AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2016

Turno de acceso general

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Título:

Structural biology of translation initiation and of proteins involved in signal transduction in bacteria

Resumen de la Memoria:

My past research experience has been mainly focused in understanding cellular function through structural mechanisms. In both my predoctoral and postdoctoral research periods I acquired not only experience in molecular biology and protein/nucleic acid biochemistry, but also in different techniques of macromolecular structure determination such as X-ray crystallography and cryo-electron microscopy.
During my predoctoral period at the laboratory of Dr. Vicente Rubio at the Biomedicine Institute of Valencia (IBV-CSIC), I mainly worked on signal transduction systems and control of transcription in bacteria. In more detail, my work was mainly focused in the study of molecular devices involved in controlling nitrogen metabolism and homeostasis. One of these devices is the protein PII, an ancient, widespread and conserved signalling protein which transduces nitrogen/carbon/energy abundance signals into metabolic and gene expression regulation, interacting with target proteins. During my thesis work I determined the crystal structures and largely characterized functionally the complex of the signalling protein PII with two protein targets, the enzyme acetylglutamate kinase (NAGK) and the cyanobacterial adaptor protein PipX. These were the second and third complexes of protein PII ever resolved structurally. Since PipX is an activator protein for the cyanobacterial transcription factor NtcA, for which the structure remained to be determined, I also determined the structure of the complex of NtcA with PipX as well as of NtcA by itself bound to its effector 2-OG and also in inactive form.
All this work was the subject of two papers published in PNAS in 2007 and 2010, of a review in Current Opinion in Structural Biology (2008). In addition to this work, I also determined the structures of NtcA-DNA and NtcA-PipX-DNA (not published) and determined the crystal structure at good resolution (1.65 Å) of the enzyme agmatine deiminase catalyzing its reaction. This work was published in the Journal of Bacteriology. I was first author in all these papers.
During my postdoctoral period in the laboratory of Dr. Venkatraman Ramakrishnan, at the MRC Laboratory of Molecular Biology (MRC-LMB, I have been working on the structural bases of translation initiation in eukaryotes. Eukaryotic translation initiation is a complex process with many different stages and involves at least 12 initiation factors (eIFs). When I started my postdoctoral period four years ago little was known about the structural basis for each of these stages. In a first work (Cell, 2014), we determined a structure by cryo-EM showing in detail how the AUG codon is recognized by the tRNAi and how different ribosomal elements and initiation factors modulate the codon-anticodon interaction. In a second work we solved cryo-EM reconstructions of yeast 48S ribosome in both scanning and scanning-arrested conformations (Mol. Cell 2015). Recently I have also played a key role on understanding prokaryotic translation initiation by providing eleven different cryo-EM structures, shedding light on the multiple steps used to position the correct tRNA and codon during bacterial initiation and into the role of each IF (Cell, 2016). Finally, I helped in the determination of the structure of the large subunit of the yeast mitochondrial ribosome by cryo-EM (Science 2014).

Resumen del Currículum Vitae:

I obtained my master degree in Biology in October 2002, and also in 2002 I obtained a master degree in Food Science and Technology, both at the University of Valencia.
My predoctoral research experience (2004-2011) was acquired entirely in the laboratory of Dr. Vicente Rubio at the Biomedicine Institute of Valencia (IBV-CSIC), first as a predoctoral fellow and then with predoctoral contracts. During that period of time I acquired significant experience in molecular biology, protein biochemistry and X-ray crystallography, while working on signal transduction systems and control of transcription in bacteria. I successfully overcame the challenges involved in determining the crystal structures of three protein-protein complexes, the first to have been done in the laboratory where I carried out my PhD work. All this work was reflected in six research papers (four of them as first author), several communications to different meetings and conferences and few awards.
From July 2012 to present, I am a postdoctoral fellow (first three years as a FEBS long-term fellow, and then as an Investigator Scientist) in the laboratory of Dr. Venkatraman Ramakrishnan, at the MRC Laboratory of Molecular Biology (MRC-LMB), in Cambridge. I recently learnt and used cryo-electron microscopy as a tool to study the various steps in eukaryotic translational initiation by determining the structure of different translation initiation complexes of the small ribosomal subunit (40S) with most of initiation factors, representing different stages of this complex process (Cell 2014, Mol. Cell 2015). More recently I have crucially contributed to understand structurally translation initiation in prokaryotes, by obtaining 11 different cryo-EM structures, representing distinct steps during initiation (Cell 2016). Finally, I also played a key role in a team-work project that required a full time dedication for almost six months. That is the determination of the structure of the large subunit of the yeast mitochondrial ribosome by cryo-EM (Science 2014). It has to be noted that this was the first time an structure was built de novo and refined in an EM map, and many tools originally designed for macromolecular crystallography were consequently adapted to work with EM, and therefore this can be considered as a pioneer work in the EM-field. All this work has been reflected in four research papers (all of them as a shared first author), and a few communications to meetings.

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Below I have listed 5 of my latest contributions

1. Llácer JL, Espinosa J, Castells MA, Contreras A, Forchhammer K & Rubio V (2010). Proc Natl Acad Sci USA 107, 15397-15402. 55 cits.
2. Amunts A*, Brown A*, Bai XC*, Llácer JL*, Hussain T, Emsley P, Long F, Murshudov G, Scheres SHW, Ramakrishnan V. (2014). Science 343, 1485-1489. 146 cits.
3. Hussain T*, Llácer JL*, Fernández IS, Munoz A, Martin-Marcos P, Savva CG, Lorsch JR, Hinnebusch AG, Ramakrishnan V. (2014) Cell 159, 597□607. 36 cits. (One figure of this work was the journal cover)
4. Llácer JL*, Hussain T*, Marler L, Echeverría-Aitken C, Thakur A, Lorsch JR, Hinnebusch AG, Ramakrishnan V. (2015). Mol. Cell 59, 399□412. 17 cits.
5. Hussain T*, Llácer JL*, Wimberly B*, Kieft JS, Ramakrishnan V. (2016) Cell 167, 133□144. 3 cits.
*These authors contributed equally

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Turno de acceso general

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Título:

Study to Predict Drug Adverse Effects in Diverse Genetic Populations of iPSC Using the Organ on a Chip " Technology

Resumen de la Memoria:

I started my PhD studies in the laboratory of Dr. Pedro A Lazo-Zbikowski, Salamanca, Spain where I was granted with a Predoctoral Trainership Award from the Castilla y Leon Community in Spain and later with a CSIC-Predoctoral I3P trainership Award. My research goal on his laboratory was to characterize in detail the Vaccinia related kinase (VRKs) protein kinase family and its implication in cancer. I characterized the phosphorylation on p53, ATF2 and c-Jun by the kinase VRK-1. From my PhD studies, I published 9 publications in Journals with high impact factor like Oncogene (IF=6.63) 83 citations, Journal of Biological Chemistry (IF=6.57) 87 citations, Molecular of Cell Biology (IF=13.30) with 103 citations, Journal of Virology and Molecular Cancer Research (IF=4.18) 25 citations.

On 2005, I was awarded with the highly competitive Travel Fellowship to assist to a FEBS & EMBO Advanced Course related to Molecular Mechanisms in Signal Transduction. I doctorated with Magna Cum Laude by the University of Salamanca on 2006. For my Post-Doctoral training, I moved to the EEUU to perform Stem Cell Research thanks to a grant from the Foundation Ramon Areces and later from a Postdoctoral fellowship from the Spanish Education and Science Ministry. At Dr. Ihor Lemischka laboratory I learned the characterization of induced pluripotent stem cells (iPSCs) from patients with Leopard syndrome. This work was published in Nature (IF=38.1) showing from first time a disease model of hypertophic cardiomyopathy on a dish which has already 509 citations.

During my stay at Ihor Lemischka lab I collaborated with many principal investigators publishing many papers in high impact factor journals. Plos Computational Biology (IF=4.5), Stem Cells (IF= 5.9), Nature Cell Biology (IF=18.6) with 94 citations where I performed single cell gene expression analysis to unravel the mouse stem cell heterogeneity. This was a very high impact study and I was invited to give a talk at the McGill University in Montreal, Canada. During my stay at Ihor Lemischka laboratory I assisted to many international conferences related with stem cells like the ISSCR. On 2010 I was elected for the prestigious and competitive travel award.
At Dr. Ihor Lemischka laboratory one of the main techniques established on his laboratory is to perform shRNA screening and competition assays to find the true regulator of the pluripotent state. This, we wrote a Nature Protocol (IF=7.9) paper to show this methodology. After 5 years at his laboratory, I published 10 papers in different journals including one book chapter and one review. Besides that, I also review other papers from my peers form the following journals: PLOS ONE, Journal of Proteomics, and bio protocols.

In 2013, I joined the New York Stem Cell Foundation as Staff Scientist to derivate iPSC from fibroblasts in a robotic platform. This work has been published on Nature Methods Journal (IF=25.32) where Im co-first author with 37 citations. We successfully have designed a revolutionary, high-throughput, robotic platform that automates and standardizes the process of transforming patient samples into stem cells. This unique platform, for the first time gives researchers the scale to look at diverse populations to better understand the underlying causes of disease and create new individually tailored treatments through drug screenings.

Resumen del Currículum Vitae:

Throughout my career my aim has been to uncover the best ways to use induced pluripotent stem cells for regenerative medicine.

I completed my PhD work at the University of Salamanca (Spain) at the Cancer Research Center under the supervision of Dr. Pedro Lazo-Zbikowski, supported by a Predoctoral Fellowship from the Junta de Castilla and Leon (Spain) and a I3P Predoctoral Fellowship from the CSIC (Spain). My research goal on his laboratory was to study the signaling pathways related with Cancer Biology. I focused my research on the characterization of the Vaccinia related kinase (VRKs) protein kinase family and its implications in cancer by characterizing the phosphorylation on p53, ATF2 and c-Jun proteins.

In total, I published (9) papers and (2) book chapters
(2) as first author (Oncogene. 2004, Biol. Chem. 2004. (2) as second author (Mol. Cell. Biol. 2004 and Atlas Genet Cytogenet Oncol Haematol. 2007 and (4) as third/ middle author (Arch Biochem Biophys. 2007: J. Virol. 2006; Mol. Cancer.Res. 2006; Journal of Biological Chemistry. 2012. and Atlas Genet Cytogenet Oncol Haematol. 2007.

On 2005 I was awarded with the Travel Fellowship to go to Spetses (Greece) and assist to the (FEBS & EMBO Advanced Course) Molecular Mechanisms in Signal Transduction.

On 2006 I started my posdoc at Mount Sinai School of Medicine (MSSM) in New York under Dr. Bernardo Nadal-Ginard with a Fellowship

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from the Ramon Areces Foundation to study cardiac cell regeneration and later I joined the laboratory of Dr. Ihor R Lemischka supported by a postdoctoral Fellowship from the Ministerio de Educación y Ciencia MEC (Spain). At his laboratory, we showed from first time a cardiac disease model on a dish from patients with Leopard Syndrome which was cover on Nature 2010 (IF=38.1) with 509 citations.

My postdoctoral time has been very prolific. I published (10) papers, (5) first or co-first author Bio-Protocol 2013; Stem Cells 2013; Epigenetics.2013; Nat cell biol.2012; Nat Protoc 2012 (2) second author Cell Reports. 2015. Nature 2010 (3) third/ middle author PLoS Comput Biol. 2014; Cell Stem Cell 2012; Blood 2011 (1) Book Chapter and (1) review. Stem Cell Research 2014.

Besides that, I was invited to give a talk at the McGill University in Montreal, Canada and I also got invited to review other papers from my peers in PLOS ONE, Journal of Proteomics, and bio-protocols.

Later, I joined the New York Stem Cell Foundation as Staff Scientist to derive iPSC for the NYSCF Array with a complete robotic system. After two years, we published our work on Nature Methods Journal (IF= 25.32), where I m co-first author.
As a researcher, in addition to the published papers (26 total, 7 first-author, 5 second author, 5 middles author). I have participated in stem cell scientific meetings, with a total of 30 contributions: 30 international scientific conferences/symposia (NYSCF, ISSCR). Being awarded with the competitive international travel award to assist to the International Society for Stem Cell Research (ISSCR) conference on 2010 in San Francisco.
During my scientific career, I have been key contributor on several research projects founded by public entities: NIH/USA, FIS/MEC (Spain), Also I have been fortunate to have opportunities to develop fruitful collaborations with researchers worldwide as well as perform teaching/mentoring duties at different levels.

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Turno de acceso general

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Título:

New mechanism of age-associated cardiovascular and metabolic disease

Resumen de la Memoria:

Aging is the greatest risk factor for cardiovascular disease (CVD), but the mechanisms by which aging contributes to CVD remain incompletely understood in spite of many years of intensive research. My research is focused on evaluating new mechanisms that link aging to CVD.

As a graduate student in Spain I investigated the role of several tumor suppressors involved in cell proliferation, senescence and death in the context of atherosclerosis. Overall, my work as a graduate student led to the publication of 7 research articles (3 as first author) and multiple reviews and book chapters. Between 2011 and 2015 I worked as a Postdoctoral Associate at the Whitaker Cardiovascular Institute of Boston University School of Medicine. During this period I combined the analysis of human samples and the generation and characterization of several new mouse strains to identify new signaling pathways involved in the control of inflammatory reactions in the adipose tissue and the cardiovascular system in the setting of obesity and aging. Among other contributions, my research revealed that non-canonical Wnt signaling plays a pivotal role in adipose tissue inflammation associated with visceral adiposity in mice and humans, which may contribute to the increased cardiometabolic risk associated with abdominal obesity. Furthermore, I contributed to studies that characterized a novel adipo-vascular non-canonical Wnt signaling axis that is dysregulated in conditions of aging and obesity and modulates vascular inflammation, insulin resistance and angiogenesis in mice and humans. Overall, these studies led to the publication of 8 research articles (one as first author; Fuster et al, Diabetes 2015) and several review articles. I was fully funded for the majority of my time as an undergraduate/graduate student and postdoctoral fellow (2004-2015), having been awarded four undergraduate research scholarships, one predoctoral fellowship and two postdoctoral fellowships.

In 2015 I was appointed as Instructor in the Department of Medicine at Boston University, a Junior Faculty position that allowed me to establish an independent line of research focused on investigating the contribution of age-associated somatic mutations in hematopoietic cells to cardiovascular and metabolic disease. Human aging is associated with an increased frequency of somatic mutations in hematopoietic cells, and several of these mutations promote the clonal expansion of the mutant blood cells. This clonal hematopoiesis correlates with an increased risk of atherosclerotic CVD in humans, but whether there is a causal link between exacerbated atherosclerosis and clonal hematopoiesis induced by somatic mutations remained unknown. My recent studies have provided the first experimental evidence supporting the notion that somatic mutations in specific genes within hematopoietic cells contribute to atherosclerosis and thus represent a novel causal cardiovascular risk factor, which could potentially be targeted for the development of new therapies or preventive care strategies for CVD. My work on this topic as Principal Investigator is currently funded by an American Heart Association R&D project grant and has generated so far one publication as first and co-corresponding author (Fuster et al, Science 2017) and a patent of which I am co-inventor.

