: Cristina González Aguilera.

I also participated in other 14 research projects

PUBLICATIONS

I have published 18 articles in high impact journals (Cell, Mol Cell, Gen Research, Gen Biol, NSMB, EMBO J, NAR, JCB) obtaining total of 794 citations and a h-index:13

CONGRESSES AND SEMINARS

I have participated in more than 23 national and international meetings and I have been invited speaker at an international meeting (2018) and at CABD institute (2016).

MENTORING

Supervision of a PhD student (2016 to date)

FP student practices (2010)

OTHERS

Reviewer of scientific journals (Cell cycle and Genome Research) and international grants (COST action).

Member of PhD defence committees.

Best student award (University of Sevilla)

Teaching at University of Sevilla (2005-2007)



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: ALVAREZ CASTELAO, BEATRIZ
Referencia: RYC2018-024435-I
Área Temática: **Biomedicina**
Correo Electrónico: beatriz.alvarez-castelao@brain.mpg.de

Título:

Neuronal Protein Homeostasis

Resumen de la Memoria:

My research career has been focused on the study of protein homeostasis. During my PhD studies at the Universidad Autónoma de Madrid, under the supervision of the Prof. Dr. Jose G. Castaño, I concentrated mainly on the study of α -Synuclein and other proteins related to Parkinson's Disease (PD). I studied four important aspects of α -Synuclein biology: (1) α -Synuclein over-expression: does not alter the expression, assembly or maturation of the subunits that compose the proteasome active complex, or the catalytic activity of the proteasome. (2) α -Synuclein phosphorylation: inhibits its own degradation by the proteasome. (3) α -Synuclein oxidation: at N-terminal methionines inhibits its own degradation by the proteasome. (4) Synphilin-1 interaction with α -Synuclein: inhibits its degradation by the proteasome. Overall these studies describe specific mechanisms that ultimately lead to the inhibition of α -Synuclein degradation favoring its accumulation within the cell, which can contribute to the formation of the aggregates that are found in PD.

Additionally, I studied the degradation of other proteins related to PD such as: (1) Nurr-1: I identified the main region of the protein (degron) that is recognized by the proteasome for its degradation. (2) DJ-1: I characterized the degradation of M26I, R98Q, A104T, D149A and L166P point mutants related to familial cases of PD. In the case of the L166P mutation, the change in this amino acid exposes a region for its recognition by the proteasome, increasing its degradation, and drastically decreasing DJ-1 protein levels in the cell. After my PhD and my first postdoc period, I moved to the Max Planck Institute in Frankfurt, as a postdoctoral researcher in the laboratory of Prof. Dr. Erin Schuman, where I focused on the study of protein degradation. Here I worked on two main projects: (1) I developed a technique for the identification of cell type specific proteins in vivo. Using this technique I identified the proteomes of the pyramidal (hippocampus) and Purkinje neurons, the comparative study of these proteomes revealed that Purkinje neurons express higher levels of proteins associated with metabolism. Additionally, I studied protein dynamics in vivo and discovered more than 200 proteins differentially regulated in hippocampal pyramidal neurons after mice were exposed to an enriched environment paradigm. (2) I studied the coordination of protein synthesis and degradation in neurons, and discovered that one kinase, whose function is poorly characterized in neurons, is involved in this coordination. I also described an atypical mechanism by which this kinase is activated.

My future aim is to apply the in vivo labeling with ANL to study protein dynamics in the context of brain diseases, and put together the knowledge I acquired during my PhD and postdocs for the study of protein homeostasis regulation from different points of view.

Resumen del Currículum Vitae:

Education:

- Doctor of Philosophy (Dec 2010, UAM)
- Grado de Salamanca (2004, USAL)
- Bs Biochemistry (2002, USAL)
- Bs Biology (2000, UNAV)

Employment:

- 2013-Present Senior Researcher at Max Planck Institute for Brain Research (Frankfurt AM, Germany)
- 2010-2012 Postdoctoral Position (UAM)
- 2003-2010 PhD Student (UAM)

Funding:

- Marie Curie IEF experienced researchers (2014-2016)
- Alfred Dollwet (2017-2018)

Awards:

- Award for the best postdoctoral researcher in the Max Planck Institute for Brain Research 2017
- Award to the most relevant publication in the Area 1, awarded by CIBERNED, (In red Biomedical investigations research center for the study of neurodegenerative diseases) for the publication: Synphilin-1 inhibits alpha-synuclein degradation by the proteasome (2012)
- Fellowship for the attendance to the Young Scientific Forum (FEBS) (2011)



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Conferences with oral communications:

- National and international conferences with 8 oral communications and 10 posters.
- 5 invited lectures in national and international research centers.

