MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **MONTSERRAT PULIDO, NURIA**
Referencia: RYC-2014-16242
Área Científica: Biomedicina
Correo Electrónico: nmontserrat@ibecbarcelona.eu

Título:

Pluripotent Stem Cells for Regenerative Medicine

Resumen de la Memoria:

Overall my research career has been focused in stem cells biology and in the identification of the molecular and cellular mechanisms driving pluripotency, cell differentiation and organ regeneration. The discovery in 2006 that any somatic cell type of our body can be converted towards cells with identical properties of human embryonic stem cells, offered me during the last eight years an unprecedented opportunity to develop novel strategies for nuclear somatic reprogramming and disease modelling by the generation of patient specific induced pluripotent stem cells (iPS).

My work has covered the generation of patient derived iPS cells for the production of in vitro platforms for compound screening and the study of tissue differentiation. I have also combined my background in organ regeneration in different animal models (teleost fish and zebrafish) and tissue homeostasis regulation developed during my pre-doctoral studies for the generation of massive strategies for the comprehension of mammalian organ regeneration.

The aims of my current research line are as follows:

Aim 1: To identify the molecular and cellular mechanisms promoting kidney regeneration in a model of kidney regeneration in mammals

Aim 2: To generate and correct patient-specific transgene-and feeder-free induced pluripotent stem cells (iPSCs) from patients with kidney genetic diseases

Aim 3: To generate protocols for renal differentiation for the establishment of kidney disease models

Whereas I understand that the results obtained during the course of my research line cannot be generalized to the generation of any other somatic cell type, I firmly believe that providing this information will open new venues for the development of therapeutics targeting a major unmet medical need. I have chosen this research topic for a number of reasons. First, the high incidence and poor prognosis of renal diseases are a major public health problem in Europe and worldwide, and although patients with End Stage Renal Disease (ESRD) can survive with dialysis or transplantation, these procedures are expensive, demanding and can be prone to life-long side effects due to the immunosuppressive regimen employed on the patient. Furthermore, there is a shortage of organs for transplantation. Second, I have generated for the first time a model of kidney regeneration in mice, offering an unprecedented opportunity to address major questions related to kidney development and regeneration. Third, others and I have reported methodologies for the generation of transgene-free human iPSCs (hiPSCs) from patients with genetic based disorders. Fourth, I have co-authored for the first time, the possibility to differentiate patient derived hiPSCs towards renal cells (ureteric bud progenitors). Fifth, the institution where I am currently conducting my research has extensive experience and resources allowing me to tackle these major questions.

Some of the objectives of my current research line have been selected for funding from the European Research Council (ERC) within the call of ERC Starting Grant from 2014, revealing the interest of the scientific community for this type of multidisciplinary approaches when developing new strategies in Regenerative Medicine and Biomedicine disciplines.

Resumen del Currículum Vitae:

I became interested in organ regeneration and stem cells during my master and PhD training that finished in 2006. The same year I got a Postdoctoral fellowship from the Fundaçao para a Ciência e Tecnología (Portugal). In 2007 I was hired as a post-doctoral researcher at the Hospital of Santa Creu i Sant Pau in Barcelona.

In 2008 I moved to the Center of Regenerative Medicine of Barcelona (CMRB), as research associateIn 2008 I moved to the Center of Regenerative Medicine of Barcelona (CMRB), as research associate. There, I participated in developing strategies for the generation and banking of new induced pluripotent stem cell (iPSC) lines. In 2010 I first co-authored how to reprogram cord blood stem cells for the first time (Nature Protocols, 2010). Based on my previous knowledge on stem cells and tissue development I reasoned that iPSCs could be

obtained by means of safe strategies using specific transcription factors determinant for lineage specification. With this in mind, I set out to test whether dermal fibroblast could be reprogrammed to pluripotency. Not only I succeeded at demonstrating that this was the case, but I also found, for the first time, that OCT4, the only transcription factor believed to be indispensable for somatic reprogramming, could be replaced by GATA3. The work resulted in a high-impact publication in Cell Stem Cell (2013), in where I am the first co-author. I also collaborated in other projects aimed to characterize the genomic integrity of human iPSCs as well as in the differentiation of iPSCs towards germ cells, neural cells, endothelial cells, retinal cells or blood cells. These studies were published in Stem Cells 2011, Nature 2012, Nature Methods 2012, Nature Communications 2013, Protein and Cell 2013, Nature Communication 2014. In the same manner I have participated in the generation of platforms for the study of disease progression and compound screening for therapy by means of hiPSCs (Nature 2012, Nature Communication 2014). Moreover, my interest on organ regeneration provide new knowledge for the generation, for the first time, of kidney organoids, suitable for the study of iPSCs differentiation towards renal lineages and compound screening for therapeutic purposes [Nature Cell Biology (2013)].

Taking advantage of my expertise in the fields of somatic reprogramming and organ regeneration I am developing a massive strategy in order to understand how to activate endogenous programs in order to regenerate the adult mammalian kidney. Indeed this approach has been selected for funding from the European Research Council (ERC) within the call of ERC Starting Grant from 2014. Within this line my studies have identified, for the first time, how the reactivation of endogenous regenerative programs that are dormant in adult murine heart can be reactivated and elicit heart regeneration [Cell Stem Cell, in press 2014]. From January 2015 I am junior group leader at the Institute for Bioengineering of Catalonia (IBEC).

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **TAPIA , NATALIA**
Referencia: RYC-2014-16359
Área Científica: Biomedicina
Correo Electrónico: natapse@hotmail.com

Título:

Stem cells and regenerative medicine

Resumen de la Memoria:

In the last 10-years, I have been working on 4 main topics related to stem cells and their potential use in regenerative medicine:

- Embryonic and epiblast stem cells. I have assessed the mechanisms underlying the regulation of pluripotency in these two murine cell types. The final goal was to ascertain their similarity to human embryonic stem cells. Our results show that human embryonic stem cells are more similar to mouse epiblast stem cells than to mouse embryonic stem cells. However, the data obtained from mouse epiblast stem cells cannot be fully extrapolated to the human model. 4 publications have been published in this topic, including 1 in Cell Stem Cell and 1 in Cell.

- Induced pluripotent stem cells (iPS). I have investigated the mechanisms underlying reprogramming to pluripotency as a new source of cells for patient-specific cell-replacement therapy. 7 reports have been published in this topic, including 1 Nature Cell Biology and 1 Nature Communications.

- Direct reprogramming into somatic cells. iPS need to be differentiated into the required cell types prior to transplantation but differentiation protocols for all cell types are still not available. In 2010, the direct conversion of fibroblasts into neurons was accomplished using a specific combination of transcription factors. However, the amount of generated neurons is not enough for transplantation since the reprogramming efficiency is very low and neurons do not proliferate. To avoid this limitation, I have been able to directly convert fibroblasts into induced neural stem cells (iNSCs) that can self-renew. Therefore an unlimited number of neurons can be produced for transplantation. My group is now trying to reprogram iNSC in vivo in order to eliminate the transplantation step. 5 reports have been published in this topic, including 2 Cell Stem Cell and 1 Nature Protocols.

- Spermatogonial stem cell (SSC) lines can be stably derived in vitro and can be converted to pluripotency under specific culture conditions without any genetic manipulation, thus representing a new source of cells for transplantation. Furthermore, SSC lines can restore spermatogenesis after testicular transplantation into infertile mice. Unfortunately, the culture conditions to establish human SSC lines have not been identified yet. One of my main research lines is focused on deciphering the conditions required to maintain SSC self-renewal in vitro. Establishing a human SSC line will have many implications in the treatment of infertility. For instance, some cancer treatments compromise the fertility of pre-pubertal patients in which sperm cannot be cryopreserved. In this scenario, patient-specific human SSC lines could be derived prior to the anticancer treatment and transplanted after tumor elimination, a process that will restore spermatogenesis. In addition, human SSC lines will be the perfect tool to study the mechanism underlying some types of male infertility. 7 publications have been published in this topic, including 1 in Cell Stem Cell and 1 in Nature.

Overall, my research is focused on stem cell topics that can improve the medical treatment of diseases such as neurodegenerative (e.g. iNSCs) or male fertility disorders (e.g. SSCs), thus it fits into the Biomedicine ANEP area.

Resumen del Currículum Vitae:

CURRENT POSITON:
June 2014, Independent Group Leader, Heinrich-Heine University (Düsseldorf, Germany).

EDUCATION:
-1999, Degree in Pharmacy (equivalent to Grade + Master) with Special Honors, Universitat de Valencia (Valencia, Spain).

-2005, Ph.D. in Immunology, Universitat Autonoma de Barcelona (Barcelona, Spain).

RESEARCH EXPERIENCE:
-June 2014, Independent Group Leader, Heinrich-Heine University (Düsseldorf, Germany).
Funded by the North-Rhine Westphalia Ministry of Innovation, Science and Research.

-Sep 2009-May 2014, Project Group Leader, Max Planck Institute for Molecular Biomedicine

(Münster, Germany).
Employed as a scientist according to the German Public Sector Labor Agreement (TVöD).

-Sep 2005-Aug 2009, Postdoctoral fellow, Max Planck Institute for Molecular Biomedicine (Münster, Germany).
Funded by a Max Planck Society postdoctoral fellowship to promote scientific cooperation with foreign countries.

-Nov 2004-Feb 2005, Guest scientist, Johns Hopkins University (Baltimore, USA).
Funded by a research fellowship from the Spanish Ministry of Health (BEFI).

-May 2000-June 2005, Predoctoral fellow, Fundacio Irsicaixa (Barcelona, Spain).
Funded by a research fellowship from the Spanish Ministry of Health (BEFI).

-Oct 1998-June 1999, Pregraduate researcher, Universitat de Valencia (Valencia, Spain).
Funded by a research fellowship from the Spanish Ministry of Education and Culture.

TEACHING:
-May 2014 Habilitation for Privat Dozentin, German accreditation required for applying to Professorship positions in Germany.

-July 2012, 3rd Royan International Summer School: Stem Cells and Developmental Biology, (Tehran, Iran). Organizer and Lecturer.

-Oct 2011-July 2013, 3 hours/week per semester (4 semesters), Westfälische Wilhelms-Universität (Münster, Germany).

THESIS SUPERVISION:
-May 2014, Doctoral thesis: Ulf Tiemann (Magna Cum Laude).

-March 2014, Doctoral thesis: Adele Marthaler (Magna Cum Laude).

-October 2013, Master thesis: Hannah Flaßkamp (Excellent).

INVITED EXTERNAL REVIEWER FOR GRANT PROPOSALS:
-Dec 2014, ANR 2015 Program (French National Research Agency).

-June 2014, CE11 2014 Program (French National Research Agency).

-Nov 2013, Call for International Stem Cell Research, Breakthrough Project (The Netherlands Organization for Health Research and Development).

INVITED REVIEWER FOR PEER-REVIEWED JOURNALS: Stem Cells, Nature Cell Biology, EMBO Journal, BMC genomics and Scientific Reports.

AWARDED GRANTS AS PRINCIPAL INVESTIGATOR:
-Title: Dissecting the molecular mechanisms that regulate human spermatogonial stem cell fate decisions
-Funding organization: North-Rhine Westphalia Ministry of Innovation, Science and Research (Germany)
-Amount: 1.250.000 euros
-Duration: 5 years
-Role: Principal Investigator

CONFERENCES: 25 conferences including oral and poster presentations.

RESEARCH ARTICLES:
- 30 articles accepted plus 2 reports that are under revision.
- 9 first authorships
- 3 corresponding authorships plus the 2 reports that are under revision.
- 9 papers have been published in journals with an impact factor higher than 10, from which 4 have been published in Cell Stem Cell (IF: 25,4), 1 in Nature (IF:38,5), 1 in Cell (IF:31,9), 1 in Nature Cell Biology (IF:20,7), 1 in Journal of Experimental Medicine (IF:13,2) and 1 in Nature Communications (IF:10).

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **ROA GOMEZ, SERGIO**
Referencia: RYC-2014-16399
Área Científica: Biomedicina
Correo Electrónico: sroa@unav.es

Título:

Molecular mechanisms of DNA editing and genomic instability through DNA deamination

Resumen de la Memoria:

Being a molecular immunologist, I have always been intrigued by the plasticity of B cells to produce a tremendously diverse repertoire of high affinity antibodies. Such diversification process in the germinal centers (GC) of secondary lymphoid organs is triggered by the Activation Induced DNA Deaminase (AID) promoting genomic instability and error-prone DNA repair. I learned this as a Volunteer Undergraduate Research Student at the U. of Salamanca. Since then, my research interest has centered on the role of DNA deamination, DNA repair and the mutagenic enzyme AID, both in the physiological function and malignant transformation of GC B cells. The award of Student (MEC-Colaboración) and PhD (MEC-FPU) Fellowships, allowed me to study the clinical relevance of AID SNPs in atopic asthma, investigate the aberrant expression of Bcl2 in malignant B cells, and identify 5 alternative splicing variants of AID; with publications in JACI, Leukemia, Clin Dev Immunol. Once I got my PhD, I moved to the lab of Prof. Matthew D Scharff (USA), funded by a Spanish Postdoctoral Fellowship (MEC). During the following 6 years, my work was published in numerous articles and reviews (5 PNAS, DNA repair, PLoS ONE, Annual Rev Immunol, Mol Med, Trends Genet*, Disc Med*, Biomed Pharmacother*, *as corresponding author) characterizing (i) the role of distinct mismatch DNA repair (MMR) proteins in the mutagenic activity of AID (i.e. MSH2/MSH6-mediated sensoring; PMS2-endonuclease activity; PCNA-ubiquitylation role in recruitment of error-prone polymerases; RNF8/168 mediation to repair DSBs); (ii) the deleterious impact of aberrant AID activity and MMR in the promotion of genomic instability, and intraclonal evolution of leukemias (CLL) and lymphomas; and (iii) the potential impact of AID in epigenetics. In late 2011, I decided to continue my primary research about DNA repair/DNA deamination-AID/lymphomagenesis in Europe at CIMA in the U. of Navarra, funded by an Inncorpora-Torres Quevedo Fellowship (MINECO) first, and a FP7-Marie Curie International Incoming Fellowship later. During this time, I was able to contribute: (i) as leading scientist: to discern the role of MLH1-ATPase signaling downstream of AID-initiated lesions (J Exp Med); initiate new projects on the field of B cells and allergy (JACI); and write a book about epigenetics of B cells in allergy (Ed. Springer), and a review about AID and MMR (Semin Immunol); (ii) as first author: to elucidate the role of the TF FOXP1 during the engagement of B cells in the GC reaction (Blood); (iii) as co-author: to the characterization of cis-elements that are critical for AID accessibility to the Ig locus (J Immunol); the description of AID malfunction in CLL cells (Blood); the identification of the Exo1-exonuclease role resecting AID lesions (PNAS); and revealing in B cells a new functional link between autophagy and BCL6 (British J Haematol). In the future, the award of a RyC Fellowship would tremendously help my long-term goal of uncovering specific druggable molecular mechanisms of DNA deaminases and error-prone DNA repair in oncogenesis, providing new targets and therapeutical strategies for patient care. I am confident that the recent award of my first 2 research grants (MINECO-Retos, GobNavarra-Salud), and my incorporation to the recently created European DeamiNET Consortium will highly contribute to this goal.

Resumen del Currículum Vitae:

TRAINING: BSc in Biology (2001) and PhD in Molecular Medicine by the University of Salamanca, Spain (2001-2006) [Molecular characterization of activation-induced cytidine deaminase (AID) gene]. For this work I received the Extraordinary Grade Award in Biology. My Postdoctoral training continued at the Albert Einstein College of Medicine, NY, USA (2006-2011) on the role of DNA mismatch repair (MMR) proteins in the generation of antibody diversity and prevention of lymphoid malignancies. Then I joined the Center for Applied Medical Research (CIMA, University of Navarra) as a Research Associate in the Oncohematology Division (2011-present), to continue my studies on the impact of DNA deaminases in the molecular mechanisms of B-cell lymphomagenesis. PARTICIPATION IN PROJECTS: I was recently awarded two grants from MINECO-Retos (145K, SAF2013-45787-R) and Gobierno de Navarra (56K, GNS-106/2014), in addition to my current European FP7-mobility-IIF grant (20K, PIIF-2012-328177) to study molecular mechanisms of lymphomagenesis. During my postdoc, I received 2 competitive intramural Pilot Project grants (10K & 15K) from the Cancer Center and Center for Epigenomics at the Albert Einstein College of Medicine, NY, USA (2010, 2011). RESEARCH FELLOWSHIPS: Currently, I am about to finish a two-year European FP7-PEOPLE-2012 International Incoming Fellowship (IIF) for career reintegration in Europe. Previously, I was awarded fellowships from different Spanish programmes: Inncorpora-Torres Quevedo Program (2012) [by MINECO]; Postdoctoral Research Fellowship (2006-2008), FPU Research Fellowship (2002-2006), and Undergraduate Research Fellowship (2000-2001) [all three by MEC]. KEY PUBLICATIONS: I have published a total of 24 articles, which have accumulated 461 cites, so far scoring an h-index of 10 (ISI Web of Science). These include 3 corresponding author articles (JACI, 2014; J Exp Med, 2012; Trends Genet. 2010); 3 corresponding author reviews (Semin Immunol, 2012; Biomed & Pharmacother, 2011; Discov Med, 2011); 6 first-author papers (PNAS, 2010; PLoS ONE, 2010; PNAS, 2008; PNAS, 2008; Clin Dev Immunol, 2009; Med Clin, 2001); 10 co-author papers (PNAS, 2013; British J Haematol, 2013; Blood, 2012; J Immunol, 2012; Mol Med, 2011; PNAS, 2010; PNAS, 2009; DNA Repair, 2009; Leukemia, 2004; J Allergy Clin Immunol, 2003); 1 editorial (Genet Res Int, 2011); and 1 co-authored review (Annu Rev Immunol, 2008), all of them in prestigious journals. Moreover, my publication as corresponding author in

