



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2017

Turno de acceso general

Nombre: HURTADO , ANTONIO
Referencia: RYC-2017-22715
Área Científica: Biomedicina
Correo Electrónico: antonihurtado@gmail.com

Título:

Cooperating transcription factors mediate the function of Oestrogen Receptor

Resumen de la Memoria:

The main interest of my research is to understand the mechanism of hormone resistance in breast cancer. In the last years my research has focused in identifying transcription factors that modulate Estrogen Receptor (ER) function. Moreover, I have investigated how different bacteria types may impact the gene transcription and epigenetics of the colon tissue. More recently, I aimed to investigate what is the impact of kinases targeting the forkhead transcription factor FOXA1 in hormone resistant cells. In particular, my research has contributed significantly to the understanding of the role of the HER2/FOXA1/ER axis in hormone resistant tumors. A recent study from my group has revealed that hormone-resistant tumors escape anti-ER inhibition by developing mechanisms of tumor growth independent of ER and that are coordinated by the activities of HER2/3 and FOXA1 (this work is under review in Nat Commun). Moreover, I am interested in determining how the estrogen antagonist Tamoxifen contributes to the inhibition of breast cancer progression. Therefore, the focus of my future research is summarized in two main projects related with breast cancer. These projects are explained in section below and are structured in two comprehensive and often overlapping areas. One area entails chemical systems approaches to: (1) functionally understand how anti-ER drugs perform their repressive effects and (2) identify novel mechanism by which hormone-resistant cells overcome ER inhibition. Specifically, we are employing a combination of targeted proteomics, drug screenings, highthroughput sequencing of chromatin and sequencing of de novo transcripts (by means of GRO-seq) in the projects related with this part of my research. The second area involves in vivo approaches from patient derived xenographs of breast cancer tumors. With this research I aim to test how drugs identified in our drug screening influence the tumor growth of breast cancer tumors. Moreover, we will validate which compounds might be used as alternative therapies for patients with poor response to current anti-ER therapies using hormone-resistant breast cancer in vivo models.

Resumen del Currículum Vitae:

My research activity has been mainly centered on the study of nuclear receptors and transcription factors in hormone-dependent tumors. In my Master's degree I studied the effects of dietary factors in breast cancer initiation and progression in animal models, activity that I complemented teaching to second year medical students at the Autonomous University of Barcelona. Later, during my PhD at the Vall-Hebron Research Institute of Barcelona, my work focused on understanding the non-genomic actions of Estrogen Receptor (ER) in Prostate cancer. All this work resulted in four publications as a first author and in collaborations with other projects. The main interest during my post-doctoral research at Cambridge University (UK) was to understand the mechanisms of resistance for endocrine treatment in luminal breast tumors, which led to four significant publications (i.e. Nature, Nature Genetics). In late 2011 I became young group leader at University of Oslo (non-tenure track position). Over the past six years, I have built a team and I have developed a research program in functional genomics and proteomics of hormone dependent tumors. My research group has: (1) a proven track record with a total of 8 papers (i.e. NAR, Nat Commun), (2) successfully established national and international research collaborations and (3) attracted significant external funding from several sources (Norwegian and European funding bodies). In addition, I have trained 3 PhD students and 3 undergraduate students. The scientific and educational supervision was complemented with teaching at the University of Oslo.



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Nombre: FERNANDEZ MARCOS, PABLO
Referencia: RYC-2017-22335
Área Científica: Biomedicina
Correo Electrónico: pablojose.fernandez@imdea.org

Título:

Crosstalks between metabolism, aging and cancer

Resumen de la Memoria:

I am a molecular biologist specialized in the fields of metabolism, cancer and aging. I am the Group Leader of the Bioactive Products and Metabolic Syndrome group, an independent research group at the IMDEA Food Institute (Madrid), focused on the potential of nutritional interventions against metabolic syndrome and aging. As Group Leader at IMDEA Food, I have been granted by the Spanish Ministry of Economy, Industry and Competitiveness - MINECO and the Ramón Areces, BBVA and Francisco Escudero Foundations as the only Principal Investigator in competitive calls. In total, I have co-authored 21 research articles, 5 reviews, 1 book chapter and 4 previews, 11 of them published after my incorporation to IMDEA Food. My research has been published in top journals, as Science, Cell, Cell Metabolism, JCI or Nature Communications, including 7 corresponding and 15 first-authorships.

My education was carried out in Spain and Switzerland: I obtained my PhD in Manuel Serrano's laboratory at the Spanish National Cancer Research Center (CNIO), working on the potent tumor suppressor Par4; on Sei1, a cell cycle regulator at -islets; and on the long-living strain of mice overexpressing telomerase and several tumor suppressors. I obtained my first postdoctoral position in the laboratory of Prof. Johan Auwerx, at the École Polytechnique Fédérale de Lausanne (EPFL), in Switzerland, granted by Marie Curie, FEBS and Alfonso Martín Escudero Fellowships, focused on the sirtuins family of regulators of metabolism and aging. In my second postdoctoral position in Dr. Manuel Serrano's laboratory at the CNIO, granted by the AECC, I studied the protective potential of G6PD against ROS-induced aging, and the role of the Notch pathway in lung and bladder cancer.

My experience as an independent Group Leader began in December 2015 at IMDEA Food Institute, in Madrid. Here, I direct a team of one postdoctoral researcher and one PhD student. I have recently been assigned a new postdoctoral and two new PhD student positions, one of them obtained in a competitive call by the Madrid Community, who will incorporate in short to the laboratory. Research in my laboratory is focused on nutritional interventions to fight aging, obesity, cancer and diabetes. We are following three research lines: (1) high throughput screenings to identify and characterize bioactive products effective against obesity and diabetes. (2) Study the potential of fasting as an enhancer of chemotherapy treatments against cancer. In this line, I have been the Principal Investigator of a human clinical trial subjecting healthy human volunteers to short-term fasting, to study the mechanisms driving the protective effects of fasting against the secondary effects of chemotherapy. (3) Study the molecular mechanisms by which two fasting-responding enzymes, Sirt1 and Sirt3, affect cancer development. These projects have been granted by the MINECO and the Ramón Areces, BBVA and Francisco Escudero Foundations, with me as the only Principal Investigator.

Resumen del Currículum Vitae:

SCIENTIFIC CAREER

- 12/2015 - present

Principal Investigator of the Bioactive Products and Metabolic Syndrome group at IMDEA Food Institute, Spain

- 2/2012 - 11/2015

Post-doctoral research in Dr. Manuel Serrano's laboratory

CNIO, Spain

AECC grant

- 10/2009 - 2/2012

Post-doctoral research in Prof. Johan Auwerx's laboratory

EPFL, Switzerland

Grants from the FAME foundation, FEBBS and Marie-Curie

- 5/2003 - 10/2009

Pre-doctoral student in Prof. Manuel Serrano's laboratory

CNIO, Spain

FPI grant from the Education and Science Ministry of Spain

MAIN PUBLICATIONS

1) High throughput image-based screening to identify chemical compounds capable of activating FOXO. Marta Barradas, Wolfgang



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- Link, Diego Megías, Pablo J. Fernández-Marcos#. Methods in Molecular Biology, 2018. Book chapter. #: corresponding author. In press.
- 2) FOXO transcription factors at the interface of metabolism and cancer. Link W#, Fernandez-Marcos PJ#. International Journal of Cancer. 2017. #: co-corresponding.
 - 3) Analysis of the advantages of cis reporters in optimised FACS-Gal. Sánchez-Luengo MA, Rovira M, Serrano M, Fernandez-Marcos PJ#, Martínez L#. Cytometry A (2017). #: co-corresponding.
 - 4) Young and lean: elimination of senescent cells boosts adaptive thermogenesis. Fernandez-Marcos PJ#, Serrano M#. Cell Metabolism (2017). #: co-corresponding.
 - 5) Tissue damage and senescence provide critical signals for cellular reprogramming in vivo. Mosteiro L, Pantoja C, Alcazar N, Marión, RM, Chondronasiou D, Rovira M, Fernandez-Marcos PJ, et al., Science (2016).
 - 6) PI3Ka inhibition reduces obesity in mice. Lopez-Guadamillas E, Muñoz-Martin M, Martinez S, Pastor J, Fernandez-Marcos PJ, Serrano M. Aging (Albany NY). (2016).
 - 7) p21Cip1 plays a critical role in the physiological adaptation to fasting through activation of PPAR γ . Lopez-Guadamillas E, Fernandez-Marcos PJ, et al., Sci Rep. (2016).
 - 8) NADPH: new oxygen to the ROS theory of aging. Fernandez-Marcos PJ#, Nóbrega-Pereira, S#. Oncotarget. (2016). #: co-corresponding.
 - 9) G6PD protects from oxidative damage and improves healthspan in mice. Nóbrega-Pereira S*, Fernandez-Marcos PJ*# et al. Nat Commun. 2016. In press. *: contributed equally to this work. #: co-corresponding.
 - 10) Notch pathway inactivation promotes bladder cancer progression. Maraver A*, Fernandez-Marcos PJ* et al. JCI. 2015. *: contributed equally to this work.

PROJECTS

1.- TITLE: Characterization of the molecular mechanisms of short-term fasting as an enhancer of chemotherapy

PI: Pablo J. Fernandez Marcos

FINANCING INSTITUTION: MINECO

HOSTING INSTITUTION: IMDEA Food

AMOUNT: 142659€ FROM: 2-2018 TO: 2-2021

2.- TITLE: New food-derived bioactive products against obesity and diabetes

PI: Pablo J. Fernandez Marcos

FINANCING INSTITUTION: Ramon Areces Foundation

HOSTING INSTITUTION: IMDEA Food

AMOUNT: 120000€ FROM: 2-2017 TO: 2-2020

3. TITLE: Nuevos Productos Alimentarios Bioactivos contra la Obesidad y la Diabetes

PI: Pablo J. Fernandez Marcos

FINANCING INSTITUTION: BBVA Foundation

HOSTING INSTITUTION: IMDEA Food

AMOUNT: 40000€ FROM: 12-2016 TO: 5-2018

4. TITLE: Bioactive Products and Metabolic Syndrome € BIOPROMET. Starting package.

PRINCIPAL INVESTIGATOR: Pablo J. Fernandez Marcos

FINANCING INSTITUTION: IMDEA Food

HOST INSTITUTION: IMDEA Food

AMOUNT: 40000€ FROM: 12-2015 TO: 12-2016



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Nombre: BUSQUETS GARCIA, ARNAU
Referencia: RYC-2017-21776
Área Científica: Biomedicina
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Título:

Targeting the endocannabinoid system to understand brain physiological and pathological processes

Resumen de la Memoria:

My research career has been focused mainly on the endocannabinoid system (ECS) since 2008. This system is widely expressed in the brain and it is necessary for several physiological processes, ranging from the regulation of cellular energy metabolism to the modulation of complex cognitive functions. Accordingly, malfunctioning of the ECS has been strongly linked to pathological conditions, such as obesity and mood disorders and other neurodegenerative and neuropsychiatric disorders. Thus, a deeper understanding of the neural circuits, the molecular signaling pathways and the behavioral impact of cannabinoid action is essential for the development of new therapeutic approaches. I am fascinated by the multiple functions of the ECS and for this reason I have been using this system to better understand how the brain controls different behavioral responses.

After obtaining my degree in Biology (Universitat Pompeu Fabra, Barcelona) and performing a Neuroscience Master at the University of Barcelona, I carried out my PhD thesis with a competitive FPU pre-doctoral fellowship (Spanish Ministry of Education) in the Laboratory of Neuropharmacology (NeuroPhar) at the Universitat Pompeu Fabra (Barcelona). My PhD thesis topic was focused on the role of the ECS in several behavioral responses in physiological and pathological conditions. During this period, I have received a solid training in behavioral and biochemical pharmacology focused on cannabinoid effects. After finishing my PhD in 2013, I obtained the competitive postdoctoral fellowship from the University of Bordeaux (IDEX fellowship) and the prestigious European postdoctoral fellowship (IEF-Marie Curie) to join the laboratory of Dr. Giovanni Marsicano at the NeuroCentre Magendie in Bordeaux, a leading group in the cannabinoid field. During these years in Bordeaux, I have been investigating the link between CB1R activation and the development of psychotic-like states. Moreover, I have been actively participating on ongoing projects of the host lab.

Resumen del Currículum Vitae:

My research career has been focused mainly on the endocannabinoid system (ECS) since 2008. This system is widely expressed in the brain and it is necessary for several physiological processes, ranging from the regulation of cellular energy metabolism to the modulation of complex cognitive functions.

After obtaining my degree in Biology (Universitat Pompeu Fabra, Barcelona) and performing a Neuroscience Master at the University of Barcelona, I carried out my PhD thesis with a competitive FPU pre-doctoral fellowship (Spanish Ministry of Education) in the Laboratory of Neuropharmacology (NeuroPhar) at the Universitat Pompeu Fabra (Barcelona). Then, I obtained a postdoctoral fellowship from the University of Bordeaux (IDEX fellowship) and the prestigious European postdoctoral fellowship (IEF-Marie Curie) to join the laboratory of Dr. Giovanni Marsicano at the NeuroCentre Magendie in Bordeaux, a leading group in the field.

During all this period, I have demonstrated my value with publications in very good journals that I have achieved during my PhD and postdoctoral periods, including 22 original scientific articles and reviews in Nature Medicine, Molecular Psychiatry, PNAS, Biological Psychiatry and Neuropsychopharmacology (as 1st author), Nature Neurosciences, Neuron, Nature, Oncogene, Philosophical Transactions of the Royal Society London B Biological Sciences, Neuropharmacology and Journal of Clinical Investigation, among others. Notably, some of these works received prizes from Spanish Society for Cannabinoid Studies (SEIC), the Biogen Idec Company or the Esteve Foundation.

I also displayed a remarkable ability to propose, implement and validate innovative actions for my experimental work. It is worth mentioning, a novel apparatus to study memory registered before the Spanish IPR authority (8/12/2008) and two patents on the use of novel cannabinoid-linked treatments of several diseases (priority dates, 26/7/2011 and 19/3/2013). These contributions have allowed my group to negotiate licensing agreements with pharmaceutical and biotechnological companies for their commercial exploitation.

I also participated in the writing of grants that we successfully obtained during these last years. In particular, my contribution was central for the following grants: FRM (2016-2019, 300.000 Euro), ANR (ORUPS, 2017-2020, approx. 300.000 Euro) and EPHE (2019, 60.000 Euro). Moreover, I am one of the coordinators of a LABEX Grant obtained (LABEX, HIPOMEAL, 100.000 Euro).

I have also supervised Master students and I obtained in 2014 an exceptional authorization from the PhD School in Bordeaux. Thus, I successfully supervised the work of several Master 1 and Master 2 students (Yarmo Mackenback, Camille Pernegre, Paula Gomez, Bastien



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Redon and Christina Ioannidou. Moreover, I am currently co-supervising the PhD of Christina Ioannidou.