Resumen del Currículum Vitae:

During my scientific research career since a PhD student (2006-present), I have co-authored a total of 27 scientific publications mainly related to new pathophysiological mechanisms of cardiovascular and metabolic disease, including the following:

- 16 Research Articles (8 in journals within the first decile; 14 in journals within the first quartile in WOS/JCR categories in the year of publication), 5 of them as main author (first or first and co-corresponding).
- 8 Invited Reviews and Editorials, 7 as main author (first or first and co-corresponding).
- 3 Book Chapters, 2 of them as main author (first or single author).

My most significant scientific publication to date is a recent Research Article in Science as first and co-corresponding author (Fuster et al, 2017), which I consider the foundation of my current line of research. The studies included in this publication also led to a patent application.

I have presented my work at multiple national and international meetings, obtaining several abstract awards and travel scholarships, and I have been an invited speaker in prestigious institutions such as the Harvard-affiliated Brigham and Women's Hospital, the Boston University Evans Center for Interdisciplinary Biomedical Research and the Centro Nacional de Investigaciones Cardiovasculares (CNIC).

My research work as PI is currently funded by an American Heart Association R&D project grant.

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I also do editorial work for a number of biomedical journals, being a frequent reviewer for high profile cardiovascular journals (e.g. Circulation) and an Editorial Board Member of Frontiers in Cardiovascular Medicine - Atherosclerosis and Vascular Medicine.

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Turno de acceso general

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Título:

Striatal and hippocampal excitatory synapses in normal and diseased brain

Resumen de la Memoria:

I started my career in 2005 in the laboratory of Dr. Jordi Alberch Vié who is a leader in Neurosciences in Spain and he has one of the most important team studying Huntington's disease in such country. I started in this lab during one year with a collaboration grant. After learning several techniques, I started my PhD in the same lab. With the acquisition of many in vivo techniques in rodents I published 8 papers, 2 as first author. During that time I also lectured during 5 years practical histology lessons to Medicine students and I also mentored two Master students during 3 months each. On the other hand I also was in the teacher staff of an international course to train postgraduate students in neuroscience (DiMI training course leaded by Dr. Anna Planas from the IDIBAPS) during the years 2006-07. My PhD trajectory allowed to me to obtain the special award from the University of Barcelona in recognition of the quality of my PhD. Then, after my PhD dissertation I continued in the same department to perform my first postdoc there from the end of 2010 until the end of 2013. This led me the opportunity to finish all my big projects as a first author such as two papers published in Human Molecular Genetics (IF: 7.6), a Nature Medicine (IF: 28.05) and a Journal of Clinical Investigation (IF: 13.2). During that period I received the annual CIBERNED prize. This is a national prize that recognizes the high quality research from young investigators in neurodegenerative diseases. Then I moved to Paris in the laboratory of Dr. Jean-Antoine Girault from October 2013 until now. Jean-Antoine is the director of the Institute du Fer à Moulin (the IFM). He is also the current president of the French Neuroscience Society. In this institute I uploaded my background by performing workshops about molecular biology and optogenetics to apply to my research which is now partially based in such techniques. I have also got big experience in confocal and electronic microscopy imaging as well as in electrophysiology in slices. After three years of postdoc in Paris, I already published three papers, two as a second author, in Nature Communications (IF:11,3) and in Neuropharmacology (IF:4.9) and one as a first author in Glia (IF:6,03). Furthermore I have a manuscript as a first author under second revision in Nature Communications (IF:11,3) highlighting the quality and efficiency of the research that I carried out in this team. I decided to follow up this trajectory until now with the idea of increasing my skills in many fields of basic research, to publish in very good journals and to work in high-quality laboratories. Altogether is helping me to start to develop my skills on leadership in order to lead a team in the future. In this sense, nowadays I could ensure that I am at the beginning of this process since I am supervising a PhD and a master student in the laboratory, I am also leading a new line of research in the lab about Alzheimer disease from which we are preparing two manuscripts in which I will be the last corresponding author in one of them. Finally and most importantly, I recently obtained my own funding from a Young Investigator Research Grant from the internationally renowned NARSAD foundation (amount: 70000 dollars for two years. Ref: 24803).

Resumen del Currículum Vitae:

I have a degree in Psychology (University of Barcelona, 2005) and I a PhD in Neurosciences (University of Barcelona, 2010). I speak Catalan and Spanish with a C2 level and English and French with a C1 level. As additional education, I attended to:
-The 1rst stereological course performed by Olympus (2008) in Barcelone. (5 days of training)
-Workshop: Genes: From brain to Cognition, celebrated in Soria, Spain; 2006 (5 days of training).
-Workshop called: Optogenetic approaches for pre-clinical studies. February 9-10/2016 At the ICM. Paris, France

My scientific evaluation from the ISI web of knowledge is:
H-index 15, I published 35 publications (papers) and I have been cited 742 times. I'm first author in 12 papers and all of them have been published in journals placed in the first quartile. All the papers as co-author (23) are published in journals of the first quartile except 5 in the second quartile. My most outstanding papers from my PhD and first postdoc in Alberch's lab are: two Human Molecular Genetics (IF: 7.6), a Journal of Clinical Investigation (IF: 13.2), a Nature Medicine (IF: 28.05). My outstanding published papers in my second postdoc in Paris are: a Glia (impact factor 6.03) and my papers as second author in Nature Communications (IF: 11.47) and in Neuropharmacology (IF: 4.9). It is also remarkable my current manuscript as first author under second revision in Nature Communications (IF: 11.47) Ref: NCOMMS-16-19675-T.

As posters and oral presentations I presented results in both, oral and poster formats in national and international congresses such as the World Huntington Disease congress (Dresden, Germany; 2008) Congreso de terapia génica (SEYTG, Granada, Spain. 2009) or in CIBERNED (2012 Madrid, Spain) or in several FENS Amsterdam (2008), Barcelona (2010) and Copenhagen (2016).

During my scientific career I have been involved in 8 competitive (national and international) projects, the most outstanding: an ERC consolidator grant (budget: 2500000 euros) obtained by the Jean-Antoine Girault's team in Paris (France). As technological transfer I was

co-leading two projects with my supervisor Dr. Jordi Alberch Vié, from the University of Barcelona, collaborating in 2009 with Digna Biotech and with SERVIER in 2013 (3K and 80K euros respectively). Finally, now I have my own funding from a Young Investigator grant from the NARSAD foundation 2016 (Ref: 24803; 70000 dollars. From 01/01/2017 to 31/12/2018).

As a teaching experience I taught practical classes in histology during 5 years in the Faculty of medicine of the University of Barcelona (24 hours/year). I also mentored 2 master students during 3 months each in the University of Barcelona and 1 master student (3 months) and a PhD student, Benoît de Pins (since one year ago) in the Institut du Fer à Moulin in Paris. Finally, I lectured practical classes (in 2007 and 2008) in the international course called Animal Models for the study of Neurological Diseases: histological, molecular and biochemical hallmarks (conducted by the DiMI).
As social transfer I participated in several educational initiatives. I gave talks in high schools in Barcelona during the so-called "Semana del cervell" (Brain week) once per year from 2007 to 2010. I also was a co-author in an educational audiovisual report which won the VII Joan Oró Prize to scientific divulgation.

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Título:

F CALVO - Research career and interests

Resumen de la Memoria:

My scientific career has focused on investigating the mechanisms that control human cancer dynamics and pathobiology. It has progressed from the study of oncogenic signalling and interactions during my PhD, up to the integrative analysis of signalling, gene expression, cancer cell biology, and complex cancer models during my postdoctoral studies. Now, as an independent principal investigator I exploit this varied background and expertise in a research program that investigates the multicellular context of solid tumours to understand the molecular mechanisms regulating cancer progression, dissemination and response to therapy. My PhD studies at Universidad de Cantabria focused on investigating signalling dysregulations in malignant cells and were instrumental in describing how Ras-ERK signalling is spatially modulated leading to the activation of diverse transcriptional programs and different pathobiological responses. These studies shaped our current understanding on how Ras/ERK signalling is the sum of multiple, site-specified sub-signals, rather than single, homogeneous entities. In this period, I contributed to 7 original research manuscripts and 2 reviews (total of 360 citations). In my postdoctoral studies at the Universidad de Cantabria and the CRUK London Research Institute (UK) I focused on deciphering the mechanisms that control cancer cell invasion and metastasis in complex environments. Using ex vivo and in vivo models of human cancer, clinical material and state-of-the-art methodology such as multiphoton intravital imaging my studies provided key insights in the role and regulation of specific cytoskeletal rearrangements in metastatic cancer cells. In addition, I contributed with influential studies into the tumour microenvironment and crucially demonstrated that the physical properties of solid tumours not only can modulate the malignant potential of cancer cells, but also affect the behaviour of non-cancerous cells such as fibroblasts. During my postdoc, I generated 2 first-authored manuscripts in Nature Cell Biology, and wrote 2 reviews (total of 311 citations). Since 2013, I am an independent principal investigator at the Institute of Cancer Research (UK) where I lead a research program investigating tumour:stroma interactions in solid tumours to understand the molecular mechanisms regulating tumorigenesis and metastasis. My studies focus on two key aims: (i) how pro-tumorigenic CAFs can be manipulated towards tumour-suppressive phenotypes for therapeutic gain; and (ii) investigating cytoskeletal dynamics, their role in cancer cell invasion in complex 3D environments and strategies to manipulate them to reduce cancer dissemination. Following my previous findings, an encompassing goal is to understand the role of mechano-biological processes (the mechanisms by which cells convert mechanical stimulus into chemical activity) in these systems. By incorporating clinical collaborations and patient-derived material into our cancer models and extensive mechanistic background, I have expanded my research into more clinically relevant scenarios. My final goal is to generate basic knowledge that can be quickly transferable to human disease, clinical practise and cancer therapeutics. As a PI, I have participated in 10 publications, including 6 as corresponding author (total of 41 citations).

Resumen del Currículum Vitae:

I am a scientist with a background of 15 years of specialised research focused on the study of the mechanisms that control human cancer dynamics and pathobiology. After graduating in Biochemistry at the Universidad del Pais Vasco (Spain), I joined Prof Piero Crespo's team at the Universidad de Cantabria (Spain) to course my PhD studies by means a Spanish Ministry of Culture (FPU) Studentship. My PhD focused on investigating the regulation and pathological consequences of the signalling cascades triggered by the Ras oncogene. I obtained my PhD in 2008 and my thesis was awarded the Best Thesis in Biomedicine, Unversidad de Cantabria. In 2010 I joined Dr Erik Sahai's team at the CRUK London Research Institute (UK) as a Postdoctoral Researcher. During my postdoctoral studies I investigated the molecular mechanisms that regulate cancer cell invasion and the role of the tumour microenvironment in tumour progression and dissemination. As esteem indicators in this period, I obtained various awards (e.g. 22nd EACR Meeting Travel Bursary, Best Poster Prize 28th AIBCR Conference). Since October 2013, I am an independent Principal Investigator at the Institute of Cancer Research (UK) where I lead a research program that investigates the multicellular context of solid tumours to understand the molecular mechanisms regulating cancer progression and dissemination. Throughout my career, I have established highly-productive collaborations that led to high impact publications in the fields of cancer metastasis and tumour microenvironment. In addition, I have mentored younger scientists (I currently supervise 2 postdoctoral fellows, 1 PhD Student and 1 research technician, having already mentored several MSc/BSc students in the past), and obtained highly competitive funding as an independent researcher (e.g. Worldwide Cancer Research Grant, CRUK Multidisciplinary Award, ICR internal funding). As additional indicators of my visibility in the field, my work has been acknowledged with awards and invitations to present at conferences and research institutes (24 invitations since I became independent). Overall, at this early stage of my career I have a very good publication record with 17 primary research papers and 7 reviews/commentaries (713 citations, h-index=12). Two of my first author papers are in Nature Cell Biology, one of the highest ranked journals in the field of molecular cell biology. Since becoming an independent researcher I have participated in 10 publications and I am the corresponding author on 6 of them.

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Título:

Targeting Hypothalamic Astrocytes in Obesity

Resumen de la Memoria:

Despite considerable efforts aimed at prevention and treatment, the prevalence of obesity and type 2 diabetes has increased at an alarming rate worldwide over recent decades. Given the urgent need to develop safe and efficient anti-obesity drugs, the scientific community has to intensify efforts to better understand the mechanisms involved in the pathogenesis of obesity. Based on human genome-wide association studies and targeted mouse mutagenesis models, it has recently emerged that the brain controls most aspects of systemic metabolism and that obesity may be a brain disease.

I have recently shown that like neurons, astrocytes also respond to circulating nutrients, and they cooperate with neurons to efficiently regulate energy metabolism. Specifically, astrocytes respond to insulin and leptin to modulate brain glucose uptake and leptin sensitivity respectively and, in turn, participate in the regulation of feeding behavior. So far, the study of brain circuits controlling energy balance has focused on neurons, ignoring the presence and role of astrocytes. Importantly, our studies were the first to describe that exposure to a high-fat, high-sugar (HFHS) diet triggers hypothalamic astrogliosis prior to significant body weight gain, indicating a potentially important role in promoting obesity. Additionally we found alterations in how hypothalamic astrocytes physically interact with neurons and blood vessels, suggesting a disruption in hypothalamic cell-cell interactions and nutrient availability in the pathogenesis of obesity.

Overall, my recent findings suggest a novel model in which astrocytes are actively involved in the central nervous system control of metabolism. Taking advantage of recent technical advances enabling targeting non-neuronal cells genetically (designer receptors, vectors based on the adeno-associated virus, and sophisticated imaging technology), my studies are focusing on uncovering the molecular underpinnings of astrocyte-neuron inputs regulating metabolism in health and disease. The resulting insights will help to inspire and enable novel therapeutic strategies to fight diabetes and obesity.