Trends in Genetics (2010) was front cover, and I have several manuscripts in preparation. BOOKS: 1 SpringerBriefs on epigenetics, immunology and allergy. INVITED LECTURES & MEETINGS: I have participated in 8 international and 10 national research meetings, as well as delivered lectures in national and international research institutions and associated hospitals. OTHERS: I have strengthened my scientific career with stays (CNIO, CIC); technology transfer activities (SHMTool algorithm, Hybridoma Facility at AECOM-USA); teaching and mentorship experience in Spain and USA (teaching courses and supervising students and technicians). Currently at the U. of Navarra, I am a Supervisor in the Research Training Program, and a Professor in the Biomedicine Master degree. Internationally, I am one of the founding members of the DeamiNET European Consortium, including 17 partners across 7 EU countries.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **RAMON AZCON, JAVIER**
Referencia: RYC-2014-15022
Área Científica: Biomedicina
Correo Electrónico: ramonazconjavier@gmail.com

Título:

Biomaterials for "organ-on-a-chip" development

Resumen de la Memoria:

My first period of my research career started in February 2002 when I join the group of Profs. M.-Pilar Marco and Francisco Sanchez Baeza in the Institute of Chemistry and Environmental Investigation J. Pascual Vila (IIQAB) (now Institute of Advanced Chemistry of Catalonia, IQAC) at the Superior Council of Scientific Research (CSIC). They are a reference in immunochemistry and in biological and artificial receptors in Spain and in the world. During two years (2002-2004) I performed a M.S. in Biochemistry, where I learned how to synthesize, purify and characterize immunogenic haptens, produce specific antibodies, modify proteins and develop and optimize an enzyme-linked immunosorbent assay (ELISA) analytical assay. Immediately after my master's degree (2004), I started my Ph.D. studies in the same group. During my Ph.D. studies I was working in the laboratory of M.-Pilar Marco at the Superior Council of Scientific Research (CSIC) in Barcelona on the development of electrochemical immunosensors for pesticides residues analysis and immunoassays technology (2004-2009). Posteriorly during my post-doc stay I was working under the direction of professor Mizutani at Hyogo University in Japan on amperometric immunosensors and dielectrophoresis technic (2009-2011). After my post-doctoral stay in Hyogo University (2011) I was hired by the Advanced Institute for Materials Research (AIMR) at Tohoku University as Assistant Researcher. The AIMR at Tohoku University is one of nine World Premier International Research Centers Initiative (WPI) Program established with the support of the Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT). The AIMR-WPI institute is the third most relevant institute in Japan and one worldwide reference in material science. I joined the group of Prof. Matsue in the device/systems group and in April 2013 I was promoted to Assistant Professor. In this position, I was working in the integration of biosensors technology with stem cell and tissue engineering research (2011-2014). In this area of research I have recently published several manuscripts in journals of high impact factor (e.g. Lab Chip, Adv. Mater. and Nano Lett., among others). In 2011, I started a new line of research that has become my main line of research. The idea was to integrate biosensor technology and nanotechnology with stem cell research with tissue engineering. This research on 3D-functional engineered tissues was expected to develop an understanding of tissue construction and their functions and relation with some human diseases. Integration of fully functional tissues with microscale biosensor technology allowed us to obtain "organs-on-a-chip." These chips could be used in pharmaceutical assays and could be a step toward the ultimate goal of producing in vitro drug testing systems crucial to the medicine and pharmaceutical industry. Engineered tissues have been integrated with biosensing technology to obtain a microdevice for detecting cellular responses to external stimuli, monitoring the quality of the microenvironment (e.g., metabolites, nutrients), and supporting diverse cellular requirements. My idea is to import this technology to my future research group and to continue working on nanotechnology, biosensors, and immunotechnology.

Resumen del Currículum Vitae:

Actually, I am working in the Chemical and Biomolecular Nanotechnology Department of the Advanced Chemical Research Institute of Catalonia (IQAC) of the CSIC as a senior researcher, concretely in the The Nanobiotechnology for Diagnostics Group (Nb4Dg) led by the Prof. M.-Pilar Marco. My main area of expertise is development of biosensors and immunoassays, integration of nanotechnology in stem cell research, biomaterials and tissue engineering. In my current position, I am the leader of a new line of research, direct responsible of 4 projects and collaborating in several more, and am supervising the work of 5 persons participating on these projects. My main project is the integration of immunosensors technology with stem cells, biomaterials and tissue engineering research (2011-2014). We are using carbon nanotubes and graphene as conductive and mechanically strong materials to make hybrid hydrogel scaffolds. We use dielectrophoresis to precisely manipulate carbon nanotubes inside hydrogels and therefore to control electrical and mechanical properties of the hybrid scaffolds. Engineered muscle tissues using hybrid hydrogel-carbon nanotubes scaffolds showed higher maturation and physiological activity compared with muscle tissues fabricated based on pristine hydrogel scaffolds. We are doing research on the controlled differentiation of stem cells using this hybrid material. We encapsulate embryo bodies in hybrid carbon nanotube gelatin hydrogel scaffolds and study the effect of the electric stimulation on their differentiation. In this area of research I have recently published several manuscripts in journals of high impact factor (e.g. Lab Chip, Adv. Mater. and Nano Lett., among others). In other project, we use biomolecular (kinesin/tubuline) motors for powering shuttles along carbon nanotubes tracks. Carbon nanotubes are aligned by dielectrophoresis and immobilized on glass surface by a covalent reaction. We are developing an electrochemical device for innovating bio-imaging of engineered tissue samples. We are doing epigenetic research of human blood cells using polymerase chain reaction, chromatin immunoprecipitation and magnetic microparticles and finally we are working to generate spatially long-range concentration gradients in a microfluidic device by dielectrophoresis. In the different groups where I have worked, I have had the opportunity to participate and lead competitive projects and supervise students (M.S. and Ph.D.), demonstrating my leadership. As a guest researcher and as a Ph.D. student,

whenever given a particular task, I have demonstrated that I can develop a new and unexplored research field and produce scientifically significant results. My primary research interests include: biomaterials and biofabrication, nano-regenerative medicine, biosensors, nanotechnology, surface chemistry, electrochemical technics and antibody design and production. During my research the results of my work have been presented in 23 scientific conferences both national and international, with 8 oral contributions and 15 poster presentations. Likewise it has given rise to 40 international scientific publications. In addition, I have obtained 2 national patents and one international patent.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **GIMENEZ-CASSINA SENDON, ALFREDO**
Referencia: RYC-2014-15792
Área Científica: Biomedicina
Correo Electrónico: agcassina@gmail.com

Título:

INTEGRATION OF CELL SIGNALING WITH MITOCHONDRIAL METABOLISM IN NEURODEGENERATION

Resumen de la Memoria:

Neurodegenerative disorders constitute an increasing burden in developed countries. Understanding the molecular mechanisms of neurodegeneration is crucial to develop therapeutic strategies. A common feature to most neurodegenerative diseases is mitochondrial failure and metabolic decline. Mitochondria play a central role in neurons by supplying energy, buffering intracellular calcium, maintaining redox balance and providing intermediate metabolites to serve as precursors of neurotransmitters and other intracellular messengers. Mitochondria also harbour the apoptotic machinery, thus contributing to cell death during development or in the event of accumulated cell damage. Importantly, compelling evidence has shown that the metabolic program executed at mitochondria may contribute to modulation of neuronal function and survival through mechanisms that are not yet fully understood.

Most cellular activities, including metabolism, are coordinated through a complex network of signaling pathways. However little is known about the direct impact of signaling pathways on mitochondrial activity and its subsequent effects on neuronal function and survival. Our current research lines aim at identifying and characterizing new mechanisms of regulation of mitochondrial metabolism by signaling pathways. Furthermore, we are studying integration of signaling and metabolism in the context of neurodegenerative diseases with a strong mitochondrial component, including Parkinson's disease and Friedreich's ataxia. Ultimately, we may uncover metabolic anomalies as new biomarkers for early diagnosis as well as novel molecular targets for therapeutic purposes.

A multidisciplinary experimental approach to carry out this proposal is devised. It encompasses the use of mouse and cellular models genetically engineered to recapitulate the progression of the selected neurodegenerative disorders under investigation. State-of-the-art technologies to assess mitochondrial function in real time will be employed, including extracellular flux analysis that offers the possibility to monitor O2 consumption and CO2 release as measurements of mitochondrial respiration and substrate utilisation; and confocal imaging that will enable us to determine mitochondrial dynamics as well as other parameters, such as mitochondrial membrane potential and reactive oxygen species (ROS) production, amongst others. Additionally, the use of cell biology, biochemistry, proteomics and molecular biology approaches will allow us to understand the regulation of mitochondrial metabolism in the brain and its role in the pathogenesis of neurodegenerative diseases. In summary, we are proposing to study and target neurogenerative disorders from an innovative angle. Importantly, our background in cellular neurobiology and cell signaling pathways in neurodegeneration combined with the extensive experience in mitochondrial physiology and bioenergetics has endowed us with the expertise and the tools to carry out the proposed research. In the fullness of time, our studies may pave the way to develop new therapeutic strategies to target neurodegeneration.

Resumen del Currículum Vitae:

EDUCACION

2002-2006 Doctorado, Universidad Autonóma de Madrid.
1997-2002 Licenciado en CC. Biológicas. Universidad Autónoma de Madrid

PUESTOS

2013 – Actual Investigador científico en el Instituto Karolinska (Estocolmo, Suecia)
2007 - 2013 Investigador postdoctoral en Dana-Farber Cancer Institute, Harvard Medical School (Boston, EEUU)
2006 - 2007 Investigador postdoctoral en Centro de Biología Molecular "Severo Ochoa", Universidad Autónoma de Madrid (CBMSO-UAM)
2002 - 2006 Estudiante de doctorado en CBMSO-UAM
2004 - 2005 Visitante en Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford (Reino Unido)
2001 - 2002 Estudiante de último año de carrera en CBMSO-UAM
2001 Estudiante de penúltimo año de carrera en Instituto Cajal (Consejo Superior de Investigaciones Científicas, CSIC)

FINANCIACIÓN COMO INVESTIGADOR PRINCIPAL

2014-2015 Hjärnfonden (Fundación Sueca para la Neurociencia)
2014-2015 Fundación Petrus och Augusta Hedlunds
2015-2016 Fundación Åke Wibergs
2015 Diabetesfonden (Fundación Sueca para la Diabetes)

PUBLICACIONES

1. Ribeiro SM, Gimenez-Cassina A, Danial NN. Methods in Mol Biology, 2015, 1241:59-69

2. Gimenez-Cassina A, [], Danial NN, Cell Metabolism, 2014, 19(2):272-284

3. Stanley IA, Ribeiro SM, Gimenez-Cassina A, Norberg E, Danial NN, En prensa en Trends in Cell Biology,

4. * Gimenez-Cassina A, Lim F, Diaz-Nido J , Neuroscience Letters, 2012, 531(2):182-187 (*: AGC & JDN co-corresponding authors)

5. Fu S, Fan J, Blanco J, Gimenez-Cassina A, Danial NN, Watkins SM, Hotamisligil GS, PLoS Genetics, 2012, 8(8):e1002902

6. Gimenez-Cassina A, Martinez-François JR [...], Danial NN, Neuron, 2012, 74(4):719-730

7. Gimenez-Cassina A, [...], Diaz-Nido J Gene Therapy, 2011, 18(10):1015-1019

8. Gimenez-Cassina A, Danial NN, Molecular Cell, 2010, 40(5):687-688

9. Danial NN, Gimenez-Cassina A, Tondera D, Advances in Experimental Medicine and Biology, 2010, 687:1-32

10. Simarro M, Gimenez-Cassina A, [...], Anderson P, Biochemical and Biophysical Research Communications, 2010, 401(3):440-446

11. Corona JC, Gimenez-Cassina A, Lim F, Diaz-Nido J. Journal of Neuroscience Research, 2010, 88(9):1943-1950.

12. Gimenez-Cassina A, [...], Diaz-Nido J. Journal of Biological Chemistry, 2009, 284(5):3001-3011

13. Simon D, Benitez MJ, Gimenez-Cassina A, Garrido JJ, Bhat RV, Diaz-Nido J, Wandosell F. Journal of Neuroscience Research, 2008, 86(3):668-674

14. Lim F, Palomo GM, Mauritz C, Gimenez-Cassina A, Illana B, Wandosell F, Diaz-Nido J. Molecular Therapy, 2007, 15(6):1072-1078.

15. Gomez-Sebastian A, Gimenez-Cassina A, Diaz-Nido J, Lim F, Wade-Martins R. Molecular Therapy, 2007, 15(2):248-254

16. Gimenez-Cassina A, Lim F, Diaz-Nido J. Neurochemistry International, 2007, 50(1):181-188

17. Gimenez-Cassina A, Lim F, Diaz-Nido J. Journal of Neuroscience Research, 2006, 84(4):755-767

18. Bhat RV, Xue Y, Berg S, Hellberg S, Ormö M, Nilsson Y, Radesäter AC, Jerning E, Markgren PO, Borgegård T, Nylöf M, Gimenez-Cassina A, Hernandez F, Lucas JJ, Diaz-Nido J, Avila J. Journal of Biological Chemistry, 2003, 278(46):45937-45945

DOCENCIA

Certificación ANECA para Profesor Contratado Doctor

PRESENTACIONES Y CONGRESOS

4 Comunicaciones orales y 5 posters en congresos nacionales e internacionales
5 Ponencias como orador invitado en distintos centros internacionales

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **DURAN DIAZ, RAUL VICTOR**
Referencia: RYC-2014-15698
Área Científica: Biomedicina
Correo Electrónico: raul.duran@inserm.fr

Título:

Crosstalk between cell growth signaling and metabolism in cancer cells

Resumen de la Memoria:

I dedicated my career to 3 main relevant projects, comprising the study of fundamental bioenergetics of redox processes, the analysis of cancer metabolism, and the investigation of the response of cell signaling to nutrients availability in cancer cells. As a main result of my investigations, I stablished a connection between the increased consumption of glutamine in cancer cells and the over-activation of mTOR signaling, a master regulator of cell growth (Durán and Hall, EMBO Rep 2012).

Glutamine, the most abundant amino acid in the blood, plays a particularly important role in cell growth and metabolism as a precursor alpha-ketoglutarate (aKG) of the tricarboxylic acid cycle, for nucleotides and for other amino acids. The importance of glutamine as a nutrient is further underscored by the observation that cancer cells are particularly dependent on this amino acid. Glutamine is metabolized through glutaminolysis, which consists of two deamination steps catalysed by glutaminase (GLS) and by glutamate dehydrogenase (GDH. GLS is regulated at the expression level by several oncogenes, and its activity correlates with tumor growth (Tennant, Durán and Gottlieb, Nat. Rev. Cancer 2010). Inhibition of GLS prevents malignant transformation and slows cell growth in certain types of gliomas. On the other hand, the essential amino acid leucine directly binds and activates GDH to stimulate aKG production. Our findings showed that glutamine in combination with leucine activates mTORC1 by enhancing glutaminolysis and aKG production (Durán et al., Mol. Cell 2012). Inhibition of glutaminolysis prevents the Rag-dependent lysosomal translocation and subsequent activation of mTORC1. Conversely, enhanced glutaminolysis or a cell permeable aKG analogue stimulates lysosomal translocation and activation of mTORC1. Finally, cell growth and autophagy, two processes controlled by mTORC1, are regulated by glutaminolysis. Thus, mTORC1 senses and is activated by glutamine and leucine via glutaminolysis and aKG production upstream of Rag (Durán et al., Cell Cycle 2012).

These findings positioned aKG as an intracellular messenger for nutrients availability and suggest new interesting questions, for instance, how is aKG sensed by the cell? On this lead, my studies also suggest that prolyl hydroxylases (PHD) are the aKG sensors that mediate the activation of mTORC1 by glutaminolysis (Durán et al., Oncogene 2013). PHDs are considered the oxygen sensors of cells, as they regulate the stability of HIF, the cellular coordinator of the response to hypoxia. PHDs also require aKG for their catalytic activity (Boulahbel, Durán and Gottlieb, Biochem. Soc. Trans. 2009). Importantly, our work showed that amino acid starvation causes depletion of aKG that leads to PHD inactivation. Importantly, loss of PHD activity during amino acid starvation does not activate HIF, likely due to a lack of HIF expression. In agreement with this result, PHD inhibition blocks the response of mTORC1 to amino acids and induces autophagy independently of HIF. Therefore, PHD proteins act as general metabolic sensors in the cell, detecting scarcity not only of oxygen, but also of amino acids, and forming a link between glutaminolysis and the mTORC1 pathway.

Resumen del Currículum Vitae:

CURRENT POSITION
Since June 2013, Group Leader at the Institut Européen de Chimie et Biologie (Pessac, France), affiliated to the U916 Unit (INSERM)

RESEARCH EXPERIENCE
2010 - 2013, Senior Postdoctoral position at the Biozentrum (University of Basel, Switzerland) in the group of Prof. Michael N. Hall (Growth and Development Area)
2006 - 2009, Postdoctoral position at the Beatson Institute for Cancer Research (Glasgow, UK) in the group of Prof. Eyal Gottlieb (Apoptosis and Tumour Metabolism Group)
2001 - 2005, PhD student at the Instituto de Bioquímica Vegetal y Fotosíntesis (CSIC / University of Seville, Spain), in the group of Prof. Miguel A. de la Rosa (Functional and Structural Proteomics Group)

EDUCATION AND CERTIFICATES
ADT: October 2014, Université de Bordeaux, Bordeaux. France, Autorisation à Diriger une Thèse.
Doctorate, December 2005, CSIC – Universidad de Sevilla, Seville, Spain, PhD in Biochemistry
Master (DEA), March 2003, Universidad de Sevilla, Seville, Spain, Diploma of Advances Studies in Molecular and Cellular Biology
Graduation, August 2000, Universidad de Sevilla, Seville, Spain, BSc in Biology

RECENT SELECTED PUBLICATIONS

Villar VH, Mehri F, Djavaheri-Mergny M and Durán RV. Glutaminolysis and autophagy in cancer, Autophagy, under review.