Finally, I have demonstrated to be a very good scientific disseminator receiving the 1st Prize for the Best Oral Presentation at the Spanish SEIC Meeting (2010). Moreover, I am currently one of the two postdoctoral representatives in the NeuroCentre Magendie and we are organizing the scientific activities for the Institute. Finally, I promoted the creation a trimestral NeuroCentre Magendie Newsletter, implementing interviews, news, and recent publications.



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Nombre: CASTELLANO SANCHEZ, ESTHER
Referencia: RYC-2017-21915
Área Científica: Biomedicina
Correo Electrónico: esther.castesa@gmail.com

Título:

Targeting RAS-PI3K signalling to re-educate the stroma of RAS mutant lung cancers

Resumen de la Memoria:

My career to date demonstrates a high level of achievement shown in the high impact papers I have produced throughout my career. My research as a PhD student showed that the different RAS isoforms have non-redundant roles and demonstrated that N-Ras regulates the expression of genes involved in immune processes. These findings led to the publication of two articles as first author in *Oncogene* and *Genome Biology*.

After obtaining my PhD I moved to Dr. Julian Downward's laboratory as a postdoctoral fellow, with the aim of applying my knowledge of Ras signalling to further understanding the different roles that it plays at different stages of cancer development. Using a sophisticated mouse model, I demonstrated that loss of Ras-PI3K binding in established tumours results in partial tumour regression and prolonged cytostasis. These results were phenocopied by chemical inhibition of PI3K activity. This work showed, for the first time, that PI3K activity is essential for tumour maintenance and its activity in this setting requires activation by Ras. These results were published in *Cancer Cell*.

Additionally, I have shown that RAS binding to PI3K is key for cell motility, since it is required for activation of Rac GTPase and regulation of the Reelin pathway. Analysis of clinical datasets showed that loss of Reelin is associated with poor survival rates in lung cancer patients, which has important translational implications: re-expressing Reelin or inhibiting Rac activity in tumours lacking Reelin expression could be explored as a therapeutic approach to reduce cancer cell migration and improve the outcome of patients in certain settings. This work has been published in *Nature Communications* where I am co-corresponding author.

I am currently a Lecturer at Barts Cancer Institute. My research program as an independent investigator aims to understand how oncogenic RAS proteins drive cancer development by regulating the interplay between tumour cells and the surrounding microenvironment in lung cancer. We want to identify the molecular mechanisms by which RAS-PI3K signalling re-educates the tumour stroma to sustain tumour growth and progression. In doing so, we expect to identify downstream processes that, when targeted, halt tumour growth while bypassing the ability of tumours to compensate direct inhibition of PI3K. My programme focuses on:

1. Determine the role of RAS-PI3K signalling in the biology of Cancer Associated Fibroblasts (CAFs). RAS signalling has been extensively studied in tumour cells, but little is known about how it affects the function of CAFs and the dynamics of the extracellular matrix (ECM).
2. Dissect the role of CAF-specific RAS-PI3K signalling in the recruitment and activity of immune cell populations. The potential of cancer immunotherapy is significant, but there is a concerning lack of mechanistic understanding of the role played by CAFs and the ECM in tumour immune cell infiltration and function.
3. Define the role of CAF-specific RAS-PI3K signalling during establishment, maintenance and spread of lung tumours. It is important to understand the effect of disrupting RAS-PI3K interaction in CAFs during tumour growth and metastasis formation and understand if and how this approach synergizes with chemotherapy, targeted agents and immune therapies (e.g. checkpoint inhibitors).

Resumen del Currículum Vitae:

I have split my CV in 3 main blocks, each corresponding to the main phases of my career:

1. PhD: I joined Prof. Eugenio Santos's group for my "Grado de Salamanca" studies in 2001 and then went on to carry out my PhD research (2002-2007) after obtaining an FPU fellowship. During my PhD, we demonstrated that HRAS and NRAS have specific, non-overlapping functions. During this time I published 6 scientific articles and 1 review describing different aspects of RAS proteins function and regulation in physiological conditions and in cancer: 3 as first author (*Oncogene*, 2007; *Genome Biology*, 2009; *Genes and Cancer*, 2011); 1 as second author and 3 as middle author (*EMBO J*, 2010; *Blood*, 2011 and *Science Signalling*, 2017). Furthermore, I presented my work in several national and international conferences in poster format and as a selected oral presentation at the CNIO Meeting DNA Arrays (2003).

2. Postdoctoral Fellow: I joined Prof. Julian Downward's group as a postdoctoral fellow (2007-2013), funded by a grant from Cancer Research UK (CRUK). I worked on two different projects aimed at understanding the functional role of RAS signalling through PI3K, one of its main effectors, in lung cancer maintenance and in cell migration. I published 5 scientific articles: 2 as first author, including 1 in which I am also corresponding author (*Cancer Cell*, 2013; *Nat Commun*, 2016); 2 as middle author (*J Clin Invest*, 2014; *Oncogene*, 2016); 1 review (*Genes Cancer*, 2011); and 1 book chapter (*Curr Top Microbiol Immunol*, 2010).

During this period I was awarded a travel grant to attend a Keystone symposium on "PI3-Kinase signalling in Disease" and I supervised 1 Summer Student and 1 Master Student.

I took a career break while on maternity leave for a period of 11 months.



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3. Lecturer: In 2013 I joined Barts Cancer Institute (Queen Mary University of London) as a Lecturer. My teaching responsibilities include tutoring several groups for Medicine and Biomedicine students. I have obtained the Postgraduate Certificate in Academic Practice, which certifies that I possess the knowledge and skills required to provide high-quality teaching in higher education settings. As an independent researcher I was awarded 4 projects/fellowships amounting to over £350,000. In addition, I have recently been invited to submit a full application for a CRUK Career Establishment Award (£1,400,000). I have supervised 1 PhD thesis to completion; currently I am supervising 1 PhD student. I have also supervised 6 Master students and the final project of 2 bachelor students. I present my work at national and international conferences and scientific seminars. Recently, the importance of my research was recognized with a "Best Talk Award" at the CRUK Lung Cancer Workshop (York, December 2016). My expertise in the RAS field has recently been recognized by an invitation to write a book chapter on the role of RAS-PI3K in human disease (Krygowska, A.A and Castellano E, Cold Spring Harb Perspect Med, 2017). I am currently a peer reviewer of scientific projects for the Medical Research Council and the Rosetrees Trust, and an ad hoc reviewer for Nature Communications and PLOS One. I am a member of the UK Cell Adhesion Society and the Spanish Society of Biochemistry and Molecular Biology. During this period, I took a career break while on maternity leave for a period of 11 months.



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Nombre: ROVIRA CLUSELLAS, MERITXELL
Referencia: RYC-2017-21950
Área Científica: Biomedicina
Correo Electrónico: meritxell.loris@gmail.com

Título:

Human, mouse and zebrafish adult pancreatic progenitors, from the organ to the plate

Resumen de la Memoria:

As a highly motivated and experienced investigator, I am seeking the opportunity to progress in my career as an independent researcher. After my PhD at IMIM and my postdoctoral training at Johns Hopkins University I built up the ability to use different systems and model organisms to help me answer research questions and test hypothesis. As my career has progressed I have focused my interests in pancreas development, especially in the study of embryonic and adult pancreatic progenitors either in homeostasis conditions or under regenerative models, such interest has been always linked to the understanding of pancreas development and to the study and development of new therapies for the treatment of pancreatic pathologies, specially diabetes and pancreatic cancer.

My ability to use different model organisms, such as mouse and zebrafish as animal models, as well as expertise in ESC culture and primary cultures of adult progenitors, such as organoids and pancreatospheres of mouse and human pancreas, helped me answer scientific questions broadly. In my last years as postdoctoral fellow I gained expertise in developing high throughput chemical screens in vivo and in vitro that will help me as well in the development of translational research projects to study new target drugs or small molecules for the treatment of human pathologies. While at Johns Hopkins I also gained expertise in imaging technologies allowing me to study pancreas development in zebrafish in vivo in real time. Lastly, I also gained expertise in the field of epigenetics and transcriptomics at Jorge Ferrer laboratory.

During my postdoctoral training I also had the opportunity to supervise several PhD students and I am actually the co-director of a PhD student thesis at IDIBAPS whose project will finish in 2018.

I was recently awarded a project "I+D+i para jóvenes investigadores sin vinculación o con vinculación temporal 2015 (SAF2015-73226-JIN) from the Spanish Ministry that allowed me to join the CMRB as principal investigator with my own research project focus in a comprehensive examination of transcriptional and epigenetic changes that occur in the pancreatic ductal population between embryogenesis and adulthood, this might aid in identifying the molecular mechanisms that restrict their differentiation potential in the adult organ. I propose that this developmental transition results from changes in cell autonomous genomic programs in concert with changes in the microenvironment or niche that regulates the balance between progenitor cell renewal and differentiation. The overarching goal of this project is to identify mechanisms that enable the reprogramming of adult pancreatic duct cells into pancreatic beta cells, thereby providing an avenue for regenerative medicine in Type 1 Diabetes.

In this research career stage my main goal is to progress as an independent principal investigator and be able to work with mouse, zebrafish and human samples to study pancreas development, pancreatic cancer and diabetes. In this context the use of zebrafish and mouse as animal models for regeneration studies together with the organoid model system will be great tools for the identification of the extrinsic signals that regulate pancreatic progenitor maintenance and differentiation as well as the perfect platform to test the functional significance of candidate regulators of multipotency.

Resumen del Currículum Vitae:

My scientific interest has been centered on the study of pancreatic progenitors in the adult pancreas, using ESC or adult pancreatic progenitors from mouse or zebrafish animal models, as well as in vitro culture models, such as, organoids derived from mouse and human ductal cells from cadaveric donors. My studies on pancreatic regenerative models have been always linked to the study and development of new therapies for diabetes and pancreatic cancer.

ACADEMIC DEGRESS

2001 Bachelor in Biology (University of Barcelona)
2007 PhD in health and life science (Pompeu Fabra University)

RESEARCH ACTIVITY

05/2007-08/2007 MRC Harwell, Postdoctoral training (Roger D Cox lab)
09/2007-10/2011 Johns Hopkins University-School of Medicine, Postdoctoral fellow (Steven D Leach lab and Michael J Parsons lab)
11/2011-10/2016 IDIBAPS, Postdoctoral fellow (Jorge Ferrer lab)
11/2016-02/2017 IRB, Research associate (Núria López lab)
02/2017-present CMRB, Principal investigator

AWARDS AND GRANTS



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Fellowships:

07/2002-07/2006 Becas Predoctorales de Formación de Investigadores (FPI)

09/2007-09/2010 Chicago Diabetes Project Postdoctoral Fellowship

17/10/2011-30/05/2015 BIOTRACK (co-funded project by the Marie Curie Actions of the 7th Framework Program of the European Commission and the IDIBAPS consortium) for the Professional Training and Career Development in Biomedicine.

Grant:

02/2017-02/2020 Proyectos de I+D+i para jóvenes investigadores sin vinculación o con vinculación temporal 2015 (JIN).

MENTORING

Director of doctoral thesis (ongoing since 2013): Student: Mar Armengol, University of Barcelona

Project: Chemical screen to identify new therapies for monogenic diabetes.

PATENTS:

Registered industrial property: Isolation, expansion, and guided differentiation of self-renewing progenitor cells from the adult human pancreas. Nº of patent: US 20140017207 A1

PUBLICATIONS: Below I have listed my most relevant publications as first or corresponding author:

1. Solomon Afelik* and Meritxell Rovira*. Pancreatic beta-cell regeneration: advances in understanding the genes and signaling pathways involved. *Genome Medicine*. 2017. Review. *Corresponding.

2. Solomon Afelik* and Meritxell Rovira*. Pancreas beta-cell regeneration: facultative or dedicated progenitors? *Molecular and Cellular Endocrinology*. 2017. Review. *Corresponding.

3. Rebecca L. Beer RL*, Michael J. Parsons, Meritxell Rovira*. Centroacinar cells: At the center of pancreas regeneration. *Developmental Biology*. 2016. Review. * Corresponding.

4. Meritxell Rovira*, Inês Cebola*; Santiago A. Rodríguez-Seguí*; Candy H.-H*. Cho; José Bessa*; et al.; TEAD and YAP regulate the enhancer network of human embryonic pancreatic progenitors. *Nature Cell Biology*. 2015. *Authors contributed equally to this work.

5. Meritxell Rovira et al.; Chemical screen identifies FDA-approved drugs and target pathways that induce precocious pancreatic endocrine differentiation. *PNAS*. 2011.

6. Meritxell Rovira et al.; Isolation and characterization of centroacinar/terminal ductal progenitor cells in adult mouse pancreas. *PNAS*. 2010.

7. Meritxell Rovira et al.; Murine embryonic stem cell-derived pancreatic acinar cells recapitulate features of early pancreatic differentiation. *Gastroenterology*. 2008.

PERIODS OF RESEARCH INTERRUPTION

Maternity leave: 01/2012-06/2012

Sick Leave: oncological treatment for several periods in 2014.



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Nombre: ROODVELDT CATELLANI, CINTIA
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Área Científica: Biomedicina
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Título:

Roles of aggregating proteins and molecular chaperones in the immune dysregulation linked to misfolding neurodegenerative disease

Resumen de la Memoria:

As a result of my PhD work (2000-2005) in the field of "protein structure and function" (The Weizmann Institute of Science, Israel), I contributed 6 articles, including 3 highly cited, seminal papers. I then performed a Postdoc (2006-2009) at Prof. Chris M. Dobson's lab (University of Cambridge, UK) having obtained a FEBS-LT Fellowship. During that period, I focused my research on the mechanism of molecular chaperones and their interaction with amyloid proteins linked to "misfolding" neurodegenerative diseases, and published 3 papers (e.g. Roodveldt et al., EMBO J. 2009 *CR corresp.). I was awarded with a Clare Hall Research Fellowship (Univ. of Cambridge, 2008) and with the "FEBS Distinguished Young Investigator Award" (2010).

In 2009, after maternity leave, I joined Dr. David Pozo's lab at CABIMER (Seville, Spain) and started a new line of research on alpha-synuclein aggregation and innate immunity dysregulation in Parkinson's disease" (3 arts. as 1st. author). Since 2011 ("Miguel Servet" Investigator, ISCIII), I have built an independent research group at CABIMER, which currently includes one PhD Student, one Postdoc, and one international Visiting Postdoc.

Since 2013, I have been PI of two MINECO grants (#SAF 2012-2015, and RETOS-Colab., 2015-2018). During this stage, I have produced 4 articles as senior-corresp. author (IID 2014; FASEB J. 2016; FASEB J. 2017; Glia 2018), and 6 articles in collab. (PNAS 2012; PLoS One 2013; PNAS 2015, Trends Mol. Med. 2016; Sci. Rep. 2017, Sci. Rep. in press). I have been PI of collaboration projects with biotech companies and registered 3 patents.