Resumen del Currículum Vitae:

Doctora en Biología por la Universidad Autónoma de Madrid con calificación Sobresaliente Cum Laude y Premio extraordinario (Curso académico 2011/2012). Desde el 2012 estoy trabajando en el Instituto de Diabetes y Obesidad de Helmholtz Zentrum Muenchen, Munich, Alemania. Primero como contratada postdoctoral y desde 2015 dirijo como jefa de grupo el Departamento de Biología del Astrocito de dicho instituto. Mi carrera científica se inicia en el 2006 con mi incorporación al Departamento de Endocrinología del Hospital Infantil Universitario Niño Jesús (asociado a la Universidad Autónoma de Madrid) primero para la realización del proyecto fin de carrera y luego como contratada predoctoral por la Fundación de Endocrinología y Nutrición, y por el CIBER de Fisiopatología de la Obesidad y Nutrición (CIBERobn). En el 2008 fui beneficiaria de una beca de Formación de Profesorado Universitario (FPU) del Ministerio de Educación y Ciencia lo que me permitió llevar a cabo la Tesis Doctoral bajo la dirección de la Dr. Julie Chowen y el Prof. Dr. Jesús Argente Oliver. Durante mi periodo predoctoral disfrute de dos estancias en el extranjero (becas de movilidad FPU) en la Universidad de Yale (New Haven, EEUU) bajo la supervisión del Dr. Tamas L. Horvath y en la Universidad de Göteborg (Gotemburgo, Suecia) bajo la supervisión de la Dra. Suzanne Dickson que me permitieron extender mis conocimientos así como aprender técnicas experimentales nuevas que me ayudaron en el desarrollo de mi Tesis Doctoral. Además dichas estancias me permitieron establecer colaboraciones científicas de larga duración que continúan en la actualidad con el Departamento de Medicina Comparativa de la Universidad de Yale (TL. Horvath). Desde el inicio de mi Tesis Doctoral me he centrado en el estudio del circuitos hipotalámicos implicados en el control del metabolismo energético haciendo especial hincapié en el papel de la glía en dicho proceso. Estos estudios me han permitido publicar, hasta la fecha, un total de 33 artículos (11 de ellos como primer autor distribuidos en 7 artículos y 4 revisiones) en revistas científicas de referencia en el campo de la endocrinología y la obesidad de los que cabe destacar mis estudios publicados recientemente (índice de impacto: 28,7) que demuestran que los receptores de insulina en los astrocitos regulan el transporte de glucose al cerebro (Garcia-Caceres C., et al., Cell 2016). He participado en 7 proyectos de investigación (2 de ellos aún en desarrollo: CIBERobn y The French National Research Agency) y he sido invitado a 5 ponencias para presentar mis estudios en congresos y seminarios. En total he contribuido en 43 trabajos presentados en congresos tanto nacionales como internacionales como autor principal o coautor. Entre los premios recibidos cabe destacar: 1 premio a la mejor publicación presentado en la Sociedad Española de Endocrinología Pediátrica (Lechuga-Sancho et al., Endocrinology 2006), 3 premios a mejor poster en los congresos: Nutrient and Metabolite Sensing (Dinamarca, 2015), 49th SEEP Annual Meeting (República Checa, 2010) y III Simposium del Ciberobn (España, 2009), 1 premio al mejor abstract concedido por The Endocrine Society y presentado en el 96th ICE/ENDO Annual Meeting (EEUU, 2013) y 1 beca de viaje concedido por Keystone Symposia para asistir al congreso "Obesity and Adipose Tissue Biology Meeting" (Canadá, 2016).

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Turno de acceso general

Nombre: BALERIOLA GOMEZ DE PABLOS, JIMENA
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Título:

Glia-to-axon exosome transfer in physiology and pathology

Resumen de la Memoria:

My general goal is to understand how the central nervous system is formed and/or altered under physiological and pathological conditions. I graduated in Biochemistry at the Universidad Complutense de Madrid (2003) and started my career as a neuroscientist when I joined the 3D lab directed by Drs. Flora de Pablo and Enrique de la Rosa at Centro de Investigaciones Biológicas (Madrid, 2004). From 2004 to 2008 I conducted research on DNA damage and its and impact on programmed cell death during central nervous system development. On 2008 I obtained my doctorate degree (PhD) from the Department of Biochemistry and Molecular Biology at Universidad Complutense. I continued my research on DNA repair and programmed cell death as a postdoctoral researcher under the supervision of Dr. Enrique de la Rosa until 2010.

To further my career in neuroscience research, in 2010 I joined the laboratory of Dr. Ulrich Hengst at the Taub Institute for Research on Alzheimer□s Disease and the Aging Brain, Columbia University Medical Center (New York, USA). My research projects aimed to characterize a possible function for intra-axonal protein synthesis in amyloid pathology, a central feature in the development of Alzheimer□s disease. When I joined the Taub Institute there was no evidence in the literature that local translation in axons could play a role in the adult central nervous system in the context of a neurodegenerative disease. I have defined a novel unexpected molecular pathway that mediates axon-to-soma spread of amyloid pathology within neurons that requires the local translation of the transcription factor ATF4 (among other proteins). My work as a postdoctoral researcher has been featured in AlzForum by its scientific advisory board, as well as in scientific journals such as Sience Signaling (Editor□s Choice) or CNS & Neurological Disorders-Drug Targets. I was also one of the only twelve candidates that Columbia University nominated for the 2015 Blavatnik Awards for Young Scientists.

Throughout these years I□ve gained extensive expertise, not only in the basic mechanisms that lead to cell death during neural development and neurodegeneration, but more importantly, in mRNA localization and local translation. The study of intra-axonal protein synthesis is far from trivial, since it requires the use of challenging techniques that allow the isolation of axons from the corresponding neuronal soma (e.g microfluidic chambers, modified Boyden chambers, etc□). Such techniques are mastered by few research laboratories.

In 2015 I was awarded with an Ikerbasque Research Fellow contract form the Basque Foundation for Science. This 5-year tenure-track style position allows me to conduct my research (starting May 2016) at the Achucarro Basque Center for Neuroscience as the group leader of the Laboratory of Axon-Glia-Interactions. My research focus is deciphering the contribution of glial cells in regulating intra-axonal protein synthesis through horizontal transfer of exosomes containing RNAs, ribosomes and other translation regulators in physiological and pathological conditions (e.g experimental models of Alzheimer□s disease). I am currently directing two master projects from students Maite Blanco Urrejola and Javier García Santana (UPV/EHU). More importantly, one of my lab projects has been funded by the R&D program □Retos□ from MINECO.

Resumen del Currículum Vitae:

I am a neuroscientist specialized in basic mechanisms that mediate cell death in neural development and neurodegeneration. During the last years I have been committed to better understand the contribution of intra-axonal signaling events in the pathogenesis of Alzheimer□s disease (AD), with a special focus on mRNA localization and local translation. In 2015 I was awarded with a 5-year Ikerbasque Research Fellow position to establish my own research lines as group leader of the Laboratory of Axon-Glia Interactions at Achucarro Basque Center for Neuroscience. My lab is focused on the role of glial exosomes in regulating local translation by supplying mRNAs and other regulatory molecules to axons under physiological and pathological conditions. I was recently granted funding through the R&D program "Programa Estatal de I+D+i Orientada a los Retos de la Sociedad" from MINECO. I currently supervise two master students enrolled in the University of the Basque Country (UPV/EHU).

Past achievements:

Postdoctoral training (2010-2016, Columbia University Medical Center):

In 2010 I joined Dr. Hengst laboratory at Columbia University, a reference laboratory in the field of intra-axonal protein synthesis. My projects focused on unravelling a possible role for local translation in the pathogenesis of AD. I described an unexpected mechanism for axon-to-soma degeneration induced by amyloid that relies on local production of the transcription factor ATF4 (and other proteins) in axons. One of my major achievements was to publish my results in the high impact factor journal Cell in 2014. My work was featured in AlzForum by its scientific advisory board, as well as in scientific journals such as Science Signaling (Editor□s Choice) or CNS & Neurological

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Disorders-Drug Targets.
The innovative techniques I use to isolate axons from the neuronal soma helped me establish the importance of axonally synthesized ATF4 in amyloid-induced neurodegeneration. These data settled the basis for a new project in which I was principal investigator and was awarded with an ADRC pilot grant from Taub Institute financed by NIH (2013-2014). In this project I proposed the identification of target genes whose transcription depend on axonally synthesized ATF4 and might also be involved in neurodegeneration (ongoing work in the Hengst lab).
In 2015 I was nominated by Columbia to the 2015 Blavatnik Awards for Young Scientists. The Blavatnik Foundation awards the excellence of young scientists that conduct their research in the tri-state area of New York, New Jersey and Conneticut. Only three winners and six finalists are recognized with this award. Universities from the three above mentioned states can present only twelve candidates and I had the honor to be nominated by Columbia University in 2015.

Predoctoral and early postdoctoral training (Center for Biological Research, CIB-CSIC, 2004-2010):

In 2004 I was awarded with a FPI predoctoral felllowship to complete my doctoral studies under the supervision of Dr. Enrique de la Rosa. As a graduate student I focused on the role of DNA damage repair proteins in central nervous system development and their repercussion in neuronal death. I identified DNA-PK and DNA polymerase mu; (Pol mu), as key players in the survival of newly generated neurons in the embryonic central nervous system (Baleriola et al. 2010; Baleriola et al. 2016).

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Turno de acceso general

Nombre: PIRIZ , JOAQUIN
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Título:

Circuitos Neuronales de Asignación de Valores Negativos

Resumen de la Memoria:

I graduated in Biology at the University of Buenos Aires, Argentina. I pursued my career with a PhD in Neurosciences (2002-2007, Cajal Institute, Madrid, Spain). During my PhD I studied brain actions of blood-circulating type I Insulin-Like Growth Factor (IGF-I) and contributed to clarify the physiological mechanisms of brain uptake of that hormone.
I performed my postdoctoral formation at the University of California San Diego (San Diego, USA) studying synaptic physiology in depression. During this stage I contributed to individualize the brain nucleus of the Lateral-Habenula as a locus of synaptic plasticity associated with depression.
I returned to Argentina, my home country, in 2010. In 2011 I was appointed as Assistant Researcher to the tenure-track career of the Argentinean National Scientific and Technical Research Council (CONICET), a position with partial independence. In 2014 I was promoted to a fully independent position. During these last two stages I investigated the synaptic physiology of the Lateral Habenula (LHb) and its role in memory formation. As independent researcher I have established my own group and nowadays I supervise PhD students, postdocs, technicians and Assistant Researchers. In addition, I have obtained national and international funding and have published articles as senior author.

The innovative essence of my work is reflected in the quality of my scientific production. On each stage of my formation, from three different countries, I have published in top journals (Neuron: Spain, Nature: United States, Science: Argentina), demonstrating that I am able to attain excellence under different circumstances. Nevertheless, I am aware science is a social enterprise where institutional support is a key factor for success. Hence, at this stage of my career, where I have to expand and consolidate my research, I have decided to move to a more stable and well funded scientific environment. In this regard, I consider Spain my first choice, a country where I started my formation as scientist; which I consider my second home. The Ramon y Cajal program constitutes an excellent and timely opportunity to achieve that goal.

Resumen del Currículum Vitae:

Positions and Employment:

2002-2007 Doctoral Fellow of the Spanish Ministry of Education, Cajal Institute, Madrid, Spain
2007 Postdoctoral contract, Spanish Consortium for Neurodegenerative Diseases (CIBER), Cajal Institute, Madrid, Spain
2008-2010 Postdoctoral Fellow, University of California San Diego, San Diego, California, US
2010- Postodoctoral Fellow of the Return Home Program of the CONICET, Buenos Aires, Argentina
2011-2014 Researcher CONICET (Assistant), Buenos Aires, Argentina
2014- Researcher CONICET (Associated), Buenos Aires, Argentina

Peer-reviewed Publications:

Number of peer reviewed indexed publications: 13
Total citations: 550
h Index: 10

Most relevant to the current application:

1. A. Lempel, L. Coll, AF. Schinder, OD. Uchitel, J. Piriz (2016). Chronic Pregabalin Treatment Decreases Excitability of Dentate Gyrus and Accelerates Maturation of Adult-born Granule Cells. J. Neurochem doi: 10.1111/jnc.13740.
2. S. Shabel, C. Proulx, J. Piriz, R. Malinow. (2014). GABA/glutamate co-release controls habenula output and is modified by antidepressant treatment. Science 345(6203):1494-8.
3. M. Tomaiuolo, M.C. Gonzalez, J.H. Medina, J. Piriz. Lateral Habenula determines long-term storage of aversive memories (2014). Frontiers in Behavioral Neuroscience, 8(May), 170
4. B. Li *, J. Piriz *, M. Mirrione *, C. Chung * (* equal contributors), C. Proulx, D. Schulz, F. Henn, R. Malinow (2011). Synaptic potentiation onto habenula neurons in learned helplessness model of depression. Nature; 470(7335):535-9.
5. T. Nishijima *, J. Piriz *, S. Duflot * (* equal contributors), A.M. Fernandez, G. Gaitan, U. Gomez-Pinedo, J.M. Verdugo, F. Leroy, H.

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Soya, A. Nuñez, I. Torres-Aleman (2010).Neuronal activity drives localized blood-brain-barrier transport of serum insulin-like growth factor-I into the CNS. Neuron; 67(5):834-46.

6. J.L. Trejo *, J. Piriz* (* equal contributors), M.V. Llorens-Martin, A.M. Fernandez, M. Bolós, D. LeRoith, A. Nuñez, I. Torres-Aleman (2007). Central actions of liver-derived insulin-like growth factor I underlying its pro-cognitive effects. Mol. Psychiatry; 12(12):1118-28.

Current Research Support:

2013-2016 PICT 2013-1523. National Agency of Promotion of Science and Technology, Argentina. Mechanisms Underlying L-DOPA Induced Dyskinesia in an Experimental Model of Parkinson Disease.
Role: Project Integrant . 436,800 AR$ ~ 26,000

2016-2017 PICT 2015-2609. National Agency of Promotion of Science and Technology, Argentina. Optogenetics dissection of brain circuits involved in long-term memory maintenance
Role: PI 200,000 AR$ ~ 13,000

2016-2017 Young Investigator Award. Brain and Behavior Research Foundation (NARSAD), USA. Synaptic Plasticity at the Globus Pallidus-Lateral Habenula Pathway in Depressive Disorders
Role: PI 70,000 US$ ~ 65,000

Current Human Resources Mentoring

Demian García Violini. Postdoctoral Fellow, CONICET (Co-director).
Lucila Kargieman. Assistant Researcher, CONICET (Co-director).
Nicolas Ivan Bertone Cueto. Predoctoral Fellow, CONICET (Director).
Tomas Sachella. Predoctoral Fellow, CONICET (Director).

Recent Awards and Fellowships

September 2015. Fulbright Fellowship for Neuroscience Training at the United States.
August 2015. NARSAD Young Investigator Award

Recent Research Stays

August 2015 Summer Workshop at Dr. Karl Deisseroth laboratory. Stanford University (California, U

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Turno de acceso general

Nombre: PAMPLIEGA ORMAETXEA, OLATZ
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Área Científica: Biomedicina
Correo Electrónico: opampliega@gmail.com

Título:

The primary cilium as a tool to modulate autophagy in neurodegenerative diseases

Resumen de la Memoria:

Through my career I have been interested in research related to biomedicine and cell biology, with emphasis in neurodegenerative diseases. My PhD thesis (2009) focused on the study of glutamatergic signaling during multiple sclerosis, supervised by Dr. María Domercq and Dr. Carlos Matute (UPV-EHU). Here we concluded that alterations of glutamatergic signaling in the peripheral blood of MS patients mimics those from the Central Nervous System (CNS), and thus, they could be developed to get new biomarkers for MS. Additionally, this training familiarized me with basic procedures in neurobiology, neuronal and glial primary cultures, immunohistochemistry and molecular biology, as well as with the handling and analysis of human samples.

My postdoctoral training in the Laboratory of Dr. Ana María Cuervo at Albert Einstein College of Medicine (NY-USA, 2010-2014) focused on the regulation of macroautophagy by nutritional conditions, with emphasis on the primary cilia (PC), a signaling organelle that senses the extracellular environment. I discovered that there is physiological interplay between autophagy and ciliogenesis, as signaling pathways that are clustered in the PC -such as Hedgehog (Hh) pathway- regulate autophagy by a mechanism that involves the recruitment of autophagy related proteins to ciliary structures. Our work was published in Nature. The novelty and importance of this finding was highlighted in the "News and Views" section, as well as in Nature Reviews in Molecular Cellular Biology, and in the journal Developmental Biology. The comments by experts in the field of cellular biology emphasize the projection and innovation of the discovery. In order to gain insights about the role of this newly discovered interaction during non-physiological conditions, I become interested in the role of cilia mediated autophagy during senescence, one of the hallmarks of aging. The results have led to a new submitted paper "Deregulated ciliary Hh signaling induces aberrant autophagy activation during cellular senescence" where we describe that alterations of ciliary Hh signaling during senescence lead to a deregulated increase of autophagy that can be modulated by restoring the Gli1 levels of the cell.