Teaching/mentoring/managing:

- Training of undergraduate, graduate students and technicians
- Master class (MPI-BR)
- Assistant in practical lessons of Biology bachelor (UAM)

Publications:

- 1.Alvarez-Castelao, B*.et al. Nature Protocols (2019) *Corresponding authors
- 2.Sambandan, S. et al. Science 355, 634-637 (2017).
- 3.Alvarez-Castelao, B.et al. Nat Biotechnol 35, 1196-1201 (2017).

Featured in:

- Miura, G. Neurobiology: Nat Chem Biol 14, 1 (2017).
- Phys.org: <https://phys.org/news/2017-11-proteins-brains-mice.html>
- Proteomics news: <http://proteomicsnews.blogspot.com/2017/11/cell-type-specific-metabolic-labeling.html>
- 4.Sanchez-Lanzas, R. Alvarez-Castelao, Bet al. BBA 1862, 1423-1432 (2016).
- 5.Hanus, C. et al. Elife 5 (2016).
- 6.Alvarez-Castelao, B. & Schuman, E.M. JBC 290, 28623-28630 (2015).
- 7.Alvarez-Castelao, B., et al. Front Aging Neurosci 6, 169 (2014).
- 8.Alvarez-Castelao, B., et al. BBA 1843, 352-365 (2014).
- 9.Alvarez-Castelao, B., et al. PLoS One 8, e55999 (2013).
- 10.Alvarez-Castelao, B.,et al. Biochem Res Int 2012, 823597 (2012).
- 11.Alvarez-Castelao, B. et al. BBA 1823, 524-533 (2012).
- 12.Alvarez-Castelao, B.& Castano, J.G. CMLS68, 2643-2654 (2011).
- 13.Kong, X., Alvarez-Castelao, B.,et al. JBC 282, 15498-15505 (2007).
- 14.Diaz-Hernandez, M. et al. J Neurochem 98, 1585-1596 (2006).
- 15.Jimenez, J., Castelao, B.A., et al. Int Microbiol 8, 33-42 (2005).
- 16.Alvarez-Castelao, B. & Castano, J.G. FEBS Lett 579, 4797-4802 (2005).
- 17.Martin-Clemente, B. Alvarez-Castelao, Bet al. JBC 279, 52984-52990 (2004).

Scientific outreach:

- 2 articles in non-peer review journals
- Support in the organization and teaching of the teaching laboratory of the MPI-BR activities (for young students, 2013-2015)
- Night of Science (2015 and 2016)



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: BRAVO SAN PEDRO, JOSE MANUEL

Referencia: RYC2018-025099-I

Área Temática: Biomedicina

Correo Electrónico: chemabsp@gmail.com

Título:

Role of autophagy in cancer, metabolic and neurodegenerative diseases

Resumen de la Memoria:

My scientific career started at Prof. José Manuel Fuentes Rodríguez laboratory in 2007 studying the role of autophagy and neurodegenerative diseases. During my PhD, I contributed to establishing a new link between the high sensibility to neurotoxins and the deregulation of autophagy observed in cells derived from Parkinson disease (PD) patients with the G2019S LRRK2 mutation.

In 2013, I accepted a postdoctoral fellowship in Prof. Guido Kroemer laboratory at Gustave Roussy Cancer Campus in Paris. During this period, I have investigated the link of autophagy with metabolism and obesity and I discovered that autophagy is the main responsible for the secretion of a highly conserved protein, Acyl-CoA binding protein (ACBP) and that it controls the extra and intracellular balance of this protein. I also discovered that lipid metabolism was regulated by ACBP intra/extracellular abundance. To carry out this project, I have acquired extensive experience in vivo research and I have developed several tools such as an inducible knockout mouse, a monoclonal antibody anti-ACBP and anti-ACBP autoantibodies. By using these novel tools and reagents, I have recently demonstrated that the neutralization of this protein constitutes a novel treatment of obesity and its comorbidities.