Currently, I hold an h index of 15 and 142 cites/art. in the last 5 years. I have obtained competitive funding as PI for ca. EUR 450,000. With a growing international visibility, I was Invited Speaker at the "International Congress on Neuroimmunology and Therapeutics" (SF, USA) in 2015, invited for a "Cold Spring Harbor Laboratory (CSHL) Meeting" (2016), and Invited Speaker at two International Meetings of the Center for Misfolding Diseases (CMD, Cambridge, UK; 2016, 2018). In addition, I was co-Organizer of a UNIA International Workshop (Baeza, Spain, 2016) together with Prof. J.M. Valpuesta (CNB, Madrid) and Prof. A.M. Cuervo (Albert Einstein College, New York).

Based on the scientific background I have developed within world leading groups as well as on my current scientific interests, my research lines focus on:

- 1) "Roles and mechanisms of aggregating proteins and chaperones in immune dys/regulation in the context of misfolding neurodegenerative disorders (Parkinson and ALS)".
- 2) "Immunotherapeutic potential of specific chaperones with immunomodulatory capabilities as a novel immunotherapeutic strategy against neurodegenerative "misfolding"/amyloid disorders".

Resumen del Currículum Vitae:

Current, Previous Position

- 01/2017-12/2019: "Miguel Servet II" Cat.A Researcher, ISCIII, MINECO.
- 01/2011-12/2016: "Miguel Servet" Researcher, ISCIII, MINECO
CABIMER-Andalusian Center for Mol. Biol. & Regener. Med., Seville, Spain

Education

- * PhD, The Weizmann Institute of Science, Israel (2006)
- * Lic. in Biotechnology. Univ. Nac. del Litoral, Argentina (1999)

Positions & Stays at Intern. Research Centers

- 2013, 2015: Visiting Scientist. 2+3m stays. Center for Neurologic Diseases (CND), Harvard Med. School (USA). Lab: Prof. FJ Quintana
- 2006-2009: Postdoctoral Research Associate, Univ. of Cambridge, UK. Lab: Prof. CM Dobson
- 2006: Visiting Postdoc. 1m-stay at Princeton Univ., USA. Lab: Prof. MH Hecht



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- 2000-2005: PhD Student. The Weizmann Institute of Science, Israel. Lab: Dr. DS Tawfik
- 2001-2002: Visiting Student (6m). Lab. of Mol. Biology (LMB), MRC, Cambridge, UK.

Research Grants as PI (compet.)

- 2015-2018: RETOS-Colaboración. MINECO. Coord.: nLife Therap., S.L. (Spain) €343,868
- 2012-2015: Proy. Inv. Fundam. No Orientada (SAF), MINECO. € 80,000

Publications

- articles: 26
- h index: 15
- cits./year (last 5y): 142
- 1st author: 9
- corresp. author: 5

*Publications in the journals:

- Glia (D1) (corresp. auth)
- FASEB J. (D1) (2016, 2017) (2x corresp. auth)
- EMBO J. (D1) (1st, corresp. auth)
- PNAS (D1) (2012, 2015)
- PLoS One (Q1) (x3)
- Biochemistry (Q1) (x2)
- Nature Gen. (D1)
- Sci. Rep. (Q1)
- Trends Mol. Med. (D1) (x2)
- Curr. Opin. Chem. Biol. (D1)
- Curr. Opin. Struct. Mol. Biol. (D1)

Invited Presentations (International)

- Inv. Speaker. V International Meeting of the Center for Misfolding Diseases (CMD, Cambridge, UK), 01/2018. Taormina, Italy.
- Inv. Speaker. IV and V International Meeting of the Center for Misfolding Diseases (CMD, Cambridge, UK), 11/2016. Seville, Spain.
- Inv. Speaker: UNIA International Workshop (Baeza, Spain), 19/10/2016
- Cold Spring Harbor Laboratory Meetings on "Protein Homeostasis in Health & Disease" (USA), 04/2016
- Inv. Speaker: International Congress on Neuroimmunol. & Therapeutics. San Francisco, USA. 22/07/2015

Supervised PhTheses & Academic Activities

- 22/05/2017: Adahir Labrador-Garrido (FPU). Mención Internacional. "Cum laude"
- 06/05/2016: Marta Cejudo-Guillén. "Cum laude"
- 2011-2018: Prof. Externo, Univ. de Sevilla
- 2013-2017: Prof. Ext. Univ. de Sevilla. Teóricas. Master en Biomedicina

Other Professional Activities

- >01/2018. Assoc. Editor: Front. in Neurosci.
- 12/2017: Guest Editor. Book.
- 10/2016. co-Organizer, UNIA International Workshop (Baeza, Spain)
- 2016-2017. Guest Editor: Front. Neurosci. (Switzerland)
- >01/2016. Member of Editorial Board: Imm. Inflamm. Dis.
- >2008. External Reviewer of Grant Projects: Parkinson's UK
- >2010. Prof. Externo, Univ. de Sevilla

Prizes, Fellowships & Awards

- 2017-2019. "Miguel Servet II". ISCIII, MINECO. (2016). Cat. 'A' (top 50%)
- 2011-2016. "Miguel Servet". ISCIII, MINECO. (2010)
- 2010. "FEBS Distinguished Young Investigator Award". FEBS. € 10,000
- 2009-2010. Programa "Juan de la Cierva". MINECO
- 2009. Programa "JAE Doc". CSIC
- 2007-2008. Clare Hall "Research Fellow". Clare Hall College, Cambridge, UK
- 2006-2009. FEBS Long-Term Fellowship. FEBS. Postdoc
- 2001-2005. "Rodolfo May" Fellowship Award. Feinberg Graduate School, Israel
- 2002, 2006, 2013. 3x EMBO Short-Term Fellowships. EMBO
- 1997-1998. Undergrad Research Fellowship (UNL, Argentina)



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Turno de acceso general

Nombre: SANZ REMON, JOAQUIN
Referencia: RYC-2017-23560
Área Científica: Biomedicina
Correo Electrónico: jsanz@bifi.es

Título:

Multi-scale approaches to Tuberculosis infection: mathematical epidemiology and functional genomics.

Resumen de la Memoria:

The study of the dynamics of TB infection through the lenses of Systems Biology and Mathematical Epidemiology has been the focus of my research since the beginning of my PhD, concluded cum laude in October 2014 at the University of Zaragoza. During my PhD, I focused on two main aspects of the Biology of TB: 1) the characterization of the gene-regulatory machinery of the bacterium from the perspective of networks theory and 2) the refinement of mathematical models of disease spreading, aimed at improving the description of cardinal features of TB such as its long latency times and its interactions with other diseases. My work during this period was published in 7 peer-reviewed articles (PRX, BMC Systems Biology, PLoS One, etc) and 1 book chapter.

Then, I moved to Canada to join Dr. Luis Barreiro's laboratory in the Hospital Sainte Justine (Université de Montreal) as a postdoc. Here, I focus on the analysis of genomic variation datasets to characterize the determinants shaping inter-individual differences in immune responses to infection. During my postdoc I published three high-impact co-first author articles where we have 1) characterized differences in immune responses between individuals of European and African ancestry (Cell, 2016), 2) used primate models to unveil the effects of social status on immune function (Science, 2016) and 3) showed that the TB vaccine BCG can be used to epigenetically reprogram hematopoietic stem cells that generate protective innate immunity in a way largely independent from the adaptive immune system, so challenging most classical views in TB immunology (Cell, 2018). My central role in these projects brought me solid experience in statistical methods and bioinformatics, which I successfully applied to the analysis of large genomic, transcriptomic and epigenomic datasets (bulk and single-cell RNA-seq, ChIP-seq, ATAC-seq). In this context, I engaged in two fruitful, still ongoing collaborations with the groups led by Drs. Jenny Tung (Duke University, Durham) and Maziar Divangahi (McGill University, Montreal).

Simultaneously, I supervise grad and undergrad students hosted both at my predoc and postdoc labs, including one PhD student whose dissertation will take place in 2018. In this role, I have recently published two articles, where we study the variation patterns in BCG efficacy across epidemic settings (PeerJ, 2016), and propose a new model for TB spreading on evolving demographic structures (PNAS, under 2nd round revision, co-last author), and at least three more will be submitted in 2018.

During my research trajectory (3 years since PhD), I have 13 peer-reviewed publications (10 as first/co-first or last/co-last author in Cell (x2), Science, PNAS, etc.), I have presented my work in 18 conferences and been awarded with most prestigious fellowships and awards, both at pre-doc (e.g. FPU fellowship, High-Performance-Computing HPC-Europa-2 award), and post-doc levels, (CIHR Banting fellowship). I have participated in 8 research projects competitively funded by different scientific institutions (European Commission, NIH, CIHR), I regularly work as reviewer for journals (PRL, PLoS One, Nat. Sci.Rep.), conferences (COMPLENET) and academic awards panels (CIHR PhD research prizes) and I have also taught several University courses and engaged in assorted dissemination activities.

Resumen del Currículum Vitae:

PRE-DOCTORAL EXPERIENCE AND EDUCATION.

- Undergrad studies in Physics (Universidad de Zaragoza, Licenciateship -2009- and Master -2010-)
- PhD in the Institute BIFI (University of Zaragoza, cum laude, international mention, October 2014).
- Research stages in Turin (ISI Foundation, 2011, 3 months) and Barcelona (UPC, 2012, 3 months).
- Awarded with 2 doctoral fellowships (FPI program, Government of Aragon (declined), and FPU fellowship, Ministry of Education) and several travel awards.

POST-DOCTORAL EXPERIENCE, FELLOWSHIPS AND AWARDS. The transition to my current lab led by Dr. Luis Barreiro, in the Hospital Sainte Justine (Montreal, Canada)- implied a radical interdisciplinary leap, from a research environment specialized in Physics of Complex Systems to a group led by a renowned Biologist and Genomicist focused on functional genomics of the immune system. This decision turned out to be extremely positive for the development of my career, as attested by my fast and solid publications record (see below), and my ability to get my work funded through a series of post-doctoral fellowships (Sainte-Justine foundation: 30K Canadian \$ (CAD), FRQNT merit scholarship for foreign students: 35K CAD, FRQS postdoctoral program for non-resident of Quebec: 60K CAD, first year declined). Among these achievements, the Banting postdoctoral fellowship I currently hold, granted by the CIHR (Canadian equivalent to NIH), is the Canadian most prestigious post-doctoral recognition (140K CAD for 2 years, application ranked 9 over 178, 24 granted). Starting



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June 2018, I will begin a double appointment between Sainte-Justine Hospital and the Genetics department at U.Chicago, where I plan to stay as a visiting scholar for a few months.

OTHER MERITS.

- ☐ Participant in 8 research projects funded competitively by Spanish institutions (total amount: 385K Euro), the European Commission (2 projects, 9.8M Euro), the NIH (1 project, 1.5 million US \$) and the CIHR, (2 projects: 1.6 million Canadian \$).
- ☐ Teaching experience (courses of Algebra and Computational Physics, academic years 2011-2012 and 2012-2013) and students supervision (2 bachelor and 1 master dissertations co-directed; 1 PhD student under co-supervision).
- ☐ Participant in the project on epidemiological participatory surveillance www.gripenet.es, aimed at monitoring flu incidence levels through the collection of periodic symptom reports from a community of volunteers. During the launch of the platform, I led the design of the website, generation of contents, and scientific dissemination tasks.

SELECTED PUBLICATIONS. During my still short research career (3 years since PhD), I have published a total of 13 publications (11 articles in indexed peer-reviewed journals, one book-chapter and 1 pre-print (under second round revision in PNAS: minor editions asked), 9 of them as first/co-first author, and 1 as co-last author, H-index=6), which accumulate 222 citations in the WoS. My 5 most relevant publications are the following:

- 1.Sanz, J. et al. Physical Review X, 4(4), 041005 (2014).
- 2.Kauffman, E. *, Sanz, J. *, Dunn, J. * et al. Cell 172, 176-190, January 11th, 2018.
- 3.Sanz, J. *, Navarro, J. * et al. . PloS one, 6(7), e22178, (2011).
- 4.Nédélec, Y. *, Sanz, J. *, Baharian, G. * et al. Cell, 167(3), 657-669 (2016).
- 5.Snyder-Mackler, N. *, Sanz, J. * et al. Science, 354(6315), 1041-1045 (2016).



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Turno de acceso general

Nombre: MARTIN MUÑOZ, ABRAHAM
Referencia: RYC-2017-22412
Área Científica: Biomedicina
Correo Electrónico: amartin@cicbiomagune.es

Título:

Neuroimaging of experimental stroke

Resumen de la Memoria:

The research applicant has focused his research on the study of the pathophysiology of cerebrovascular diseases as the ischemic stroke in rodents. The aim of his research has been to understand and visualize pathological processes as well as biological mechanisms that might be related with the functional recovery of this pathology over time by using non-invasive molecular imaging modalities. In order to achieve these purposes, the applicant has been familiarized with radioisotope techniques (positron emission tomography and single photon emission computed tomography), magnetic resonance imaging, computed tomography, optical imaging and ultrafast doppler ultrasound imaging. The applicant has provided valuable information in the field of the experimental stroke as follows; (i) the characterization of the in vivo spatiotemporal activation of the inflammatory reaction with both PET [11C]PK11195 and [18F]DPA-714, (ii) the in vivo evaluation of early Metalloproteinase expression using optical imaging after ischemia onset, (iii) the study of Lymphocyte-T depletion as a response to cerebral ischemia by using tomography optical imaging, (iv) the characterization of the early hyperperfusion phenomena as a result of ischemic conditions with both PET [15O]H₂O and SPECT [99mTc]HMPAO and (v) the evaluation of the dopaminergic and serotonergic neurotransmission role in the functional recovery following stroke with PET [11C]raclopride, [11C]DASB and [18F]altanserin. His track record and expertise in the molecular imaging field have allowed him to expand his research interests into the study of other brain pathologies as neurodegenerative and mental disorders. Likewise, the applicant has set up several collaborations in order to apply the potential of the nanobiotechnology into the diagnosis and therapy of the brain diseases. The current research lines of the applicant are focused in the neuroimaging of inflammatory processes after brain diseases. Despite the neuroinflammatory processes are relatively well understood, there is still a lack of effective anti-inflammatory strategies for the human treatment of brain pathologies. This fact is possibly due to the lack of knowledge of the spatiotemporal dynamics of microglial polarization after neuroinflammation. For this reason, the major aim of his research is to identify biomarkers for the in vivo visualization by molecular imaging of the pro-inflammatory and anti-inflammatory microglial subpopulations. There are many evidences that a large variety of neuroreceptors are over-expressed in activated microglia/macrophages and that their modulation might promote differential responses. There are many evidences that a large variety of neuroreceptors are over-expressed in activated microglia and that their modulation might promote differential responses. Therefore, the correct in vivo PET imaging characterization of the neuroreceptors in both microglial populations with specific radiotracers is essential for the establishment of novel tools to monitor and modulate neuroinflammation in neurological pathologies such as stroke. In summary, the identification of the spatiotemporal spectrum of neuroreceptors on microglial cells should be determining for the modulation of neuroinflammation and this knowledge may open new avenues on the diagnosis and therapy of all spectra of neurological diseases.