The discovery of cilia-mediated autophagy and my dual expertise in cell biology and neuroscience enable an innovative approach for my independent research line. My ongoing projects at the Institute of Neurodegenerative Diseases of the University of Bordeaux (2015-) aim to understand the molecular mechanisms behind cilia-mediated autophagy, and its impact on neurodegeneration. More specifically, I am interested in deciphering the impact of ciliary p75-NTR receptor signaling in the autophagy decline during Alzheimer's disease and beta-amyloid pathology. In this regard I have already received independent funding from LECMA-Vaincre Alzheimer, and my proposal CILIAD was selected for the second round of the ERC-StG-2016, for which I was invited for a personal interview in Brussels.

Based on the fact that a growing number of neurodegenerative and age-related diseases curse with malfunctioning autophagy, selective manipulation of ciliary signalling pathways could become a novel therapeutic approach to restore autophagic activity and slow down the progression of neurodegeneration and aging.

Resumen del Currículum Vitae:

Education

2004-2009	PhD in Biology Department of Neurosciences, University of the Basque Country, Spain
2002-2003	M.S. in Biomedicine and Biotechnology University of Alicante, Spain
2002-2003	M.S. in Reproductive Biology Miguel Hernández University, Spain
1997-2002	BSc. in Biology (Biomedicine) Autonomous University of Barcelona, Spain

Appointments

2017 -	Senior Postdoctoral Fellow Equipe Bézard. Institute of Neurodegenerative Diseases, University of Bordeaux, France.
2015 - 2016	IdEx Junior Chairs Senior Postdoctoral Fellow Equipe Bézard. Institute of Neurodegenerative Diseases, University of Bordeaux, France.
2010-2014	Postdoctoral Fellow Laboratory of Dr. Ana María Cuervo. Dpt. Developmental and Molecular Biology, Albert Einstein College of Medicine, Bronx-NY, USA.
2009 - 2010	Postdoctoral Fellow Laboratory of Dr. Carlos Matute. Dpt. Neurosciences, University of the Basque Country, Spain.

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2004 - 2009 Graduate Research Fellow Laboratory of Dr. Carlos Matute. Dpt. Neurosciences, University of the Basque Country, Spain.
2007 Visiting scientist Laboratory of Dr. Frauke Zipp. Neuroscience Research Centre. Charité-Universitätsmedizin. Berlin, Germany.

Honors, Awards and Fellowships

2016 Poster Award. 7th Proteasome & Autophagy Workshop. Clermont-Ferrand, France.
2015-2016 IdEx Junior Chairs Postdoctoral Fellowship.
2014 Dennis Shields Postdoctoral Award for Outstanding Postdoctoral Research.
2013 EMBO Meeting 2013 travel award.
2011 Keystone Symposia in Autophagy travel award.
2010-2011 Basque Government Postdoctoral Fellowship.
2009 Excellent Cum Laude by unanimous decision Thesis Dissertation. Doctor Europeus mention.
2007 Spanish Ministry of Education and Science Short-Term Abroad Fellowship.
2005-2009 Spanish Ministry of Education and Science Predoctoral Fellowship for Research Personnel Training.
2004-2005 Basque foundation BIOEF and University of the Basque Country Fellowship.

Scientific Production

14 Scientific Publications, which include papers in Nature (1), Autophagy (1), Current Opinion in Cell Biology (1), and Glia (2). Five of them as main author, and 2 as corresponding author. One international patent.
Total number of citations: 368 in Google Scholar (subtracted 4439 from the review in Autophagy to the 4807 in total). H-index 6.
Thirteen conference communications, from which 1 as invited speaker, 2 oral communications, and 10 posters. Three awards related to presentations in meetings.
Supervision of 5 master projects, and 3 final-year projects of undergraduate students.

Funding as Independent Researcher

2015 2016 IdEx Bordeaux: Cilia related autophagy in Alzheimer s disease and neurodegenerative disorders. Amount: 126000 (included salary of the PI)
2016 - 2017 LECMA-Vaincre Alzheimer: Study of Primary Cilia Receptors that modulate Autophagy in Alzheimer's disease. Amount: 40,000

Reviewer activities

Acta Neuropathologica, Autophagy, Biochemical Journal, Cells-Open Access Cell Biology Journal, Cell Stress and Chaperones, FEBS Journal, Free Radical Biology & Medicine (FRBM), Journal of Cellular Biochemistry, Journal of Molecular Neuroscience, Molecular Biology of the Cell, Neurobiology of Aging, Neurobiology of Disease, PLOS One, Progress in Neurobiology, Science Reports

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Turno de acceso general

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Título:

Breast cancer stem-like cells specific glycosylation as therapeutic target

Resumen de la Memoria:

Breast cancer is still the most frequent cause of female cancer death in Europe. A small population of cells that display stem cell characteristics in breast cancer (BCSCs) have been proposed as the mediators of tumour metastasis and acquisition of treatment resistance. However, selective targeting of BCSCs is still challenging, as they are very similar to normal stem cells in the body.

Normal mammary stem cells characteristically show high expression of CD44, low expression of CD24, and high ALDH activity. The main transcriptional differences in BCSCs are the expression of onco-fetal proteins, the upregulation of stem cell markers and specific mutations. In addition, specific post-translational modifications have also been associated to BCSCs, including addition of onco-fetal glycan structures to surface proteins.

Differential glycosylation can alter important biological processes including cell adhesion, migration, interactions with the extracellular matrix, immune surveillance, cell signalling and cellular metabolism. Altered glycosylation has been more frequently found in stem cell protein markers and could be contributing to altered biological behaviour of these cells. The role of glycans in tumour biology and their potential use as biomarkers has been explored but the effect of the glycosylation changes in the stem cell compartment of tumours is widely unknown.

Plan of investigation

Most BCSCs markers are also present in normal mammary stem cells but differences in their glycosylation patterns have been described. Interestingly, the null mouse for GnT-V/MGAT5, an enzyme that catalyses posttranslational modifications of glycoproteins, shows attenuated tumour formation and a significant reduction of the stem cell compartment. I plan to study if the changes in protein glycosylation contribute to the stem cell phenotype and/or drive the reprogramming of these cells.

1. Generation of the CRISPR library

I will generate a pooled library of CRISPRs to target each of the protein glycosylation genes (GO:0006486). gRNAs will be cloned into the lentiCRISPR v2 vector and equal representation of each of them tested by NGS. Then, the library will be deposited in Addgene repository to ensure public access.

2. Screening

The library will be used to infect a panel of breast cancer cell lines that recapitulates breast cancer heterogeneity. Stem cell populations will be isolated taking benefit of their high ALDH activity. The gRNAs lost in tf when compared to t0 could be targeting genes essential for BCSC survival or for the stem phenotype.

3. Validation

Candidate genes will be individually depleted and changes in the ALDH+ cells analysed. I will measure changes in their viability, tumorigenesis, metastasis and response to treatment. The effect on the microenvironment and immunotherapeutic potential will be evaluated as well.

After more than fifteen years of experience in breast cancer research, I aim to study the insights of protein glycosylation in cancer. My experience in whole-genome shRNA screens gathered at Columbia University and Mount Sinai (New York, USA) will greatly contribute to the success of this proposal. The identification of BCSCs specific vulnerabilities has important implications, not only to enrich our knowledge about their biology, but also they could represent outstanding candidates to develop targeted therapies.

Resumen del Currículum Vitae:

From the beginning, my research has been tied to the biomedical field in the academia. I graduated in Biochemistry from the Autonomous University of Barcelona in 2001. Then, I joined Dr Sierra¿s groups in the Oncologic Research Institute of Barcelona (Spain), where I analysed the differential expression of genes involved in apoptosis and breast cancer metastasis, by using two-dimension protein electrophoresis and microarrays. This research was part of my Master¿s project on TIP30/CC3, a protein that we described to be under-expressed in breast cancer bome metastasis.

After this first experience, I joined Dr Pandiella¿s laboratory whithin the Cancer Research Center of Salamanca (Spain) that is associated to the Spanish Council of Science (CSIC). Dr Pandiella¿s group has been mainly working in breast cancer, and represents an international reference in the the study of the EGF family. There, I was involved in several projects, most of them directed towards elucidating the role of Neuregulins in tumour development (MBC 2007, Clin Can Res 2008, JBC 2011). In my doctoral thesis entitled "Neuregulin Domains Involved in Their Synthesis, Sorting to Plama Membrane and Biologic Action", I described essential traits of this family of ErbB ligands in breast cancer, later proposing them as targetable molecules for treatment. In parallel, I explored potential therapeutic effects of small tyrosine kinase inhibitors in breast and head-and-neck squamous cell carcinoma (Ann Oncol 2008).

Then I moved to Dr Silva's laboratory in New York, which was initially based at the Columbia University Medical Center and later

relocated to Mount Sinai School of Medicine. During my tenure at the Silva lab, I was granted a National Cancer Center Fellowship to complete my training as a postdoctoral researcher under his mentorship. Dr Silva generated a whole-genome RNAi library (Nat Genet 2005, Science 2008). This is an extremely versatile toool that could be used in multiple settings so I established several collaborations and gained extensive exprience in RNAi screenings (Cell Host Microbe 2013, Oncogene 2015, Genes Dev 2015, Breast Cancer Res 2015, Oncotarget 2015). Interestingly, we found that the JAK/STAT3 pathway is activated and essential in HER2+ breast tumours and completed preclinicical animal studies, using the FDA-approved drug Ruxolitinib (Genes Dev 2015). Given the successful results, we launched a multicenter phase I/II clinical trial in patients with metastatic HER2+ breast cancer. This provided me an important experience in translational research. In addition, I participated in the study of the role of microRNAs in mammary gland development (Genes Dev 2014, MCB 2014) and other projects in breast and prostate cancer (Cell 2012, Cancer Cell 2012, Cell Res 2014, Cancer Cell 2015).

In May 2016, I joined Newcastle University following a Faculty Fellowship appointment. This is a very competitive scheme aimed to support and guide the scientific leaders of the future in the establishment of their own research groups. In addition to the salary, the position included a start-up package, laboratory and office space. Since I arrived in Newcastle, I have completed another first author paper recently accepted in the journal Autophagy and I have received very positive comments in another first author paper currently under review in Genes and Development.

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Turno de acceso general

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Área Científica: Biomedicina
Correo Electrónico: arfolgueras@gmail.com

Título:

Generation of mutant mice and stem cell-based models for the study of human pathologies

Resumen de la Memoria:

My scientific career started at Prof. Carlos López Otín laboratory in 2003. There, I had the opportunity to contribute to the functional characterization of the degradome (a term that was created at that time to define the complete set of proteases within the genome), by using in vivo approaches. Thus, during my PhD I contributed to the generation of 3 different murine models deficient in protease genes: the matrix-metalloproteinases (MMPs) Mmp19 and MT5-MMP (Mmp24); and the serine protease, matriptase-2 (Tmprss6). Hence, I characterized for the first time the in vivo function of these proteolytic enzymes in a variety of physiological processes such as adipogenesis (Mmp19), pain and nociception (Mmp24) or iron metabolism (Tmprss6). I also explored the relationship among MMPs and two pathological conditions: cancer and inflammation. In particular, I studied the dual role of Mmp19 in cancer development, demonstrating that MMPs, originally considered as pro-tumoral proteases, can also exert protective functions in tumor progression. In addition, by using mice deficient in an MMP mainly expressed in immune cells (Mmp8), I demonstrated that the genetic or pharmacological inhibition of this protease protects against the development of experimental autoimmune encephalomyelitis, the murine model of multiple sclerosis.
With the experience accumulated working with in vivo models, in September 2009 I moved to the lab of Prof. Elaine Fuchs at The Rockefeller University (New York), funded by an EMBO post-doctoral Long-Term Fellowship, with the aim of developing a new line of research within the field of stem cells (SCs), given its enormous physiological relevance and potential for clinical approaches. I joined Dr. Fuchs lab with the aim to study the regulatory mechanisms governing SC transition from a quiescent to a proliferative/committed state. In particular, I worked in the functional characterization of the lim-homeodomain transcription factor Lhx2, which is highly expressed in skin SCs. Thus, I was able to identify in vivo Lhx2 stem cell targets and understand why the lack of Lhx2 causes the disruption of the SC niche, the loss of stem cell quiescence and a bald phenotype in mice. After 4 years as a postdoc at The Rockefeller University, I returned to the University of Oviedo with a Juan de la Cierva contract, which allowed me to start the new lines of investigation that I am currently pursuing on the basis of my previous experience in the fields of degradomics and stem cells.

Resumen del Currículum Vitae:

During my scientific career I have had the opportunity to contribute to the fields of degradomics and stem cells. These two lines of research have provided me an enormous range of possibilities and skills in the search for molecular mechanism underlying human diseases and therapeutic opportunities by using in vivo approaches, which has always been the main common goal of my scientific career. I have published 19 articles (including Cell Stem Cell, Nature, PNAS, Blood, Trends Immunol, Trends Cancer, Cancer Res, Mol Cell Biol, Oncogene, Oncotarget, Oncoimmunology and J Biol Chem), most of them working with in vivo models and I sign 11 of them as first or second author and 2 of them as corresponding author. In addition, I am co-editor of a scientific book. According to Web of Science, my articles have been cited 1376 times. Likewise, I have also participated in a number of international and national meetings and research projects and I am currently a co-PI of an international grant, funded by the PRF-USA. In addition, I have been the co-advisor of one PhD student and, at present, I am supervising a new Thesis work, which will follow new lines of research based on my previous fields of expertise, degradomics and stem cells, and the use of in vivo approaches to the study of human pathologies. This new Thesis work has already yield a publication, in which I am the corresponding author, and a manuscript that is currently under second revision in Nature Commun, in which I am also the corresponding author.

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Turno de acceso general

Nombre: MOLES FERNANDEZ, ANA BELEN
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Área Científica: Biomedicina
Correo Electrónico: amolestgn@gmail.com

Título:

Study of cellular and molecular biological pathways driving fibrosis and cancer

Resumen de la Memoria:

My research has focused over the years on understanding the cellular and molecular mechanisms driving fibrotic diseases in different organs (liver and kidney) in order to find new therapeutic candidates for drug development. Fibrosis accounts for 45% of the deaths in the developed world and has no treatment available. Thus, increasing our biological understanding around this disease is crucial to design new and specific treatments.

During my PhD I discovered a new biological signalling pathway involving lysosomal enzymes, acidic sphingomyelinase and cathepsin B. Modulation of this novel pathway using specific inhibitors showed reduction in liver fibrosis in preclinical models, demonstrating promising therapeutic potential. My PhD results were reproduced by Virobay Inc whom currently have a cathepsin B inhibitor for the treatment of liver fibrosis in phase I clinical trials.