Durán RV, MacKenzie EM, Boulahbel H, Frezza C, Tardito S, Heiserich L, Bussolati O, Rocha S, Hall MN and Gottlieb E (2013) HIF-independent role of prolyl hydroxylases in the cellular response to amino acids. Oncogene 32, 4549-56.
Durán RV and Hall MN (2012) Glutaminolysis feeds mTORC1. Cell Cycle 11: 4107-8.
Durán RV, Oppliger W, Robitaille AM, Heiserich L, Skendaj R, Gottlieb E and Hall MN (2012) Glutaminolysis activates Rag-mTORC1 signaling. Mol. Cell 47, 349-58.
Durán RV and Hall MN (2012) Regulation of TOR by small GTPases. EMBO Rep. 13, 121-8.
Tennant DA, Durán RV and Gottlieb E (2010) Targeting metabolic transformation for cancer therapy. Nat. Rev. Cancer 10, 267-77.

UNIVERSITY TEACHING RESPONSIBILITIES

2014 - 2015, Master Course Lecture, Cancer metabolism, 4 h, Master Course, Université de Bordeaux
2010 - 2013, Lab Practice Coordinator, Biochemistry, 90 h (aprox.), Department of Biochemistry (University of Basel, Switzerland)
2002 - 2005, Lab Practice Coordinator, Experimental Techniques on Biochemistry, Structure of Macromolecules, and Biochemistry, 90 h (aprox.), Department of Plant Biochemistry and Molecular Biology (University of Seville, Spain)

SELECTED INVITED TALKS

10/04/2015, mTOR and glutamine metabolism in cancer cells, Prof. Sergio Moreno, Instituto de Biología Funcional y Genómica, Salamanca, Spain
24/06/2014, Linking metabolic transformation and cell signaling deregulation in cancer, Prof. Mario Pende, Institut Necker Enfants-Malades, Paris, France
10/01/2014, Linking metabolic transformation and cell signaling deregulation in cancer, Prof. Maria Jose Sanchez Sanz, CABD, Seville, Spain
11/01/2013, Regulation of mTOR signaling by glutamine metabolism, Prof. Lluis Fajas Coll, Université de Lausanne, Lausanne, Switzerland
8/10/2012, Crosstalk between cell growth signaling and metabolism in cancer cells, Prof. Eric Solary, Institute Gustave Roussy, Paris, France
27/09/2012, Glutamine metabolism and mTOR signaling in cell growth regulation, Prof. Ashok Venkitaraman, MRC Cancer Cell Unit - Hutchison Institute, Cambridge, UK

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **FAZZARI , PIETRO**
Referencia: RYC-2014-16410
Área Científica: Biomedicina
Correo Electrónico: fazzari.bio@gmail.com

Título:

Neurociencias

Resumen de la Memoria:

RESEARCH INTEREST
I am a molecular neurobiologist devoted to molecular psychiatry. Specifically, my aim is to investigate neuronal wiring and function in physiological and pathological conditions. To accomplish this aim, I take advantage of state of art tools and approaches by performing a multidisciplinary research that combines genetic, molecular neurobiology, electrophysiology and morpho-functional analysis.

RESEARCH TRACK
I carried out my PhD at the University of Torino in the lab of Prof. Luca Tamagnone, who discovered Plexins as the receptors for Semaphorin guidance cues. There, I generated one of the first KO mice for Plexins, specifically PlexinB1. Already from the PhD, I gained experience in different labs of developmental neurobiology in different countries such as the lab of Dr. Flavio Maina (IBDM, Marseille, France), of Dr. Britta Eickholt (MRC King's College, London, UK) and in the lab of neuronal regeneration lead by Prof. Ferdinando Rossi. In my main PhD work I performed an extensive characterization of PlexinB1 i) expression in different tissues, ii) relevance in Semaphorin induced growth cone guidance and iii) involvement in axonal regeneration after spinal cord injury. This study was among the firsts to investigate the role of Plexins also outside the nervous system and it had an important impact on the Semaphorin/Plexin field (Fazzari et al., BMC Dev Biol, 2007; 41 citations).

Next, I moved to Alicante in the lab of Oscar Marin and Beatriz Rico, where I was awarded a Marie Curie Postdoctoral fellowship to investigate the role of the schizophrenia risk genes NRG1 and ERBB4 in cortical wiring. Using a multidisciplinary approach that combined cell biology, electron microscopy and electrophysiology, I showed that Nrg1/ErbB4 signalling controls the development of inhibitory cortical circuits. Specifically, I found that ErbB4 is expressed by basket and chandelier interneurons and I showed Nrg1/ErbB4 signalling controls the establishment of inhibitory cortical assemblies in two ways: on one side, it is required for perisomatic and axo-axonic inhibitory synapses over pyramidal neurons; on the other, ErbB4 promotes the formation of excitatory input received by interneurons. Overall, this landmark work provided a novel perspective on the involvement of inhibitory circuits in Schizophrenia (Fazzari et al., Nature, 2010; 123 cit.).

To continue, I became interested in the poorly understood Nrg1 intracellular signalling which is regulated by gamma-secretase protease (see Pedrique & Fazzari, J Neuro, 2010). Hence, I moved as Staff scientist to the VIB in Leuven to the lab of Prof. Bart De Strooper, a leader in the field of gamma-secretase biology. Here, I demonstrated that specific Aph1b-gamma-secretase complexes are selectively involved in the processing of Nrg1. Moreover, I showed by gain and loss of function experiments that Aph1b–gamma-secretase/Nrg1 signalling promotes excitatory synaptic transmission, synaptic plasticity and spine formation in pyramidal neurons. This study was recently published (Fazzari et al., eLife, 2014).
Altogether, my work unveiled the complexity of Nrg1 intracellular and forward signalling in cortical wiring and provided precious insights on the etiological role of this major schizophrenia risk gene in human pathology.

Resumen del Currículum Vitae:

Curriculum Vitae
Pietro FAZZARI, PhD

Sex: Male Nationality: Italian
Born: 23/11/1974 Address: Quai du Batelage 5/261, 1000 Bruxelles, Belgium

CURRENT POSITION
Senior Staff Scientist

EXPERTISE
Neurobiology, Molecular Psychiatry, Cortical wiring, Synaptogenesis, Schizophrenia, Alzheimer's disease

WORK EXPERIENCE

01/11-present
Staff Scientist,
Project: "Selective role of gamma-secretase complexes in neuronal physiology and in Alzheimer's disease"
VIB-CME K.U.Leuven. Laboratory for Research on Neurodegenerative Diseases,
Leuven, Belgium
Supervisor: Prof. Bart De Strooper

04/07-09/10
Marie Curie Post-Doctoral Fellow
Project: "Analysis of Neuregulin-1 function in the maturation of cortical GABAergic interneurons: Implications for the etiology of schizophrenia"
Department of Neurobiology, INA Neuroscience Institute of Alicante, Spain
Supervisor: Prof. Oscar Marín, Prof. Beatriz Rico

11/2002-03/2007
PhD Student, PhD Course in Cell Science and Technology
Project: "PlexinB1 functional role during mouse development and in tumour angiogenesis"
Institute for Cancer Research and Treatment, Division of Molecular Oncology,
University of Torino, School of Medicine, Candiolo, Torino, Italy
Director: Prof. Paolo Comoglio, Supervisor: Prof. Luca Tamagnone

4/2006-7/2006
EMBO Visiting fellow
Project: "Study of the functional interaction between B subfamily Plexins and Scatter Factor Receptors during growth and differentiation of hippocampal neurons"
Department of developmental neurobiology, KCL-Medical Research Council, London, UK
Supervisor: Prof. Britta J.Eickholt

3/2004-11/2004
Visiting researcher
Project: "Study of PlexinB1 and Sema4D expression and function in cerebellar development and in neural regeneration upon axotomy and spinal cord injury"
Department of Neuroscience, University of Torino, Torino
Supervisor: Prof. Ferdinado Rossi

01/2001-10/2002
Telethon visiting fellow
Project: "Characterization of PlexinB1 and Sema4D expression during embryonic development by In Situ Hybridization"
Unit of Motoneuron Development and Pathology, IBDM, Marseille, France
Director: Prof. Christopher Henderson, Supervisor: Prof. Flavio Maina

01/1999-12/2000
Master Thesis Student
Thesis Title: "Study of GnRh neuronal system development in urodela amphibian"
Department of Animal Biology, FSMFN, University of Torino, Torino
Supervisor: Prof. M.F. Franzoni

EDUCATION AND TRAINING

05/2012
Course: "Leadership and team management"
VIB, Flemish Institute for Biotechnology, Leuven, Belgium

06/2009

Workshop: "Cortical interneuron in health and disease"
EMBO, European Molecular Biology Organization, Mallorca, Spain

11/2002-03/2007
PhD in Cell Science and Technology
Thesis Title: "PlexinB1 functional role during mouse development and in tumour angiogenesis"
Division of Molecular Oncology, School of Medicine, University of Torino, Torino

09/2005
Course: "Mouse models for human disease"
EMBO, European Molecular Biology Organization, Strasbourg, France

09/2003
Workshop: "The assembly of neural circuits"
EMBO, European Molecular Biology Organization, Varenna, Italy

09/1995-11/2000
Master in Molecular Biology / Bachelor of Science in Biology
Grade: 110/110 (full marks)
Faculty of Mathematical Physical and Natural Science,
University of Torino, Torino

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **LOPEZ SANCHEZ-LAORDEN, BERTA**
Referencia: RYC-2014-15422
Área Científica: Biomedicina
Correo Electrónico: berta.lopez@umh.es

Título:

Unravelling the mechanisms of melanoma initiation, metastasis and resistance to targeted therapies

Resumen de la Memoria:

My scientific career has been focused on cancer research, particularly on melanoma, the deadliest form of skin cancer. The RAS-RAF-MEK-ERK signalling cascade is a known driver of melanoma. RAS is a small G protein activated downstream of receptor tyrosine kinases and RAF, MEK and ERK are protein kinases activated downstream of RAS. BRAF is mutated in 45% of melanomas, and RAS is mutated in 25% of cases. In its early stages, melanoma can be cured by surgery, but the advanced metastatic disease is invariably fatal and unfortunately, strategies to treat these cases are still inefficient. I have used different strategies to gain insight into the mechanisms underlying melanoma susceptibility, initiation, metastasis, resistance to targeted therapies and new therapeutic approaches. During my PhD with Prof Garcia-Borron at the University of Murcia (Spain) by characterizing the melanocortin 1 receptor (MC1R), I showed that melanoma risk can be modulated by an aberrant intracellular trafficking and dimerization of natural variants of the MC1R (4 first-author publications). During my postdoc in Prof Richard Marais laboratory at The Institute of Cancer Research (London, UK) and the Cancer Research UK Manchester Institute (Manchester, UK), I used BRAF and RAS-driven mouse models of melanoma, patient samples, and cutting-edge tecniques such as whole exome sequencing or mass spectrometry to show that (1) UVR accelerates BRAF-driven melanomagenesis and that sunscreen provides only partial protection from the effects of UVR. I identified p53 as a bona fide target of UVR in melanoma in mice and humans and showed that mutant p53 and oncogenic BRAF cooperate to drive melanoma (cofirst-author publication in Nature). (2) Myeloid-derived cells are necessary for melanoma growth and that melanoma immuno-environment promotes resistance to targeted therapies (cofirst-author publication in Cancer Discovery); (3) Paradoxical activation of ERK by the BRAF inhibitors used in clinic promotes invasion and metastasis in RAS mutant and BRAF inhibitor-resistant melanoma cells which can be blocked by MEK inhibitors, in this way supporting the use of this drug combination in the clinic (first-author publication in Science Signaling) and (4) Oncogenic BRAF drives melanoma metastasis by downregulating the phosphodiesterase PDE5A, which in turn, promotes cell contractility (second-author publication in Cancer Cell). I recently moved to the Instituto de Neurociencias CSIC-UMH to enlarge my expertise in the mechanisms underlying metastasis and additional animal models and I am currently investigating the role of the tumour microenvironment in carcinoma metastasis, to pursue my longer-term aim of finding new targets for antimetastatic therapies.

Resumen del Currículum Vitae:

After obtaining two major degrees, in Biology and Biochemistry, I did my PhD in Biochemistry and Molecular Biology at the University of Murcia (2008), under the supervision of Prof Garcia-Borron. During my PhD my research was focused on the structure-function relationship of the human melanocortin 1 receptor (MC1R) and its functional characterization. I also performed two scientific stays to learn new techniques, at the Imperial College (London, UK) and National Institutes of Health, Bethesda, (Maryland, United States) for 3 months each. My thesis obtained a Cum Laude grade with European Doctor mention and the Extraordinary PhD Award. During this time I published 11 articles (with 4 first-author papers, 1 review, and 1 paper from a collaboration that was supervisor-independent). In addition, I presented my work in several international conferences and participated in Biochemistry teaching courses for Medicine and Nursery students and obtained the Acreditación de la ANECA para Profesor Ayudante Doctor (2009). After my PhD, attracted by the highly competitive scientific environment of The Institute of Cancer Research, I moved to London (UK) In October 2008 to join Prof Richard Marais Group, a well recognized laboratory with huge expertise in the underlying causes of melanoma. In October 2012, together with Richard Marais and his group, we moved to the CRUK Manchester Institute (Manchester, UK). During my postdoc in this lab, my work was focused on different aspects of melanoma biology including melanomagenesis, metastasis mechanisms, and resistance to targeted therapies and I published another 9 articles, 3 of them as first-author in Nature, Cancer Discovery and Science Signaling, 1 second-author paper in Cancer Cell, 1 preview in Cancer Cell and other articles in Cancer Cell, Nature Communications, and Cancer Discovery among others. I also presented my work in several international conferences (oral and poster presentations). I am currently working at the Instituto de Neurociencias CSIC-UMH with Dr Angela Nieto, a renowned expert in cell movements in health and disease and my line of investigation is focused into the role of tumour microenvironment metastasis. In addition, I have designed and written proposals that allowed me to get funding to cover my salary during my postdoc -Esteban Cobos Short-Term Fellowship, Postdoctoral Fellowship from the Spanish Ministry of Science and Innovation, FEBS Long-term Postdoctoral Fellowship and a grant from Cancer Research UK awarded to Prof Marais where I was the main investigator and that covered my salary and project costs-. In addition, I have mentored PhD students. All of the described above indicates my research skills, independency and capabilities to lead my research career.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **CASTRO TUBIO, JOSE MANUEL**
Referencia: RYC-2014-14999
Área Científica: Biomedicina
Correo Electrónico: JMCTUBIO@GMAIL.COM

Título:

The impact of structural variation in genome function and disease

Resumen de la Memoria:

The main focus of my research interests along my scientific career has been the impact of genomic structural variation (especially retrotransposition) in genome function, and its role in disease.
My PhD thesis focused on the annotation of retrotransposons in the genome of the Malaria mosquito Anopheles gambiae. In the Mosquito genome, I discovered 60 new retrotransposon families and characterized their evolutionary patterns (see, for instance, Tubio et al. Mol. Biol. Evol. 22:29-39). After this work, I was invited to collaborate in several international insect genome sequencing projects funded by the NIH. Our findings were published in several papers in high-impact journals (Science 316:1718-1723; Science 330:86-88; Science 347:DOI: 10.1126/science.1258522).
After my PhD I moved to the field of cancer genomics. First, in 2010, I joined the Chronic Lymphocytic Leukemia (CLL) genome project, of the International Cancer Genome Consortium (ICGC), at Centre for Genomic Regulation (Barcelona). Here, I specialized in the identification of cancer structural variation by next-generation sequencing data analysis using bioinformatic tools. In the CLL project, I participated in the identification of the genes that drive the disease (Nature 475:101-105; Nature Genetics 44:47-52).
In 2011, I proposed the hypothesis of 'aborted apoptosis' to explain 'chromothipsis', a phenomenon discovered in cancer genomes that consists in hundreds of clustered chromosomal rearrangements (Tubio & Estivill. Nature 470:476-477).
In 2012 I moved to the Wellcome Trust Sanger Institute at Cambridge (UK), under the supervision of Dr. Peter J. Campbell and Professor Mike Stratton. At Sanger, I joined the osteosarcoma, blood cancers, breast cancer, and prostate cancer genome projects of the ICGC, to analyse the structural variation acquired somatically during cancer development. Here, I collaborated in the discovery of two new cancer genes: COL2A1 in osteosarcoma (Nat Genet 45:923-6), and ATF7IP in acute lymphoblastic leukemia (Nat Genet 46:116-25).
In 2013 I was awarded a Marie Curie grant (FP7-PEOPLE-2012-IEF) to analyze the somatic genomic insertions of transposable elements and viruses associated with 1,000 cancer genomes. The results obtained within the framework of this project, which will be active until May 2015, led to an important discovery in the field of cancer genomics: a new mutational process in human cancer called L1-transduction. We found that L1-transduction is a common event in human tumours. Because this mechanism can scatter genes and regulatory sequences across the genome, it may represent another mechanism by which tumour cells acquire new mutations that help them tu survive and grow. This project produced a research article published in the journal Science, of which I am the first author (Tubio et al. Science 345, DOI: 10.1126/science.1251343).
Currently, I'm playing a coordinating role in the "Retrotransposition Subgroup" of the "Pancancer Initiative" of the ICGC and TCGA.
For the last two years, I have also contributed to the understanding of the biology of transmissible (contagious) cancers. I am in charge of the structural variation analyses (including retrotransposition) of the canine transmissible venereal tumour (CTVT) and the Tasmanian Devil Facial Tumour (DFTD). We published the preliminary results of this research in Science 343:437-440.

Resumen del Currículum Vitae:

1. Current position
2013-2015: Marie Curie postdoctoral fellow at Wellcome Trust Sanger Institute (Cambridge, UK).

2. University degrees and Doctorates:
- 2001: First degree in Biology, University of Santiago de Compostela.
- 2009: PhD degree in Biology (Genetics), Department of Genetics, University of Santiago de Compostela.