During my postdoctoral stage, in addition to the finding derived from my main project, I had the opportunity to study more in-deep the mechanistic process of autophagy (Sica V.*, Bravo-San Pedro J.M.* et al., Oncotarget. Inhibitor of growth protein 4 interacts with Beclin 1 and represses autophagy) and cell death studies (Sica V.*, Bravo-San Pedro J.M.* et al., Cell Reports. Lethal poisoning of cancer cells by respiratory chain inhibition plus dimethyl alpha-ketoglutarate). Also during my postdoctoral stage, I had the opportunity to explore different fields and the privilege of interacting with top researchers from these fields, highlighting the Dr. Beth Levine collaboration. In 2015 I published, as the first author, in collaboration with Dr. Levine's group a work entitled BAX and BAK1 are dispensable for ABT-737-induced dissociation of the BCL2-BECN1 complex and autophagy. In this paper, published in the journal Autophagy, we described the role of the pro-apoptotic BAX and BAK1 proteins in the interaction between BCL2/BECN1 in the context of autophagy induction. I have also participated in the elaboration of reviews as the main author, with some of the most outstanding autophagy researchers, in some of the most important international journals.

An additional scientific field where I have been able to grow is the editorial field. Being lead editor of the prestigious book Methods in Enzymology: Molecular Characterization of Autophagic Responses of Editorial Elsevier. This book, published in 2017 presents a collection of methods for the qualitative and quantitative evaluation of virtually all the morphological, biochemical, and functional manifestations of autophagy.

Therefore, we can summarize that during my career I have focused my research on the search for therapeutic targets, based on the modulation of the autophagy, for different diseases as cancer, metabolic or neurodegenerative diseases.

Resumen del Currículum Vitae:

In summary, I have published 74 scientific works including:

15 papers as first author in journals with Impact factor higher than 5: Nature Reviews Drug and discoveries (47.1), Nature Reviews Neuroscience (29.3), Nature Cell Biology (19.6), Autophagy (12.0), The EMBO Journal (9.6), Autophagy (9.1), Cellular and Molecular Life Science (5.8), Aging (5.1).

26 papers as second author in journals with Impact factor higher than 5: Toxicological Science (5.0), Cell Death&Disease x2 (5.1), Free Radical Biology & Medicine (5.7), Cellular and molecular life science (5.8), Cell death and differentiation (8.3), Cell reports (8.5), Current Biology (8.9), Seminars in Cancer Biology (9.1), Autophagy x4 (11.4), Trends in Cell Biology x3 (12), Molecular Cell (14.0), Cell Metabolism (16.7), Nature Reviews Clinical Oncology (18.7), Nature Cell Biology (20.6).

According to ISI web of knowledge, I have an h-index of 24 and more than 4000 citations. Moreover, I have been the Editor of two international books and I published 12 chapters in several books of international publishers. I have presented 37 communications at national or international meetings. Furthermore, during my postdoc stage, I have actively participated in the development of other aspects related to the scientific career, as the developing of important new tools, highlighting the developing of the Metabolomic and Cell Biology platforms in the Gustave Roussy Cancer Campus. In addition, I have participated in nine research project and I participated as co-directions in the elaboration of two doctoral thesis and three Master Degrees and I am currently supervising two additional PhD thesis, which follow new lines of research based on combining and integrating my previous studies on autophagy and neurodegeneration (Spain) with my current research on autophagy and metabolic disorders (France).



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: TOMÁS LOBA, ANTONIA
Referencia: RYC2018-025622-I
Área Temática: Biomedicina
Correo Electrónico: atomas@cnic.es

Título:

Cáncer y sus mecanismos: una visión integradora de un fenómeno complejo

Resumen de la Memoria:

Before graduating in Biology (Universidad de Murcia, 2004) my interest on knowledge and science was more than a fact. During the university studies I was working in different laboratories to understand the lab work and the methodology underlying in the daily life and early my curiosity on cells governing laws and the effects on escaping to them was clearly defined. To pursue my interest on cell s-laws, I decided to do my PhD in the Spanish reference center in cancer research (2005-2010): Centro Nacional de Investigaciones Oncológicas (CNIO, Madrid) under the supervision of Dr. Blasco. My interest was mainly focused in deciphering the role of telomerase (tert, the enzyme that protects the chromosomes to be critically short and, thus, genetically unstable) beyond what it was established. Tert was previously defined as a pro-tumorigenic effector, however, and it was a breakthrough in telomerase field, I described that tert had an effect not only in maintaining tissue homeostasis but also in the wellness and life span of tumor suppressor overexpressing mice. The work was published in Cell (Tomas-Loba, et al., 2008, IF: 31.253) and raised a huge impact in the social press. From this period I had two more publications: i) where we described blood metabolites associated with aging (Tomás-Loba, et al., 2010, IF: 5.939); ii) a second publication as a result of a collaboration with Dr. Serrano (García-Cao, et al., 2007, IF: 8.175). After my PhD, and as a result of my interest on DNA biology and its relation with tissue homeostasis and cancer, I decided to do my first postdoctoral stay in the prestigious Cancer Research UK, in Clare Hall laboratories, under the supervision of Dr. Boulton (2010-2012) where I was granted by EMBO and Marie Curie fellowships. During these 2 years I stablished several mouse models to understand the role of a new chromatin remodeler (ALC1, Amplified in Liver Cancer 1) in cancer and more in detail, in liver cancer. I have described that ALC1 is an mTORC2 (mammalian Target of Rapamycin Complex 2) regulator through its binding to RICTOR promoter (Tomas-Loba, et al., in preparation). From this period and derived from 2 collaboration y I have also published 2 more papers (Chapman JR, et al., 2013, IF: 14.178. Kulkarni A, et al., 2013, IF: 5.300). To fully address the role of ALC1 in liver cancer, I stablished a collaboration with Dr. Sabio at Fundación Centro Nacional de Investigaciones Cardiovasculares (CNIC, Madrid). As a result she offered me to continue in her lab. Since then, I got my own funding and currently I have a semi-independent position with a JIN-MINECO fellowship (SAF2014-61233-JIN). My interest is mainly in describing the role of p38gamma (a Mitogen activated kinases) in liver cancer. I have described that p38gamma acts Cyclin dependent kinase, driving hepatocytes from G0 to G1 when a liver stress occurs. The work was accepted in Nature. I am also co-directing one theses project, I supervised 4 undergraduate students and I am currently a member of the PhD committee of 4 PhD students. My interest in science is not only based in the generation of knowledge but also in communicating to society the importance of it. This is the main goal of iDEAM, innovation in education foundation, where I am the co-founder with a group of scientist and pedagogues.

Resumen del Currículum Vitae:

After graduating in Biology (Universidad de Murcia, 2004) I did my PhD in Centro Nacional de Investigaciones Oncológicas (CNIO, Madrid) under the supervision of Dr. Blasco (2005-2010), where I published several papers in relevant journals: 2 as first author: Cell (2008) and Aging Cell (2010) and one more paper as co-author in EMBO Report (2006).

I did two postdoctoral stays, one at the prestigious Clare Hall Laboratories (Cancer Research UK, 2010-2012), under the supervision of Dr. Boulton; and second, with Dr. Sabio at Centro Nacional de Investigaciones Oncológicas (CNIC, Madrid, 2013-December 2018). During this period I was able to find my own funding: EMBO long-term, FP7-People Marie Curie, Juan de la Cierva and JIN-MINECO fellowship (SAF2014-61233-JIN) where I was the PI allowing me to have a semi-independent position. Moverover, I finished this chapter publishing the work in Nature. Based on what we have found and published in Nature, we are processing a patent which application number is 15382308.3-1464.

I have participated in several national e international meetings where I was awarded twice with the best poster (American Association of Cancer Research: 6th-9th December 2008, San Francisco, California and EMBO meeting: 23-26 April 2017, Palma de Mallorca, Spain). During the last 5 years I have participated in more than 10 research project where I was the IP in one of them (Spanish Ministry of Education and Science. SAF2014-61233-JIN).

To sum up, these are my indicators of quality in scientific production:

- 1 thesis co-directed currently ongoing.
- 6 publications (indexed-journals); 3 as first author; 1 in Cell. In addition, 1 in Nature (accepted still not in press) at the present time.
- H Index = 5 (in accordance with Web of Science; Researcher ID.; Scopus author ID:).
- 675 citations (in accordance with Web of Science).
- Average citations per article: 135

Moreover, I was completely involved in students training and, as a result, I am co-directing one thesis project, I have supervised 1 final



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AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

project and 1 master project (that got the highest qualification,) 1 CICERONE, 1 AECC summer students and I am currently a PhD committee member of 4 PhD students.