Resumen del Currículum Vitae:

Abraham Martin studied Biology at the Autonomous University of Barcelona (UAB). In 2002, the applicant spent three months at the University of California Los Angeles (UCLA), USA as visiting student. After this stay, he started his PhD at the Institute of Biomedical Research of Barcelona (IIBB-CSIC) under the supervision of the Dr. Anna M. Planas. During his PhD, the applicant worked as visiting scholar for six months in the lab of Dr. Jorge Ripoll at the Institute of Electronic Structure and Laser (IESL-FORTH), Greece. He received his PhD in 2007 and he moved to the Inserm Unit 803, Institut d'Imagerie Biomedicale (I2BM), Service Hospitalier Frederic Joliot, Commissariat à l'Énergie Atomique (CEA). The research applicant spent 29 months in the Professor Bertrand Tavitian's lab. In 2010, he joined the Molecular Imaging Unit at CIC biomaGUNE in San Sebastian, Spain. Recently, the applicant has been granted an Ikerbasque research fellow to carry his research between Achucarro-Basque Center for Neuroscience and CIC biomaGUNE.

The main research of the applicant has been focused on the study of the pathological processes underlying experimental stroke in rodents by using molecular imaging techniques. Likewise, during the last years the applicant has gained great experience in new applications of the nanotechnology to the biomedicine and molecular imaging fields. The contribution of the author to these research lines has been the publication of 38 papers in peer-reviewed journals and 2 book chapters providing the H citation number of 14 and 650 citations. The applicant has been the first author of a total of 14 papers, the corresponding author of 10 papers and 1 book chapter evidencing his capability of leadership, to carry out independent research plan and to take decisions.

The applicant has participated in several national and international projects as pre-doc, post-doc and research associate. During his stay at CICbiomaGUNE the researcher applicant has been the principal investigator of a regional (PI2011-3) and a national (SAF2014-54070-JIN) project grants. The research applicant has taken the responsibility for the intellectual leadership of research projects.

The researcher applicant has presented a total of 30 communications in national and international meetings from which a total of 8 were selected as oral and 22 as poster communications. In the year 2009, the applicant received the Young Investigator Award by the European Society of Molecular Imaging for the following study "Evaluation of the TSPO (18kDa)/PBR radioligand [18F] DPA-714 in a rat model of



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focal cerebral ischemia² at the 4th European Molecular Imaging Meeting in Barcelona, Spain. He also received the World Molecular Imaging Congress 2009 and 2010 Student Travel Stipend Awards based on the abstract score. Furthermore, the applicant has been invited to give 15 talks in national and international research institutes/universities.

The research applicant has set up several ongoing national and international research collaborations with Dr. Jordi Llop and Dr. Mónica Carril (CICbiomaGUNE), Prof. Carlos Matute and Dr. Maria Domercq (Achucarro), Prof. Ignacio Lizasoain (UCM), Dr. Teresa Iglesias (CSIC), Prof. Jean-Claude Baron (Saint Anne Hospital, France), Prof. Frédéric Dollé (SHFJ-CEA), Orsay, France) and Prof. Makoto Higuchi (NIRS, Japan). These collaborations have promoted the publication of 22 papers in in peer-reviewed journals during the last 5 years.



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Nombre: TORRANO MOYA, VERONICA
Referencia: RYC-2017-22295
Área Científica: Biomedicina
Correo Electrónico: vtorrano@cicbiogune.es

Título:

Transcriptional control of prostate cancer metabolism

Resumen de la Memoria:

I am a scientist with dedicated training and work of 16 years to cancer research and one central question has driven my career: how does transcriptional control influence biological events usually altered in cancer?

During my PhD at the University of Cantabria I worked in the field of leukaemia interested in the transcriptional control of myeloid differentiation and nucleolar transcription by CTCF. Along those years, I periodically visited Prof. Elena Klenova lab at the University of Essex (UK) allowing me to improve and diversify my knowledge on molecular and biochemical techniques, as well as the interaction with other scientists around the world. After defending my PhD, I was awarded with the Lady Tata International Award for Leukaemia Research aimed to develop a project as co-principal investigator (co-PI) in studying the interactions between CTCF and p27Kip1 in myeloid differentiation.

My training motivated me to further focus my research in the field of leukaemia and mutational alterations that alter the transcriptional landscape. In 2008, I joined as a postdoctoral researcher the lab of Prof. Mel Greaves (ICR, UK), a leading laboratory in the field of clonal evolution of childhood acute lymphoblastic leukaemia (ALL). In that stage of my career, being co-PI in my projects, I was interested in how the genetic events occurring in ALL control the survival of pre-leukemic stem cells through transcriptional reprogramming.

In 2011, I decided to continue my training in a path towards independence, and joined Dr. Carracedo's lab (CIC bioGUNE). I developed two main lines of research focused on (i) the transcriptional regulation of prostate cancer (PCa) metabolism and (ii) the development of non-invasive tools for PCa diagnosis based on gene expression. Emanated from one of my research lines, we have found a genetic signature that is able to stratify aggressive-PCa patients. This gene signature is protected under a European patent. As a collaborative team, I was involved in five additional projects studying (1) the transcriptional regulation of SOX9 by the protein PML; (2) the regulation of polyamine metabolism by mTOR; (3) the tumorigenic role of statins in PCa; (4) the tumor suppressor activity of PPARdelta in PCa and (5) the description of clinical methodologies to study PCa biology.

Since 2016 I lead a team formed by one postdoc, one PhD student, one bioinformatician and one technician. My current research lines are the stratification of aggressive PCa patients using a metabolic-transcriptional signature, and the study of EVs in the process of PCa dissemination and I have obtained 3 grants as PI to fund my projects. Importantly, I have established collaborations with experts in a broad range of areas, from clinical research to bioinformatics, which have been and will be key for my achievements.

I have been actively involved in directing PhD thesis (2), mentoring undergraduate students (1) and teaching in the UC/UPV Master in Molecular Biology and Biomedicine.

Overall, my combined years in national and international laboratories has given me a broad knowledge of different techniques, animal and cellular models, grant writing, manuscript preparation and student training and has provided me with the skills necessary to successfully apply them to my own line of research.

Resumen del Currículum Vitae:

I am a scientist with a background of more than 16 years of specialised research in cancer biology.

During my pre-doctoral training at the Universidad de Cantabria (Spain), my work in the field of transcriptional control of myeloid proliferation and differentiation in leukaemia were published in 5 articles (first author in Journal of Biological Chemistry and Journal Cell Sciences) and presented in 8 international meetings. After defending my PhD, I was awarded with the prestigious Lady Tata International Award for Leukaemia Research, to develop a project in which I was co-principal investigator (PI) and resulted in the publication of a research article.

In 2008 I joined the ICR (UK) as Postdoctoral Fellow. As first author, I published my work in Blood journal, presented it in two international meetings and I was invited as speaker in one national congress. I successfully obtained competitive funding as PI.

In 2011, I joined CICbioGUNE (Spain) and developed my own projects that have been the biggest achievements of my career and were published in 4 first-author research&review articles in journals such as NatureCellBiology. I was co-author in two scientific articles, published in NatureCommunications and Methods. I was awarded with EACR_Poster_Prize at the 15th ASEICACongress. I mentored younger scientist and co-direct the thesis of a PhD student.

Since September 2016, I'm an independent PI belonging to the Cancer Signalling and Metabolism Group (CICbioGUNE). I lead a team formed by one postdoc, one PhD student (the second I co-direct), one technician and one bioinformatician. I successfully got funding as PI from 3 public agencies and I have been invited to write a preview in CellMetabolism journal (first author) and a minireview in Frontiers (corresponding author). I'm first author in a review article (TEM) and corresponding author in a scientific article recently submitted. As a



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result of my co-working spirit and the establishment of highly-productive collaborations I've been co-author in four research articles published in Nature, CancerResearch, Hepatology and Oncotarget, and three additional ones that are submitted or under review in NatureMedicine, MolecularCancerTherapeutics.

Overall, I have a very good publication record with a total of 15 primary research papers, 5 reviews/preview and 4 additional papers that are submitted or under review. Among my publication record, I'm first author in 9 of them and corresponding author in two. My work has been presented in 18 international meetings, I'm inventor in a registered European patent and I have been invited to present my work in 3 international institutions. I have co-directed the thesis of two PhD students, obtained funding as PI for 3 projects and lead a 4-people-team (1)focus on the crosstalk between transcription and metabolism during cancer progression and (2)committed to scientific dissemination.



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Nombre: MUÑOZ MANCHADO, ANA BELEN
Referencia: RYC-2017-22594
Área Científica: Biomedicina
Correo Electrónico: abemuman@gmail.com

Título:

Neuronal diversity in cortex and striatum and role of striatal interneurons in Parkinson's disease pathology

Resumen de la Memoria:

I started my research career with a work, as an undergraduate student, focused in the regulation of the carotenogenesis in the fungus *Phycomyces Blakesleeanus* (2002-2004).

But I promptly became interested in the Neuroscience field that I found very attractive and challenging for its complexity and proximity to the core of human existence. For that, I continued my research with the PhD Project "Trophic action of intrastriatal carotid body transplants in a systemic and chronic parkinsonian mouse model and its therapeutic implications" awarded Summa Cum Laude (2011). As a PhD student I developed a chronic and robust toxic parkinsonian mouse model that was of great use to investigate different aspects of the neuroprotective action of the antiparkinsonian cell therapy based in striatal carotid body transplants, that was also part of my thesis project. This model is still being used in other research lines with different purposes (For instance, Pérez-Villalba et al 2017).

In 2012 I started as a postdoc in Karolinska Institutet. During these years I have investigated the neuronal diversity of brain structures as striatum, hippocampus and cortex. That research comprised the set up and use of the novel technique RNA single cell sequencing, that results in the individual transcriptome of each cell. I described new interneuron classes and a huge dataset that includes novel molecular markers for the described cell types and unexpected hierarchical modular arrangements of gene expression. My recent work (under review in Nature Neuroscience) has a special focus in the striatum where I first described a new interneuron population that I further continued investigating with a combination of RNA sequencing and electrophysiology (using another novel technique, Patchseq), that allows to link the molecular and firing properties of the cell. I am also currently working in a collaborative work with Mats Nilsson's lab using the in situ sequencing technique that they developed to investigate the detailed distribution of 100+ molecular identities (revealed by the single cell sequencing data) in tissue in a single experiment. This technique allows for cheap, high throughput screening not only in mouse but also in patient material in a way that is not feasible through single nuclei sequencing. This allows to translate the findings into the human system.

My work from the thesis and postdoc period resulted so far in 9 publications in prestigious journals as Science, Cerebral cortex, Journal of neurochemistry, Neurobiology of aging and Journal of Neuroscience among others (total number of citations: 751, h index 7), holding first authorship in 4 of them.

The striatum and cortical datasets have being also of great use in different projects whose results are starting to get published (Nguyen HT et al 2017, Genome Medicine; Skene N et al bioRxiv doi: <https://doi.org/10.1101/145466>, 2017; Savage J.E. et al bioRxiv doi: <https://doi.org/10.1101/184853>, 2017).

I have being awarded with a competitive starting grant from the Swedish Research Council, which will allow me to start my own research line, where I will be focusing on the molecular pathways in the striatum triggering the onset and development of Parkinson's disease.

Resumen del Currículum Vitae:

In 1999 I started my studies in Biology at University of Seville. During this time (1999-2004) I began my research career with the project "Regulation of the carotenogenesis in the fungus *Phycomyces Blakesleeanus*" in the Genetics department, supervised by full professor Enrique Cerdá Olmedo. For this project I was awarded with the fellowship from the Ministerio de Ciencia e Innovación.

In 2004 I became a PhD student in the Medicine School, University of Seville, under the supervision of full professor Juan J. Toledo Aral. For this period I was awarded with the pre-doctoral fellowship FPU from the Ministerio de Ciencia e Innovación. On 27th July 2011 I defended my thesis titled "Trophic action of carotid body transplants in a chronic and systemic parkinsonian mouse model. Therapeutic Implications" awarded with Summa Cum Laude. I actively participated during this time in official teaching at the University, both in laboratory work and lectures, in different degrees as Odontology, Medicine, Nurse Diploma and Physiotherapy Diploma.

In 2012 I started a postdoc position in Hjerling-Leffler lab, Karolinska Institutet, Stockholm. Since then I have been investigated the diversity



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in the neural populations of different brain areas as cortex and striatum. For that purpose I have taken advantage of very novel and sensitive techniques as RNA single cell sequencing, in situ sequencing and patchseq.

Publications:

- Nguyen HT et al 2017, Genome Medicine
- Pérez-Villalba et al. 2017, Journal of Neuroscience
- Muñoz-Manchado et al. 2016, Journal of Neurochemistry
- Muñoz-Manchado et al. 2016, Cerebral Cortex
- Marques et al. 2016, Science
- Nikouei et al. 2016, Journal of chemical neuroanatomy
- Zeisel and Muñoz-Manchado et al. 2015, Science
- Muñoz-Manchado et al. 2013, Neurobiology of Disease
- Ortega Saenz et al. 2013, The Journal of Physiology
- Rodríguez-Pallares et al. 2012, Regenerative Medicine

Total number of citations: 751

h index: 7

i10 index: 6

I am currently participated as a teacher in the Biomedicine degree, in Karolinska Institutet.

Regarding conferences I have been very active since I started my PhD attending and presenting my work in national and international meetings as Neuroscience, FENS forum, IBAGS, Cortical Development among others and in different years.

I am currently in the process of starting my own research line. I have been awarded with the prestigious starting grant from the Swedish Research Council. My goal is deciphering the transcriptional changes that take place in the striatal cell populations in parkinsonian mouse models and patients. I already attended the EMBO Laboratory Management Course "The art of leadership" that took place last June (2017) in Alicante, Spain.

I have been official supervisor of the bachelor student Alexandra Kouznetsova with the project "Striatal neuronal populations revealed by single cell sequencing and in situ sequencing" and I am currently an official supervisor of the PhD student Carolina Bengtsson with the project "Striatal GABAergic interneuron diversity, from characterization to function".

I have also being very active in other scientific aspects including science dissemination, as an active member of the Karolinska Postdoc Association and StratNeuro.