3. Scholarships and Fellowships:
Along my career I have been the main intellectual driving force to secure funding for my doctoral thesis and my postdoct.
Predoctoral:
- 2003-2005: Predoctoral Contract, from Xunta de Galicia and European Social Fund (ESF).
- 2003-2005: Mobility fellowship from Xunta de Galicia and ESF
Postdoctoral:
- 2010-2012: ANGELES ALVARIÑO Research Contract, from Xunta de Galicia and ESF.
- 2010-2012: Two Mobility fellowships from Xunta de Galicia and ESF.
- 2012: JOSE CASTILLEJO Mobility Fellowship, from Spanish Ministry of Economy and Competitiveness.
- 2013: SARA BORELL Research Contract, from Institute of Health Carlos III.

- 2013-2015: MARIE CURIE Fellowship, from European Research Council (ERC).

4. Publications:
I have published 21 research articles, 11 of them in high-impact journals (5 Science, 3 Nature, 3 Nature Genetics). I have published 5 papers as first author, 2 of them in high-impact journals (1 Science, 1 Nature). I would like to highlight: Tubio et al. Science 345.

5. Research stays:
I carried out one predoctoral stay at the University of Notre Dame (Indiana, USA) and two postdoctoral stays: at Center for Genomic Regulation (Barcelona) and at Sanger Institute (Cambridge, UK). Until the deadline of this Ramon y Cajal call, I spent a total of 4 years, 11 months and 5 days as follows:
09/2004-12/2004 (3 months): University of Notre Dame
15/02/2010 - 31/01/2012 (1 year -11 months - 15 days): Centre for Genomic Regulation
01/02/2012 - 20/01/2015 (2 years -11 months -20 days): Wellcome Trust Sanger Institute

6. Grants and funding:
I have been the main applicant and coordinator of two successful grants from public funding bodies:
- Project: "characterization of transposable elements in the genome of the Lyme disease tick Ixodes scapularis". Funding body: Xunta de Galicia; project code: 10PXIB918057PR; amount 9,200".
- Marie Curie IEF grant FP7-PEOPLE-2012-IEF (project acronym: "CANCER INSERTOME", project number: 328264). The application was scored 94.70 out of 100, and received a total funding budget of "221,606.40 for two years.

7. International collaborations and leadership qualities:
- As part of my PhD project, I have established collaborative research with six international consortia for the sequencing and annotation of the genome of arthropods involved in vector-borne disease; all projects funded/supported by the National Institutes of Health of the United States (NIH).
- As a postdoc, I am member of the International Cancer Genome Consortium (ICGC) since 2010. Currently, I am playing the role of coordinator of the "Retrotransposition Subgroup" of the "Pancancer Initiative", which involves hundreds of researchers from tens of institutions around the world.

8. Teaching and student supervision:
- 2003-2005: Teaching assistant in Genetics, University of Santiago de Compostela.
- 2010: Master in Genetic Consultancy, Pompeu Fabra University

9. Outreach activities:
- Honorary columnist of the Galician newspaper "La Voz de Galicia".

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **TOVAR CARRO, SULAY A.**
Referencia: RYC-2014-15811
Área Científica: Biomedicina
Correo Electrónico: sulay.tovar@usc.es

Título:

Central regulation of Energy Homeostais

Resumen de la Memoria:

SUMMARY OF SCIENTIFIC PRODUCTION

- 44 articles in international research journals Published in journal of high impact index in endocrinology (Endocrinology, JCEM), Obesity and Metabolism (Cell Metabolism, Diabetes, International Journal of Obesity y Diabetologia), Neuroscience (European Journal of Neuroscience), and more generals (Nature medicine, FASEB Journal, EMBO J). High cited for scientific community.
- Times cited: 3995
- IF:266
- H-index: 32 (source Google Scholar).
- More than 50 presentations to national and international congresses and 4 National awards.
- Reviewer for international journals

SUMMARY OF THE RESEARCH CAREER

- Bachelor in Sciences (B.S.c) University of Santiago de Compostela (2000).
- Master in Sciences (M.S.c) (2001)
- Ph D student (2001-2007): University of Santiago de Compostela..

Thesis project: New evidences in the interaction between metabolic status with PYY, Adiponectin, Resistin, Ghrelin.
05/02/2007. Doctor in Biology Department of Physiology. University of Santiago de Compostela). PhD Degree Prize.
25 publications during this period.
Join 2 European projects and more than 5 national and autonomic projects

- Postdoctoral stay in Dpt of Mouse genetics and metabolism (2007-2011). Institute for Genetics, University of Cologne,Germany.

-Postdoctoral Fellowship from the Ministry of Education to Spanish Government
- Fellow Alexander Von Humboldt Foundation
- Postdoctoral Research Fellow from Max Planck Institute.

Research line: study of signalling pathways in different hypothalamic and extra- hypothalamic neuron populations in relationship with energy homeostasis and glucose metabolism.
Principal project: The study of KATP channels in noradrenergic and dopaminergic neurons (cathecolaminergic) in the regulation of energy homeostasis. (Tovar S, et al Cell Metab 2013)
2 more papers in collaboration (Cell Metab)
I joined in 2 European projects

- Selected Isidro Parga Pondal program from Consellería de Economía e Industria de la Xunta de Galicia, University of Santiago de Compostela (2011-until now):
- Principal Investigator: Diabesity group (term for the Study of Diabetes and Obesity).

-Funding as PI Funded by a grant from the Acción Estratégica en Salud from the Spanish Instituto de Salud Carlos III. Hypothalamic control of Ghrelin and UAG in the Glucose Homeostasis.
- 2 paper as senior and corresponding author (see cv).
- 1 Thesis defended under my supervision.
- 3 Master and 1 bachelor thesis defended under my supervision
- 3 PhD thesis under supervision
- 1 Master thesis
- Others future lines: Central regulation of p107 in energy homeostasis.

Resumen del Currículum Vitae:

Previous activity

- Bachelor in Sciences (B.S.c) (Licenciado in Biological Sciences). University of Santiago de Compostela (2000).
- Master in Sciences (M.S.c) (2001) and Diploma of advanced studies. (2002) University of Santiago de Compostela
- Doctor in Biology (Magna Cum Laude). Department of Physiology, Faculty of Medicine. University of Santiago de Compostela (05/02/2007). PhD Degree Prize..

- Postdoctoral stay in el Dpt of Mouse genetics and metabolism (2007-2011). Institute for Genetics, University of Cologne,Germany
- -Selected Isidro Parga Pondal program from Conselleria de Economía e Industria de la Xunta de Galicia, University of Santiago de Compostela (2011-until now):
- Principal Investigator: Diabesity group (term for the Study of Diabetes and Obesity).
- Funding as PI: Hypothalamic control of Ghrelin and UAG in the Glucose Homeostasis. Funded by a grant from the Accion Estrategica en Salud from the Spanish Instituto de Salud Carlos III.
- 1 Thesis defended under my supervision.
- 3 Master and 1 bachelor thesis defended under my supervision

SUMMARY OF SCIENTIFIC PRODUCTION

- 44 articles in international research journals Published in journal of high impact index in endocrinology (Endocrinology, JCEM), Obesity and Metabolism (Cell Metabolism, Diabetes, International Journal of Obesity y Diabetologia), Neuroscience (European Journal of Neuroscience), and more generals (Nature medicine, FASEB Journal, EMBO J). Some of these papers are high cited for scientific community.
- Times cited: 3995
- IF:266
- H-index: 32 (source Google Scholar).
- More than 50 presentations to national and international congresses.
- Reviewer for international journals.

Prizes

- Academia Medico-Quirurgica/Conselleria de Sanidade (Xunta de Galicia) Research Award Date: 26/02/2004. Title: New experimental models for obesity studies Authors: Trujillo M, Seoane LM, Tovar S et al
- Roche Farma Award in Research in Basic Obesity. Madrid, May 2005
- Roche Farma Award in Research in Basic Obesity. Sevilla 2006. Title: Un posible papel del neuropéptido Y AgRP y las isoformas del receptor de leptina en la programación hipotalámica por la ingesta perinatal en la rata. López M, Seoane LM, Tovar S et al.
- Sergio Vidal Award 2006 in Biomedical Research. Effects of single or repeated intravenous administration of kisspeptin upon dynamic LH secretion in conscious male rats. Tovar S, Vázquez MJ et al Endocrinology. 2006 Jun;147(6):2696-704
- PhD Degree Prize Universidad de Santiago de Compostela

Research expertise

- In vivo manipulation: Phenotyping in genetic modify organism, manipulation and surgery in laboratory animals (rats, mice), implantation of intra-cerebral-ventricular, intracardiac cannula, peripheral treatments (mini-osmotic pumps, subcutaneous, intraperitoneal, intravenous injections), adrenalectomy, gonadectomy, clamp hyperinsulinemic-euglycemic, microdialysis, hormonal pulsatil secretion assays, Indirect calorimetry system, Body composition analysis system Thermogenic analysis system, Behavioural analysis system.(open field, water maze, rotarod) Manipulation Drosophila melanogaster lines, Gene-Switch system UAS-GAL
- Molecular Biology: cloning, subcloning, transgenic organism generation, Associated Adenovirus (AVV) manipulation, Northern blot, Southern blot, Western blot, In situ hybridization, Immunohistochemistry

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **GARAIGORTA DE DIOS, URTZI**
Referencia: RYC-2014-15805
Área Científica: Biomedicina
Correo Electrónico: ugaraig@scripps.edu

Título:

Virus-host interactions in hepatitis C and B virus infections

Resumen de la Memoria:

My research career has been focused on studying host-pathogen interactions that regulate human pathogenic virus infections (i.e. influenza, hepatitis C virus (HCV) and hepatitis B viruses (HBV)).
During my Ph.D. studies in Prof. Ortin's laboratory I studied the functions of influenza virus NS1 protein in the regulation of (i) viral gene expression and (ii) late steps in the virus life cycle preceding virus morphogenesis, leading to two publications in Nucleic Acid Research and Journal of Virology, respectively. In this period, I had the chance to supervise 3 undergraduate students in their university-end projects allowing me to gain mentorship and leadership skills that together with other experimental and technical skills prepared me for my next step: the postdoctoral training.
As soon as I joint Prof. Chisari's laboratory I obtained a very competitive and prestigious postdoctoral fellowship from the Cancer Research Institute that supported my research for 3 years. During this time my scientific interests moved from influenza towards hepatitis C virus (HCV) and innate immunity fields, where I've been focused on understanding the mechanisms that HCV employs to activate the innate immune system and escape from its antiviral activity. In collaboration with other postdoctoral fellows we discovered a new mechanism of recognition of infected cells by plasmacytoid dendritic cells (pDCs). We showed that HCV-infected or HCV-replicating cells secrete HCV RNA containing exosomes that activate pDCs, which produce type 1 interferon (IFN) in response and contribute this way to the control of HCV infection. In a different project I discovered a new mechanism by which HCV escapes from the antiviral action of IFN. This mechanism involves the inhibition of translation, including that of antiviral IFN-stimulated mRNAs, by the activation of protein kinase R (PKR). The results of these two projects led to several publications in high impact journals i.e. Nature Communications, PNAS, Cell Host & Microbe and Journal of Virology.
As part of my training, I've often helped Prof. Chisari in peer-reviewing manuscripts and I've actively participated in the design and writing of two NIH grant proposals awarded to him that had since then supported my research till I obtained my own funding from NIH.
As an Assistant Professor at TSRI and as independent Principal Investigator my research is now focused on studying basic aspects of hepatitis B virus (HBV) biology as well as on identifying new molecular targets that could be exploited to develop new treatments against HBV. We are currently collaborating with Isis Pharmaceuticals in the pre-clinical testing of new antisense molecules designed to target HBV infection using both in vitro cell culture and in vivo HBV mouse model systems. In this regard, we have already identified candidate compounds that are in Phase I clinical trials and will hopefully move forward Phase II trials by the end of 2015. In recognition of my work in virology, I am a member of the Editorial Board of Virus Research and I serve as reviewer for 4 international journals: PNAS, Virus Research, Virology Journal, and International Journal of Antimicrobial Agents.

Resumen del Currículum Vitae:

PERSONAL INFORMATION:
Name: Urtzi Garaigorta de Dios
Email: ugaraig@scripps.edu

ACADEMIC DATA:
PhD. in Molecular Biology. Universidad Autónoma de Madrid. Qualification: Summa Cum Laude (2007).
B.S. in Biology and B.S. in Biochemistry. Universidad de Navarra. Qualification: Excellent (2002).

SCIENTIFIC POSITIONS:
Assistant Professor at The Scripps Research Institute (TSRI), La Jolla, USA. July 2014 – present.
Postdoctoral fellow: Prof. Chisari's laboratory (TSRI). July 2007 – June 2014.
Graduate student: Prof. Ortín's laboratory (Dept. of Molecular and Cellular Biology at CNB, Madrid, Spain). August 2002 - May 2007.

PUBLICATIONS:
1. Padmanabhan P., Garaigorta U. and Dixit M.D. Emergent properties of the interferon signaling network may underlie the success of hepatitis C treatment. Nature Communications, 2014. PMID: 24834957.
2. Dreux M, Garaigorta U, et al. Short-range exosomal transfer of viral RNA from infected cells to plasmacytoid dendritic cells triggers

innate immunity. Cell Host & Microbe. 2012. PMID: 23084922.
3. Garaigorta U, et al. Hepatitis C virus induces the formation of stress granules whose proteins regulate late steps in the virus life cycle. J. Virol. 2012. PMID: 22855484.
4. Takahashi K, Asabe S, Wieland S, Garaigorta U, et al. Plasmacytoid dendritic cells sense hepatitis C virus-infected cells, produce interferon, and inhibit infection. PNAS. 2010. PMID: 20231459.
5. Garaigorta U and Chisari FV. Hepatitis C virus blocks interferon effector function by inducing protein kinase R phosphorylation. Cell Host & Microbe. 2009. PMID: 20006840.
6. Garaigorta U and Ortín J. Mutation analysis of a recombinant NS replicon shows that influenza virus NS1 protein blocks the splicing and nucleo-cytoplasmic transport of its own viral mRNA. Nucleic Acids Research, 2007. PMID: 17488845.
7. Garaigorta U, et al. Genetic analysis of influenza virus NS1 gene: a temperature-sensitive mutant shows defective formation of virus particles. J. Virol. 2005. PMID: 16306596.

SCIENTIFIC ACTIVITIES:
Member of the Editorial Board of Virus Research.
Reviewer of: Virus Research, Virology Journal and International Journal of Antimicrobial Agents.

GRANTS:
Antisense Mediated Treatment of Hepatitis B Virus Infection. NIH (04/2014-03/2016).

FELLOWSHIPS:
Postdoctoral fellowship: Cancer Research Institute (01/2008–12/2010).
Graduate fellowship: CSIC (08/2006–05/2007).
Graduate fellowship: Formación Personal Investigador (08/2002–07/2006).

INVITED SEMINARS
Institute Pasteur. Paris. France. 27th February 2013
CNB-CSIC. Madrid. Spain. 25th February 2013
CIMA. Pamplona. Spain. 15th February 2013

SELECTED ORAL AND POSTER COMMUNICATIONS AT MEETINGS:
19th International Symposium on HCV and Related Viruses. October 2012 Italy.
18th International Symposium on HCV and Related Viruses. September 2011 USA (oral).
9th International Symposium on Positive-strand RNA viruses. May 2010 USA.
Cell Biology of Virus Entry, Replication and Pathogenesis. Keystone Symposia. February 2010 USA (oral).
16th International Symposium on HCV and Related Viruses. October 2009 France (oral).
15th International Symposium on HCV and Related Viruses. October 2008 USA.
13th International Conference on Negative Strand Viruses. June 2006 Spain.
13th Congress of Virology. Microbes in a changing World. July 2005 USA (oral).
2nd European Congress of Virology, Eurovirology. September 2004 Spain.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **AGIS BALBOA, ROBERTO CARLOS**
Referencia: RYC-2014-15246
Área Científica: Biomedicina
Correo Electrónico: roberto.carlos.agis.balboa@hotmail.com

Título:

Studying the epigenetic link between PTSD and depression with Alzheimer¿s disease (AD) in human patients

Resumen de la Memoria:

Research career: I obtained a Bachelor in Biology (2001) and a Master in Neuroscience (2005) at the Univ. of Santiago de Compostela (Spain). Then I pursued my PhD in Physiology and Biophysics (2008) at the Univ. of Illinois at Chicago (USA) studying the neurosteroid biosynthesis and the epigenetic theory of schizophrenia. Afterwards, I moved to Goettingen (Germany) to work as a postdoc at the European Neuroscience Institute-Goettingen (2008-2013). There, I focused on the genome-environment interactions (ie, epigenome) that occur during the cognitive impairment associated with normal ageing, psychiatric disorders and neurodegenerative diseases.

Since 2013 I am a senior researcher on neuroepigenetics at the Institute of Biomedical Research of Vigo under the European Project BIOCAPS (FP7-316265). I study the epigenetic mechanisms associated to psychiatric, neurodegenerative and autoimmune diseases using human samples and mouse models. I also search for biomarkers and therapeutic targets for diagnosis, prognosis and treatment of such devastating diseases. I am also a Research Associate Professor at the PhD Program in Neuroscience and Clinical Psychology. At present, I am the supervisor of two PhD students. I am part of the "Red Gallega de I+D de Medicamentos (REGID)". Moreover, I am actively involved in popularizing science using diverse media. I have two scientific blogs in "GCiencia" and "El Huffington Post".

Main line of research: Traumatic events can lead to excessive fear and certain psychiatric disorders such as PTSD. Here, fear extinction is crucial as a therapeutic strategy to inhibit excessive fear. I showed in a mouse model that IGF2 facilitates fear extinction, while IGFBP7 impairs fear extinction in an IGF2-dependent manner. Similarly, I showed that fear extinction-induced IGF2/IGFBP7 promotes survival of new neurons generated in the adult mouse hippocampus. In addition, we have shown recently that IGFBP7 regulates memory consolidation and could be a potential target to treat Alzheimer¿s disease (AD).