I moved to Newcastle,UK to perform my postdoc and deepen my understanding in molecular biology specifically the NF-kB transcription factor family, which is involve not only in liver disease but also in cancer, etc. Due to its pleiotropic functions, targeting NF-kB is incredibly challenging and side effect such as tumours can easily arise. My postdoctoral work investigated targeting NF-kB phosphorylation sites to modulate some specific NF-kB functions. I discovered that phosphorylation at serine 536 or threonine 505 played important roles in liver fibrosis or cancer respectively. Using competing peptides for serine 536 phosphorylation site I reduced liver fibrosis without affecting other NF-kB functions, such as the innate immunity, proving specific targeting of NF-kB as a possible therapeutic option.

Fibrosis affects several organs, therefore my next research challenge was to find common signalling pathways for fibrotic diseases. In 2013 I was awarded with a competitive Newcastle University Faculty Fellowship to develop my own independent research around the role of lysosomal cathepsins in renal fibrosis. During my fellowship I have funded and produced three senior author papers. In them I described for the first time that cathepsin D controls two important biological processes in tubular epithelial cells: collagen degradation and apoptosis. Inhibition of cathepsin D in preclinical models resulted in reduction of renal fibrosis and improvement of renal function ameliorating chronic kidney disease progression and improving acute kidney injury. This findings have translated into an agreement with Meck Group to test two new clinical candidates against cathepsin D in different fibrotic models.

Moving forward I would like to investigate the role of lysosomal proteases such as cathepsin D in the liver fibrosis/cancer axis. Hepatocellular carcinoma is the 2nd most common cause of cancer death worldwide. It is highly resistant to chemotherapy and present very poor prognosis (5-year survival of 11%) with frequent recurrence and metastasis. Most patients present similar disease progression involving an inflammation-fibrosis-cancer axis. Despite the role of cathepsins have been previously described in several cancers, their role in liver cancer is still unknown.

The Ramon y Cajal Programme is the perfect way to reintegrate into the Spanish research system. If awarded, I plan to apply to national and international calls, including the ERC Starting Grants, to fund my research.

Resumen del Currículum Vitae:

My translational research has focused on identifying new therapeutic targets for liver and kidney disease treatment by studying the cellular and molecular pathways involved in disease progression, with an emphasis on protease biology.

My PhD was supervised by Prof JC Fernandez-Checa, an international expert studying the role of mitochondrial stress in liver disease and was based upon the role of lysosomal proteases in liver fibrosis. I discovered lysosomal cathepsin B and D as important for fibroblast activation and liver fibrosis progression. I completed my PhD in 2009 with a scientific output of 6 publications, 3 of them as first author (Hepatology 2009, IF: 11.06, Am J Pathol 2010, IF: 4.59, J Biol Chem 2012, IF: 4.57).

I moved to Newcastle University in 2010 to work with Prof Mann and Prof Oakley, world experts in the study of NF-kB. During my three years as postdoc I led three independent projects which generated three first author, high-impact factor, publications. My first paper demonstrated the use of competing NF-kB peptides as beneficial therapy to reduce mouse liver fibrosis without affectation of the NF-kB-driven immune response (Hepatology 2012, IF: 11.06). My second paper unravelled a new TLR2/S100A9/CXCL-2 signalling network which is essential for neutrophil recruitment in liver disease (J Hepatol 2014, IF: 11.34). Finally, my last paper, in collaboration with Prof Perkins,

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described for the first time a novel regulatory mechanism for NF-kB in vivo and dissected its implications for liver regeneration and cancer (Oncogene 2016, IF: 8.46). I also contributed to the development of three other publications within Prof Mann□s team, including a Nature Medicine published in 2011 (IF: 27.36) were I am third contributing author. I was invited to chair an early morning workshop at the 2011 International Liver Meeting organised by the European Liver Association for the Study. This indicator of esteem demonstrated recognition of my potential as a future leader in the hepatology field.

In 2013 I was awarded a Newcastle University Faculty Fellowship which are competitive positions (2-3 years) aimed to support talented young scientist in their transition towards independence. As a fellow I have funded my independent research through small internal and external grants (totalling £122,879 ~ 146.000□). I have co-supervised 2xPhD, 1xMRes and 2xBSc. During my 3 years as a lead PI, I have become a fully independent researcher generating five research outputs, three of them as senior author, two published in Scientific Reports in 2016 (IF: 5.58) and the third under review in Cell Death Dis. I have built strong national and international scientific collaborations and established collaborative links with pharmaceutical industry, Merck Group. I have disseminated my research in national and international conferences (28 accepted abstracts) raising my profile as a researcher. I have been invited to chair workshops, sessions and to deliver talks at external international seminars. During my career I have produced 17 original research papers, all of them Q1, (6 as first author and 3 as senior author), work in top-class Universities and collaborated with world leading scientists within Newcastle (Prof Mann, Perkins and Sheerin) and abroad (Prof Karin and Seki) increasing my scientific knowledge and shaping my own independent career as PI.

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Turno de acceso general

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Área Científica: Biomedicina
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Título:

Immunity to infections and vaccines

Resumen de la Memoria:

After graduating in Biology (Universidad Complutense de Madrid, 1999), I became interested in understanding the relationship between pathogens and hosts. I followed my interests to pursue a career in Immunology with an underlying desire to see my efforts emerging into useful applications. During my PhD thesis I developed vaccines against leishmaniasis (Universidad Autónoma de Madrid, 2000-2005. I published several papers in relevant journals for this field (Vaccine, Infection and Immunity). I also co-authored a patent featuring the use of parasite histones for the treatment of the disease. I also spent a short stay in the Laboratory of Parasitic Diseases (lead by David Sacks) at the National Institutes of Health. Later, I joined the Viral Immunology Unit headed by Margarita del Val (ISCIII, 2005-2011). I co-supervised a PhD student during this period. In collaboration with Edgar Fernández-Malavé (UCM), I explored the role of the different Ras GTPases in T cell development and differentiation (Blood. 2011). Afterwards, I demonstrated that the generation of protective memory CD8+ T lymphocytes requires N-ras mediated signalling (J. Exp. Med. 2013). Finally, I joined David Sancho□s laboratory (CNIC) to fulfil my interests in dendritic cells (DC), antigen presentation and innate immunity. I have determined that DNGR-1, a C-type lectin receptor (CLR) that recognizes damaged cells, is critical to cross-prime cytotoxic T cells during virus infection (J. Clin. Invest. 2012). Next, we demonstrated that DNGR-1+ DC are critical to instruct the generation of resident memory CD8+ T cells (Immunity, 2016), and that drive local Th1 immunity against Leishmania (Eur. J. Immunol. 2015). We have shown that these parasites secrete a ligand for a CLR expressed on DC (Mincle), that dampens its activation promoting parasite survival (Immunity, 2016). Finally, I am still involved in the development of vaccines against leishmaniasis (PLoS Negl. Trop. Dis., 2015).

Resumen del Currículum Vitae:

My research has contributed to the following achievements:

1. I have found vaccine candidates, formulations, routes of administration and antigen-processing pathways that induce memory T-cell-mediated responses and protective immunity. (Iborra et al. Infection and Immunity 2003; Iborra et al. Vaccine 2004; Iborra et al. Infection and Immunity 2005; Soto et al. PLoS Neglected Tropical Diseases 2015, I am co-corresponding author of this paper; Patent PCT/IB2004/004078)

2. I have contributed to decipher essential key host factors for T helper lymphocyte differentiation into type 1 (Th1) and immunity against intracellular parasites. (Iborra et al. Blood. 2011)

3. I have also contributed to define early signalling pathways downstream of the T-cell receptor that regulates the generation of functional protective memory (Iborra et al. J. Exp. Med. 2013).

4. I have described the role two receptors expressed by dendritic cell (DC) that recognizes necrotic cells. I demonstrated that DNGR-1 plays an essential role during infection with a cytophatic virus to promote CD8+ T cell responses (Iborra et al. J. Clin. Invest. 2012). I have found that Mincle can recognize Leishmania ligand(s) that triggers an inhibitory signal and promotes susceptibility to the parasite (Immunity, 2016).

5. I have contributed to understand the division of labour within different DC subsets. First, I demonstrated the role of Batf3-dependent DC during infection with Leishmania (Martínez et al. Eur. J. Immunol. 2014; I am co-corresponding author of this paper). Further, I have found that this DC subset is essential for the generation of resident memory CD8+ T lymphocytes in the skin (Immunity, 2016).

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

- 1 thesis co-supervised and 2 PhD students currently under co-supervision.
- 32 peer-review publications: 12 as first author; 4 as co-corresponding author.
- H Index = 14 (in accordance with Web of Science; Scopus author ID: 6701708092).
- 536 citations (in accordance with Web of Science; 617 citations according to Scopus).
- Average citations per article: 19.14
- Awarded project: SAF2015-74561-JIN (PROYECTOS DE I+D+I, PARA JÓVENES INVESTIGADORES SIN VINCULACIÓN O CON VINCULACIÓN TEMPORAL).

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Turno de acceso general

Nombre: NAVARRETE LLINAS, MARTA
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Correo Electrónico: mnavarrete@cbm.csic.es

Título:

Synaptic Modulation Mediated By Astrocyte Signaling

Resumen de la Memoria:

Bachelor Degree in Chemistry (Extremadura University, 2008), Master¿s Degree in Chemistry (Extremadura University, 2004), Doctoral Degree in Medicine (Autonoma University of Madrid, 2009).
Master□s Degree (2003-2005) Undergraduate student at Extremadura University (supervisor: J. Espinosa-García). Experimental work: construction of potential energy surfaces for polyatomic reactions and theoretical calculation of enthalpies of free radical formation. My work resulted in 6 original publications.
PhD student (2005-2009) at the Cajal Institute (FPI fellowship; supervisor: A. Araque). Experimental work: studying the role of endocannabinoids on astrocyte-neuron communication, which resulted in the publication of 1 original paper (Neuron 2008) and 1 review (TINS 2009).
Visiting scientist (4 months total in 2008 and 2009) at Albert Einstein College of Medicine (New York, USA; Supervisor: Alberto Pereda) studying Mauthner□s cell synaptic physiology in goldfish.
Postdoctoral Researcher (2009-2013) at the Cajal Institute (supervisor: A. Araque) studying the consequences of astrocyte-neuron signaling on synaptic transmission. My work resulted in the publication of 6 original and 5 review papers.
Postdoctoral Researcher (2014-2015) at the Centro de Biología Molecular □Severo Ochoa□ (CBMSO) (supervisor: J.A. Esteban), I developed to research lines: 1) synaptic signaling changes associated with aging; and 2) astrocyte-neuron signaling in synaptic plasticity. The results obtained revealing the role of astrocytes in the hippocampal long-term depression will be reported in a manuscript ready to be submitted as co-corresponding author. This stage resulted in the publication of 3 papers.
Principal Investigator (2016-) of the SAF2014-58598-JIN project at the CBMSO (CSIC).
My contributions as first (or co-first) author include: first demonstration of astrocyte involvement in endocannabinoid signaling (Neuron 2008); elucidation of endocannabinoid effects on astrocytes and their consequences on synaptic transmission (Neuron 2010); demonstration of astrocyte-mediated hippocampal synaptic plasticity in vivo (PLoS Biol 2012); demonstration of astrocyte-neuron signaling in human brain tissue (Cereb Cortex 2013); demonstration of structural and functional plasticity between astrocyte processes and dendritic spines (J Neurosci 2014); demonstration of lateral synaptic plasticity mediated by endocannabinoids through astrocyte signaling (Cereb Cortex 2015).
I have been awarded 3 projects as principal investigator (PI) from competitive calls. I was awarded L'Oreal-Unesco-Spain Award and Olympus Young Investigator Award.
The bibliographical analysis of my contributions show 22 publications that have been cited >1800 times. I am the first (including equal contribution) or second author in 87% of the papers and 5 of them are authored by 2 authors (including two papers in Neuron). H-index: 14.
My goals aim to understand how astrocytes participate in learning and memory, and how their alterations contribute to brain disorders, such as Alzheimer's disease, aiming to identify new cellular targets for potential therapeutic approaches.

Resumen del Currículum Vitae:

ACADEMIC DEGREES
Doctor, Universidad Autónoma de Madrid, 2009.
Graduate in Chemistry, University of Extremadura, 2004.
Degree in Chemistry-Physics, University of Extremadura, 2004.

CURRENT SITUATION
Principal Investigator. Centro de Biología Molecular Severo Ochoa (CSIC-UAM),

RESEARCH ACTIVITY
2009- 14: Postdoctoral researcher. Cajal Institute. Madrid, Spain. (Advisor Dr. A. Araque).
2005-2009: Predoctoral fellow Cajal Institute. Madrid, Spain. (Advisor Dr. A. Araque).
June-August 2009 and August 2008: Visiting scientist. Albert Einstein College of Medicine. New York, EEUU. (Advisor Dr. A. Pereda).
2003-2005: Undergraduate student. University of Extremadura (Advisor Dr. J. Espinosa-García).

BIBLIOGRAPHY
(H-index: 14; Total number of citations > 1800; Mean IF: 10.2; I have been 1st or 2nd author in 87% of the papers)

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Top 10 publications over the past 10 years:

1. Rodríguez-Tornos FM, Briz CG, Weiss LA, Sebastián-Serrano A, Ares S, Navarrete M, Galazo M, Frangeu L, Jabaudon D, Esteban JA, Nieto M. 2016 Cux1 enables inter-hemispheric connections of layer II-III neurons by regulating 1 Kv1-dependent firing. Neuron, 89:494-506
2. Gómez-Gonzalo M*, Navarrete M*, Perea G*, Covelo A*, Martín-Fernández M, Luján R, Araque A. 2015 Endocannabinoids induce lateral long-term potentiation of transmitter release by stimulation of gliotransmission. Cereb Cortex, pii: bhu231
3. Perez-Alvarez A*, Navarrete M*, Covelo A, Martín ED, Araque A. 2014 Structural and functional plasticity of astrocyte process and dendritic spine interactions. J Neurosci, 34:12738 12744
4. Navarrete M, Perea G, Maglio L, Pastor J, García de Sola R, Araque A. 2013 Astrocyte Calcium Signal and Gliotransmission in Human Brain Tissue. Cereb Cortex, 23:1240-1246
5. Navarrete M, Perea G, Fernandez de Sevilla D, Gómez-Gonzalo M, Núñez A, Martín ED and Araque A. 2012 Astrocytes mediate in vivo cholinergic-induced synaptic plasticity. PLoS Biology, 10:e1001259
6. Araque A and Navarrete M. 2011 Electrically driven insulation in the central nervous system. Science, 333:1587-1588
7. Navarrete M and Araque. A. 2011 Basal Synaptic Transmission: Astrocytes Rule! Cell, 146:675-677
8. Porto-Pazos AB, Veiguela N, Mesejo P, Navarrete M, Alvarellos A, Ibáñez O, Munteanu CR, Pazos A and Araque A. 2011 Artificial astrocytes improve neural network performance. PLoS ONE, 6:e19109
9. Navarrete M and Araque A. 2010 Endocannabinoids potentiate hippocampal synaptic transmission through stimulation of astrocytes. Neuron, 68:113-126
10. Navarrete M and Araque A. 2008 Endocannabinoids mediate neuron-astrocyte Communication. Neuron, 57:883-893

RESEARCH GRANTS (as Principal Investigator)
2015-18: Ministry of Economy and Competitiveness. SAF2014-58598-JIN.
2016: L¿Oreal-Unesco for woman in Science
2014-15: BBVA Foundation, Spain.