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Turno de acceso general

Nombre: FEMENIA CANTO, TERESA
Referencia: RYC-2017-22666
Área Científica: Biomedicina
Correo Electrónico: tefemenia@gmail.com

Título:

Mecanismos y dianas terapéuticas en las alteraciones emocionales y en el deterioro cognitivo.

Resumen de la Memoria:

My research trajectory has dedicated on determining the molecular mechanisms underlying neurological alterations in animal models of psychiatric diseases, with emphasis on emotion and cognition. By combining a wide range of approaches, which include behavioral, pharmacological and molecular techniques in rodent models of psychiatry for addressing the fundamental alterations on specific brain systems as well as the associated signaling pathways.

During my doctorate at Dr. Manzaneres' group at the Neuroscience Institute of Alicante I was involved in several projects centered on the role of opioid and cannabinoid system in animal models of neurologic and psychiatric diseases and the action of drugs used for their treatments.

In January 2011 I moved to Sweden (Stockholm) to start my postdoctoral research at the Neuroscience Department- Karolinska Institute (KI) in the laboratory of Dr. Maria Lindskog. My research focused in the study of the mechanisms underlying depression and the cognitive deficits associated. Further, I became interested on the interaction between the periphery and central nervous system and how the activity of specific brain circuits involved in the regulation of emotion and behavior can be regulated from the periphery. Thus, at the same time I was part of the group of Dr. Jorge Ruas at Physiology and Pharmacology department-KI (FyFa). I investigated the mechanisms whereby physical exercise protects from depression considering the interaction between brain and muscle.

Thereafter, motivated by the interaction between the immune system and the brain, in a recent project carried out at the Dr. Diaz-Heijtz group at the same Neuroscience department I have been studying the impact of innate immunity alterations in brain systems and behavior (emotional and social) focusing in the role of Toll-like receptor-4. Along the same lines, in collaboration with Dr. Gomez-Galan, (at the group of Prof. Lars I Eriksson (FyFa)) in a current project I am studying how an immune activation and subsequent inflammation in the periphery triggered by a surgical trauma is related to a cognitive decline (known as post-operative cognitive decline-POCD) and dementia later in life. Hence, targeting master regulatory pathways within glutamatergic signaling, innate immunity and inflammation involved in central nervous system complications after a surgical trauma. In April 2017 I obtained by merits an Assistant Professor position in neuroimmunology with focus on behavior and cognition at the department of Physiology and Pharmacology-Section of Anesthesiology and Intensive Care, KI.

Resumen del Currículum Vitae:

Current position

Assistant Professor since April 2017 at the department of Physiology and Pharmacology, C3, Eriksson I Lars group - Section of Anesthesiology and Intensive Care, Karolinska Institutet, Stockholm, Sweden

Undergraduate studies

In 2006, I obtained the bachelor in Pharmacy and in 2012 the bachelor in Biochemistry at the Miguel Hernandez University-Elche in Spain.

In March 2010, I defended my Doctoral Thesis at the Neuroscience Institute of Alicante-Miguel Hernandez University, Spain, under the supervision of Dr. Jorge Manzaneres. Thesis Title: Role of prodynorphin gene in the mechanisms regulating the emotional responses and their implication in alcohol dependence.

Post-doctoral experience

In January 2011, I moved to Stockholm in Sweden at the Karolinska Institutet (KI), Neuroscience Department, in the laboratory of Dr. Maria Lindskog. In this laboratory, I developed several projects dedicated to investigate the mechanisms underlying depression and the cognitive deficits associated. At the same time, I was affiliated at the Pharmacology and Physiology department at KI in Dr. Jorge Ruas' laboratory.

In July 2013, I joined Dr. Diaz-Heijtz group at Neuroscience department-KI to investigate the impact of innate immune alterations in emotional and social behaviors with special interest in the role of Toll-like receptor-4.

In October 2015 I became part of the group of Prof. Lars I Eriksson, Section for Anesthesiology and Intensive Care at Karolinska University Hospital/Physiology and Pharmacology department-KI, to investigate pivotal mechanisms linked with the innate immunity and inflammation underlying postoperative impairment of brain functions related to cognitive performance.

Experimental skills

I have gained considerable experience in the use of animal models for neuropsychiatry disorders and have a significant track record in animal behavior, histological and molecular techniques for gene expression studies and protein analyses. I developed and used chronic implants and local drug delivery methods into specific brain areas to quantify evoked pharmacological responses in the awake and behaving animal.



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Teaching and student supervision

Between 2007-2009, I taught at the University Miguel Hernandez and now I am currently taking part in the teaching program in the Physiology and Pharmacology department for the Biomedicine bachelor and Optics bachelor at the Karolinska Institutet, while also providing supervision to a number of under- and post-graduate students in their research activities.

Scientific records

I have received 3 project grants in open competition to finance and direct my individual research. I have published 18 articles (9 first author, 1 corresponding author, 3 reviews, 1 book chapter) and other 2 manuscripts are in preparation, and have a total of 27 international conference contributions.



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Turno de acceso general

Nombre: CRUZ ADALIA, ARANZAZU
Referencia: RYC-2017-21837
Área Científica: Biomedicina
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Título:

Function of "Innate Lymphoid cells" in cancer and infectious diseases for future applications in biomedicine.

Resumen de la Memoria:

My scientific career is focused on the study of the immune system regulation. I obtained a competitive contract [FPU] (2005-2010) to perform the PhD at Dr. Sánchez-Madrid laboratory ([Hospital de la Princesa] and [CNIC]; Madrid). My research work was focused on identifying the ligand/s of CD69, which remained elusive for more than 25 years, and the study of its role in the immune response in vivo during the development of different autoimmune diseases. These studies were published in the journal of highest impact factor of Cardiology Area (Circulation) as a first author (I.F: 19,3), and in other top journal of Molecular and Cellular Biology Area, as co-first author (Mol Cell Biol. I.F: 5,3). I performed two stays abroad to develop my projects, one at Institute of Immunology (Vienna; AUSTRIA) for 6 months and other at [Center for Allergy and Immunology] (Tokyo; JAPAN) for 2 months. I defended my thesis in 2010 and I graduated magna cum laude from Universidad Autónoma de Madrid (UAM) and obtained the Extraordinary Doctorate Award.

Afterwards, I was awarded with a competitive postdoctoral contract "Juan de la Cierva" (2012-2015) to join the laboratory of Dr. Veiga at CNB/CSIC (Madrid), where I performed a very challenging project discovering that T cells could capture bacteria by transinfection from infected dendritic cell during antigen presentation. These results were published in a high profile journal of the Microbiology and Parasitology area, as first author (Cell Host & Microbe. I.F: 14,9).

Later, I got a very competitive project [Project for young investigators] as Principal Investigator (PI) financed by Ministerio de Economía y Competitividad in 2015 (CNB/CSIC; Madrid). The project is focused on the characterization of T cells as antigen-presenting cells, although they belong classically to the adaptive immunity compartment. We have demonstrated that conventional CD4+ T cells, after bacteria engulfment and digestion, were able to present bacterial antigens to CD8+ T cells, which massively proliferate and become cytotoxic. CD4+ T cells-mediated antigen presentation in vivo induced the generation of central memory CD8+ T cells with interestingly low levels of PD1. Moreover, we have showed that transphagocytic CD4+ T cells induced strong protective anti-tumor immune response. All these data have been published in a top journal, in which I sign as first and corresponding author (Cruz-Adalia et al. Nature Communications. IF: 12,1). Currently, I have been doing a stay in the Dr. Eric Vivier laboratory at Aux-Marseille Université (FRANCE). I have started an ongoing collaboration project focused on the function of the new characterized type of cells called "Innate lymphoid cells" (ILCs). The project is focused on the function of ILCs during infectious diseases and cancer. ILCs are the innate counterparts of T cells and their functions are still being characterized in homeostasis, during infections, inflammatory diseases or cancer. Eric Vivier laboratory was one of the first groups that have recently characterized both human and mouse ILCs. This opportunity has improved my skills in a new and very promising research field and has allowed me to continue my own project as PI.

My professional aim now is to continue this translational research that could represent a step forward in immunology and biomedicine.

Resumen del Currículum Vitae:

I studied the degree of Biochemistry at University Autónoma de Madrid (UAM) and I graduated with honors in 2003. Then, I obtained a competitive contract from Ministry of Science (Formación de Personal Universitario, FPU) in 2005 to perform the PhD at Dr. Sánchez-Madrid laboratory (Madrid, SPAIN), where I published in several top journals in the area of cellular biology and biomedicine; as a first author in Circulation (I.F: 19,3), and Mol Cell Biol.(I.F: 5,3). During this period, I performed two stays abroad to develop my projects; one was in Vienna (AUSTRIA) for 6 months and the other one was in Tokyo (JAPAN) for 2 months. I graduated magna cum laude and I obtained the Extraordinary Doctorate Award at Facultad de Medicina (UAM) in 2010.

Afterwards, I was awarded with a competitive postdoctoral contract "Juan de la Cierva" financed by [Ministerio de Economía y Competitividad] in 2015, to join the laboratory of Dr. Esteban Veiga (Madrid; SPAIN), where I published my work in a top journal, as first author, Cell Host and Microbe (I.F: 14,9). In parallel to my research work, I continued my formation, studying the degree of Biology at University Autónoma de Madrid and I graduated with honors in June 2013.

Later, I got a very competitive project [Project for young investigators] as Principal Investigator (PI) financed by [Ministerio de Economía y Competitividad] in 2015 (Madrid, SPAIN) for 3 years, which allowed me to fund my own project. Some data of this work have been recently published in a prestigious top journal, where I sign as first and corresponding author (Nat. Commun., I.F: 12,1). These data have been the basis for a patent (Application. Nº: P201531177) protecting the use of tpCD4+ T cells as novel agents in anti-tumor



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immunotherapy. We have also published a methods paper showing the protocol of T cell transinfection (Cruz-Adalia et al. J Vis Exp; IF: 1,232; 2016) and a review paper discussing recent published data demonstrating that the strict separation has blurred by the discovery of lymphoid cells behaving in an innate-like manner (Cruz-Adalia et al. Front Immunol; IF: 6,429; 2016), in which I sign as first and corresponding author.

During this period, I have supervised, as co-director, the Doctoral Thesis of Guillermo García Santiago who has graduated magna cum laude at UAM in 2017.

Currently, I have got an EMBO fellowship from Europe Grants and "Estancias José Castillejos" financed by "Ministerio de Economía y Competitividad" to perform a stay for almost one year in the laboratory of Dr. Eric Vivier at Centre d'Immunologic de Marseille-Luminy and Hôpital de la Timone (CIML, Marseille, FRANCE). There I started an ongoing collaboration project focused on the function of a recently characterized type of cells called "Innate lymphoid cells" in September 2017, which has been a great opportunity for me to improve my skills in a new and very promising research field. This year, I will apply for Europe ERC Starting Grants, to get financy to continue this exciting project as PI.



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Nombre: MORENO GONZALEZ, INES
Referencia: RYC-2017-21879
Área Científica: Biomedicina
Correo Electrónico: ines.m.gonzalez@uth.tmc.edu

Título:

Risk factors for Alzheimer's disease. Effect on neuropathology development and molecular mechanisms.

Resumen de la Memoria:

I performed undergraduate and graduate studies in the Alzheimer's disease field, specifically focused on the characterization of transgenic mice models of Alzheimer's at the University of Malaga (Spain). My main research topics involved amyloid-beta deposition, neuronal loss and inflammatory processes related with the onset and progression of the disease, and the study of biomarkers needed for early diagnosis. This work provided a detailed characterization of a new animal model for the disease and the identification of potential biomarkers of disease progression to be used in preclinical studies and drug screening. In fact, two of these biomarkers are currently being used by Sanofi in its screening program for novel AD drugs. During my PhD, I was trained in tauopathies at the Dept. of Neurological Diseases Research in Sanofi (France).

I performed my postdoctoral research training at The University of Texas Health Science Center at Houston (UTHealth) under the supervision of Dr. Claudio Soto and I performed a short training on organotypic slice culture in the Institute of Bio-Engineering (Switzerland) with Dr. Luc Stoppini. I focused my postdoctoral research on analyzing AD transmissibility and risk factors of AD, including smoking, meat consumption and diabetes. In 2013, we published in Nature Communications (IF:12.12) how cigarette smoke can affect AD pathology in transgenic animals. We successfully showed for the first time that inhalation of environmental tobacco smoke can play a major role in AD onset and development by increasing the probability to develop the disease, to initiate a faster and earlier pathology, and to worsen the symptoms. When these results are translated into humans, an active smoker could double his or her risk of developing the disease up to 10 years before a non-smoker.

In addition, after careful analysis of the brain of more than hundred animals, I have found that aging cattle develop amyloid plaques and neurofibrillary tangles in a similar way as humans affected by AD. To determine whether exposure to diseased animal tissue can accelerate AD progression, I administered this material to transgenic animal models of AD. These studies determined that brain inoculation of cow brain harboring amyloid aggregates can accelerate AD neuropathology in vivo. The results of this study have been submitted to Nature Communication and are currently under review with me as a first and corresponding author.

Furthermore, we have demonstrated that type 2 diabetes may potentiate AD pathology through cross-seeding of misfolded proteins, increasing the coexistence of both diseases. This data generated during my postdoctoral training and the first two years as an assistant professor was published in Molecular Psychiatry (IF:13.2).

Currently, I am an Assistant Professor in the Department of Neurology at UTHealth. My independent program, funded by the USA Department of Defense and the Alzheimer's Association as principal investigators, focuses towards the effect of traumatic brain injury in protein misfolding aggregation and its implication in Alzheimer's pathology and chronic traumatic encephalopathy, both in vitro and in vivo, combined with several strategies to monitor the brain damage and its development into a tauopathy, including PET imaging techniques to detect misfolded proteins and the associated neuroinflammatory process.

Resumen del Currículum Vitae:

Regarding education, I got a Bachelor's degree in Biology by the University of Malaga in 2003. In 2009, I obtained my PhD degree in Cellular and Molecular Neuroscience at The University of Malaga (UMA). From 2010 to 2013, I performed my postdoctoral training at The University of Texas Health Science Center at Houston (UTHealth) and I become Assistant Professor of Neurology in 2013. I have been trained as an invited trainee in Sanofi Aventis (Paris, France), the University of Seville (Spain), and the Institute of Bio-Engineering (Geneva, Switzerland). I have attended more than 50 specialized training courses in neuroscience, and 5 in teaching and mentoring. I am also currently enrolled in a course for faculty leadership development.

Concerning honors and awards, I have several editorial positions. I have been appointment as a review editor for Frontiers in Aging Neuroscience, and I am ad hoc reviewer in several international journals, including Acta Neuropathologica and Alzheimer's & Dementia. I serve in the grant review panel for the Alzheimer's Association and the Arizona Biomedical Research Commission. I have received 14 different travel awards, some of them very competitive both in Europe and internationally.