The greatest risk factor for dementia is aging. The most severe form of dementia is AD. The search for biomarkers in order to prevent and detect AD in its earliest form is essential. Recent studies in humans have shown that PTSD and depression are also risk factors for AD, accelerating cognitive decline associated with AD. These data suggest a relationship between PTSD and depression with the progression of AD; however, this link is not characterized yet. In this context, IGFBP7 is de-regulated in both PTSD and AD as shown by my previous work. We postulate that IGF2/IGFBP7 signaling could be a candidate for the link between PTSD and depression with the progression of AD. However, little is known about the role of IGF2/IGFBP7 signaling and the associated molecular (eg. epigenetic) mechanisms in the human brain.

There are not available drugs targeting IGF2/IGFBP7 signalling to treat diseases such as PTSD, depression or AD. My studies will help to design epi-drugs that would regulate IGF2/IGFBP7 signaling and the associated epigenetic mechanisms. In this context, the level of signaling molecules belonging to IGF2/IGFBP7 signaling in blood or CSF (e.g. miRNAs) could be a potential biomarker for diagnosis of PTSD, depression, and AD. In future IGF2/IGFBP7 signaling could be used as a therapeutic target to treat such brain diseases.

Resumen del Currículum Vitae:

Education

08/2003 to 12/2007	Physiology and Biophysics (Ph.D.), UIC, USA
10/2003 to 06/2005	Neuroscience (M.Sc.), USC, Spain
10/1995 to 06/2001	Molecular Biology (B.Sc.), USC, Spain

Work experience

06/2013 to present	Senior Researcher (BIOCAPS, FP7-316265), IBI-VIGO, Spain
06/2013 to present	Collaborator with Prof. A. Fischer (AG 179/1-1), DZNE-Goettingen, Germany
04/2013 to 05/2013	Principal Investigator (DFG grant, AG 179/1-1), ENI-Goettingen, Germany
04/2011 to 03/2013	Postdoct, ENI-Goettingen, Germany
04/2009 to 03/2011	EMBO Postdoctoral Fellow (ALF 652-2008), ENI-Goettingen, Germany
04/2008 to 03/2009	Postdoct, ENI-Goettingen, Germany
01/2008 to 03/2008	Postdoct, UIC, USA

08/2003 to 12/2007	Graduate Research Fellow, UIC, USA
12/2001 to 08/2003	Research Specialist in Health Sciences, UIC, USA
10/2000 to 06/2001	Research Student, USC, Spain

Recent accomplishments and awards:
- Early Stage Researchers grant and Prize for the Best Poster Presentation. COST action (TD0905) "Epigenetics: From Bench to Bedside Conference". Athens, Greece. May 5th-8th, 2014.
- Leadership in Action. Competitive Program organised by the Health Innovation Platform and Foundation Barrie. La Coruña, Spain. October 28th-30th, 2013.
- BIOCAPS project (FP7-316265). I got 20.000 euros for research / 3-years contract. IBI-Vigo, 06/2013 to present.
- Recipient of a DFG research grant (336.100 euros / 3 years), AG 179/1-1 "Epigenetic regulation of IGF2/IGFBP7 signaling in anxiety disorders and neurodegenerative diseases", 04/2013-03/2016.
- Recipient of the Inge and Fritz Kleekamm Research Award of the Alzheimer-Foundation Goettingen (5.000 euros), 09/2012.
- EMBO Long-Term Fellowship (ALF 652-2008), 04/2009-03/2011.
- Humboldt Research Fellowship (2009). Declined.
- Graduate Teaching Assistantship with tuition and fee waiver. UIC, USA. 08/2003–12/2007.

I have organised and presented my work via posters (24) or speeches (32) at national and international conferences. I review grants and scientific papers. I am author of several research articles in high impact journals (Science, PNAS, EMBO J, J Neurosci, Schizophr Res, JAD,). Selected publications:

- Agis-Balboa RC et al. Psychopharmacology, 2014.
- Ortolano S, Vieitez I, Agis-Balboa RC & Spuch C. Molecular Brain. 2014.
- Agbemenyah HY, Agis-Balboa RC. Neurobiol. Dis, 2014.
- Agis-Balboa RC* and Fischer A. CMLS, 2013 (*, Corresponding author).
- Kerimoglu C, Agis-Balboa RC, et al, J Neurosci, 2013.
- Agis-Balboa RC* et al. J Alzheimers Dis, 2013 (*, Corresponding author).
- Zovoilis A*, Agbemenyah HY*, Agis-Balboa RC, et al. EMBO J, 2011 (*, Equal contribution).
- Agis-Balboa RC et al, EMBO J, 2011.
- Govindarajan N, Agis-Balboa RC, et al, J Alzheimers Dis, 2011.
- Peleg S*, Sananbenesi F*, Zovoilis F*, Burkhardt S, Bahari-Havan S, Agis-Balboa RC, et al, Science, 2010 (*, Equal contribution).
- Agís-Balboa RC et al, PNAS, 2007.
- Veldic M, Kadriu B, Maloku E, Agis-Balboa RC, et al, Schizophr Res, 2007.
- Agís-Balboa RC et al, PNAS, 2006.
- Pinna G, Agis-Balboa RC et al. PNAS, 2006.
- Dong E, Agis-Balboa RC, et al, PNAS, 2005.

In addition, I am part of the Divulgacción AGC CCT "Galician Association of Communication of Scientific Culture and Technology" and popularise science using diverse media.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **CUBERO PALERO, FRANCISCO JAVIER**
Referencia: RYC-2014-15242
Área Científica: Biomedicina
Correo Electrónico: cuberj01@hotmail.com

Título:

Compound function of Jnk1 and Jnk2 during acute and chronic liver disease

Resumen de la Memoria:

Liver disease encompasses a wide spectrum of injury including acute liver failure such as drug-induced liver injury (DILI) or inborn-errors of metabolism (IEM) or chronic liver disease such as alcoholic liver disease (ALD), non-alcoholic steatohepatitis (NASH) which may progress to cirrhosis and end-stage hepatocellular carcinoma (HCC).

During my M.Sc. and later my Ph.D. studies I became strongly interested in fetal hepatocyte isolation. Thus we worked on optimizing the technique to isolate hepatocytes with the view of transplanting them in order to restore liver function impaired by IEM (Sierra, 2000; Arahuetes, 2001). Next, we aimed to purify hepatocyte suspensions (Arza, 2001) and used them at the most appropiate stage of development for transplantation into hyperbilirubinemic rats (Cubero, 2001; Bustamante, 2006). Finally, we formulated a strategy for selective proliferation of transplanted cells (Cubero, 2005; Cubero, 2007).

For my postdoctoral investigations I first focused on the context of Kupffer (KC) and hepatic stellate cells (KC), and their role in alcoholic liver disease (ALD) (Cubero, 2006; Cubero, 2009). Our results unveiled a synergism between ethanol and polyunsaturated fatty acids (PUFAs) such as arachidonic acid (AA) to the mechanism whereby KC mediate ECM remodeling (Cubero, 2008; Cubero, 2012). Futhermore, we found out that reactive oxygen (ROS) and nitrogen species (RNS) can induce a protective mechanism in HSC in early stages of liver injury (Urtasun, 2009; Urtasun, 2012).

My second postdoctoral has focused on the study of molecular mechanisms of cell death. We first investigated the activation of caspase-8 (Casp8) and its role in death receptor-mediated apoptosis (Liedtke, 2011) and later in NASH (Hatting, 2013). Furthermore, we have shown that death receptors in hepatocytes and immune cells have different roles in chronic liver injury and tumorigenesis (Cubero, 2013; Arshad, 2012; Hatting, 2015) and its therapeutic potential (Malato, 2012; Kaldenbach, 2014). My main focus during the past years has been the role of JNK during acute and chronic liver injury (Cubero, 2010; Cubero 2011). We first identified Jnk1 in HSC as a profibrotic kinase (Zhao, 2014) and then provided evidence that JNK1 in hematopoietic cells is crucial not only for liver regeneration but also for the progression of chronic liver disease (Schaefer, 2015; Cubero, 2015). Furthermore, we have very recently found that the current dogma of JNK inhibition as a treatment for acute liver failure might have been misinterpreted (Cubero, 2015; Gastroenterology, In Revision).

For my independent career, I aim to unmask the compound and distinct functions of Jnk1 and Jnk2 in different forms of liver injury. Very recent results suggest that (1) the oxidative stress response is essential for the modulation of JNK during different forms of DILI and (2) the compound function of Jnk1 and Jnk2 in hepatocytes determines the fate of cancer cells. These viable projects have the potential to increase in a significant manner our understanding of key molecular mechanisms involved in essential aspects of liver disease. Therefore, millions of people around the world could be benefited from therapies that modulate the function of the JNK genes.

Resumen del Currículum Vitae:

Soon after I finished graduated in the Universidad Complutense Madrid (UCM), I started my predoctoral stage as a student-collaborator in Dr. Rosa Maria Arahuetes's lab, granted with a Fellowship from the Regional Government of Madrid. During this period, we began a profitable collaboration with Dr. Paloma Maganto, at the Service of Experimental Surgery in Puerta de Hierro Hospital. We focused my M. Sc. thesis on the expression of bilirubin UDP-glucuronosyl transferase throughout fetal development. With the financial support of a predoctoral fellowship of the Spanish FISS (ISCIII), we focused on hepatocyte transplantation as an alternative to orthotopic liver transplant in liver-based inborn errors of metabolism, such as the Crigler-Najjar syndrome type I. My doctoral thesis, outstanding cum laude, was titled "Intrasplenic transplantation of hepatocytes in an experimental model of type I Crigler-Najjar syndrome". During this stage, I also taught practical and theorical classes at UCM.

My postdoctoral experience began at Trinity College Dublin where I could finish my PhD papers and simultaneously acquire teaching experience in Anatomy and Physiology under the Supervision of Prof. Gabrielle McKee. Later, I joined Dr. Natalia Nieto's lab, in the Division of Liver Diseases at Mount Sinai School of Medicine as a postdoctoral fellow first and then as a recipient of a postdoctoral fellowship from the Spanish Ministry of Science and Education (Beca MEC), under the auspices of Prof. Scott Friedman. Using my expertise in primary hepatocyte isolation (both fetal and adult), I experimentally approached the study of the pathophysiology of alcohol-induced

liver fibrosis. As a result of my work in New York, I was awarded the prestigious Liver Scholar Award (AASLD), and the postdoctoral fellowship of the New York Center for Systems Biology (NYCSB) in 2008.

In 2009, I joined the research group headed by Prof. Trautwein who has been several years investigating the functional relevance of cell-type specific signaling pathways in animal models of liver injury. During this time I have actively collaborated in two MD theses and directed one. I currently supervise the Doctoral theses of 5 people. Moreover, I have collaborated with the Teaching in the Faculty of Medicine at the RWTH, giving at least 2 h of classes per week. In addition I have received the Glaxo Smithkline Travel Award 3 years in a row (2012-2014) to attend the European Association for the Study of the Liver (EASL) Conference and received 3 Research grants as Principal Investigator. In addition, I have been invited as Invited Speaker to CNIC (Madrid) in 2013 under the auspices of Dr. Guadalupe Sabio), and took part of the Thesis Committee of a doctoral thesis (CNIO, Madrid). Furthermore, I have been part of the Thesis Examination as Secretary two times (2013 and 2014), both in CNIO. Moreover, I have submitted over 40 proceedings to national and international congresses, many of them awarded with Distinguished Distinctions and as Oral Presentations. In total I have up-to-date 31 published papers indexed in Pubmed including reviews, some as senior and corresponding author. Also, I have written 2 book chapters and acted as a Reviewer for several Scientific Journals and the German Research Foundation (DFG). I am a member of the EASL.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **RODRIGUEZ BRAVO, VERONICA**
Referencia: RYC-2014-15616
Área Científica: Biomedicina
Correo Electrónico: rodriguv@mskcc.org

Título:

Mechanisms of Genome Instability in Human Cells and Consequences in Cancer

Resumen de la Memoria:

Genome aberrations such as chromosomal instability (CIN) and aneuploidy are a hallmark of cancer, however their molecular and cellular underpinnings and contribution to cancer are not completely understood. I have focused my research on the study of cell cycle control mechanisms or "checkpoints" that safeguard genome integrity. During my PhD I studied ATR/ATM-independent replication checkpoint mechanisms in human cells. My work revealed different responses of tumor and non-tumor cells to replication stalling. While non-tumor cells integrate multiple pathways involving activation of Chk1 and p38 kinases to ensure robustness of the checkpoint response, cancer cells lack this redundancy giving a rational for specific cancer treatment combinations (Rodriguez-Bravo V, et al. Cancer Res. 2006; Rodriguez-Bravo V, et al. Cancer Res. 2007).

During my postdoctoral research I have applied genome-editing methods to precisely dissect mechanisms controlling error-free chromosome segregation in human cells. I have participated in the study of Plk1 kinase roles in cytokinesis (Burkard ME, Maciejowski J, Rodriguez-Bravo V, et al. PLoS Biol. 2009) and I have shown that nuclear pore complexes (NPCs) ensure proper speed of mitosis and fidelity of chromosome segregation to protect genome integrity (Rodriguez-Bravo V, et al. Cell. 2014) (Highlighted by: Abigail Butchwalter, Martin W Hetzer. Cell. 2014; Kirsty Minton. Nat Rev Mol Cell Biol. 2014). My work uncovered mitotic timing fine-tuning by NPCs as a safety mechanism to prevent structural and numerical chromosome alterations and revealed NPCs deregulation as a new mechanism of genome instability opening new avenues of research to understand the intricate NPC-checkpoint network that guards genome integrity and potentially protects against cancer.
During the last years I have also participated in the study of how cancer cells acquire chemotherapy resistance to anti-mitotic agents, such as taxanes, commonly used in the clinics. These studies have uncovered new mechanisms of chemotherapy resistance in cancer cell models and patient tumor samples (Domingo-Domenech J, Vidal S, Rodriguez-Bravo V et al. Cancer Cell. 2012) and a transcriptional program controlled by the master regulator GATA2 that drives aggressiveness and survival to chemotherapy (Vidal S, Rodriguez-Bravo V et al. Cancer Cell, in press, February 2015) allowing me to gain expertise in cancer biology and translational oncology.

My research goal as an independent investigator is to study the molecular and cellular mechanisms controlling error-free human cell division, analyze the contribution of their failure to genome instability and the consequences for cancer pathogenesis and therapeutic responses. To achieve this, I will take a multi-disciplinary approach building on my expertise in cell, molecular biology (genome-editing) and cancer biology, to elucidate how nuclear pores and the mitotic checkpoint monitor faithful chromosome segregation and the consequences of deregulation in cancer.

Resumen del Currículum Vitae:

I studied Biology at the University of Barcelona (Spain) supported by the "Extraordinary College Award". Motivated to understand the molecular processes underlying cancer I did my PhD studying cell cycle checkpoint mechanisms in the School of Medicine of the University of Barcelona. Supported by predoctoral fellowships from the Catalan Government (FI, 2002-2005) and from the School of Medicine (2006) in Dr. Neus Agell's group, I showed that non-tumor cells activate robust checkpoint mechanisms in response to DNA synthesis inhibition involving redundant signaling by several kinases that cancer cells lack. This work gave a rational for selective targeting of tumor cells combining DNA replication and replication checkpoint inhibitors (Cancer Res. 2006 and 2007) and was recognized with the "Extraordinary Doctorate Award" by the University of Barcelona in 2007. To gain expertise on cell cycle control mechanisms of DNA damage, I visited Dr. Rene Medema laboratory at the University Medical Center of Utrecht (UMC, The Netherlands) as a postdoctoral fellow where I got interested in the mechanisms controlling fidelity of mitosis during human cell division (J. Cell Biol. 2009).

Pursuing to further study error-free chromosome segregation in human cells, chromosome instability (CIN) impact in cancer and eager to learn innovative genome editing methods to create conditional knock out human cells (cKO), I joined Dr. Prasad V. Jallepalli laboratory at MSKCC (New York, USA) as a postdoctoral researcher in 2008. During the last years I have worked on Plk1 kinase regulation of cytokinesis (PLoS Biology, 2009) and focused my research on the cell division control mechanisms that ensure mitosis fidelity and avoid chromosome aberrations common in human cancers such as aneuploidy and CIN. Using genome-editing I discovered that nuclear pore complexes (NPCs) produce an anaphase inhibitory signal in interphase that ensures proper speed of the next mitosis, high-fidelity chromosome

separation and genome integrity. Failure of this pathway accelerates mitosis inducing the accumulation of chromosome errors associated to CIN cancers. My work was published in Cell (Feb. 2014) and highlighted by Nat. Rev. Mol. Cell Biol., Cell preview, Faculty 1000 and frontiers in Oncology where it was listed as a new mechanism of chromosome instability with cancer implications. In addition it has been selected for oral presentations in international conferences.

Moreover, to integrate my molecular and cell biology background with cancer biology approaches I have collaborated in studies dissecting mechanisms of chemotherapy resistance to anti-mitotic agents (taxanes) commonly used in cancer treatment. These studies have been published in Cancer Cell (2012, and Feb. 2015 in press) and allowed me to obtain extensive experience in cancer biology and therapeutic responses that will be instrumental in my own laboratory.