I have been invited to several prestigious international conferences (IBRO; FENS; Euroglia). I act as a referee ad hoc for specialized journals (Science, glia, Cerebral Cortex, PLoS One) and I review grants proposals for recognized agencies (ANEP, FNS, Switzerland; ANR, France, ISF, Israel). I organized a symposium for SENC.

I have received awards at all stages of my career highlighting L'Oreal-Unesco-Spain Award and Olympus Young Investigator Award, and my work has been reported at the non-specialist's level (e.g. Spanish TV, radio interviews; Magacines, newspapers).

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Turno de acceso general

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Título:

MOBILE DNA: CHARACTERIZATION, REGULATION AND IMPLICATIONS FOR HUMAN DISEASES

Resumen de la Memoria:

I developed my PhD (2007) in the laboratory of Dr. Manuel Carlos Lopez Lopez (López Neyra Parasitology and Biomedicine Institute, National Research Council, Granada, Spain) funded by a prestigious FPU. During this period, I worked to elucidate the mechanism of mobilization of a LINE-1 element from Trypanosoma cruzi and its impact in gene expression. I performed some aspect of the project during short stays in two laboratories abroad: Sandra L. Martin□s lab (University of Colorado, Denver, USA) and Martin D. Ryan□s lab (University of St. Andrews, UK). My PhD work gave rise to six research publications, four as first author.
In late 2008, I joined the laboratory of Dr. Javier Caceres (MRC Human Genetic Unit, Edinburgh, UK) trough a prestigious Marie Curie Intra-European Fellowship to study different aspect of post-transcriptional regulation of gene expression in humans. Interestingly, I demonstrated that the splicing factor SRSF1 couples pre-mRNA splicing and translation of several mRNAs and this activity is required for normal mitotic progression (first co-autor eLife). Importantly, combining my previous knowledge in the mobile DNA field and the miRNA expertise from the host lab I showed that the Microprocessor complex controls mammalian LINE-1 activity (first author, Nat Struc Mol Biol). In 2011, I joined to Jose Luis Garcia-Perez lab as an independent researcher in Genyo, a center for Genomic in Granada. I started an independent line of research based on my postdoctoral results but with a translational goal: study the connection between LINE-1 deregulation and human diseases. Recently, we demonstrated that LINEs are active in mature neurons lending a new perspective to the impact of LINEs in mental disorder (second co-author, Genome Res.). During this period, I obtained two grants as a Principal Investigator, a Marie Curie Career Integration Grants and a National grant from MINECO and funding to support a PhD student.

Resumen del Currículum Vitae:

ACADEMIC TRAINING
-May 2007 Ph.D. in Biochemistry and Molecular Biology (Cum Laude) University of Granada and Spanish National Research Council (CSIC), Spain.
-Oct. 2000 B.S. in Pharmacy Molecular Biology orientation (grade point average: 3,2/4). University of Granada, Spain.

RESEARCH EXPERIENCE
□ 2011- Research Investigator. GENYO (Pfizer-University of Granada-Andalusian Goverment-Centre for Genomics and Oncological Research). Supervisor: Dr. Jose L. Garcia-Perez
□ 2008-2011 Postdoctoral Fellow in the laboratory of Dr. Javier Caceres
MRC Human Genetic Unit. Chromosomes and Genes Expression, Edinburgh, UK
□ 2007-2008 Postdoctoral Fellow in the laboratory of Dr. Manuel Carlos Lopez
Spanish National Research Council (CSIC) Department of Molecular Biology.
Institute of Parasitology and Biomedicine □López-Neyra□, Granada, Spain.
□ 2001-2007 Ph.D. student in the laboratory of Dr. Manuel Carlos Lopez
Spanish National Research Council (CSIC). Institute of Parasitology and Biomedicine □López-Neyra□, Granada, Spain.
□ Sept.2004-Dic. 2004 Short stay in University of St. Andrews, School of Biology, St. Andrews, Scotland, UK. Supervisor: Dr. Martin D. Ryan
□ May 2002- Agos. 2002 Short stay in University of Colorado, USA. Supervisor: Dr. Sandra L. Martin.

RESEARCH PUBLICATIONS (*equally contributing authors)
-Macia A, Widmann TJ*, Heras SR*, et al. (2016) Genome Res.pii: gr.206805.116
-Morales-Hernández A, González-Rico FJ, Román AC, Rico-Leo E, Alvarez-Barrientos A, Sánchez L, Macia Á, Heras SR, et al. (2016) Nucleic Acids Res. 44(10):4665-83.
-Maslon MM*, Heras SR*, et al. (2014) Elife:e02028
-Heras SR, et al (2014) Mob Genet Elements e28439. eCollection 2014 (co-corresponding author).
-Heras SR*, Macias S*, et al (2013)Nat Struc Mol Biol. 20(10):1173-81.
-Heras SR, et al (2009) Biochem J. 10, 479-90.
-Heras SR, et al (2007) Nucleic Acids Res 35, 2199-214
-Heras SR, et al (2006) Cell Mol Life Sci, 63, 1449-1460.
-Heras SR, et al (2005) Mol Cell Biol, 25, 9202-9220.

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-Bringaud F, Garcia-Perez JL, Heras SR, et al (2002) Mol Biochem Parasitol, 124, 73-78.
-Olivares M, Garcia-Perez JL, Thomas, MC, Heras SR (2002) J Biol Chem, 277, 28025-30.

FELLOWSHIPS AND AWARDS
-2009- 2011 Marie Curie Intra-European Fellowship.
-2001- 2005 PhD Fellowship (FPU) for the formation of research personnel by Spanish Ministry of Education and Science.
-Sept. 2006 Promega Biotech Ibérica young scientist award.

GRANTS
--SAF2015-71589-P.The role of microRNAs in human retrotransposon LINE-1 mobility and impact in cancer. Funded by: Ministerio de Economía y Competitividad. Budget: 147.000 Dates: 01/01/16 30/12/18 (36 months) Principal Investigator: Sara Rodríguez Heras.
-PEJ-2014-A-31985.Two years contract for a PhD student funded by Ministerio de Economía y Competitividad en el Programa de Empleo Joven e Implantacion de Garantia Juvenil.
-PCIG10-GA-2011-303812. Role of LINE-1 retrotransposons in the human disease DiGeorge Syndrome Marie Curie Career Integration Grants (CIG). FP7-people-2011-CIG.2012-2016.
Budget: 100000 . IP: Sara Rodríguez Heras.

MENTORING EXPERIENCE.
-Co-director of a Master Thesis (2014) .Student: Pablo Tristan.
-Co-director of a Doctoral Thesis (In progress).Student: Pablo Tristan.

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Turno de acceso general

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Título:

Estudio de la cromatina desde el punto de vista epigenético y de organización tridimensional

Resumen de la Memoria:

Biola María Javierre Martínez posee un extenso conocimiento teórico y práctico de los campos científicos que abarcan el estudio de la organización tridimensional (3D) de la cromatina, de la epigenética, de la autoinmunidad y del cáncer.

Durante su etapa universitaria, como estudiante de investigación analizó el papel de la angiogénesis en la progresión del cáncer de próstata (Int J Cancer, 2007).

Posteriormente, durante su doctorado, estudió el papel de la alteración epigenética asociada a enfermedades autoinmunes y a cáncer. Concretamente llevó a cabo el primer análisis global sobre las diferencias de metilación del ADN existentes entre gemelos monozigóticos discordantes para diversos trastornos autoinmunes. Dicha investigación permitió describir alteraciones globales y especificas, de determinados promotores génicos, en el contenido de metilación asociadas al lupus eritematoso sistémico (Genome Res, 2010). De forma paralela investigó la desregulación epigenética de genes clave para el proceso de autoinmunidad en el contexto del cáncer y su contribución a la carcinogénesis (Mol Cancer Res, 2011).

Durante el periodo postdoctoral estudió la organización 3D de la cromatina y su función en el control de la expresión génica. Estuvo directamente involucrada en el desarrollo y la optimización de una nueva técnica experimental denominada "Promoter Capture Hi-C" (PCHi-C) que permitió por primera vez describir las regiones genómicas que interactúan físicamente con cada promotor génico. Parte de dichas regiones genómicas regulan la actividad del gen diana a través del contacto físico.

Con este enfoque experimental ha demostrado que PRC1 funciona como un regulador maestro de la arquitectura del genoma de células madre embrionarias murinas. PRC1 es capaz de organizar genes inactivos en redes de interacción 3D que promueven el silenciamiento de estos. Además, la eliminación de la actividad catalítica de PRC1 desencadena la perdida de los contactos promotor-promotor de la red, manteniéndose intactos los contactos promotor-potenciador, acompañada de la adquisición generalizada de marcas de activación epigenética y la correspondiente sobreexpresión génica (Nat Genet, 2015).

Recientemente ha desarrollado un proyecto que constituye la primera colección de interacciones de los promotores génicos humanos en células primarias. Concretamente ha caracterizado las regiones genómicas que se entran en contacto físico con cada promotor en diecisiete tipos de células hematopoyéticas humanas. Ha mostrado que las interacciones de promotores vinculan preferentemente promotores activos y potenciadores, y que son altamente específicas del tipo celular, preservando las relaciones de linaje entre tipos celulares. Colectivamente, los patrones de interacciones recapitulan el árbol hematopoyético, consistente con una arquitectura nuclear robusta y dinámica. Usando estos mapas de interacción de alta resolución se han conectado variantes no codificantes asociadas a enfermedades con sus correspondientes promotores diana, identificando decenas de nuevos genes candidatos asociados a patologías (Cell, 2016).

Como un científica independiente, altamente motivada y trabajadora, su objetivo es continuar el estudio del papel de la organización 3D de la cromatina e integrar dicho conocimiento con la investigación clínica con el objetivo de mejorar la salud pública.

Resumen del Currículum Vitae:

Biola María Javierre Martínez, nacida en 1983 en Huesca, es investigadora postdoctoral en el laboratorio dirigido por el Doctor Peter Fraser en el "Babraham Institute" (Cambridge, Reino Unido).

Estudio paralelamente las licenciaturas de Biología y de Bioquímica en la Universidad de Navarra (2000-2006), obteniendo en ambas una calificación de matricula de honor y el primer y segundo premio extraordinario de Licenciatura respectivamente. Durante este periodo fue alumna interna del departamento de Genética de dicha universidad donde realizo labores de docencia. Además, durante el ultimo año de licenciatura fue estudiante de investigación en el laboratorio del Doctor Alfonso Calvo, en el Centro de Investigación Medico Aplicada (CIMA), donde llevo acabo un proyecto de investigación sobre la angiogénesis en cáncer de próstata. Dicho proyecto contribuyó a su primera publicación científica.

Cursó sus estudios de doctorado en la Universidad Autónoma de Madrid (2006-2011) financiados por una Beca Predoctoral Puente del

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Centro Nacional de Investigaciones Oncológicas (CNIO), una Beca Predoctoral PFIS del Instituto de Salud Carlos III (ISCIII) y dos proyectos competitivos de I+D+i del ISCIII. Bajo la supervisión de los Doctores Manel Esteller y Esteban Ballestar estudio los procesos de desregulación epigenética asociados a autoinmunidad y cáncer en el CNIO y en el Instituto de Investigaciones Biomédicas de Bellvitge (IDIBELL). Para ampliar su formación predoctoral realizó una estancia en el laboratorio del Doctor Reiner Siebert ubicado en la Universidad Christian Albrechts (Kiel, Alemania). Durante esta etapa publico 6 artículos científicos (2 de ellos como primera autora), 3 reseñas y 3 capítulos de libro.

Posteriormente se unió al laboratorio del Doctor Peter Fraser, en el "Babraham Institute" (UK), para realizar sus estudios postdoctorales (2012-actualidad). Financiada por una Beca Postdoctoral de la "Federation of European Biochemical Societies" (FEBS) y un proyecto competitivos de I+D+i del "Medical Research Council" (MRC) ha estudiado la organización tridimensional (3D) de la cromatina. De forma paralela a su investigación, la doctora Javierre ha estado implicada en una extensa formación de estudiantes y en la codirección de una tesis doctoral. Durante este periodo ha publicado 6 artículos científicos (2 de ellos como primera autora en las prestigiosas revistas "Nature Genetics" y "Cell") y 1 reseña. Ha presentado y defendido su trabajo postdoctoral en numerosas ocasiones internacionalmente.

Su formación académica le ha permitido obtener extenso conocimiento teórico y práctico en los campos de la organización 3D de la cromatina, de la epigenética, de la autoinmunidad y del cáncer. Además ha adquirido una extensa experiencia para investigar de forma independiente, liderar y obtener financiación, así como ha establecido una extensa red de contactos y colaboraciones.

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Turno de acceso general

Nombre: NISO SANTANO, MIREIA
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Área Científica: Biomedicina
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Título:

Autophagy regulation in human diseases.

Resumen de la Memoria:

My research career has been focused on the study of autophagic process in human pathologies such as cancer or neurodegenerative disorders.

During my PhD studies, the role of autophagy as a survival mechanism in the pathogenesis of Parkinson's disease (PD) was an emerging topic in neuroscience. Autophagy plays a critical role in cellular homeostasis, adaptation to multiple types of stress as well as the removal of protein aggregates. Therefore, we decided to explore the autophagic process as a mechanism of neuroprotection in neuronal cell lines. In order to find out the link between autophagy and PD-related proteins, we focused on the role of DJ-1 in paraquat-mediated toxicity and its relationship with autophagy. We have demonstrated that environmental toxins can trigger autophagy as a mechanism of neuroprotection, and that DJ-1 is essential in this process.

In 2011, given my interest in autophagy research, I joined the lab of Prof. Guido Kroemer who is an internationally recognized leader in this field. My research project was focused on the identification and characterization of new proteins associated with autophagy. Indeed, Beclin 1 has been the first mammalian protein shown to play a critical role in the initiation of autophagy. Its complex interactome has a major influence on the positive and negative regulation of autophagy. Due to its implication in autophagy regulation, we performed a screen to identify novel Beclin 1-interacting proteins. TAB2 and TAB3 (two upstream activators of the TAK1-IKK pathway) were found to interact with Beclin 1 in a direct fashion. These findings provide evidence in favour of an unsuspected intersection between autophagy regulation and upstream portions of the canonical NF-κB activation pathway. In parallel to my studies focused on Beclin 1 regulation, I performed another screen to identify novel autophagy inducers, leading to the discovery that chemical inhibitors of STAT3 upregulate the autophagic flux, and driving the characterization of the mechanisms through which STAT3 regulates autophagy. Our results indicated that cytoplasmic STAT3 tonically suppresses autophagy by binding to PKR, hence inhibiting the phosphorylation of eIF2α, which is required for autophagy induction by multiple stimuli. Therefore, we unravelled an unsuspected crosstalk between proinflammatory signalling (STAT3), innate immunity (PKR), and translational control (eIF2α). In spite of these findings it was not easy to provide a physiologically-relevant information. Consequently, we analysed a library of autophagy triggers for their dependence on PKR. This screen led to the identification of palmitate (and other fatty acids (FA)) as PKR-dependent inducers of autophagy. Moreover, we reported the unexpected finding that saturated FA (SFAs) and unsaturated FA (UFAs) promote autophagy by activating different molecular mechanisms.
In 2014, I returned to Spain through the Juan de la Cierva Program. As soon as I arrived, I have started to coordinate several ongoing research projects at Prof. Fuentes's lab where I am currently supervising 2 PhD students and 1 Bachelor student.