In terms of publications, I have 25 peer-reviewed publications, including 20 original articles, and 5 review publications. Almost all of them are in Q1 quartile. In 5 of them I am the first author. My top articles are published in Molecular Psychiatry (2 of them, one as the first author; IF:13.2), Nature Communications (first author, IF:12.12), Journal of Experimental Medicine (IF:11.99), and Acta Neuropathologica (IF:12.21). My publications have been cited more than 1,000 times, providing me an H-index of 13. I currently have 7 publications pending: 2 under review (in Nature Communications (first and corresponding author, IF:12.12) and Nano Today (IF:17.47)) and 5 in preparation. Out of them, I am the senior author in 5 and the first author in 2.

With respect to teaching and mentoring, I am the course director on a PhD and a postdoctoral program at UTHealth. In both of them, I



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have developed the course syllabus. I participated in other 12 different courses in bachelor, master's and PhD programs, and I have been a teaching assistant for more than 6 years at UMA. I have mentored 3 PhD students, 1 Master's, and I have participated in the advisory committee and PhD committee of several PhD students. In addition, I have trained more than a dozen of rotation and graduate students. I have been able to secure funding for my research program on risk factors for Alzheimer's disease. I have obtained almost \$1,000,000 in total funds as the principal investigator of two grants from the prestigious Alzheimer's Association junior independent investigator program and the highly competitive USA Department of defense. I am also collaborator in 3 grants from the National Institutes of Health. In terms of dissemination of my results, I have attended 17 international meetings, given 5 oral communications, and have almost 70 abstract communications in poster format. I have been invited to national and international institutions to provide 11 invited talks, and have 11 media presentations in TV, online press, and radio in USA, including the FOX channel.



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Nombre: ROTLLAN VILA, NOEMI
Referencia: RYC-2017-22879
Área Científica: Biomedicina
Correo Electrónico: noemirotlan@yahoo.es

Título:

Identification and characterization of novel mechanisms by which cholesterol and lipoprotein metabolism are regulated in order to develop therapeutic approaches to treat cardiovascular diseases.

Resumen de la Memoria:

Through my career I have been interested in research related to biomedicine and cell biology, with emphasis in lipoprotein metabolism and cardiovascular diseases.

As a graduate student in Dr. Francisco Blanco-Vacalés laboratory in Hospital de la Santa Creu i Sant Pau in Barcelona, I was classically trained in experimental biochemistry and molecular biology, obtaining an expertise in the field of lipoprotein metabolism, specifically the high-density lipoprotein (HDL) and atherosclerosis susceptibility using different models of transgenic mice. I had described in different manuscripts the importance of ApoAII, CETP, ABCA1 and ABCG5/G8 in controlling reverse cholesterol transport (RCT), a physiological process by which HDL removes cholesterol from injured arteries and transports it back to the liver for elimination. Overall, these studies led to the publication of 14 research articles (4 as a first author) and 1 review. I was fully funded for the majority of my time as a graduate student having been awarded with one predoctoral fellowship

In my first year as a postdoctoral Fulbright fellow in the laboratory of Dr. Edward Fisher in NYU, I had the opportunity to learn his pioneered animal models in which we can stimulate the plaques in the arteries to regress, as well the laser capture microdissection technique. After this short postdoc, I had joined Dr. Carlos Fernández-Hernando laboratory, first in NYU and then at Yale University. From 2012 to 2014 I was awarded with a postdoctoral fellowship. My research had focused in studying the role of miRNAs in regulating lipoprotein metabolism and the progression of atherosclerosis. I had investigated the role of miR-33, a key miRNA regulator in cholesterol metabolism, in regulating RCT and the progression of atherosclerosis. I demonstrate that the anti-miR-33 therapy protects against the progression of atherosclerosis (ATVB 2013). In addition to the microRNA field, I also had developed two side projects, which aimed to elucidate the role of two different protein kinase B, AKT1 and AKT2, during the progression of atherosclerosis (Circ. Res 2015, FASEB 2015). In 2014, I was promoted to Associate Research Scientist, a faculty position at Yale University School of Medicine. Moreover, I define the contribution of Akt during hepatic regeneration. I found that absence of Akt1 or Akt2 does not influence liver regeneration after partial hepatectomy and the Akt-FoxO1 signaling pathway is essential for proper liver regeneration (Hepatology 2016) In addition to these studies, I had been a key contributor of seminal studies that have uncovered the role of non-coding RNAs in regulating lipoprotein metabolism and the progression of atherosclerosis (Nat Med, Nat Commun, EMBO Mol Med, Cell Reports)

My training and background has provided me with extensive experience and immersion in the fields of lipid metabolism and vascular biology. Most recently I was awarded with the prestigious Scientific Development Grant from the American Heart Association where I am the principle investigator. As an independent investigator, my research focuses on the identification and characterization of novel mechanisms by which cholesterol and lipoprotein metabolism are regulated in order to develop therapeutic approaches to treat cardiovascular diseases.

Resumen del Currículum Vitae:

In order to pursue my scientific career I move to New York University and Yale University to perform my postdoctoral research (2010-2014) with Dr. Edward Fisher the first year, and then with Dr. Carlos Fernández-Hernando. I was promoted as an Associate Research Scientist in 2014 a faculty position at Yale University School of Medicine. Through my career I have been interested in research related to biomedicine and cell biology, with emphasis in lipoprotein metabolism and cardiovascular diseases. As an independent investigator, my research focuses on the identification and characterization of novel mechanisms by which cholesterol and lipoprotein metabolism are regulated in order to develop therapeutic approaches to treat cardiovascular diseases.

Scientific Production

I have co-authored a total of 46 scientific publications, 39 research articles and 7 invited reviews. From this 39 research articles, 8 of them I was first author (4 of them during my PhD), 9 of them I was second author and 13 of them I was the third author. The first author papers are in high profile peer-reviewed scientific journals: Hepatology (IF:11,7), Circ Res (IF:11,5), Arterioscler Thromb Vasc Biol (2) (IF:5,5), FASEB (IF:5,2), Atherosclerosis (IF:4,6), Biochim Biophys Acta (IF:5,0) and J.Lipid Res (IF:4,4). As well the ones as a second author: Nat Med (IF:30,3), Nat Commun (1) (IF:12,1), EMBO Mol Med (2) (IF:9,2), Cell Reports (1) (IF:8,2) among others.

Total number of citations: 1500 in Google Scholar, since 2013 the total number of citations is 1225. H-index is 22

Author of 14 communications in several congresses at international level (8) and national level (SEA)



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Honors, Awards and Fellowships

I had been awarded with a pre-doctoral and postdoctoral fellowship (MEC and Fulbright). More recently I was awarded with the very competitive Scientist Development Grant as an independent researcher (AHA) (17SDG33110002) Amount \$231.000

Reviewer activities

-Journal Reviewer: Disease Markers, Molecular and Cellular Biology, PLOS ONE, Nutritional Neuroscience, Experimental Cell Research, Molecular Immunology, Advances in Nutrition, GENE, Journal of Molecular and Cellular Cardiology

-Review Editor: Cardiovascular Genetics and Systems Medicine



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Nombre: GUASCH CAMELL, JUDIT

Referencia: RYC-2017-22614

Área Científica: Biomedicina

Correo Electrónico: jguasch@icmab.es

Título:

Multifunctional Materials for Technological and Biomedical Applications

Resumen de la Memoria:

The research career of the candidate has been focusing on the design, synthesis, and development of novel multifunctional molecular and polymeric materials based on supramolecular structures with technological and biomedical applications.

The candidate performed a truly multidisciplinary research during her PhD designing, synthesizing, and characterizing molecular and supramolecular materials based on stable organic radicals. The main accomplishments of this research were the elucidation and tuning of intra- and intermolecular interactions of multifunctional molecular materials based on self-synthesized electron donor-acceptor dyads to generate specific responses. For example, the bistability phenomenon of organometallic dyads was analyzed and experimentally tuned in solid state, which could lead to versatile memory devices. Moreover, switchable supramolecular structures which, if self-assembled on surfaces, behave as unimolecular rectifiers, were also produced. Additionally, the candidate was involved in a project in which she correlated the electronic and cytotoxic properties of certain anticancer molecules, thus establishing a method to further produce new efficient dyads to eliminate cancer cells. This experience opened a new horizon for her and she decided to apply her knowledge in multifunctional materials to tackle biomedical challenges, especially those related to cancer research.

With this objective, her postdoctoral research was targeted the cell-material interface, developing nanostructured surfaces to elucidate mechanisms related to metastasis and creating tools for novel cancer immunotherapies to treat malignancies with poor prognosis. On the one hand, she developed several surface chemistry strategies to elicit specific responses such as cell adhesion and migration, which were used to shed light on integrin-related mechanisms of metastasis. On the other, she designed and prepared tools for novel cancer immunotherapies. Such therapies are achieving encouraging results but suffer from technical challenges that prevent their broader use in clinics, such as the production of large amounts of T cells in vitro. To overcome this limitation, different strategies to expand T cells using nanostructured surfaces and costimulatory agents were designed that outperform the current state-of-the-art expansion techniques. For that, the candidate acquired first-hand knowledge and experience in cell culture, biophysics, immunology, and cancer, expanding even further her multidisciplinary background and research. Acquiring and applying all this new knowledge and toolset has impacted her immediate publication record, but opened a vast territory of multidisciplinary research that she is currently unraveling.

More specifically, the candidate is focusing her research career in the field of multifunctional materials and tissue engineering for cancer immunotherapy. Her work revolves around the design of biomimetic lymph nodes based on supramolecular structures. In this project, she combines her expertise in supramolecular chemistry, gained during her PhD, with the biomedical experience that she acquired in her postdoctoral research; thus bringing to the Spanish research system new horizons, which are already contributing to boost the new Multifunctional Nanostructured Biomaterials research line of her current institution.

Resumen del Currículum Vitae:

The candidate was initiated to research through an internship in Prof. Albericio's group (Scientific Park of Barcelona) when she was a BSc student (University of Barcelona). Her work in peptide synthesis contributed to 1 article (Eur. J. Org. Chem. 2005) and 1 proceeding.

She then accepted a JAE predoctoral grant (CSIC) to perform her PhD at the Institute of Materials Science of Barcelona (ICMAB-CSIC), under the supervision of Prof. Veciana and Dr. Ratera, elucidating and tuning intra- and supramolecular interactions of multifunctional materials based on dyads for technological and biomedical applications. The candidate co-authored 10 publications (* indicates first author): J. Am. Chem. Soc., 2008; CrystEngComm, 2009; *Chem. Mater., 2013; J. Phys. Chem. B, 2009; *Angew. Chem. Int. Ed., 2012; *J. Amer. Chem. Soc., 2013; J. Phys. Chem. Lett., 2013; J. Phys. Org. Chem., 2014; *Acta Cryst., 2013; J. Org. Chem., 2011) and presented her results in 7 national and international conferences. Moreover, she experienced a few stays in international labs (University of Parma, Italy; Tel Aviv University, Israel; etc.) and was awarded by the European Institute on Molecular Magnetism for her PhD thesis (2014) and by the Catalan Chemical Society (2009) for her MSc thesis.

After her PhD, she obtained an Intra-European Fellowship (Marie Curie Actions, EU) and did a postdoctoral stay in Prof. Spatz's group at the Max Planck Institute for Intelligent Systems and the University of Heidelberg (Germany). There she deepened her expertise in cancer research, working at the frontier of multifunctional materials and cell biology. For that, she acquired first-hand experience in cell culture, biophysics, and immunology. This learning process slowed down her publication record, but gave her access to a vast interdisciplinary



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territory that she is venturing into. She obtained 4 publications (* indicates first and corresponding author): Chem Eur. J., 2013; *Adv. Mater., 2015; *Chem. Mater., 2016; *Nano Lett., 2017), 1 patent is under revision (European Patent Office), and presented her research in 8 national and international conferences. Moreover, she supervised several BSc and MSc students from a few German universities (Reutlingen University, Ulm University, etc.) and taught in a course for BSc students of Technical Biology (Stuttgart University).

The candidate accepted a TecnioSpring fellowship (EU Cofund for experienced researchers) in Prof. Veciana's group (ICMAB-CSIC) over a Juan de la Cierva Incorporacion grant. She is currently working in the fields of multifunctional materials and tissue engineering for cancer immunotherapy. For that, she has been appointed head of a Max Planck Partner Group in collaboration with the Max Planck Institute for Medical Research (Germany) and is the Co-IP of a project from the ICMAB-CSIC Severo Ochoa Excellence Program. The candidate is co-supervising 2 PhD students and supervised 4 MSc thesis from the Autonomous University of Barcelona and presented the work in 2 conferences. She is a member of the Bioengineering, Biomaterials and Nanomedicine Networking Biomedical Research Centre (CIBER-BBN) through which she established collaborations with medical partners such as the Vall d'Hebron Institute of Oncology.

Her h factor is 11 and she is a reviewer of Nanoscale, Nano Lett., ACS Appl. Mater. Interfaces, Integr. Biol., and Small.



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Nombre: YAÑEZ BOYER, ALBERTO
Referencia: RYC-2017-22895
Área Científica: Biomedicina
Correo Electrónico: alberto.yanez@uv.es

Título:

Role of TLRs in hematopoiesis and trained innate immunity: impact on new immunotherapeutic strategies

Resumen de la Memoria:

My research interests are focused in the study of the function and production of myeloid cells (neutrophils, monocytes/macrophages and dendritic cells) under steady-state or during emergency conditions. I pursued 6 main projects in total: (1) During my undergraduate training, I defined innate immune responses against several fungal pathogens. (2) During my predoctoral training, I studied the effects of *Candida albicans* infection on hematopoiesis. I demonstrated that hematopoietic stem and progenitor cells (HSPCs) use Toll-like receptors (TLRs) to directly detect *C. albicans* and that TLR signaling induces their proliferation and differentiation to myeloid cells. I also developed a novel adoptive transfer approach to demonstrate that HSPCs respond directly to TLR agonists and yield macrophages in vivo. During my postdoctoral training, I showed that: (3) direct detection of microbial components by HSPCs programs the function of the macrophages they subsequently produce, which provides a mechanism to explain observations of innate immune memory; (4) I defined the role of the transcription factor IRF8 in neutrophil versus monocyte cell fate choice by myeloid progenitors, with relevance to steady-state and emergency myelopoiesis, as well as myeloid leukemias; (5) I demonstrated that commensal gut microbes promote myelopoiesis; (6) I discovered two independent pathways for monocyte production, relevant for the response to different pathogens during emergency myelopoiesis. Moreover, I have also participated in 2 very relevant collaborations in the fields of neurodegenerative diseases and aging. We showed that (i) *C9orf72* (a gene involved in the development of amyotrophic lateral sclerosis) regulates macrophage and microglial function in mice and (ii) rejuvenation of the hematopoietic system by transplantation of young bone marrow preserved cognitive function in old recipient mice. In my ongoing research as an independent investigator I am focusing my studies on three relevant aspects for the treatment of myelomonocytic and monocytic leukemia: 1) to reduce quiescence and self-renewal of leukemic stem cells (LSCs), 2) to induce terminal differentiation in leukemic cells, and 3) to promote an efficient anti-AML immune response. The interdisciplinary experience of my research training has enabled me to build a research career that bridges the fields of microbiology, immunology, stem/progenitor cell biology and hematology. In addition to deepening our understanding of the molecular regulation of myelopoiesis, my research also has the potential to impact the treatment of infection and myeloid malignances.