In summary, my research training has allowed me to gain the expertise in cell and molecular biology (genome-editing) I will apply in my own laboratory. Importantly, the interaction with multi-disciplinary collaborators made me grow as a scientist and broaden my knowledge in cancer biology. These productive research activities have empowered me to develop my own research program to address the fundamental mechanisms underlying chromosome instability in cancer.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **LLOBET NAVAS, DAVID**
Referencia: RYC-2014-15569
Área Científica: Biomedicina
Correo Electrónico: david.llobet@mssm.edu

Título:

Cáncer de endometrio, mama y papel del tejido adiposo en la regulación de la tumorogénesis

Resumen de la Memoria:

I graduated in Genetics and Cell biology in the Autonomous University of Barcelona (Spain). After finishing my bachelor degree in 2003, I pursued a PhD degree in Dr. Xavier Matias-Guiu&#65533;s molecular pathology group in the Biomedical Research Institute in Lleida (IRB-LLEIDA, Spain).
In Dr. Matias-Guiu&#65533;s laboratory I was initiated in the study of molecular alterations involved in development and progression of type I endometrial cancer and their implication in apoptosis resistance.
Briefly, the work during my PhD was focused on the study of the molecular mechanisms underpinning apoptosis resistance to TNF-family ligands in endometrial cancer cells (Laboratory Investigation 2005; Oncogene 2008; American Journal of Pathology 2009; American Journal of Pathology 2011). In parallel I also participated in the analysis of additional prosurvival factors such as expression of NF-kappaB subunits and Survivin (Journal of Pathology 2004, International Journal of Gynecological Pathology 2005), in the identification of PIK3CA gene mutations (Human Pathology 2006) and explored in vitro the potential therapeutic effects of NF-KappaB inhibitors as well as the receptor-tyrosin kinase inhibitor Sorafenib (Journal of Biological Chemistry 2006; Anti-Cancer Drugs 2008; European Journal of Cancer 2010).
During the course of my PhD I joined Dr. John C. Reed&#65533;s laboratory in The Sanford-Burnham Institute for Medical Research in 2007 (La Jolla, CA, USA) as a visitor scientist to continue studying the role of TNF ligands. In Dr. Reed&#65533;s laboratory I worked in the characterization of genetically engineered mouse models of Autoimmunity and Chronic Lymphocytic Leukemia (CLL) (Blood 2009, Journal of Immunology 2012).
Subsequently in 2010 I joined Dr. Jose Silva at the Herbert-Irving Comprehensive Cancer Center in Columbia University (NY) and at The Mount Sinai School of Medicine (NY) to discover genes in the mammary gland development with relevant roles in tumorigenesis.
In his laboratory I identified the miR-424 and miR-503 to be differentially expressed during remodeling of the mammary gland after lactation. By generating a miR-424-/-/503-/- knockout mouse model I reported the characterization of the miR-424/503 cluster as a master regulator of postlactational involution regulated by TGFβ (Genes & Development 2014; Molecular and Cellular Biology 2014). Moreover, analysis of the genomic loci of miR-424/503 revealed that this cluster is deleted in a significant proportion of breast tumors. Interestingly, the miR-424-/-/503-/- knockout mouse model develop tumors in the mammary gland and also a hyperplastic phenotype in the adipose tissue which I will continue to study in the near future.
In addition, I have also participated in the design and development of side-projects in the laboratory that were focused in the identification of new tumor suppressors and the discovery of new breast cancer vulnerabilities by using genome-wide loss of funtion assays through shRNA pooled screenings. As a result, several manuscripts are under preparation or in revision in prestigious journals (Marshall N et al 2014 Nature-under review; Rodriguez-Barrueco R et al 2014 Cancer Discovery-under review).

Resumen del Currículum Vitae:

David Llobet Navàs, Ph.D.
david.llobet@mssm.edu

INSTITUTIONS:
1-The Mount Sinai Hospital-Icahn Medical Institute: Post-doctoral Fellow
2-Institute for Cancer Genetics Irving Cancer Research Center Columbia University: Post-doctoral Fellow
3-The Sanford-Burnham Institute for Medical Research: Visitor Scientist
4-IRB-LLEIDA: Pre-doctoral Student

FELLOWSHIPS
1-Pre-doctoral:
a) ISCIII-Instituto de Salud Carlos III Fellowship
b) Spanish Association Against Cancer (AECC)
c) Pifarré Foundation Fellowship
2-Post-doctoral:
a) Beatriu de Pinós (Catalan Agency of Research)
b) Spanish Ministry of Science and Technology

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

AWARDS
1-IEC_Premio Sant Jordi Award: August Pi i Sunyer Award of Biochemistry and Physiological Sciences. 2010
2-UdL (University of Lleida) Best doctoral thesis. 2010

ARTICLES
1-Hua-Sheng Chiu*, David Llobet-Navas* et al. Genome Research. 2015 [Epub ahead of Print]
2-Félix Sanchez-Garcia, et al. Cell. 159:1461-75. 2014
3-David Llobet-Navas et al. Molecular and Cellular Biology. 34:4216-31. 2014
4-Herranz D, et al. Nature Medicine. 20:1130-7. 2014
5-Llobet-Navas D, et al. Genes & Development. 28:765-82. 2014
6-Eritja N et al. American Journal of Pathology. 183:277-87. 2013
7-Pérez-Chacón G, Llobet D et al. Jounal of Immunology. 189:1053-61. 2012
8-Eritja N et al. Journal of Cell Science. 125:1929-44. 2012
9-Montserrat N et al. Human Pathology. 43:632-43. 2012
10-Sumazin P et al. Cell. 147:370-81. 2011
￼11-Yeramian A et al. Laboratory Investigation. 91:859-71
12-Llobet D et al. American Journal of Pathology. 178:1529-1543. 2011
13-Eritja N, Llobet D et al. American Journal of Pathology. 176:2722-31. 2010
14-Llobet D et al. European Journal Of Cancer. 46:836-850. 2010
15-Tarragona J et al. Archiv Virchows. 456:39-44. 2010
16-Zapata JM, Llobet D et al. Blood. 113:4595-603. 2009
17-Pallarés J*, Llobet D* et al. American Journal of Pathology. 174:287-96. 2009
18-Llobet D et al. Journal of Clinical Pathology. 62:777-85. 2009
19-Pallares J et al. Analytical and Quantitative Cytology and Histology. 31:217-26. 2009
20-Llobet D et al. Oncogene. 27:2513-24. 2008
21-Llobet D et al. Anti-Cancer Drugs. 19:115-124. 2008
22-Gallel P et al. Human Pathology. 39:994-1001. 2008
23-Sorolla A et al. British Journal of Dermatology, 158:496-504. 2008
24-Ortega E et al. Seminars in Diagnostic Pathology. 25:262-73. 2008
25-Dolcet X*, Llobet D* et al. Journal of Biological Chemistry. 281:22118-30. 2006
26-Velasco A et al. Human Pathology. 37:1465-72. 2006
27-Dolcet X, Llobet D et al. Laboratory Investigation. 85:885-94. 2005
28-Pallarés J et al. International Journal of Gynecological Pathology. 24:247-53. 2005
29-Pallarés J et al. Modern Pathology. 18:719-27. 2005
30-Dolcet X, Llobet D et al. Archiv Virchows. 446:475-82. 2005
31-Pallarés J et al. Journal of Pathology. 204:569-77. 2004

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **GONZALEZ GRASSI, FEDERICO**
Referencia: RYC-2014-16751
Área Científica: Biomedicina
Correo Electrónico: gonzalf1@mskcc.org

Título:

Modeling PDAC initiation through gene editing in hPSCs

Resumen de la Memoria:

I conducted my PhD in the laboratory of Dr. Duboule lab (University of Geneva, Switzerland) where I acquired a solid background in molecular biology and genetics and published several articles uncovering the identification and characterization of remote enhancer sequences responsible for the long-range regulation of Hox genes during development.

Next, I joined the laboratory of Prof. Juan Carlos Izpisúa Belmonte as a postdoctoral fellow of the Swiss National Science foundation (SNSF), to study stem cell biology and regenerative medicine, first at The Salk Institute for Biological Studies (La Jolla, USA), and then at the Center for Regenerative Medicine in Barcelona (CMRB) (Barcelona, Spain). My work focused on developing strategies to generate therapeutically relevant iPSCs. In 2009, I published one of the first strategies allowing the generation of "transgene-free" iPSCs.

In 2011, I joined the laboratory of Dr. Huangfu as a New York State Stem Cell (NYSTEM) Science fellow. I addressed the role of DNA repair pathways during reprogramming. I showed that DNA damage is increased during reprogramming, and homologous recombination genes are required for this process. This study is the first report identifying reprogramming as a major trigger of DNA damage and contributes to the design of safer approaches for creating iPSCs.

More recently, I developed a novel platform for rapid, efficient and inducible genome editing of human pluripotent stem cells (hPSCs), named iCRISPR. This platform allows modifying the genome of hPSCs with unprecedented ease and efficiency. It provides an effective tool to address the function of complex gene networks altered in multigenic diseases such as cancer, and has the potential to support high-throughput genetic analysis in hPSCs.

My main research line is to model and study pancreatic ductal adenocarcinoma (PDAC) initiation using human Pluripotent Stem Cells (hPSC). Pancreatic ductal adenocarcinoma (PDAC) has a dismal 5-year survival rate of 6% and is projected to be the second leading cause of cancer death by 2030. Unfortunately, no available human models of PDAC initiation recapitulate the genetic context found in early stages of this disease.

Using iCRISPR, I propose to create a PDAC initiation model by introducing single or multiple PDAC initiating mutations in hPSCs. By sequentially generating the mutations characterizing different stages of PDAC initiation, I will be able to recapitulate the genetic events leading to PDAC and assess their function in vivo, through injection into recipient mice or in vitro, through generation of pancreatic organoids. This approach will greatly improve our understanding of the early steps of this disease, allowing identifying biomarkers for its early detection, and easily perform drug or genetic screens using CRISPR libraries, providing new therapeutic approaches to detect and treat PDAC patients.

Resumen del Currículum Vitae:

PhD in Science, mention Biology, Department of Zoology and Animal Biology, University of Geneva-Switzerland (2000-2006)
Master in Biology, University of Geneva-Switzerland, 1998
Degree in Biology University of Geneva-Switzerland, 1996

Research activity

April 2011 to present Post-doc in the Developmental Biology Program
Dr. Danwei Huangfu. Sloan-Kettering Institute MSKCC, New York, USA. New York State Stem Cell (NYSTEM) Science fellow.

2008 to April 2011. Post-doc at the Centre of Regenerative Medicine. Prof. Juan Carlos Izpisua Belmonte at CMRB, Barcelona, SPAIN. Fellow of the Swiss National Science Foundation (SNSF).

2007. Post-doc in the Gene Expression Laboratory. Prof. Juan Carlos Izpisua Belmonte at The Salk Institute, La Jolla, USA. Fellow of the

Swiss National Science Foundation (SNSF).

06/2006 - 12/2006. Post-doc in the Laboratory of Molecular Embryogenesis and Morphogenesis. Prof. Denis Duboule at University of Geneva, SWITZERLAND

2000 - 06/2006. PhD in the Laboratory of Molecular Embryogenesis and Morphogenesis
Prof. Denis Duboule at University of Geneva, SWITZERLAND.

1996 - 1998. Master in the Laboratory of Molecular Embryogenesis and Morphogenesis
Prof. Denis Duboule at University of Geneva, SWITZERLAND.

Most relevant publications

Zhu, Z. *, Gonzalez, F. *, and Huangfu, D. (2014). The iCRISPR Platform for Rapid Genome Editing in Human Pluripotent Stem Cells. Methods in enzymology 546, 215-250.

Gonzalez, F. *, Zhu, Z. *, Shi, Z.D. *, Lelli, K., Verma, N., Li, Q.V., and Huangfu, D. (2014). An iCRISPR platform for rapid, multiplexable, and inducible genome editing in human pluripotent stem cells. Cell stem cell 15, 215-226.

Andrey, G., Montavon, T., Mascrez, B., Gonzalez, F., Noordermeer, D., Leleu, M., Trono, D., Spitz, F., and Duboule, D. (2013). A switch between topological domains underlies HoxD genes collinearity in mouse limbs. Science 340, 1234167

Gonzalez, F., Georgieva, D., Vanoli, F., Shi, Z.D., Stadtfeld, M., Ludwig, T., Jasin, M., and Huangfu, D. (2013). Homologous recombination DNA repair genes play a critical role in reprogramming to a pluripotent state. Cell reports 3, 651-660.

Gonzalez, F., Boue, S., and Izpisua Belmonte, J.C. (2011). Methods for making induced pluripotent stem cells: reprogramming a la carte. Nat Rev Genet 12, 231-242.

Gonzalez, F., Barragan Monasterio, M., Tiscornia, G., Montserrat Pulido, N., Vassena, R., Batlle Morera, L., Rodriguez Piza, I., and Izpisua Belmonte, J.C. (2009). Generation of mouse-induced pluripotent stem cells by transient expression of a single nonviral polycistronic vector. Proc Natl Acad Sci U S A 106, 8918-8922.

Gonzalez, F., Duboule, D., and Spitz, F. (2007). Transgenic analysis of Hoxd gene regulation during digit development. Dev Biol 306, 847-859.

Spitz, F., Gonzalez, F., and Duboule, D. (2003). A global control region defines a chromosomal regulatory landscape containing the HoxD cluster. Cell 113, 405-417.

Spitz, F., Gonzalez, F., Peichel, C., Vogt, T.F., Duboule, D., and Zakany, J. (2001). Large scale transgenic and cluster deletion analysis of the HoxD complex separate an ancestral regulatory module from evolutionary innovations. Genes Dev 15, 2209-2214.

Patents
Pub. No.:WO/2010/105257
Title: "Generation of mouse induced pluripotent stem cells by transient expression of a single non- viral polycistronic vector"

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **CASINO FERRANDO, PATRICIA**
Referencia: RYC-2014-16490
Área Científica: Biomedicina
Correo Electrónico: pcfcri@ibmb.csic.es

Título:

Structural biology applied to the study of bacterial signal transduction and rare diseases

Resumen de la Memoria:

My research career comprises working periods in several national and international laboratories where I have learnt different techniques and developed different skills. After my bachelor, I worked with Prof. Ángel Maquieira to develop immunoassays for the determination of pesticide residues in water and soil samples. Afterwards, I did a predoctoral stay of two years with Prof. Michael F. Dunn to work on the catalytic mechanism of the tryptophan synthase bienzyme complex using stopped-flow rapid kinetics and diverse spectroscopic techniques. During my PhD studies I worked with Dr. Alberto Marina to decipher the molecular and structural bases of two-component signal transduction systems (TCS) performing functional and crystallographic studies on their components, the sensor histidine kinase and the efector response regulator. Within the PhD studies period I did a three months stay in Dr. Bert van den Berg lab to work in the crystallization of membrane histidine kinases using detergents. As a postdoc, I worked for the CIBERER performing structural biology in recombinant human non-collagenous domains of collagen type IV chains 1-6 involved in the rare diseases Goodparture's and Alport's syndrome obtaining the structures NC112, NC566, NC1, NC2, NC3, NC4 and NC5, as well as I continued working in TCS. Since 2012, I have a contract Juan de la Cierva to work with Prof. Ignacio Fita in the Institute of Molecular Biology of Barcelona (CSIC) working on structural biology in proteins related with motility and virulence in Mycoplasma genitalium, obtaining as a result the 3-D structure of the phosphatase MG_207 involved in virulence.

The main research line that I have developed during the last twelve years is the study of the molecular and structural bases of TCS, the main signal transduction pathway in bacteria. TCS are key regulators of bacterial and fungal life acting as sensors of the environmental changes and efectors producing adaptative responses. I have studied the three basic reactions that catalyze simple TCS in order to transduce signals and I have done pioneer contributions in the field solving the first crystal structure of a complex between the catalytic machinery of the histidine kinase HK853 and its cognate response regulator RR468 which gave novel mechanistic clues of this systems, including the demonstration of cis-autophosphorylation in histidine kinases, a breakthrough in the field since autophosphorylation was accepted to occur just in trans. Later, I solved the first crystal structure of a HK performing cis-autophosphorylation, a reaction that has been elusive for structural characterization. Furthermore, I solved structures of rewired HK853 and RR468 alone and in complex that has helped us to understand the specificity in the recognition between a HK with its RR as well as the structures of the DNA-binding RRs OmpR, maeR in its activation state. After all these years of research, I have acquired a great knowledge in structural bilogy and in enzymatic characterization of TCS, however, there are still many questions left behind, therefore, I am pursuing new projects, related basically with the study of complex TCS, present mainly in fungi. All this structural knowledge will serve as a platform for the rational design of new molecules with antibiotic and/or antifungal activity, as TCS are absent in humans (in mammals, in general).

Resumen del Currículum Vitae:

Soy licenciada en Ciencias Químicas (1997) y Ciencia y Tecnología de los alimentos (2000) por la Universidad de Valencia y la Politécnica de Valencia (UPV), respectivamente. Realicé el grado (tesina) en Químicas en el Departamento de Química de la UPV bajo la dirección del Dr. Ángel Maquieira poniendo a punto inmunoensayos enzimáticos (ELISA) para la determinación de plaguicidas, publicando dos artículos. A continuación, realicé una estancia predoctoral de dos años (2001-2002) en el laboratorio del Dr. Michael F. Dunn del Departamento de Bioquímica en la Universidad de California de Riverside (EE.UU). Durante este periodo realizacé estudios enzimáticos con la enzima triptófano sintetasa, publicando tres artículos. Como becaria FPI, en 2003 comencé la tesis doctoral en el laboratorio de Cristalografía de macromoléculas del Dr. Alberto Marina en el Instituto de Biomedicina de Valencia, CSIC. El objetivo de mi tesis fue el estudio del mecanismo de transducción de señales en los sistemas de dos componentes (TCS), mediante una aproximación en biología estructural y bioquímica. Además, realicé un estancia de dos meses en el laboratorio del Dr. Bert Van den Berg en el Departamento de Medicina molecular en la Universidad médica de Massachusetts en Worcester (EE.UU). Fruto de mis estudios de doctorado (2008) se obtuvo la primera estructura cristalina de un TCS formado por una histidina quinasa y un regulador de la respuesta y se demostró por primera vez la autofosforilación en cis en histidina quinasas. Desde Diciembre 2007 hasta 2012, fui contratada CIBERER del programa de Medicina metabólica hereditaria dirigido por el Dr. Vicente Rubio en el Instituto de Biomedicina de Valencia, CSIC. Como investigadora post-doctoral, continué con el estudio de TCS y comencé nuevos estudios estructurales de los dominios no colagenosos (NC) del colágeno tipo IV humano, resolviendo la estructura cristalina de varios NCs. En Mayo 2012 comencé un contrato postdoctoral Juan de la Cierva (Área: Biología fundamental y de sistemas), en el laboratorio del Dr. Ignacio Fita en el Departamento de Biología Estructural en el Instituto de Biología Molecular de Barcelona, CSIC estudiando la maquinaria de movilidad de Mycoplasma genitalium. Como resultado de estos estudios, he conseguido resolver la estructura cristalina de la fosfatasa MG207 implicada en virulencia. A su vez, he realizado estudios en paralelo relacionados con TCS, en colaboración con el Dr. Michael T. Laub del Instituto tecnológico de Massachusetts en Boston (EE.UU)

sobre el reconocimiento en TCS y en colaboración con el Dr. Alberto Marina que ha dado lugar a la primera estructura cristalina de una histidina quinasa en cis-autofosforilación, así como las estructuras cristalinas del dominio receptor activado de dos reguladores de la respuesta maeR y OmpR.