Resumen del Currículum Vitae:

My scientific career started in 2002, at the Department of Biochemistry and Molecular Biology and Genetics of the University of Extremadura, as a graduate student in Biochemistry, under the supervision of Dr. José M. Fuentes. Immediately after graduating, I pursued my career with a Master□s Degree in Biochemistry (2006) and PhD Degree in Biochemistry (2010) (which I obtained with Extraordinary Recognition). In 2006, I spent 8 months in the Cancer Research Center (CIC- CSIC) in Salamanca, under the supervision of Prof. Jesús San Miguel and Prof. Sergio Moreno.
In this period, I was funded by a predoctoral fellowship from the Valhondo-Calaff Foundation (Cáceres, Spain) and a CIBERNED contract (ISCIII, Madrid, Spain).
My PhD formation progressively focused on autophagy, strengthening my interest in this exciting field of investigation. I therefore decided to move to Prof. Guido Kroemer's lab in Paris, financed by a 2-year postdoctoral fellowship from the Goverment of Extremadura (Extremadura, Spain) and a 2-year postdoctoral fellowship from Fondation Recherche Medicale (Paris, France). In December 2014, I returned to Spain through the Juan de la Cierva Program, since then, I work as an independent scientist in the lab of Dr. Fuentes, where I am currently supervising 2 PhD students and 1 Bachelor student.
My past activity resulted in 41 scientific articles (11 of them as first or co-first author) in top-ranked peer-reviewed international scientific journals (including Science, Nature Medicine, Molecular Cell (x2), EMBO J (x2), Autophagy (x5), Cell Reports, Cell Death and Differentiation and Leukemia), 5 reviews (including one in Nature Rev. Mol. Cell. Biol.), 5 book chapters in international books and 1 patent. According to the ISI Web of Knowledge, my current H-index is 20. I have an average impact factor of 8,9 as first author and a cumulative impact factor of 345,03. Besides, I have presented 48 communications to national and international meetings and participated in 20 research projects of both national and international breadth. I have been co-director of 1 Bachelor student, 2 Master students and 3 PhD students (Sobresaliente cum laude and Extraordinary Recognition (x2)). Finally, I operate regularly as referee for Oncotarget (Autophagy section; IF (2014): 6.6) and Parkinson□s disease and I have been part of the Thesis examination in University of Extremadura.

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In summary, during my scientific career, I have worked on different aspects of the autophagic process using diverse types of experimental approaches, allowing me to expand my expertise and to have the knowledge that is required to open new lines of investigation in the field.

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Turno de acceso general

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Área Científica: Biomedicina
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Título:

miRNA control of immune tolerance, tumor immunology and autoimmunity

Resumen de la Memoria:

My primary scientific interest is to understand the cellular and molecular mechanisms that lead to autoimmune disease and cancer with a central focus on immune tolerance. Since I started my research career as an undergraduate student, I have consistently produced scientific contributions to these fields that are reflected in my authorship in 12 publications, in which I am the leading author of 7, published in high-impact journals including Nature Immunology, Immunity, Journal of Experimental Medicine and Nature Communications. Throughout my career, I have been awarded numerous competitive fellowships including a Beca de Colaboración del Ministerio de Educación y Ciencia and a Beca de Formación de Personal Investigador de la Comunidad de Madrid, and performed stays in three national and two international research institutions.

During my PhD at the Spanish National Center for Biotechnology I focused my main studies on tumor immunology, specifically T cell-mediated antitumor responses, which provided insightful and well-recognized results. I also contributed to other projects regarding the potential use of statins for tumor immunotherapy, and took the initiative to perform a short-term stay in the Institute of Molecular Genetics of Montpellier (France) to train on T cell tolerance breakdown in diabetes. This training abroad was pivotal for the success of my PhD projects, and for the development of a patent in which I am co-inventor.

I next moved to The Scripps Research Institute in California (USA) where I led fundamental studies on the role of microRNAs in B cell tolerance and autoimmunity. I identified the first miRNA, miR-148a, that regulates B cell tolerance, and elucidated its mechanism of action. I also demonstrated that this miRNA, whose expression is frequently increased in the lymphocytes of lupus patients, plays a causative role in autoimmune disease. Furthermore, I discovered and characterized the critical role for the miR-17-92 cluster in B cell development and tolerance. In addition, I collaborated in other projects studying the roles of miR-155 in the germinal center response and of miR-183-96-182 in the pathogenicity of Th17 cells in multiple sclerosis. Overall, my studies establish miRNAs as critical players in the regulation of B cell tolerance and autoimmunity, and have been highlighted in specialized journals and in national and international press.

As an independent investigator, I will continue to study the roles of miRNAs in immune tolerance, autoimmunity and tumor immunology, with the long-term goal of designing new immunotherapies for the treatment of these diseases.

Resumen del Currículum Vitae:

- Degree in Biochemistry (2003) and PhD in Molecular Biology (2009) by the Universidad Autónoma de Madrid.
- 15 years of research experience with extensive and deep expertise in immunology. Primary research interest in immune tolerance, tumor immunology and autoimmunity.
- Awarded numerous competitive grants to fund my scientific training including a Beca de Colaboración from Ministerio de Educación y Cultura and a Beca FPI de la Comunidad de Madrid.
- Scientific training in 3 different countries (Spain, France and USA) and 5 different institutions: Centro de Biología Molecular Severo Ochoa, Instituto de Investigaciones Biomédicas Alberto Sols and Centro Nacional de Biotecnología in Madrid, Institut de Génétique Moléculaire de Montpellier, and The Scripps Research Institute in California.
- 12 high-quality publications in international peer reviewed journals, 7 as first author. Main postdoctoral first-author work published in Nature Immunology (IF=20.004) and Nature Communications (IF=11.329). Additional articles published in Immunity (IF=24.082) and Journal of Experimental Medicine (IF=11.240), among others. Many of these articles have been highlighted in specialized journals and in the press.
- Patent granted describing a new strategy for the adjuvant immunotherapy of cancer.
- Research Associate appointment in the prestigious The Scripps Research Institute in La Jolla, California (USA) for five years. After this time I was promoted to Senior Research Associate, a position that involves the establishment and development of independent lines of research, supervision and mentoring of undergraduate and graduate students, and active contribution to obtaining grant funding for the lab.
- Participation in numerous national and international research projects and ample experience in managing international collaborations.
- Supervised two master students for the completion of their research projects. Currently supervising a graduate student for the completion of her PhD.
- Ad hoc reviewer for peer reviewed international journals.

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Nombre: DE LA ESCOSURA MUÑIZ, ALFREDO
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Título:

Nanotechnologies in biomedicine: point-of-care diagnostic systems using innovative nanomaterials-based biosensors

Resumen de la Memoria:

I earned my B.A. in Chemistry from the University of Oviedo (Oviedo, Spain) in 2000. I then completed my doctoral work in electroanalytical immunochemistry and received my PhD in Chemistry in 2006 from the University of Oviedo (Excellent Cum Laude). During my PhD I acquired a strong formation in immunoelectrochemistry and its application for the sensitive detection of biomolecules in different biosensing designs.

After that, I joined the Institute of Nanoscience of Aragon (INA, University of Zaragoza, Zaragoza, Spain) as post-doctoral fellow supported by a Juan de la Cierva Research Fellow from the Ministry of Science in Spain (MEC) within the area of Biomedicine. That fellow was obtained in the framework of the project Nanotechnologies for applications in biomedicine: NANOBIOMED CSD2006-12 (MEC) where I acquired a strong formation in the field of the nanoscience/nanotechnology applied in biomedicine, which together with my previous knowledge and expertise in the field of the electrocatalytic biosensors gave rise to the design of novel biosensing systems based on nanoparticles and other nanostructures, such as nanochannels for the sensitive detection of proteins, DNA and cells of clinical interest. Due to the strong collaborative character of that project my work was in permanent collaboration with the different partners of the project, including research stays at the group of Prof. Arben Merkoçi at the Catalan Institute of Nanotechnology (ICN, Barcelona) and at medical doctor s laboratories at the University of Vigo and the University of Santiago de Compostela designing novel nanobiosensors for the detection of clinical biomarkers and tumor cells.

During the Juan de la Cierva fellow, I also did a research stay at the MC2 Microtechnology and Nanoscience Center, Chalmers University of Technology, Göteborg (Sweden), through a grant from the European Commision under the Program Structuring ERA, Research Infrastructures Action (Call identifier FP6-2004-Infrastructures-5 ; contract number 026029) learning about the characterization of micro- and nanoparticles for biosensing, using scanning probe microscopy techniques (magnetic force microscopy MFM- and electric force microscopy EFM-). The information obtained during that research stay was very useful for the applications of the studied nanobioconjugates for genosensors and immunosensors with interest in several areas, mainly clinical analysis.

Of special relevance are my works related to the development of the first cancer cell biosensor, the detection of protein biomarkers using nanochannels/nanoparticles, the monitoring of prostate cancer biomarkers and cancer cell secreted proteins using paper platforms and the pioneering integration of nanoparticles in isothermal DNA amplification.

From August 2011 I have a contract as Senior Researcher at the Catalan Institute of Nanoscience and Nanotechnology (ICN2, Spain) where I m currently co-IP of ICN2 and co-coordinator of a recently granted FP7-EuronanoMed 2 project. My ongoing and future projects are focused on the application of innovative properties of nanomaterials for (i) cancer and other diseases in-vitro diagnostics; (ii) study of cancer mechanisms through evaluation of cancer cell secreted proteins; (iii) drug delivery systems and (iv) implantable systems for in-vivo analysis.

Resumen del Currículum Vitae:

I m co-author of 57 peer-reviewed scientific publications, including 45 scientific articles (25 in the last 5 years; 40 in the Q1; 31 with IF > 5; 24 with IF > 7; First author in 22; Senior author in 14; Co-author in 9) and 12 book chapters, with 874 citations and a h-index of 19 according to Isi Web of Science (h-index of 25 and i10-index of 33 according to Google Scholar), and filled as inventor of 3 patents. I ve also been co-director of 4 finished PhD theses in addition of several master and end course projects. I ve presented my work in over 75 international congresses (21 oral presentations and 4 invited lectures). I've been member of the evaluation panel of 17 PhD theses and regularly act as referee of high-impact journals (88 articles reviewed; currently credited as the most valuable reviewer by Publons: https://publons.com/author/1173620/alfredo-de-la-escosura-muniz#profile and awarded as outstanding referee by Biosens. Bioelectron. journal on May 2015). I participated as organizer in 6 international R&D activities and I m involved in different academic activities in the field of Nanobiomedicine, including my tasks as teacher in Master Courses. I m also member of the international education net Worldwide Diagnostics. I also contributed to several activities of science dissemination (Jornadas Jóvenes y Ciencia, Jornadas puertas abiertas ICN2, temporary exhibitions at Science Museums).

I ve been involved in 21 national and international projects mostly related to nanomaterials application in biosensing and diagnostics (1 project from the EC s H2020 program, 5 from the EC s FP7 program, 1 from the EC s FP6 program, 1 from the EC s FP5 program, 1 from NATO, 3 renewable from the MEC/MICINN/MINECO, 2 international bilateral from the MICINN, 1 CONSOLIDER-INGENIO from MEC, 1 from CELLEX private foundation and 5 technological development ones from national and regional governments). In most of these projects I worked in active collaboration with national and international clinical partners, including medical doctors from international groups. I m currently co-IP of ICN2 tasks and co-coordinator of a recently granted FP7-EuronanoMed 2 project (Development of a nanodiagnostic platform for monitoring of cancer cell secreted proteins (NACANCELL). European Commission; Program: FP7-EuroNanoMed 2; Ref. PCIN-

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2016-066; 01/11/2016-31/10/2019; Group funding: 150.000) related to the study of cancer mechanisms through the monitoring of cell secreted proteins, with the objective of developing a non-invasive method to evaluate tumor evolution and response to treatments. I participated in the preparation of the proposal of 13 of the rest of projects and actively participated in all them, being of special relevance my contribution to the EC s projects Nanosystems for early diagnosis of neurodegenerative diseases: NADINE (Program: FP7-NMP-2009-4.0-3; Reference: CP-IP 246513-2) and Point of care diagnostics for rapid and cheap pathogen detection of companion animals: POC4PETS (Program: FP7-SME-2012-1; Reference: 315653). In addition to NACANCELL project, I m currently involved in 4 running projects: 1 EC s H2020, 1 EC s FP7, 1 MINECO s renewable and 2 MINECO s and regional s technological ones. I also participate in 3 technological transfer actions from my patents.

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Turno de acceso general

Nombre: MATEOS GOMEZ, PEDRO ANTONIO
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Título:

Trayectoria Pedro A Mateos Gomez

Resumen de la Memoria:

During my PhD, I studied the transcription mechanisms of Coronavirus, members of a larger family of viruses that are considered as important pathogens causing respiratory diseases. I focused in the characterization of the recombination process that allows the generation of a set of viral nucleic acids from its single RNA genome. During the five years dedicated to this topic I held a FPI fellowship for my PhD training at the National Centre for Biotechnology (CNB), under the direction of Dr. Luis Enjuanes and Dra. Isabel Sola. I also demonstrated productive and collaborative efforts leading to several publications in high tier journals.
As a post-doc, my research goal is to understanding the molecular basis of tumorigenesis. I decided to join the Sfeir□s lab, at the New York University, for my post-doctoral training and focus on deciphering the link between genomic instability and tumorigenesis. Throughout the past years I have been primarily focusing on the alternative non-homologous end-joining pathway (alt-NHEJ) of DNA repair, a poorly understood and highly erroneous DNA repair pathway that plays a unique role in the etiology of cancer.
Investigating the enzymatic activity responsible for the random insertions at repair sites I identifid polymerase theta (encoded by Polq) as a crucial alternative NHEJ factor in mammalian cells. In addition, I also found that loss of Polq results in increased rates of homology-directed repair, and that depletion of PolQ has a synergistic effect on cell survival in the absence of BRCA genes. The inhibition of this mutagenic polymerase represents a valid therapeutic avenue for tumors carrying mutations in homology- directed repair genes. These findings were published in Nature and gave me the opportunity to present it on several international meetings, including me as invited speaker at the 3rd Annual Re‐writing Genomes Symposium.
During last two years, I have been characterizing the mechanism of action of Polq and participating in the development of chemical inhibitors for this polymerase. I have used the CRISPR genome editing tool to generated mouse embryonic stem cell lines carrying mutations and deletions at the endogenous locus of Polq. These studies also allowed to me to improve the efficiency of the CRISPR targeting methods by inhibition of Polq, what we have patented recently (PCT/US16/55967). In parallel, I have established a new mouse model to study the impact of Polq in the formation and development of breast tumors. Currently, I am in the process of preparing two articles for publication.
My goal in the future is to understand the regulation of Polq gene, whereas is barely expressed in normal cells it is overexpressed in cancer tissues, lymphocytes and testis. In addition, I would like to highlight novel factors that mediate repair by alt-NHEJ and to elucidate their relevance in the progression cancer.
Finally, seeing a laboratory develops from the beginning and taking part in that development (I joined a nine-months old laboratory) has provided me with valuable experience and with the opportunity to mentor several technicians and PhD students. Furthermore, I have contributed to the funding of the lab being awarded with a Breast Cancer Research Program Postdoctoral Fellowship Award. This 3-years grant includes a budget of 0.5 million dollars where I am the principal investigator.