Resumen del Curriculum Vitae:

I obtained my Bachelor, Master and PhD degrees in the University of Valencia, Spain. During that period, I received several undergraduate and predoctoral fellowships. I was also awarded with a "Premio Extraordinario de Doctorado" from the University of Valencia. My graduate training in anti-fungal innate immunity was very productive, with 5 first-author and 9 co-authored papers. In 2011, I joined the Regenerative Medicine Institute at Cedars-Sinai Medical Center, Los Angeles, USA, as a postdoctoral fellow. During this time, I have been studying the differentiation and function of myeloid cells (macrophages, dendritic cells and neutrophils) with specific application to anti-microbial immunity, neurodegenerative diseases and cancer. I have obtained a Careers in Immunology Fellowship Award by The American Association of Immunologists. In 2016 I was promoted to Project Scientist and obtained independent funding from a competitive Career-Enhancement Award Program from the American Society of Hematology. In Dec 2017, I was promoted to Research Scientist and I established my own research group at the Blood Program of the Regenerative Medicine Institute, Cedars-Sinai Medical Center, Los Angeles, USA. In Jan 2018, I obtained the academic title of Assistant Professor. During this period, I have published 6 first-author papers (in journals such as *European Journal of Immunology*, *Blood*, *Nature Immunology*, and *Immunity*) and 6 co-authored papers (in journals such as *Journal of Immunology*, *Cell Host and Microbe*, and *Science*). I have published a total of 26 articles (11 as first author). My research has been recognized internationally. I have been selected for oral presentations and received travel awards at international conferences and invited to give seminars. Moreover, in 2014 I earned the prestigious "Young Investigator Award" from the International Endotoxin and Innate Immunity Society (IEIS). My teaching experience includes classes at the Biological Sciences Degree at the University of Valencia, classes at PhD programs from the University of Valencia and from Cedars-Sinai Medical Center. I have trained several technicians, masters and graduate students and I am currently the thesis director of a PhD student at the University of Valencia. I am an active member of the Cedars-Sinai Medical Center community where I have participated giving lectures and at outreach activities. Moreover, I am an ad hoc reviewer for the journals *PLoS ONE* and *Leukemia*.



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Turno de acceso general

Nombre: MORENO MATEOS, MIGUEL ANGEL
Referencia: RYC-2017-23041
Área Científica: Biomedicina
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Título:

New biotechnological approaches to understand cancer, early animal development and human diseases

Resumen de la Memoria:

My field of research has been focused on genetics and molecular biology with specific applications in microbiology, cancer, early development in vertebrates and human brain diseases.

I obtained my PhD from the University of Seville (Spain) under the supervision of Professor Tahía Benítez in the Department of Genetics. I studied how Pac1 (a transcription factor evolutionarily conserved in fungi) mediated ambient pH regulation and antifungal activity in *Trichoderma harzianum*. These studies were published in reference journals in microbiology and fungal genetics.

Once I completed my PhD, I wanted to develop research projects more focused on new technologies and biomedical research and I joined to Jose A. Pintor-Toro's lab at CABIMER (Sevilla, Spain) for my first postdoctoral training. While there, I conducted and led the development of new small RNA expression libraries to carry out functional screens. The results of these studies yielded three patents and a first and corresponding author paper in which we uncovered miR-30b/c as key oncogenic factors inhibiting cell death. In addition, I uncovered new molecular roles for the oncogene *pttg1* i) in cell differentiation by up-regulating gene expression of *dlk1*, a gene involved in the inhibition of adipogenesis, and ii) in promoting cell polarization and migration that contributes to its malignant transformation activity. Both studies were published in *Molecular Biology of the Cell*.

Interested by new biotechnological approaches and their applications in Developmental Biology and Biomedicine, I moved to the Giraldez Lab at Yale University (USA) to work on the optimization of the CRISPR technology in vivo, using zebrafish as a model system to ultimately study early development and human diseases. As part of this second postdoctoral training (awarded with the very competitive "Perfeccionamiento y Retorno" Grant from Junta de Andalucía) I uncovered the rules that govern CRISPR-Cas9 activity (CRISPRscan: <http://www.crisprscan.org>) and CRISPR-Cpf1 in vivo. These results have been published in the prestigious journals *Nature Methods* (First author) and *Nature Communications* (First and Corresponding author), respectively and I acquired a CRISPR-related patent. In addition, I used our optimized CRISPR-Cas9 system in an in vivo screen to uncover new genes involved in vertebrate brain development and related to human brain disorders (*PLOS Genetics*, under revision). Currently, I am developing new in vivo applications of the CRISPR system to better understand embryonic totipotency and cellular reprogramming (manuscript in preparation to be submitted to *Nature*) and I am supervising a PhD student as a thesis co-director.

Resumen del Currículum Vitae:

During my thesis and my postdoctoral training, I carried out multiple projects combining different disciplines (genetics, biotechnology, cancer, brain diseases) and model systems (filamentous fungi, yeast, mammalian cell lines and zebrafish). Throughout my PhD (University of Seville), I studied how ambient pH controls gene expression in a mycoparasitic fungus, which resulted in 3 papers (one of which as first author) in reference journals in microbiology and fungal biology and 3 book chapters. For my PhD, I was awarded with the FPI fellowship allowing me to work in CIB (Madrid) as visiting student for three months and to teach genetics in the grade of Biology. Once I completed my PhD, I wanted to develop research projects more focused on new technologies and biomedical research and I did my first postdoc in CABIMER-CSIC (Seville, Spain) at the Pintor-Toro's lab studying cancer biology in mammalian cell lines. First, I analyzed the role of the oncogene, *pttg1*, in adipocyte differentiation and microtubule nucleation and cell migration, which resulted in two papers published in *Mol. Biol. Cell* (2009 and 2011). Second, I worked on a biotechnology project where I generated and patented novel small RNA libraries to carry out functional genetic screens. From this project, I published a paper in *RNA* as first and corresponding author and a second paper is now being written. In addition, I acquired three international patents. During this period, I was awarded with a Torres Quevedo postdoctoral grant from the Spanish government and a postdoctoral fellowship from the Andalusian government as part of a lab grant. I also attended several national and international meetings to present these results and I was the Master project co-director of a PhD student. In 2012, I was awarded with a very competitive Grant from the Andalusian Government (Perfeccionamiento y Retorno). This grant provided me with funding for four years, with two years of postdoctoral training in an outstanding research institute in a country different from Spain and also with the possibility to return to Andalucía for two years to start as a Senior Researcher/Emerging PI. In 2013, I joined the Giraldez lab at Yale University as an Associate Research Scientist to work in CRISPR genome editing technology and its application to study early development and human diseases in zebrafish. As part of this second postdoctoral training, I uncovered the rules that govern CRISPR-Cas9 activity (www.crisprscan.org) and CRISPR-Cpf1 in vivo. These results have been published in the prestigious journals *Nature Methods* (first author) and *Nature Communications* (First and Corresponding author), respectively and I acquired a patent. In addition, the



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results of this project have been presented as invited talks in 10 research institutes in Spain and USA and 11 international and national meetings. I have also published a CRISPR-Cas9 review and a protocol in the Cold Spring Harbor Protocol journal that is part of a book on CRISPR-Cas9. Using our optimized CRISPR systems we have recently uncovered new genes involved in vertebrate brain development and in human diseases (PLOS Genetics, under revision). Currently, I am studying new in vivo applications of the CRISPR system to better understand embryonic totipotency and cellular reprogramming and I am supervising a PhD student as a thesis co-director.



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Turno de acceso general

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Área Científica: Biomedicina
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Título:

Genetics and molecular basis of neurodevelopmental disorders

Resumen de la Memoria:

My scientific career focuses on the study of complex and rare neuropsychiatric diseases, with emphasis on their genetic basis and molecular mechanisms. I have worked in 4 centers in Barcelona and San Diego (USA), and received training at Harvard. I have participated in 10 international research projects. I was granted as PI one project by the "Todos Somos Raros" foundation, and received a Marie Curie fellowship H2020. I have published 20 articles in international journals (70% Q1, 1083 cites) and 1 book chapter. I have extensive teaching experience, received training, and directed 3 Master's and 13 students.

1. Genetic basis of synaptopathies

We studied monogenic and complex forms of migraine using multiple approaches: linkage studies identified a locus at chr14q32. Mutational screens detected a large set of mutations in CACNA1A and ATP1A2 genes causing paroxysmal disorders. We performed innovative case-control association studies of large and well clinically characterized cohorts of variants selected following genetic coverage parameters (before GWAS). I was first author of "Association study of the serotonergic system in migraine in the Spanish population" Am J Med Genet B, 2010; and "Two-stage case-control association study of dopamine-related genes and migraine" BMC Med Genet, 2009.

2. Molecular basis of psychiatric disorders using systems biology approaches

The aim of the projects was to identify pathways that connect psychiatric disorders related genes, with the goal to discover pathways that may be targeted for therapeutic approaches. We performed high-throughput screens of isoform level protein interactions, and integrated this data with additional sources of evidence to gain insight into the molecular mechanisms of psychiatric disorders. We published two relevant articles "Spatio temporal 16p11.2 protein network implicates cortical late mid-fetal brain development and RhoA pathway in psychiatric diseases" Neuron, 2015; and "Protein interaction network of alternatively spliced isoforms from brain links genetic risk factors for autism" Nature Comm., 2014, selected for oral presentation at International Meeting for Autism Research in 2012.

3. Characterization of 7q11.23 reciprocal aneusomy syndromes: from patients to functional pathways

My interest in 7q11.23 CNVs started early in my career with the article "Copy number variation at the 7q11.23 segmental duplications is a susceptibility factor for the Williams-Beuren syndrome deletion" Genome Research, 2008. I received funding as PI to performed molecular characterization of patients with 7q11.23 syndromes (in submission to Genome research), the generation of in vitro models using hiPSC and neuronal differentiation, and to perform transcriptomic analyses with omics approach. Currently, the brain in vitro models are finished and I am analyzing the expression data and preparing another manuscript.

These demonstrate my capacity to reach and re-enforce a position of professional maturity in research. I have consolidated leadership, management, communication, and numerical skills. My international and multicentric view allows me to design, write and develop successfully research projects. These research lines reflect I have acquired multidisciplinary knowledge on neuropsychiatric disorders, and that I have an extensive experience in molecular biology, genetics and systems biology.

Resumen del Currículum Vitae:

University education:

- Degree in Biology, Pompeu Fabra University (UPF) 2003
- Advanced Studies Diploma (DEA), University of Barcelona (UB) 2005
- PhD Genetics Department, UB 2009

Current professional situation:

- Postdoctoral researcher Marie Sklodowska Curie, Genetics Unit, UPF (1/042016- 30/03/2018)

Previous positions:

- Postdoc Juan de la Cierva, UPF 2014-16
- Postdoc, University of California San Diego (UCSD) 2010-14
- Pre/Postdoc CIBER Enfermedades Raras (CIBER-ER) 2009
- Predoctoral fellow, Vall Hebron Research Institute (IR-HUVH) 2005-08
- Researcher, IR-HUVH 2003-04

Obtained grants and scholarships:

- Marie Sklodowska Curie Individual Fellowship (Reintegration panel, H2020) 2016



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-Juan de la Cierva, Ministerio de Economía y Competitividad 2014

-Predoctoral fellowship, IR-HUVH 2005

Scientific production (Scopus 2018):

-H index: 14

-Original articles in peer reviewed journals: 20, 70% (14) in top 25% journals Q1.

-Book Chapters: 1 Methods in Molecular Biology

-Cites: 1083 total citations by 1030 documents

-First author (or co-first) in 7 articles published in the journals: Neuron, Nature commun, Am J Med Genet B, BMC Medical Genetics, Neurosci Lett, European J Neurology, Genome Research.

Collaborator in research articles published in: Nature, Cell, PNAS, Mol Genet Genomic Med, European Neuropsychopharmacology, World J Biological Psychiatry, Am J Med Genet B, Neurogenetics, J Neurol Sci, Cephalalgia, and Neuropediatrics

Works submitted and attendance to national or international conferences:

-Poster presentation in 37 scientific conferences, the majority of them international, including: ASHG, ESHG, World Congress of Psychiatric Genetics.

-Oral presentation at IMFAR International Society For Autism Research (IMFAR) Toronto 2012. Travel award.

R&D projects funded through competitive calls:

-10 projects from Spain and USA

-Principal Investigator of the project: Characterization of 7q11-23 reciprocal aneusomy syndromes: from patients to functional pathways (and back). 100.000€ "Todos Somos Raros, Todos Somos Únicos" foundation.

University Teaching experience (195h):

-Basics Genetics, Biology and Medicine degree UPF

-Medical Genetics, Biology and Medicine degree UPF

-Master in Clinical Analysis Laboratory UPF

-Genetic Counselling University Master UPF

-Campus Junior, High school summer course UPF

-Human genetics, Biology degree UB

Training received to improve teaching skills (200h, UPF):

-Initial Training in University Teaching Programme

-Teaching and Mentoring programme

Supervisor of:

3 Master's Thesis supervisor

13 Undergraduate students

Others:

-Projects evaluator: Fundación Pública Andaluza Progreso y Salud (2015-2017)

-International journals manuscripts reviewer (8)

-Assistance to local and international training courses

Dissemination activities:

-Jury in XI PRBB Health Science Research project 2016

-PRBB Open day volunteer 2014-16

-Collaboration with families of patients associations

-Junior Faculty and Postdoctoral Research Symposium, Dep. Psych. UCSD 2011-14

Languages:

-English & French: excellent

-Catalan & Spanish: maternal



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Turno de acceso general

Nombre: DEL TORO RUIZ, DANIEL
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Área Científica: Biomedicina
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Título:

FLRTs: Novel mechanisms of cortical migration and cerebral cortex folding

Resumen de la Memoria:

Neuronal migration is a fundamental mechanism that strongly impacts the development of the brain architecture. This process shares similar features with axon guidance because it is also regulated by a variety of extracellular cues, and these signals can be either attractive/adhesive or repellent. During my postdoc at the laboratory of Prof. Ruediger Klein (Max Planck Institute of Neurobiology, Munich), I have studied the role of the Fibronectin Leucine-Rich Transmembrane (FLRT) protein family in axon guidance and cell migration during cortical development. Among all my postdoctoral publications, I highlight two, published in *Neuron* and *Cell* that represent my main project and the basis of my future research.