Mis objetivos futuros son ampliar el conocimiento en el mecanismo de transducción mediado por TCS más complejos, resultado de la permutación de dominios sensores, catalíticos y reguladores que imponen un nivel superior de regulación en microorganismos, mediante una aproximación estructural y funcional. Estos sistemas, no presentes en humanos, están implicados en procesos de gran relevancia para los microorganismos, por ello, dicho estudio presenta también importancia para el desarrollo racional de nuevos antimicrobianos altamente específicos.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **NICOLAS MOLINA, FRANCISCO ESTEBAN**
Referencia: RYC-2014-15844
Área Científica: Biomedicina
Correo Electrónico: fnicolas@um.es

Título:

Regulatory role of the RNAi mechanism in emerging pathogens.

Resumen de la Memoria:

The candidate has achieved a highly successful scientific career on the field of RNA interference (RNAi) and its applications to human health during the last fourteen years. In this trajectory, the candidate has published a total of 32 scientific contributions: 26 scientific articles, 4 book chapters, 1 edited monographic special issue and 1 editorial. The list of scientific articles reveals top international journals of widely recognized quality such as NATURE, EMBO J, Nucleic Acids Res, Plos Pathogens, Arthritis Rheum, RNA, RNA biology, etc. The candidate started his PhD period with the opening of a new RNAi research line in the molecular genetics group headed by Professor Rosa M. Ruiz-Vázquez. In an exceptionally competitive field, the candidate managed to publish an exceptional work (Nicolás et al., 2003; EMBO J) that was quoted by Andrew Z. Fire when he received the Nobel Prize for his work in the field of RNA interference. The international postdoctoral period was carried out at the University of East Anglia (United Kingdom), working three and a half years in the group of Professor Tamas Dalmay. During this early postdoc, the candidate published again highest quality contributions both as first and corresponding author (Nicolás et al., 2008, RNA; Nicolás et al., 2010, Nucleic Acids Res; Nicolás et al., 2013, Arthritis Rheum). Later, the candidate returned to Spain with a "Juan de la Cierva" contract and soon after, the candidate obtained a Marie Curie contract and his own project as Principal Investigator, funded and granted by the European Commission (Marie Curie Actions). In this late postdoctoral period, the candidate orientated the research line to the study of the role of RNAi in fungal pathogenesis and mucormycosis (reviewed in Nicolás et al., 2013, Plos Pathogens), producing extraordinary high impact results (Calo et al., 2014, NATURE). At this phase, the research career of the candidate has reached a final stage in which he has created a young research group with several students under his leadership and supervision.

Resumen del Currículum Vitae:

1 Scientific contributions:
A total of 32 scientific publications: 26 scientific articles, 4 book chapters, 1 edited monographic special issue and 1 editorial. The list of scientific publications reveals top international journals of widely recognized quality such as Nature, EMBO J, Nucleic Acids Res, Plos Pathogens, Arthritis Rheum, RNA, RNA biology, etc. A total of 11 research projects, 1 of them as the Principal Investigator. Three different research contracts in open and competitive calls: "Senior Researcher" (SIROCCO consortium, European Commission, 6th framework), "Juan de la Cierva" (Ministry of Science, Spain) and "Marie Curie" (European Commission, 7th framework program, UMU Incoming Mobility Programme Action). Five research fellowships in open and competitive calls. Up to 26 participations in scientific conferences including all the possible modalities: invited plenary talks, talks, posters, participant, organizer, national and international.
2 International Research Activity:
Two projects (one as Principal Investigator) and two contracts, all of them granted by the European Commission. The first project is a sub-project of the international consortium SIROCCO, which joined 24 groups from 11 different countries (European Commission, 6th framework) and was funded with 11.781.445 euros (725.000 euros for our sub-project). The second project was granted to the candidate as the Principal Investigator (European Commission, 7th framework) with 7000 euros. A "Senior Researcher" contract (SIROCCO consortium, European Commission, 6th framework) and a "Marie Curie" contract (European Commission, 7th framework program). The candidate participated in the ERC Starting Grants 2014 of the European Commission, being ranked at the final phase as "A", which states the potential of the candidate to obtain resources at the European level.
3 Others achievements:
10 years of university teaching experience for a total of 930 hours (360 hours in the United Kingdom and 570 hours in Spain) including Honor Degrees, Degrees, Masters and 12 different subjects. Positive evaluation granted by "ANECA" for the Spanish position of "Profesor Titular".
4 Independence, relevance and leadership:
The candidate has its own and young research group which currently is formed by two PhD students, two master students, two undergraduate students. The candidate is Principal Investigator in one granted project (European Commission). First author in 22 publications out of a total of 32. Corresponding author in 13 publications out of a total of 32. Supervisor of two Thesis, two Master dissertations and three Degree dissertations. A total period of 43 months of international stays. A first pre-doctoral stay of 3 months in the United Kingdom that justified the European Doctor Degree and a second post-doctoral stay of 40 months in the University of East Anglia (United Kingdom). The candidate has received up to 6 invitations to write specialized reviews in the field of RNAi, one of them in the

prestigious journal PLOS Pathogens. Edition of one special monographic issue about RNAi. Numerous requests to referee scientific articles related to RNAi. Two participations in Thesis committees. Member of the Editorial Board of the journal ‘Recent Pat DNA Gene Seq’ (recently upgraded to Regional Editor). Invitations to four plenary talks.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **CARMONA LOPEZ, FRANCISCO DAVID**
Referencia: RYC-2014-16458
Área Científica: Biomedicina
Correo Electrónico: fdcarmona@gmail.com

Título:

Genetics of Autoimmune Diseases

Resumen de la Memoria:

Autoimmune diseases are complex disorders that develop when there is a loss-of tolerance of the immune system to the own body's tissues without any discernible cause. In other words, the defence mechanisms fail to tell the difference between self and non-self molecules and trigger a chronic immune response against different organs and tissues with very severe consequences in most cases. These diseases affect between 5-8% of the general population in Western countries and they are characterised by a cascade of immunologic and physiologic abnormalities as a consequence of the interaction of multiple genetic and environmental factors.

In 2010, I started working on the genetics of autoimmune diseases in the group of Prof. Javier Martín Ibáñez (Institute of Parasitology and Biomedicine "López-Neyra", CSIC, Spain) who has a vast experience and recognition in this field (H-index=56). I was mostly motivated by my growing interest in working on human genetics (my scientific career until them was focused on the study of the molecular mechanisms involved in developmental processes). I must say that my scientific productivity since I joined Prof. Martín's group largely surpassed the most optimistic previsions by far as reflected in my CV. I have contributed with publications in high impact journals to the understanding of the genetic basis of systemic sclerosis, a fibrotic disease of the skin and internal organs, and giant cell arteritis (GCA), an inflammatory vasculitis that may lead to severe phenotypes such as polymyalgia rheumatica, stroke or blindness.

I currently lead and coordinate, together with Prof. Martin and in collaboration with different internationally recognised rheumatologists, an international collaborative effort to perform the first large scale genetic studies on GCA. The publication of recent genome-wide association studies is increasing substantially the understanding of human diseases with a complex genetic component, such as cancer or autoimmune diseases, but rarer pathologies like GCA have not yet taken advantage of this methodology. To date, all the genetic studies on this disease have followed a candidate gene approach, and most of them were compromised by a considerable low statistical power due to small cohort sizes. Because of that, the genetic component of GCA is not well understood, and only the HLA region has been consistently associated with the disease (most genetic associations were close to the statistical significance border and lacked replication in independent populations). Therefore, the research line I currently lead and in which I would work on the following years, if I had the stability provided by the "Ramón y Cajal" program, would mark a turning point in the research of the GCA genetics, being a reference for possible novel therapies.

Resumen del Currículum Vitae:

Although my scientific career has been relatively multidisciplinary, Genetics has been always a common topic in my research. My PhD was focused on the study of the molecular mechanisms driving sex determination and gonad development in mammals, under the supervision of Dr. Rafael Jiménez (Department of Genetics, University of Granada, Spain). I obtained my PhD as "Doctor Europeus" with the mark "Summa Cum Laude Unanimously" in December 2006.

During my first postdoct in Aberdeen (UK), I opened and led a new research line in the group of Prof. J Martin Collinson (Institute of Medical Sciences, University of Aberdeen, UK) to study the developmental biology of the visual system in a new animal model of dysgenic eye (the true moles Talpidae), which could inform our understanding of eye functionality, evolution, and genetic disease in humans. My research in UK was published in relevant scientific journals and had large media coverage, receiving much public attention worldwide.

On May 2010, I decided to work on Human Genetics and joined Prof. Javier Martín's group (Institute of Parasitology and Biomedicine "López-Neyra", CSIC, Granada, Spain). The main research line I am involved since then is the study of the genetic basis of autoimmune diseases, in particular systemic sclerosis and giant cell arteritis. During this period of time I participated in the publication of 21 papers in impact journals (12 in journals within quartile 1 in its category) with an average impact factor of 6.046, appearing in 15 of them as first author and in 10 as corresponding author. I also contributed as first author to the publication of three chapters in medicine books, participated as speaker of selected abstracts in 6 international congresses (including the two most relevant international congresses in Rheumatology worldwide: The American College of Rheumatology "ACR" congress and The European League Against Rheumatism "EULAR" congress, in which I also chaired two sessions on Genetics), gave 3 talks by invitation in national meetings, and participated actively in 5 research project including an European collaborative project (PRECISESAD) within the Innovative Medicines Initiative (IMI) that participated with 23 research centres and 5 companies from 12 European countries, which ultimate goal is to find innovative diagnostic

technology to relate systemic autoimmune disease to detectable changes in individual molecular signatures. In addition, I become reviewer on a number of scientific journals on Genetics and Rheumatology, such as "Human Molecular Genetics" (Impact Factor JCR: 6.677 and Q1 in "Genetics & Heredity") and "Annals of the Rheumatic Diseases" (Impact Factor JCR: 9.270; number one original research journal in the field of "Rheumatology"), and Lecturer in the University Doctorate Master Degree in "Genetics and Evolution" (M58/56/1; ref: 4312364). Finally, it should also be noted that I was supervisor of the Doctorate Master Project "Analysis of a functional variant of the CSK gene in patients with systemic sclerosis" performed by the PhD student Elena López Isac, who obtained the qualification with an Excellent mark, and I am currently supervising the Doctorate Master Project of the PhD student Tamara Fernández Aranguren.

As reflected in my CV, my scientific productivity and teaching experience in every step of my career has been considerably high.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **PAEZ GONZALEZ, PATRICIA**
Referencia: RYC-2014-16980
Área Científica: Biomedicina
Correo Electrónico: patripg2005@gmail.com

Título:

Manipulation of brain resident neural stem cells control: new future therapies by which the brain may be manipulated to induce its own repair.

Resumen de la Memoria:

Fifteen years of progress in neural stem cell therapy has unveiled great promise for brain regenerative medicine. Harnessing adult neural stem cells (NSCs) to generate new neurons may provide much needed therapies for patients suffering brain injuries or neurodegenerative/ congenital diseases, such as hydrocephalus. Since beginning my career as a research scientist, I have sought to understand ways in which NSCs are endogenously regulated during brain development and maturation in health and disease.

During my PhD research, I first demonstrated how a single mutation in NSC progenitors leads to hydrocephalus and neurodegeneration in mouse and human (J.Neuropathol.Exp.Neurol. 2005, Neurobiology of Disease.2006, J.Neuropathol.Exp.Neurol.2007). This direct relationship between NSC progenitors and congenital/neurodegenerative disease was a key concept that provided precedence for NSC mediation of these and other pathological conditions. Secondly, we observed that reactive astrocytes acquire attributes of the ependymal surface after damage to the ventricular wall (Acta Neuropathologica.2012). This strongly suggested that NSCs or other ventricular progenitors might provide additional therapeutic avenues for treatment of neurodegenerative disease, beyond the limited scope of new neuron production.

Unfortunately, current NSC treatments are typically based on transplantation and suffer from very low-efficiency. One major barrier-to-progress in transplantation is unreliable production of cells needed by the host. With knowledge of this deficiency, I endeavored as postdoc, to explore alternative approach of ‘modulating’ the brain’s own resident stem cells. I have since demonstrated that 1) local stem-cell environments are critical in providing appropriate signals for proper NSC function and progeny generation (Neuron 2011, Cover-Story), 2) NCSs in vivo are capable of elaborating appropriate responses under different requirements (Nature 2013), and 3) we can extrinsically control stem cell function and progeny by modulating local neuronal circuits using laser stimulation (Nature Neuroscience 2014, Cover-Story). By successfully manipulating intrinsic NSC control, I have revealed future therapies by which the brain itself may be manipulated to induce its own repair.

I intend to now investigate whether NSCs and other radial-glial-like progenitors in the ventricular niche can be harnessed for repair of the ventricular surface. The ependymal/ventricular surface is a critical component of the developing and mature brain. As others and I demonstrated, it is intricately involved in neuropathic/degenerative processes like hydrocephalus. Whether NSCs and other progenitors could repair or transform the ependymal surface in diseased/injured conditions is unknown. Using established developmental and neurobiological techniques acquired during my training, as well as published and unpublished in vitro assays that I developed during my postdoc, I will investigate this new avenue of research. By researching the transformative potential of NSCs as well as examining other ventricular progenitors/precursors for repair of the ependymal ventricular surface, I will move beyond the limited scope of purely NSC based neuron production. Success here will identify additional processes for clinical intervention and treatment of neuropathological injury and disease.

Resumen del Currículum Vitae:

Throughout my career my aim has been to uncover the best ways to manipulate NSCs as a tool for brain regenerative medicine.

I completed my PhD work at the Malaga University (Spain), under supervision of Dr. Fernandez-Fígares, supported by a FPU Fellowship (MEC, Spain). My thesis work was awarded the grade of Outstanding/Summa Cum Laude in 2006.

By the completion of my PhD, I had successfully established a direct relationship between NSCs and congenital/neurodegenerative disease. This work resulted in:
- Technology Patent
- 11 main papers: 3 as first author (Neurobiol of Disease.2006, J.Neuropathol.Exp.Neurol.2007), 3 as second author (Int.J.Dev.Biol.2001, Neuropathol.Exp.Neurol.2005, Acta.Neuropathol.2012), and 5 as third/middle author (J.Neuropathol.Exp.Neurol.2001, 2003, 2009; Mol Cell Probes.2009, Acta Neuropathol. 2011). The impact factors for these publications are medium to medium/high, and the journals were primary and secondary within the field of neuropathology. In addition, some of these results were published as 5 additional articles in open

access journals: 2 as first author (CSF 2005a,b), 2 as second author (CSF 2005c, CSF 2006).

In 2008, I started a postdoc at Duke University (USA) under Dr. Kuo supervision. In 2009, I independently developed a grant proposal for The Ruth K. Broad BRF, Inc and was awarded with the Ruth K. Broad International Postdoctoral Fellowship. This competitive grant supported my independent research from 2009-2011.

I focus my postdoctoral research on developing a new direction for future NSC therapies based on "modulating" the brain's own resident stem cells after brain damage. This work has resulted in 3 high impact factor papers:
- Neuron 2011 (first authorship; Neuron Cover Story; NIH-Highlights.2011),
- Nature 2013 (Top Story Neural Cells News 2013)
- Nature Neuroscience 2014 (first authorship; Nat.Neurosc. Cover Story).
I am also a key author in four additional manuscripts, one in revision and three are under final preparation for submission.

I have received different award/fellowships: Research Starting Fellowship (Beca Colaboracion, Junta de Andalucia), FPU Fellowship (MEC, Spain), The Ruth K. Broad Biomedical Research Foundation Inc. Fellowship (USA).

Furthermore, I was nominated for Outstanding Postdoc by Duke University in 2012. I have been selected as a member of F1000 faculty as an F1000 prime reviewer since 2010. My research has been frequently recognized as top story (Top Story Neural Cells News 2011, 2013, 2014; NIH Highlight 2011; Cover Story in Neuron 2011 and Nat.Neurosc. 2014).

As a researcher, in addition to the published papers (18 total, 7 first-author, 5 second-author; 139 total impact factor), I have participated in scientific meetings relevant to the neuroscience audience, with a total of 40 contributions: 11 at the national scientific level and 29 international scientific conferences/symposia (FENS, SFN, Keystone Symposia, CSHL meeting). Of these contributions, 22 were oral presentations.

During my scientific career, I have been essential contributor on several research projects funded by public entities: NIH/USA, FIS/MEC (Spain), SAS/Junta de Andalucia. Also, I have been fortunate to have opportunities to develop fruitful collaborations with researchers in other institutes and to perform various teaching/mentoring duties at different levels.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **GONZALEZ MUÑOZ, ELENA**
Referencia: RYC-2014-15410
Área Científica: Biomedicina
Correo Electrónico: elena.gonzalez.munoz@juntadeandalucia.es

Título:

Molecular and epigenetic study of adult somatic cell reprogramming, and application in disease modeling for potential therapies.

Resumen de la Memoria:

My research trajectory centers in the study and understanding of human somatic cell reprogramming, and the application in neurodegenerative disease modeling for potential therapeutic applications.

My PhD period and first postdoctoral training at University of Barcelona helped me to achieve a solid knowledge of a great amount of molecular and cell biology concepts and techniques, to get 4 indexed publications and importantly to get eager of my biomedical research career.

During my first international postdoctoral training at University of California San Francisco Neurosurgery Department (2009-2010) my research deal with the role of asymmetric cell division and differentiation of neural stem cells in brain tumor development, using cell culture, mice models and human samples.