I also have a huge interest in communicating the relevance of Science to society, therefore, I have participated in several teaching activities such as: lessons and scientific theatres at Estudiantes School, Tagore School and Zurbarán School (with children from 4 to 13 years); I am a co-founder of iDEAM, an educational association where the aim is to implement the scientific method in children education: <http://ideam10.wix.com/ideam>; and finally, I was a main organiser of PhDay, the first meeting organised by pre and postdocs from CNIC with the goal to promote the interaction between student and famous scientists from different fields. <https://cnicphday.wordpress.com>.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: SAADE , MURIELLE
Referencia: RYC2018-025379-I
Área Temática: **Biomedicina**
Correo Electrónico: msabmc@ibmb.csic.es

Título:

Understanding molecular mechanisms underlying Zika virus associated neuropathy

Resumen de la Memoria:

After my degree and Master in Cell Biology, Biochemistry and Genetics at USJ, Lebanon (1998-2002), I moved to France for my doctorate studies (2003-2009, TAGC-INSERM U1090 lab., Dr. Catherine Nguyen), where I obtained competitive fellowships from INSERM-PACA and from the French Muscular dystrophy Association (AFM). I identified stromal genes involved in thymus ontogeny and determine how they work to organize the different compartments important for Tcell differentiation (J Immunol 2004). I further characterized one gene that we called SPATIAL/Tbata (BMC Genomics 2004). I found that this gene generates different isoforms specific of the thymus and others shared with the nervous and the testis where they are directly involved in neurite outgrowth (Mol Cell Neurosci. 2014, Eur J Immunol. 2010, Exp Cell Res. 2007, Exp Cell Res. 2007). My second project was focused on validating a non viral system of gene electrotransfer to restore thymus linked immunodeficiency disorder (SCID) (PLoS ONE. 2008). With this system we corrected a murine SCID model by reconstituting mature lymphocytes displaying a normal immune reaction. In addition, financed by and EMBO-STF and Boehringer, I moved to the lab of Dr. Nathalie Scholler (UPenn, USA) for an internship to participate in developing a new clinical trial for potent antitumor immune response in ovarian cancer.

For my PhD, I also worked in the field of neurobiology that boosted my collaboration with two recognized international institute (INMED, IBDM, France) and further triggered my interest to search for a postdoctoral training in the neuro-developmental field. I moved to Spain to join the laboratory of Dr. Elisa Marti (IBMB-CSIC,) as a postdoctoral scientist, (2009- present) to enlarge my fields and switch to developmental biology. My work was focused on understanding how growth and cell specification are coordinated in the developing chick spinal cord. To obtain the single cell resolution necessary for this, I developed new lineage tracing tools to follow separately the three modes of división (PP/PN/NN). Combining these tools to a mathematical model, I studied the dynamic of motor neuron generation and the involvement of Shh in the coordination of growth and patterning in this domain (Cell Reports 2013). The tools sparked a wide interest and have been shared between European laboratories well known in the field. I also contributed on studying the activity of the BMP signaling in dictating the mode of division during interneuron generation (JCell Biol 2014) and in studying Wnt/b-catenin signaling effect on neuroepithelial aberration through the modification of cell polarity (Nat Commun 2014). In this last and more important contribution I have unveiled for the first time the centrosomal intrinsic mechanism by which Shh-signaling maintains the symmetric proliferative PP division mode of neuroepithelial cells (Nature Cell Biology 2017). This contribution has been highlighted in an invited review paper as corresponding autor (Development, 2018).

As an independent scientist, I am proposing a research project aimed to determine the molecular mechanisms of Zika Virus pathogenesis underlying congenital microcephaly. This project perfectly fits the strategic lines of IBMB to consolidate the structural biology as driving force to understand morphogenetic processes (see attached letter from the IBMB Director).