Resumen del Currículum Vitae:

Education:

- BS in Biology (Universidad de Salamanca)
- PhD in Molecular Biology (Universidad Autonoma de Madrid)

Publications:

□ Mateos-Gómez PA, Zuñiga S, Palacio L, Enjuanes L, Sola I. (2011). Gene N proximal and distal RNA motifs regulate coronavirus nucleocapsid mRNA transcription. J Virol. 85(17):8968-80.
□ Mateos-Gomez PA, Morales L, Zuñiga S, Enjuanes L, Sola I. (2013). Long-distance RNA-RNA interactions in the coronavirus genome form high-order structures promoting discontinuous RNA synthesis during transcription. J Virol. 87(1):177-86.
□ Dufour D*, Mateos-Gomez PA*, Enjuanes L, Gallego J, Sola I. (2011). Structure and functional relevance of a transcription-regulating sequence involved in coronavirus discontinuous RNA synthesis. J Virol. 85(10):4963-73. (*) Both authors contributed equally.
□ Morales L*, Mateos-Gomez PA*, Capiscol C, Del Palacio L, Enjuanes L, Sola I. (2013). Transmissible gastroenteritis coronavirus genome packaging signal is located at the 5' end of the genome and promotes viral RNA incorporation into virions in a replication independent process. J Virol. 2013 Nov;87(21):11579-90. (*) Both authors contributed equally.
□ Mateos-Gomez PA, Gong F, Nair N, Miller KM, Lazzerini-Denchi E, Sfeir A. (2015). Mammalian polymerase θ promotes

alternative NHEJ and suppresses recombination. Nature. 2015 Feb 12;518(7538):254-7

Funding:

2013 Breast Cancer Research Program Postdoctoral Fellowship Award.
CDMRP Log Number: BC134020. Grants.gov ID Number: GRANT11558051.
Project Duration: 36 months
Total Budget: $508,500
Principal Investigator: Pedro Mateos-Gomez
Department of Defense, U.S. Army Medical Research and Materiel Command Congressionally Directed Medical Research Programs.

Talks:

1. X Annual meeting of the Spanish Society for Virology. University of Salamanca, Salamanca, Spain. June 21-24th, 2009. Oral presentation.
2. 28th Annual meeting of the American Society for Virology. University of British Columbia, Vancouver, British Columbia, Canada. July 11-15th, 2009. Oral presentation.
3. XI Annual meeting of the Spanish Society for Virology. University of Granada, Granada, Spain. May 29th-June 1st 2011. Oral presentation.
4. 30th Annual meeting of the American Society for Virology. University of Minnesota, Minneapolis, Minnesota, USA. July 16-20th, 2011. Oral presentation.
5. Keystone Symposia on Molecular and Cellular Biology. Genomic Instability and DNA Repair. Whistler Conference Centre, Whistler, British Columbia Canada. March 1-6th, 2015. Oral presentation.
6. Cold Spring Harbor Meetings. Telomeres and Telomerase. Cold Spring Harbor, NY 11724-2213, USA. April 28-May 2, 2015. Oral presentation.
7. Invited speaker: 3rd Annual Re‐writing Genomes Symposium, A one-day symposium hosted by QB3 Berkeley and the Innovative Genomics Initiative. August 24th, 2015 University of California, Berkeley. ?How Does Polθ Regulate DNA DSB Repair??. Pedro A. Mateos-Gomez and A. Sfeir.

Patents:

I have invented certain new and useful improvements in COMPOSITIONS AND METHODS FOR ENHANCING CRISPR ACTIVITY BY POLQ INHIBITION, for which a Patent in the United States was filed as International Serial No. PCT/US16/55967 on October 7, 2016.

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Turno de acceso general

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Título:

Transcriptional Regulation and Intercellular Signalling During Cardiac Development

Resumen de la Memoria:

From the beginning of my research trajectory, I have been interested in understanding the mechanisms regulating the different steps of cardiac formation and my entire career has been oriented in this direction. At the beginning of my PhD training, I contributed to the description of how the activity of the Notch signaling pathway in the embryonic endocardium is required to induce the differentiation and proliferation of the early ventricular myocardium. This process is crucial for the formation of the cardiac trabeculae, essential structures for proper development and functionality of ventricular myocardium. I continued my PhD training carrying out a 3 years project where I focused on the study of the interaction between different signaling pathways (BMP2, NOTCH) and cardiac tissues. We described how the interplay between the Notch pathway from the endocardium and BMP from the myocardium restricts the process of Epithelial to Mesenchymal Transition (EMT), responsible for the beginning of cardiac valve formation, to the proper territory. We also showed how the manipulation of the various elements involved can modulate or delocalize this process, changing the identity of the cardiac regions. These findings helped us to better understand the origin of cardiac valve and septal defects, which are the most common types of cardiac congenital abnormalities and a major cause of adult morbidity and mortality. The findings described in this work also served as the basis for the generation of a simulation model representing the behavior of cells undegoing EMT. Later, during my postdoctoral stay in San Francisco (USA) I developed a complex and interdisciplinary project where I focused on the understanding of the role of two key cardiac transcription factors (TFs), TBX5 and NKX2-5, in the control of cardiogenesis. The use of mouse embryonic stem cells with mutations for Nkx2-5, Tbx5 or both, differentiated into cardiomyocytes allowed us to identify the specific genetic programs regulated by these two TFs. In the same study, we uncovered on a genome-wide scale the cooperative interactions between NKX2-5, TBX5, and GATA4 and described how these interactions coordinate gene expression during cardiac differentiation and morphogenesis. The most exciting finding was a novel mechanism by which cooperative DNA binding serves not only to activate lineage-appropriate genes, but also to prevent a transcription factor from redistributing to other genomic sites where it could activate lineage-inappropriate genes. We also described a ⍰motif logic⍰ relying on the different interdependent relationships between cardiac TFs. The recognition of specific binding sites by each TF depends to a high degree on the interaction with other TF, giving rise to TF complexes, where the strength of the interaction is dictated by the combination of TF-TF and TF-DNA affinities. The identification of permissive binding motif configurations highlighted the role of DNA as an instructive partner for pairs of heterotypic TFs. On May 2016, I joined the Jose Luis de la Pompa⍰s lab, at CNIC, as a Senior Postdoctoral. During my stay in this lab I am studying the negative effect of NKX2-5 on cardiomyocyte differentiation, and trying to understand the complex signaling between different endocardium and myocardium carried out by the Notch signalling pathway during cardiac development.

Resumen del Currículum Vitae:

After a 5 years stay in Dr. José Luis de la Pompa⍰s lab at the Centro Nacional de Biotecnología ⍰ CSIC, and later the Centro Nacional de Investigaciones Cardiovasculares (CNIC), I obtained my PhD in 2010 (Universidad Autonoma de Madrid). During this time, I studied the role of the Notch signaling pathway in ventricular chamber and cardiac valve development, describing the different molecular interactions implicated in these processes. I also became familiarized with the culture and manipulation of mouse embryonic stem cells and the generation of genetically modified mouse models. During my stay in Dr. José Luis de la Pompa⍰s lab, I was awarded two fellowships, one from the ⍰Fundación Española del Corazón para Investigación Clínica y Básica en Cardiología⍰ and one from the ⍰Heart Repair European Consortium⍰. At the end of my Ph.D I was awarded the Extraordinary Thesis Award 2010 prize (Universidad Autonoma de Madrid). I also had the opportunity to attend various international meetings, where I shared my work in scientific posters and oral presentations with some of the most prestigious researchers in the cardiovascular field. In 2012 I joined Dr. Benoit Bruneau⍰s lab at the Gladstone Institute of Cardiovascular Disease in San Francisco, California, where I stayed until March 2016. Besides a scientific review describing the role of chromatin modulators during cell reprogramming, I developed a complex and interdisciplinary project where I focused on the understanding of the role of two key transcription factors, TBX5 and NKX2-5, in the control of cardiogenesis. We examined the overlapping function of TBX5 and NKX2-5 in mouse cardiac differentiation and their relationship with other cardiac transcription factors like GATA4. We found the existence of a cooperative function to regulate gene expression programs required for expansion of cardiac progenitors and for cardiac differentiation. Besides the work with embryonic stem cells and the routine use of differentiation protocols to generate the required cardiomyocytes, my stay in Dr. Benoit Bruneau⍰s lab offered me the opportunity to learn and develop specialized genome-wide analysis methods, like ChIP-seq, ChIP-exo , RNA-seq or 4C-seq. To analyze the large and complex datasets generated with our experiments, I worked alongside experts in the field and learned how to use elaborate bioinformatics tools and to develop specific analysis pipelines. During my stay in Dr. Benoit Bruneau⍰s lab, I was awarded the California Institute of Regenerative Medicine (CIRM) Postdoctoral Fellowship. I was part of an international consortium of cardiovascular researchers (CVDC) and shared my work with other outstanding

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groups in the field. I have participated in highly prestigious international meeting (keystone Symposia, Weinstein cardiovascular meeting) with posters and oral presentations, and I was awarded the travel award in the Weinstein Cardiovascular Meeting 2014. In 2016, I was awarded the UE Cofund CNIC IPP (International Postdoctoral Programme), which allowed me to join Jose Luis de la Pompa□s lab, at CNIC, as a Senior Postdoctoral Researcher. My interest is to continue my career in the cardiovascular field having as main focus the signaling between different cardiac tissues during the process of myocardial differentiation, and the regulatory events occurring at the genomic controlling gene expression.

AYUDAS RAMÓN Y CAJAL
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Título:

Uncovering the rules of neural connectivity and its changes associated to neurodegeneration

Resumen de la Memoria:

The research career of the candidate has been focused in Neuroscience and it has been developed with a logic structure to understand the synaptic function from single neurons to brain circuits in vivo. The applicant started his scientific career as a PhD student at Prof. Fernández Chacón's lab, working on electrophysiological studies of the synaptic transmission in hippocampal cultured neurons from knock-out mice lacking Cysteine String Protein-alpha. He used patch-clamp and imaging techniques in cell cultures to figure out the essential role of CSP-alpha as a molecular chaperon for neurons with high levels of synaptic activity, mainly parvalbumin interneurons. The candidate was first author of this work, published (and cover illustration) in The Journal of Neuroscience. After finishing the PhD, the applicant moved to Joshua Trachtenberg's lab at the University of California Los Angeles, where he initially started a collaboration with the laboratory of Prof. Peyman Golshani to study the role of PTEN in a mouse model of autism, using patch-clamp techniques in slices and in vivo. The work was published in PNAS, and the candidate was the first author. Thanks to the expertise of Prof. Trachtenberg using in vivo two-photon imaging, the candidate started a new project to understand the connectivity of different populations of neurons in the cortex using genetically encoded calcium indicators in awake animals. The combination of cranial surgeries and two-photon calcium imaging allowed the study of cortical networks at a microcircuit level. The main work of this project was recently published in Nature Neuroscience, being the applicant first and corresponding author. The study of neuronal circuits function in awake animals combining -state of the art- two photon microscopy and behavior is an exciting emerging field in Neuroscience. Nevertheless, there is not yet any laboratory in Spain carrying out these type of studies. The applicant recently moved back to Spain, to Prof. Fernandez Chacon's lab, with the main purpose of introducing those approaches to study brain function using mouse models of synaptic degeneration. Prof. Fernandez Chacon and the Research General Services of the University of Seville have obtained a grant supported by FEDER to acquire a fully equipped two-photon microscope for in vivo imaging that would be operating along 2017. The applicant has been an essential adviser to get the funds.
The compromise of the candidate with his scientific career could be, in part, estimated from the quality of publications obtained, 3 publications during his PhD, 5 publications during his postdoctoral stay. A new paper was recently sent to Nature Neuroscience for review.

Resumen del Currículum Vitae:

Degree in Biological Sciences from the University of Seville (average: 8.37). Internal student of the Cell Biology Dept. in the laboratory of Prof. Felipe Cortés, obtaining a Collaboration Scholarship from the Spanish Ministry of Education. Studies of doctoral thesis in the laboratory of Prof. Rafael Fernández Chacón, belonging to the Department of Medical Physiology and Biophysics of the University of Seville (2001-2008). The PhD was financed by a BEFI fellowship from the Instituto de Salud Carlos III, as well as by predoctoral contracts associated with research projects financed by public entities (national and international). In 2008, the applicant defended the Doctoral Thesis titled Electrophysiological study of synaptic transmission in cultured hippocampal neurons of mice lacking Cysteine String Protein alpha (CSP-alpha) with Cum Laude Distinction. Also he obtained the Extraordinary Prize of Doctorate of the University of Seville. Between July 2008 and March 2010 he continued his stay in the laboratory of Prof. Fernández Chacón as a postdoctoral researcher. Throughout this period two research articles were published: The Journal of Neuroscience (first author and cover illustration) and The Journal of Physiology (fourth author). The first article was awarded by Endesa / Univ. Sevilla as the best research work carried out in collaboration with the General Services of the University, as well as at the Gordon Research Conference (Oxford, 2008) as the best poster presentation. Two reviews were published in this period, in which the candidate figure as the first and third author (Molecular Psychiatry and Brain Research Review, respectively). In this period, the candidate specialized in neural culture techniques, molecular biology and electrophysiology. In July 2011 he obtained a competitive postdoctoral mobility scholarship abroad from the Ministry of Education, Culture and Sport for a stay in the laboratory of Prof. Joshua Trachtenberg at the University of California Los Angeles (UCLA). In November of 2014 he was hired as Assistant Project Scientist in the same laboratory. There, the candidate acquired knowledge of advanced techniques in electrophysiology (in vitro and in vivo), publishing two papers of which he is the first author (PNAS and Commun Integr Biol.). In a second stage he also specialized in in vivo imaging techniques using multiphoton microscopy, which allows the study of connectivity in neural networks. The result of this work was just published in the journal Nature Neuroscience, of which the candidate is first author, as well as corresponding author. There is another collaborative work published in Nature Communications (Fifth author). In February 2016 he was recruited by Prof. Fernández Chacón (IBiS) with an Excellence contract from the Junta de Andalucía. In collaboration with the University of UCLA, another research paper has recently been sent to the journal Nature Neuroscience, which is currently under review, and in which he is the first author and corresponding author. During these research periods, the candidate has published a total of 8 articles, with an average impact factor of 8.33 and presented communications at national and international meetings (40). From and educational point of view, the applicant has taught 78 hours of official teaching (theory and practice).

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