We identified oligoprogenitor markers that were secreted asymmetrically during cell division to give rise to two cell populations with different proliferating and differentiating potential. Their characterization and implication in glioma development was the major topic of my research during this period.

At the end of 2010, I joined Dr. J. Cibelli¿s group "Cell Reprogamming Laboratory" at Michigan State University (MSU). I established a transgenic zebrafish model with in vivo labeling of heterochromatin during reprogramming (pending of publication) and essentially, I studied the reprogramming process that happens from adult somatic cell to induced pluripotent cell (iPSC)

Importantly I could start to develop an independent project focused into the screening of new oocyte-specific factors and their implication in pluripotency and reprogramming. I could continue it after I moved to Dr. Cibelli¿s lab in Spain at LARCEL (Andalusian Laboratory for Cell Reprogramming). This project¿s results have been published in a high impact article, showing that ASF1A histone chaperone is crucial for pluripotency acquisition and maintenance, and a new reprogramming combination was described.

I continue now with this project where I want to go deeper in the reprogramming mechanisms by understanding the importance of somatic cell origin, and analyzing transcriptional and epigenetic characteristics of ASF1A reprogramming.

I am also developing projects that couple my knowledge of reprogramming field with neurodegenerative disease modeling and potential therapies.

My short term goal is to generate iPSCs and specific cell types affected in different neuropathies to develop in vitro models in which perform functional assays to uncover altered cellular pathways that may explain the origin of the specific pathological states. Through scientific collaborations we anticipate the discovery of new drug targets that may enable the development of pharmacological interventions.

I currently count on funding for Huntington disease modeling using iPSCs through our participation in AMER (Acción Multidisciplinar en Enfermedades Raras y Medicina Personalizada)(project that belongs to FEDER-INNTERCONECTA I+D statal program), I have just get funding from GENZYME for Multiple Sclerosis modeling and search of new altered neurotrophic factors, and I am collaborating with Dr. M.A. Dolado (PI at CABIMER Cell Therapy for Neuropathologies department) for Friedreich Ataxia (FA) iPSC-derived neural in a FA modelling project with special focus on cells transplantation into mice nervous system.

Resumen del Currículum Vitae:

Index summary:
Total cites: 249
Average cites/year last 5 years: 26.2
Q1 Total publications: 5
D1 total Publications :2
H index: 6 (Note: my last high impact article is very recent, August 2014 so it doesnt have many cites yet)
Average impact factor: 11.22 (19.8 in last 5 years)
http://scholar.google.es/citations?user=CkH7GRoAAAAJ&hl=es

I am currently an emergent researcher of Andalusian cell therapy and regenerative medicine program launched by "Fundación Progreso y Salud" in LARCEL.
I got my biology degree at University of Seville and my PhD at University of Barcelona (Nov 2007).

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

During my PhD, my project deal with the role of caveolae in adipocyte physiology. I could get to master a wide variety of molecular and cell biology techniques and I published four ISI indexed articles.

I joined Prof. M. Palacin laboratory as postdoctoral researcher at IRBB (Biomedical Research Institute) studying the role of the aminoacid transporter 4F2 in epiblast development and mouse stem cells. We published one ISI-indexed publication and a second article is in preparation.

In 2009, I started my first international postdoctoral training at University of California San Francisco with Dra. Petritsch, to study the role of asymmetric cell division and differentiation of neural stem cells (NSCs) in glioma development. I acquired knowledge of mouse and human NSCs culture, in vitro differentiation to different neural lineages, mouse colony maintenance, brain dissection, brain cell transplantation and luminiscence-based tumor tracking. We published an article in a high impact journal (Cancer Cell) and a second manuscript is still pending for its publication.

In October 2010, I joined Dr. Cibelli Cell Reprogramming Laboratory at Michigan State University, where I focused my effort in the reprogramming field. I established a transgenic zebrafish model with in vivo labeling of heterochromatin during reprogramming (pending of publication) and essentially, I studied the reprogramming process that happens from adult somatic cells to induced pluripotent cells (iPSCs).

Importantly, during this period I could start developing an independent project focused into the screening of new oocyte-specific factors and their implication in pluripotency and reprogramming. I could continue it after I moved to Dr. Cibellis lab in Spain at LARCEL (Andalusian Laboratory for Cell Reprogramming). The results have recently been published in a high impact article (Science, 2014).

Also I currently count on funding for Huntington disease modeling using iPSCs through our participation in AMER (Acción Multidisciplinar en Enfermedades Raras y Medicina Personalizada), I have just get funding from GENZYME for Multiple Sclerosis modeling, and I am collaborating with Dr. M. Dolado (PI at CABIMER Cell Therapy for Neuropathologies department) for Friedreich Ataxia project with special focus on cells transplantation into mice nervous system.

The solid experience adquired during my postdoctoral trainings on different techniques of cell reprogramming, coupled with my previous experience on the biology of NSC as well as my knowledge of many techniques of molecular and cell biology, in addition to the recent funding I have just obtained to develop reprogramming based projects that are already started, makes a great potential to successfully develop reprogramming and disease modeling research projects

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **PRADOS ROSALES, RAFAEL CARLOS**
Referencia: RYC-2014-15655
Área Científica: Biomedicina
Correo Electrónico: pradosrosales@gmail.com

Título:

A membrane vesicle-based export system in Mycobacterium tuberculosis

Resumen de la Memoria:

I obtained my BS in Environmental Sciences with a specialty of Analytical Chemistry at the University of Cordoba with a "Premio Extraordinario de Carrera" distinction in 2003. Before graduating I joined the Analytical Chemistry department to work on the automatization of continuous and discontinuous systems for analytical processes. In 2004 I joined the Genetics department of the University of Cordoba with a fellowship from the Ministerio de Ciencia y Tecnología (FPU) to undertake my Ph.D. studies using molecular biology and genetics tools to carry out the molecular dissection of a signaling pathway of the fungal pathogen Fusarium oxysporum. In 2009, I started my postdoctoral studies in the Department of Microbiology and Immunology at the Albert Einstein College of Medicine in New York on the characterization of a membrane vesicle-based export system in Mycobacterium tuberculosis. I have published 27 articles, 13 first author and 2 corresponding author with a H-index of 10 and a cumulative impact factor of 165.345. Before completing my BS I had published five articles (4 as first author). My doctorate studies produced a total of six publications (4 as first author) in recognized international peer-reviewed journals such as "PLANT CELL IF 9.396", "PROTEOMICS IF 5.6" "JOURNAL OF BIOLOGICAL CHEMISTRY IF 4.65" and "EUKARIOTYC CELL IF 3.83". During my postdoctoral years I was the first to isolate and describe mycobacterial vesicles and establish that these structures have powerful immunological properties, publishing the results as first author in the "JOURNAL OF CLINICAL INVESTIGATION IF 13.765". These findings represent the base of my main research line, which is focused on the understanding of the vesicle-based transport in Mycobacteria. I am currently interested in the biogenesis of mycobacterial vesicles and in collaboration with other groups we have identify the first mycobacterial gene implicated in vesiculogenesis and results were published in "PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES of AMERICA IF 9.737". We also demonstrated that mycobacterial vesicles have the capacity to modify the antigen presentation process in a model of myocarditis. These results were published in the prestigious journal "CIRCULATION IF 15.202". I am currently studying the feasibility of mycobacterial membrane vesicles as a new effective anti-tuberculosis vaccine. The initial results of these studies were recently published in "mBIO IF 6.78". Due to the work on mycobacterial vesicles two independent patents have been developed. I have been invited to talk in some of the most prestigious Tuberculosis meetings in the past 3 years indicating that my research is worldwide recognized. I have recently published two reviews in the two most prestigious journals in the Microbiology and Immunology field: "IMMUNOLOGICAL REVIEWS IF 12.909 (as first author)" and NATURE REVIEWS MICROBIOLOGY IF 23.054 (as corresponding author)". I have been appointed as Research Assistant Professor, which has allowed me to supervise the Master of thesis of one student. I have recently accepted an Adjunct Professor position at Hostos Community College from College University of NY (CUNY). to teach Microbiology. I am an ad hoc reviewer for Mycologia, Journal of Immunology, Plos One and Clinical and Vaccine Immunology.

Resumen del Currículum Vitae:

I completed my BS studies in Environmental Sciences at the University of Cordoba in 2003 with "Premio Extraordinario de Carrera" distinction. I obtained a FPU fellowship to do my doctoral studies in the Department of Genetics from the same University on the Molecular dissection a signaling pathway of the fungal pathogen Fusarium oxysporum. I joined the Department of Microbiology and Immunology at the Albert Einstein College of Medicine under the supervision of Prof. Arturo Casadevall to do my postdoctoral studies focused on the characterization of a membrane vesicle-based export system in Mycobacterium tuberculosis. I have published 27 articles, 13 first author and 2 corresponding author with a H-index of 10 and a cumulative impact factor of 165.345. I have been cited 333 times with an average of 25.62 cites per year.

- Selected publications from my postdoctoral work:

1.Brown L, Wolf J, Prados-Rosales R* and Casadevall A (2015) Nature Reviews Microbiology, accepted. *Corresponding author.

2.Prados-Rosales R*, Majlessi L*, Casadevall A, Brosch R (2015) Immunological Reviews, accepted. *Equally contribution.

3.Prados-Rosales R*, Leandro J. Carreño et al (2014) mBio, 5(5):e01921-14. *Corresponding author.

5.Rath P, Huang C, Wang T, Wang T, Li H, Prados-Rosales R, Elemento O, Casadevall A, Nathan CF. (2013) PNAS 110(49):E4790-7.

6.Kania G, Siegert S, Behnke S, Prados-Rosales R, Casadevall A, Lüscher TF, Luther SA, Kopf M, Eriksson U, Blyszczuk P. (2013) Circulation

127(23):2285-94.

7.Prados-Rosales R, et al (2011) Journal of Clinical Investigation 121(4):1471-83.

8.McClelland EE*, Nicola AM*, Prados-Rosales R, Casadevall A (2010) Journal of Clinical Investigation. 120(4):1355-61. *Equally contribution

- Selected publications from my thesis work:

1.Prados-Rosales RC, Roldán-Rodríguez R, Serena C, López-Berges MS, Guarro J, Martínez-del-Pozo Á, Di Pietro A. (2012) J Biol Chem. 287(26):21970-9.

2.López-Berges MS, Rispail N, Prados-Rosales RC, Di Pietro A (2010) Plant Cell. 22(7):2459-75.

3.Prados-Rosales RC, Gil C and Di Pietro A. (2009) Proteomics 9:4755-69.

4.Prados-Rosales RC and Di Pietro A. (2008) Eukaryotic Cell 7: 162-171.

- Patents:

1.Use of a membrane vesicle based vaccine against M. tuberculosis for subcutaneous administration. 33% share.

2.Serologic test for the rapid diagnosis of active tuberculosis. Inventors: Dr. Jacqueline achkar, Arturo Casadevall, Rafael Prados-Rosales and Anke Ziegenblag.

- Invited talks:

1.March 2013. Third Global Forum on TB vaccines. Cape Town. South Africa.

2.December 2012. Multimédia bactériens et résistance. Société Française de Microbiologie. Centre d'Information Scientifique, Institut Pasteur. Paris. France.

3.June 2012. Eighth International Conference on the Pathogenesis of Mycobacterial Infections. Grand Hotel Saltsjöbaden, Stockholm, Sweden.

- Thesis supervised:

1. Stacy Toriola. Scheduled for January 28th 2015.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **JAN , TONNESEN**
Referencia: RYC-2014-15994
Área Científica: Biomedicina
Correo Electrónico: janton@gmail.com

Título:

Function and dysfunction of synaptic signaling

Resumen de la Memoria:

I did my BSc project on endogenous morphine signaling in Mytilus edulis (blue mussel) during a stay in the lab of Prof. GB Stefano at SUNY (Old Westbury, New York, USA), where I contributed to ongoing projects and co-authored two papers.

My MSc project investigated the limits of cerebral blood flow regulation assessed by the intra-arterial 133Xenon injection method and by laser-Doppler flowmetry in rats. This work was performed at the Neurobiology Research Unit at the Univ. Hospital of Copenhagen, under Prof. GM Knudsen, and resulted in two papers (Tønnesen et al, Exp Physiol, 2005; Pryds, Tønnesen et al, Pediatr Res, 2005).

Part of my PhD work in the group of Prof. M Kokaia at Lund University, Sweden, focused on making stem cells develop into dopaminergic neurons for cell replacement therapy in Parkinson's disease. I co-authored two papers where I was responsible for characterizing stem cells through whole-cell electrophysiological approaches, and lead another characterization study (Tønnesen et al, Exp Neurol, 2010)[7].
To assess the functional integration of stem cells after injection into host tissue, I independently developed an innovative optogenetic approach and experimentally demonstrated bidirectional synaptic integration of dopaminergic stem cells (Tønnesen el at , PLoS One, 2011). This work was completed with help from collaborators in Stockholm (Prof. E Arenas, Karolinska Institute).

Other part of my thesis work was a collaboration with the lab of Prof. K Deisseroth (Stanford). I developed optogenetic approaches to silence synchronized bursting in hippocampal tissue and established an epilepsy model in brain slice cultures. This enabled me to provide proof of concept that optogenetic cell control can be used to control epileptiform activity (Tønnesen et al, PNAS, 2009). I review the literature on optogenetics in experimental models of neurological disorders here (Tønnesen, Behav Brain Res, 2013).

During my PhD studies I participated in large-scale interdisciplinary efforts to develop online analysis platforms for monitoring cell growth and development. This was done under the supervision of Prof. J Emneus, Dept. Analyt. Chem. Lund University. I co-authored two proceedings on our progress.

In 2010 I began my current postdoc with Prof. UV Nägerl (Interdisciplinary Institute for Neuroscience) in Bordeaux, France. The first step was to build a two-color superresolution STED microscope for imaging synapses in live brain slices, which was done in collaboration with 2014 Nobel laureate Prof. SW Hell (Max Planck Institute, Göttingen) (Tønnesen et al, Biophys J, 2011). The paper describing the setup was selected by Faculty of 1000. We since upgraded the setup to be able to do more complex physiological experiments (Tønnesen & Nägerl, Methods Mol Biol, 2013).

I used the microscope to study dendritic spines and implemented several advanced optical techniques, including 2-photon glutamate uncaging and 2-photon FRAP. I was able to provide the first direct evidence for nanoscale changes in spine necks during synaptic plasticity (Tønnesen et al, Nature Neuroscience, 2014). We review the literature on superresolution imaging studies in neurobiology here (Tønnesen & Nägerl, Exp Neurol, 2013). I am currently in the late stage of a follow-up project on t spine morphology and electrical synaptic signaling (Tønnesen & Nagerl, in prep)

Resumen del Currículum Vitae:

Name Jan Tønnesen (male, Danish)
Birth March 22, 1977, Sweden

ACADEMIC EMPLOYMENT
2010-currently Post-doctoral researcher
Interdisciplinary Institute for Neuroscience/ CNRS and University of Bordeaux, France
Synapse physiology, STED microscopy, 2-photon microscopy, patch-clamp electrophysiology, brain slices.
Supervisor Prof. U. Valentin Nägerl

EDUCATION AND ACADEMIC TRAINING
2005-10 PhD student

Experimental Epilepsy Group, Department of Clinical Science, Lund University Hospital, Sweden.
PhD Thesis: Gene Therapy for Neurological Disorders, Stem Cell and Optogenetic Strategies
Patch-clamp electrophysiology, optogenetics, epilepsy, stem cells, Parkinson's.
Supervisor Prof. Mérab Kokaia

2002-04 MSc in Biology
Neurobiology Research Unit, University Hospital of Copenhagen, Denmark.
Master thesis: Validation of laser Doppler flowmetry against the intra-arterial 133Xenon injection method for measurement of cerebral blood flow in rats.
Supervisors Prof. Gitte Moos Knudsen and Prof. Erik Hviid Larsen

2001 BSc Biology
BSc Project: Research visit (4 months) at Neuroscience Research Institute under Prof. George B. Stefano, College at Old Westbury, State University of New York (SUNY), US.

1998-04 Science student
Faculty of Natural Sciences, University of Copenhagen, Denmark.

AWARDS AND HONORS
2014-15 EMBO Long Term Fellowship
2012-14 EU Marie Curie Postdoctoral Fellowship
2011-12 Lundbeck Foundation postdoctoral fellowship
2009 Lund University, Neuroscience Day Oral Presentation Award 1st price
+fourteen personal travel/equipment/running cost grants during Master's and graduate studies (2002-2010).

INVITED TALKS
2014/06 Achucarro, Basque Center for Neuroscience, Zamudio, Spain
2013/12 Annual retreat of Hell lab (Max Planck Inst. Biophys. Chem.), Tegernsee, Germany
2013/10 Frontiers in Neurophotonics Meeting, Bordeaux, France
2013/03 Synapse Day Meeting, Bordeaux, France
2010/11 Gurdon Institute, University of Cambridge, UK
2010/10 EPICURE annual meeting, Marseille, France
2009/09 Bordeaux Neurosciences Institute, Bordeaux, France
2009/06 International League Against Epilepsy meeting, Budapest, Hungary
2009/05 Neuroscience Day, Lund, Sweden
2009/04 NeuroStemCell annual meeting, Bellagio, Italy

TEACHING AND SUPERVISING EXPERIENCE
2014 Short practical course for M2 students on optical superresolution imaging
2013 Short practical course for M2 students on optical superresolution imaging
2013 Supervising of M2 student Kahina Kourdache
2012 Short practical course for M2 students on optical superresolution imaging
2012 Supervising of M2 student Geraldine Louvet

LANGUAGES
Danish (Native tongue), English, Swedish, German, French, Spanish

OTHER QUALIFICATIONS
2015/02 EMBO Laboratory Management course (planned)
IINS committee for Research Ethics and Good Laboratory Practice
Organizing committee of "2014 Career Development Day" at IINS, on behalf of the French Society for Neuroscience
1997-98 National service; Royal Danish Army, 1st Royal Danish Life Regiment

PEER REVIEW ASSIGNMENTS
Stem Cells
British Journal of Pharmacology