Resumen del Currículum Vitae:

EDUCATION

2008 Ph.D. in Immunology (with distinction) by the Université de Aix-Marseille II, France.
2003 Master in Immunology (Diplome d'Etude Avancée) by the Université de Aix-Marseille II, France.
2002 Master in Cell Biology, Biochemistry and Genetics, by the Université Saint-Joseph (USJ), Lebanon.
2001 Degree in Cell Biology, Biochemistry and Genetics, by the Université Saint-Joseph (USJ), Lebanon.

RESEARCH ACTIVITIES

MAY/2009-present: Postdoctoral fellow, Laboratory of Elisa Marti, IBMB-CSIC, Spain
04/2008 - 12/2008: Postdoctoral fellow, TAGC-INSERM U1090, France
01/2007 - 03/2008: Internship, Center for Research on Early Detection and Cure of Ovarian Cancer, School of Medecine, UPenn, USA
01/2007 - 12/2007: AFM PhD, TAGC-INSERM U1090, France
04/2004 - 12/2006: INSERM-PACA PhD, TAGC-INSERM U1090, France
2002-2003: Degree and Master practicum, Familial Mediterranean fever, Université Saint-Joseph (USJ), Lebanon



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

PUBLICATIONS & INDICATORS OF SCIENTIFIC PRODUCTION:

- Number of publications: 12 (First or Co-first author: 7/12; Corresponding author: 1/12; Second author: 3/12)

-h-index: 8

-Total citations: 167

-Impact factor of the last 10 years publications: Nature Cell Biology (19.064), Nature communication (12.353), Cell Reports (8.282), Journal of Cell Biology (8.784), Development (5.413), European Journal of Immunology (4.248), Mol Cell Neuroscince (3.312)

PARTICIPATION IN I+D+i PROJECTS

REF: BFU2016-77498-P, 2014 GRC 00161, BFU2014-55738-REDT, BFU2013-46477-P, BFU2010-18959 among others

FELLOWSHIPS AND FUNDINGS

PhD fellowship Association Française contre les Myopathies -AFM A465761

Ph.D. fellowship from PACA-INSERM, France-ADR2/ PACA/CA 00205029

Short-term fellowships (2008-2009, EMBO ASTF 186.00-2007)

Short-term fellowships Boehringer Ingelheim Fonds

SUPERVISION OF GRADUATE STUDENTS

2016-present PhD co-supervisor of Jose Blanco Ameijeiras

12/2010-12/2015 PhD co-supervisor of Irene Gutiérrez Vallejo

Co-supervision of Degree practicum (2010) and two Master practicum (2007, 2008)

AWARDS AND DISTINCTIONS

2008 PhD defense (very honourable)

2005 Best oral presentation award (800 euros), the13th Meeting of doctoral schools from Aix-Marseille universities, France

CONTRIBUTIONS TO SCIENTIFIC MEETINGS AND INVITED TALKS

4 Invited talks (UCSF, UPenn, University of British Columbia, IRB)

15 contributions (9 posters and 6 oral contributions) in national and international meetings

TEACHING EXPERIENCE

practical work in Immunology for two years (University of Aix-Marseille II, france).

REFeree FOR OXFORD JOURNAL

Biology of Reproduction (MS ID#: BIOLREPROD-2009-078980; MS ID#: BIOLREPROD-2008-070193)



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: OBRI , ARNAUD
Referencia: RYC2018-026024-I
Área Temática: **Biomedicina**
Correo Electrónico: arnaud.obri@gmail.com

Título:

Neuroepigenetic mechanisms in disease

Resumen de la Memoria:

I was a PhD candidate in the laboratory of Dr. Ali Hamiche, at the Department of Functional Genomics in IGBMC (Strasbourg, France). My main achievement at Dr. Hamiche laboratory was to identify for the first time ANP32E and YL1 as histone chaperones for the histone variant H2AZ in mammals. Using state-of-the-art technics my work contributed to describe how these histone chaperones recognize H2AZ and how they regulate its deposition into chromatin. Consequently, I earned my first-author paper published in Nature (2014). As a result of my doctoral training, I became an expert in chromatin biology with a strong and transferable knowledge in biochemistry and molecular biology. My training in research continued under the guidance of Dr. Gerard Karsenty, at the Department of Genetics and Development in Columbia University Medical Center (New York, USA). I joined Karsenty laboratory with the clear goal of acquiring competence in physiology and mouse genetics. Based on my previous background, the goal of my first postdoctoral project was to study the role of an epigenetic factor, the histone deacetylase HDAC4, in the differentiation of osteoblasts and the regulation of bone mass. This resulted in my second first-author paper, published in the Journal of Cell Biology (2014). Next, I moved my attention to a new project in the field of neuroscience, with the goal of studying the relationship between the osteoblast-derived hormone osteocalcin and cognition. My main achievement was to identify Gpr158 as a receptor for osteocalcin that mediates its functions in the brain. This work earned me another first-author paper in the Journal of Experimental Medicine (2017) and a review in Nature Reviews Endocrinology in 2018. During the development of this project I gained a solid knowledge in neuroscience and behaviour as well as the molecular aspects of cognition regulation.