The first publication in *Neuron* (2014) shows that FLRTs have a unique property of acting as adhesion molecules by homophilic and heterophilic binding to Latrophilin proteins, and heterophilic repulsive ligands of Unc5/Netrin receptors. These two different functions allow FLRTs to control different aspects of cortical migration, mediating repulsion to control radial migration and homophilic adhesion to direct tangential distribution. These findings lead to the identification of a new subgroup of cell adhesion molecules (CAMs) designated as repelling CAMs (reCAMs). reCAMs provide a guidance system that combines the finely tunable cell adhesion of classical homophilic CAMs with repulsive functions through the addition of a heterophilic receptor.

The second publication in *Cell* (2017) shows that mice with deletions of FLRT1/3 proteins result in cortical folding. This process depends on changes in intercellular adhesion of migrating cortical neurons that allows them to acquire faster migratory speeds and new tangential arrangements leading to sulcus formation. Further, our results show that endogenous expression of FLRT proteins is much lower in human cortical layers compared to mouse and less abundant in a future sulcus than gyrus area in the gyrencephalic cortex of the ferret. Thus, our model suggests a new mechanism by which altering FLRT expression levels (and therefore intercellular adhesion) might have influenced both migrating neuron dynamics and cortical folding during evolution.

Folding of the cerebral cortex represents a fascinating evolutionary step that highly impacts on neuronal network and cognitive capacity of large mammals. This process is thought to be favored by the amplification of basal progenitor cells and their tangential migration, leading to cortical surface expansion with the appearance of valleys (gyri) and ridges (sulci). My results provide a molecular mechanism for the role of migration in this process. Thus, my current research interest focus on understanding how neuronal migration in combination with progenitor proliferation modifies its tissue properties leading to cortical folding. I intend to tackle this project using a multidisciplinary approach including conditional mutant mice, protein structure, cerebral organoids and co-operative networks.

Moreover, several neurological disorders, including schizophrenia, epilepsy, autism and mental retardation are associated with abnormal brain folding. Thus, my research has obvious connections to human biology, and may thus pave the way to identify new genes potentially mutated in human malformations of cortical development.

Resumen del Currículum Vitae:

Academically, I am biologist, degree obtained in the University of Pompeu Fabra with honours (Spain, 2004) and Honourable mention in the National extraordinary award for BSc. in Biology of Spain (ECI/2188/2005). In 2009, I obtained my PhD in neuroscience studies in the Dept. of Cell Biology, Immunology and Neurosciences (Faculty of Medicine, University of Barcelona) investigating neurodegenerative mechanisms occurring in Huntington's disease. My thesis, entitled "Study of post-Golgi transport and cholesterol homeostasis in Huntington's disease" (PhD mentorship: Dr. Jordi Alberch and Josep Maria Canals), aimed to study the effects of mutant huntingtin on cell trafficking and cholesterol homeostasis. My research was supported by a PhD fellowship from FPU program (Ministerio de Educación y Ciencia, Spain) and the experimental results were published in 4 peer-reviewed international journals, all of them ranked in the first quartile of their category. These publications lead to the "Extraordinary prize of PhD thesis 2008/2009" award from the University of Barcelona (Spain).

After my PhD, I joined the laboratory of Prof. Ruediger Klein (Max Planck Institute of Neurobiology, Munich, Germany), where I have studied the role of the Fibronectin Leucine-Rich Transmembrane (FLRT) protein family in axon guidance and cell migration during cortical development. During my postdoctoral period I have been involved in two main projects and several successful collaborations that have led



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to 8 publications, all of them ranked in the first quartile. Among them, I highlight two publications published in *Neuron* and *Cell* that represent my main postdoctoral project. The first publication in *Neuron* (2014) shows that FLRTs family protein mediate repulsion to control radial migration and adhesion to direct tangential distribution of pyramidal neurons. The second publication in *Cell* (2017) shows that mice with deletions of FLRT1/3 adhesion molecules result in cortical folding. This process depends on changes in intercellular adhesion of migrating cortical neurons, and it provides new insights into the evolution of this fascinating process.

During my career, I have written successful applications in European competitive calls like EMBO long-term fellowship, and the Marie Curie Intra-European Fellowships (FP7). As a lab management skills, I have organized the work of 1 technician and mentor/supervised the projects of 3 PhD and 1 master student.

Furthermore, I have a proven track record of teaching and very much look to continue this in my future, to motivate students as they start their careers. I have been Instructor of the FP6-funded project DiMI (2007-8, IDIBAPS, Barcelona) and the Practical Course for "Master in Neuroscience" (2011-17, Ludwig-Maximilians University (LMU), Munich). I have also been invited as lecturer for master students of the LMU (Munich) since 2015, where I have taught "Axon guidance - signaling mechanisms" and for the International Max Planck Research school (IMPRs) lectures for PhD students (2018).

Finally, I am interested in communicating my research to a broader public. For this reason, I participated in the Brain Awareness week (2005-8), the Open days of the Max Planck Institute (2010-17), and in the elaboration of articles for the general public in printed (*Omnis Cellula*, 2009) and online magazines (*NewScientist*, 2017).



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Título:

Sistema Nervioso desde el desarrollo a la patología

Resumen de la Memoria:

The guiding thread that has defined my scientific career is the nervous system, first working with a molecular perspective. My PhD project focused on the insulin gene. I discovered two strategies that help to maintain embryonic pro-insulin (the not processed form of insulin) levels low. Since proinsulin excess causes aberrant nervous system development. The novel mechanism redefined the importance of insulin beyond the control of glucose homeostasis, and pioneered a new expression control mechanisms with physiological relevance. As a further step in the field of gene expression regulation, I moved to David Rubinsztein's laboratory. His lab is a world reference in protein degradation as related to neurodegenerative human diseases. There, I studied the Parkinson's disease protein LRRK2 and how it impairs proteasome substrate clearance without affecting proteasome catalytic activity. Thus, I contributed to the understanding of Parkinson's disease pathology. In addition, I defined the deleterious consequences of autophagy inhibition over proteasome activity, that was a key conceptual advance to the field. The mechanism is based on the accumulation of p62 that inhibits the clearance of ubiquitinated proteins destined for proteasomal degradation. Since this postdoctoral training I am considered an expert in the field and I have been invited to PhD committees and paper reviews. Upon returning to Spain, I joined the lab of Alberto Ferrús at the Cajal Institute where I have continued studying protein degradation mechanism in neurological disease. I first worked with a novel ubiquitin-ligase that controls steroid receptor levels in Drosophila and its role in growth and development. In recent times I started working on the neural calcium sensor NCS1 and its mechanisms to regulate synaptogenesis. We discovered that NCS1 is involved in the control of synapse number and probability of neurotransmitter release per synapse. This calcium sensor is involved in autism spectrum disorders and other cognitive disorders. In that context, I am leading a collaborative project with crystallographic experts at Institute for Physical -Chemistry CSIC and the department for Medical Chemistry CIB- CSIC, aimed to test novel drugs that intercept NCS-1 activity in animal models of autism. The first promising results are protected by a patent and were published in PNAS last year. In the meantime, and thanks to my knowledge in protein degradation mechanism I was asked for collaboration with a laboratory at INGEMM in Hospital La Paz. The result of the collaboration was finally published in 2014. And in 2016 I was also awarded with funding as principal investigator to study the role of trehalose, an autophagy inducer, in the treatment of neurodegenerative diseases. In the same context, recently I have also obtained funding from Comunidad Autónoma de Madrid for the recruitment of a Predoctoral fellow.

Resumen del Currículum Vitae:

I graduated in Biology from the Complutense University of Madrid in 2000, and the following year I was awarded a FPI fellowship to carry out a research project towards my PhD. Under the supervision of Prof. de Pablo and Dr. Hernández-Sánchez at CIB-CSIC, I worked in the project entitled: "Regulation of proinsulin embryonic mRNAs alternative to pancreatic mRNA: Developmental and functional implications" with which I doctorate from the Autónoma University of Madrid in 2005 with maximum qualifications. The work was published in EMBO J (Impact factor IF: 10.7, Citations C: 45), in EMBO Reports (IF:8, C:36) and Nucleic Acids Res. (IF:9, C: 10) and everything review in Diabetologia. (IF: 6.8, C:48). In parallel, I investigated the molecular phylogeny of vertebrate insulin receptor family in collaboration with Dr. Rafael Zardoya and the work was published in 2008 in Mol Biol Evol. (IF:14.3, C: 46). Pursuing my interest in regulatory mechanisms of gene expression, I moved to the lab of Prof. David Rubinsztein at the CIMR, Cambridge, UK. Initially, I was funded by the Wellcome Trust and later on, by a fellowship from Spanish Ministry (MEC-fullbright). There, I investigated the consequences of autophagy inhibition upon proteasome activity. The resulting work was published in Molecular Cell 2009, (IF:14.5, C:377). In addition, I also studied the Parkinson's disease protein LRRK2 and how it impairs substrates from reaching the proteasome, published in Cell Death Dis. 2011. (IF:5,1 C:31). In 2008, I obtained a contract from Juan de la Cierva program to work at Alberto Ferrús's lab in the Cajal Institute, where I have continued studying protein degradation mechanism in neurological disease. I first worked with Troponin I and its role in cell polarity, a work published in J Cell Sci. (IF:5.4 C:17). In addition, I also investigated a novel ubiquitin-ligase that controls steroid receptor levels in Drosophila. Genetics (IF:5, C:8). In 2010, I obtained a JAE contract to investigate how steroids control cell death. This work was published in Cell Death and Differ. (IF:8,2 C:2). In this period I have 3 children, despite the challenge, it didn't affect my efficiency or dedication to research. I started to work as an independent investigator with the project based on the neural calcium sensor NCS1 and its mechanisms to regulate synaptogenesis. I am coordinating a consortium, aimed to test novel drugs that intercept NCS-1 activity and its use on disease models of autism. The study that sustained the collaborative project was published in J. Cell Science (IF:5.4, C:8) and in PNAS (IF:9.7 C:2) and it is also protected by a patent. In 2016 I was awarded with a grant from MINECO (JIN) in which I am the PI, to develop the use of trehalose for the treatment of neurodegeneration; In order to do so I have joined IRYCIS (Hospital Ramon y Cajal). Recently I have also been granted with funding from the Community of Madrid for the recruitment of a predoctoral fellow (Garantía Juvenil). Other scientific output and expertise include at least 14 contributions to Congresses, 1 co-direction of PhD project, 2 directions of Master projects and 4 supervisions of American summer



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students. I collaborate in teaching activities as master studies and student training programs. I have participated in 2 scientific PhD committees and I am often a reviewer for scientific papers.



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Área Científica: Biomedicina
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Título:

Study of Signaling Pathways and Gene Expression Regulation During Stem Cell Differentiation

Resumen de la Memoria:

With two degrees in Biology and Biochemistry and a PhD in Biomedicine, I accumulate over five years of postdoctoral experience working as Molecular Biologist. I carried out my PhD thesis under the supervision of Dr. Marian Martinez Balbas at the Instituto de Biología Molecular de Barcelona (IBMB-CSIC, Barcelona, España) and in mid 2012, I joined Dr. Kathy Jones laboratory at Salk Institute for Biological Studies (La Jolla, US) for my postdoctoral stay.

Throughout my scientific career I have made another short stay in an international laboratory (Dr. K. Helin lab, Denmark, CPH), attended national and international conferences and participated in the training of undergraduate and graduate students. During these years, I obtained highly competitive fellowships from Spanish Ministry of Culture and Education (FPU) to perform my Ph.D, and later the Pioneer Foundation and Salkexcellerator postdoctoral grants.

I have a wide expertise in basic laboratory techniques including in vitro and in vivo experimental approaches such as cell culture of embryonic stem cells and generation of induced pluripotent stem cells. I am skilled in cutting edges genome-wide sequencing techniques; such single cell-sequencing, ChIP-seq (Chromatin Immunoprecipitation coupled to sequencing), RNA-seq and GRO-seq (Global Run On sequencing) and Bioinformatic analysis.

My main research focus has been on the study of the transcriptional and epigenetic mechanisms involved in the regulation of developmental genes. Particularly, I focused on studying the mechanism by which signaling pathways effectors together with epigenetic regulators and the basal transcriptional machinery integrate into the chromatin to activate the transcription of genes involved in cell differentiation. My PhD work focused on the activity of the TGF β signaling and the histone demethylases in the context of neural development. During my postdoctoral years I worked also on the analysis of Wnt and Hippo signaling pathways in the regulation of genes involved in embryonic stem cell differentiation toward mesoderm and cardiac progenitors. My immediate future research plans will focus on studying regulatory mechanisms important for pluripotent stem cell differentiation toward distinct cardiac lineages.

Resumen del Currículum Vitae:

- Degree in Biology and Biochemistry (2006) by the Universidad de les Illes Balears (UIB)
- PhD degree Cum Laude in 2011 by the University of Barcelona (at IBMB-CSIC). The main focus of my PhD research was the study of the epigenetic mechanisms that regulate neural development.
- Since 2007 I published 12 publications in high profile impact journals. I owe four first-author publications in the journals: Genes & Development (December, 2017), Molecular Cell (April, 2015), Molecular Biology of the Cell (2013) and Development (2012).
- My publications add 526 citations (Google Scholar)
- Currently, I work as Senior Postdoc (2011-present) in the Salk Institute for Biological Studies (La Jolla, USA).
- I have presented my research work in international and local meetings such the prestigious Cold Spring Harbor (Genes at Work, April 2015) and I have been personally invited to give a talk in the Stem Cell Foundation Retreat (CIRM CESC, San Diego, 2016 and Stanford, 2017).
- Funding: I obtained fellowships and grants for nearly my entire graduate and postdoctoral training: Spanish Ministry of Culture and Education Fellowship (FPU) to perform my Ph.D, and later the Pioneer Foundation and Salkexcellerator postdoctoral grants.
- Mentoring: Training of undergraduate and graduate students. I am a member of Education Outreach team of the Salk Institute; I teach science classes in middle school and I do e-mentoring (online science career guidance).
- Reviewer activity: I have been personally invited to review papers for several journals such International Journal of Molecular Sciences and American Journal of Molecular Biology, which I am part of the Reviewer Editorial Board.
- Current and Future Research Focus: Currently working on the study of the transcriptional mechanisms that regulate human Embryonic Stem Cell differentiation toward cardiomyocytes lineages. These research and motivation constitute the focus of my independent research program on the understanding of mechanisms involved in development and cardiac-related disorders.