Resumen del Currículum Vitae:

My name is Arnaud Obri and I have a PhD in Molecular and Cell Biology from IGBMC-University of Strasbourg 1 (Strasbourg, France). In 2017, I was awarded a Beatriu de Pinós grant to join the Neuronal Control of Metabolism laboratory lead by Dr. Marc Claret in IDIBAPS (Barcelona, Spain). My current research is aimed at discovering if (and which) epigenetic modifications in the brain might contribute to the development of obesity.

I have 9 years of experience in research including 5 years as a post-doctoral scientist. I have a strong background and expertise in epigenetics and neuroscience. In the course of my scientific career I have published 6 articles in journals within the first decile (4 of them as a first or co-first author) and 1 review as a first author. In total, these articles have been cited 163 times and my h-index is 5 (Scopus). My work has been presented four times in national and international conferences and seminars, which has led to 3 abstract publications.

From 2008 to 2012, I was a PhD candidate in the laboratory of Dr. Ali Hamiche (Department of Functional Genomics) in IGBMC (Strasbourg, France). My work during my PhD training contributed to the identification of new molecules that modulate chromatin structure in mammals (Obri et al., Nature 2014).

In 2013, I started my post-doctoral training in the laboratory of Pr. Gerard Karsenty (Department of Genetics and Development) in the prestigious Columbia University Medical Center (New York, USA). During that time (2013 to 2017), I led three projects that were ultimately published in high-impact journals and in which I am first author or first co-author (Obri et al., JCB 2014, Kode et al., Nature Medicine 2014 and Khirman et al., Journal Experimental Medicine 2017). For one of these projects, I received the Young Investigator Award from the American Society for Bone and Mineral Research (ASBMR) in 2014. The most relevant achievement of my post-doctoral research was the identification of a new receptor in the brain for the bone-derived hormone osteocalcin. This work was done in collaboration with the Nobel Prize Laureate Pr. Eric Kandel and was reviewed recently in Nature Reviews Endocrinology (Obri et al., Nat. Rev. Endocrinol. 2018). Noteworthy, our discovery might have significant therapeutic implications for the treatment of neurodegenerative disease and age-related memory loss and for that has been protected by the registration of a patent in which I am listed as inventor.

Overall, my professional experience, record of high-impact publications and international mobility reflect my innovative thinking and my ability to successfully lead project in various research fields (from chromatin biology to neuroscience). My long-term objective is to establish my independent research team in the field of neuroepigenetics to study how epigenetic gene regulation affect brain function and is important for the progression of a disease.



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2018

Turno de acceso general

Nombre: ARANDA ARAGON, SERGIO
Referencia: RYC2018-025002-I
Área Temática: **Biomedicina**
Correo Electrónico: Sergi.Aranda@crg.eu

Título:

AHCY function during embryo development: Implications for human disorders and infertility

Resumen de la Memoria:

My scientific interest is focused on setting the foundations for conceptually new therapies for human developmental diseases. My research experience combines a strong training in molecular and cellular biology, biochemistry and functional genomics, together with a solid background in stem cells, embryo development, gene regulation and epigenetics research fields.

All along my scientific career, I have trained in different laboratories in Spain and Sweden. During my pre-doctoral period at IRO and CRG (Barcelona), I contributed to elucidate the role of signaling pathways in heart development and to clarify the functionality of the human chromosome 21 gene DYRK1A in the control of neural stem cells homeostasis and neural cell death during embryo development. As a postdoc at Karolinska Institute (Sweden), I expanded my knowledge on understanding the molecular mechanisms regulating cell division in embryonic stem cells. Finally, as Staff Scientist at the CRG (Barcelona), I started to create the ground for an independent career and launched new research lines in gene regulation and epigenetics during embryo development.

My research for the next five years will be focused in two areas. First, the identification of novel therapeutic targets for an incurable human developmental disease due to AHCY deficiency (OMIM: 180960), and the functional and clinical evaluation of human AHCY variants during embryo development. For that, I will combine and integrate multi-omic experimental and computational approaches encompassing state-of-the-art technologies (NGS, CRISPR-Cas9, Chromatin Capture and mass spectrometry). Second, I aim to develop novel analytical methods and technologies to be applied in biomedicine and fundamental research. For that, I will expand a recent methodology that I have developed to characterize, in an unprecedented manner, malignant proliferating tumoral cells and rare (i.e. low abundant cells) adult stem/progenitor cells in situ at the proteomic level.

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 collaborations both in academia and with biotech companies; and, (5) proven leadership capacity to recruit and train junior researches. Overall, I believe that I have acquired the professional maturity to warrant for a successful independent scientific career.

Resumen del Currículum Vitae:

1) Scientific contributions: 16 peer-review articles/reviews, 4 submitted articles, 1 commissioned review in preparation, 1 book chapter (Elsevier), and 1 scientific handbook. Among them, 8 articles as first author, of which 6 are also as corresponding author and one is as last author, and 4 as second author. Average impact factor of 10.12, 1499 total citations, and an h-Index of 10 (source Google scholar).

2) Grants and awards: 3 competitive grants as Principal Investigator (1 research grant and 2 innovative teaching projects), 6 competitive fellowships (including Marie Curie FP7 and FEBS fellowships), and the Gold Medal at the international iGEM-2018 competition in synthetic biology. I have actively participated in 14 competitive research projects, including an ERC Advanced Grant, an FP7-european collaboration project (4DCellFate), and a recently granted EU Marie Skłodowska-Curie-ITN network (Chromdesign).

3) Mentoring and outreach: (1) I have supervised 2 PhD students, 2 master students, 2 internship PhD/master students, and 3 undergraduate students. The 2 PhD and 1 Master students were recipients of competitive fellowships from Generalitat de Catalunya, Caixa-INPhINIT, and INSERM-Liliane Bettencourt School. I will co-supervise an additional PhD student that will be recruited in September 2019, as part of my collaborative commitment with the EU Marie Skłodowska-Curie-ITN network Chromdesign. (2) I have mentored 19 high-school students as scientific co-director of the Genetics and Molecular Biology program at Youth and Science program (Catalunya-La Pedrera Foundation). (3) I have a tenure-track lecturer accreditation by the Agency for the Quality of the University System of Catalonia (AQU), and I have participated in the CRG PhD Course as a teacher. Finally, (4) I have been very active in outreach activities giving seminars and organizing scientific activities for the general audience, especially for high school students and teachers, with a total reaching audience of >1,200 people, and participating in disseminating the scientific activity in national and international general press articles (EIDiario.es, Universitetsläraren).

4) International activity: I have been invited as a speaker to three international meetings/congresses from different associations, including FEBS and SEBBM. I have assisted in the organization of an international Keystone Symposium (USA). I have also been member of scientific evaluation committees for Fundació Catalunya-La Pedrera, member of PhD defense thesis committees and PhD follow-up thesis committees, as well as reviewer for scientific journals, including Blood, Current Opinion in Genetics and Development and Journal of Molecular and Cellular Biology.



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Turno de acceso general

5) Collaborations: I have an extensive international collaboration network, including: Prof. Àngel Raya (CMRB Director, Barcelona); Dra. Anna Veiga (R&D+i Director, Dexeus Hospital); Lluís Armengol (CSO & CEO of qGenomics, S.L.); Dr. Francesc Solé (Josep Carreras Institute Director, Barcelona); Prof. Christian Thiede, MD (Universitätsklinikum Carl Gustav Carus, Dresden); Dr. Josep Nomdedeu, MD, PhD (Hospital de la Santa Creu i Sant Pau, Barcelona); Prof. Neus Agell (University of Barcelona); Prof. Patrik Ernfors (Karolinska Institutet, Sweden); Dr. Holger Heyn (National Center for Genomic Analysis, Barcelona)