AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2015

Turno de acceso general

Nombre: **REAL LUNA, PEDRO JOSÉ**
Referencia: RYC-2015-18382
Área Científica: Biomedicina
Correo Electrónico: pedro.real@genyo.es

Título:

Trayectoria Investigadora del Dr. Pedro José Real Luna

Resumen de la Memoria:

Dr Pedro José Real Luna holds a degree in Biochemistry from University of Granada and a PhD from the University of Cantabria. He completed his PhD period in the laboratory of Dr José Luis Fernández Luna in the Molecular Genetics Unit of the Marqués de Valdecilla University Hospital in Santander, Spain. He studied the effect of chemotherapy in the transcriptional regulation of apoptosis mediators in breast cancer. During this period he was first author and co-author of 8 publications in major journals in the field of Oncology and Molecular Biology. In 2005, Dr. Real joined the laboratory of Dr Adolfo A. Ferrando in the Institute for Cancer Genetics at Columbia University in New York, NY, USA. During his postdoctoral period he focused on the understanding of the molecular mechanisms responsible for T-cell Acute Lymphoblastic Leukemia (T-ALL) development. In Ferrando's lab he participated in 8 publications, three as first author or co-author, and one patent. These publications have helped to elucidate the role of NOTCH1 and TLX1 proteins in the establishment and the response to chemotherapy in T-ALL patients. In April 2009, Dr Real joined the laboratory of Dr Pablo Menéndez in the Andalusian Stem Cell Bank (BACM) in Granada, Spain. Since February 2010 Dr. Real is a Miguel Servet Researcher of the National Health Institute Carlos III leading his own line of research focused on the molecular regulators of human hematopoietic development. From July 2013, Dr Real leads the Gene Regulation, Stem Cells and Development group in GENyO, Granada, Spain. Since his return to Spain Dr Real has participated in 21 scientific publications in international journals and 26 contributions to national and international meetings. Dr Real has led 8 research projects, participated in 2 patents and has formed graduate students, doctoral students and postdoctoral researchers.

Resumen del Currículum Vitae:

Dr. Pedro José Real Luna holds a degree in Biochemistry from University of Granada in 1999. Then, he started his PhD at the Molecular Genetics Unit of University Hospital Marques de Valdecilla in Santander (Spain) receiving his doctorate from the University of Cantabria in 2005. After completing his PhD he performed a postdoctoral period at Dr Adolfo Ferrando's lab in the Institute for Cancer Genetics at Columbia University, New York, NY, USA. In April 2009, Dr Real joined Dr Pablo Menendez's lab in the Andalusian Stem Cell Bank in Granada. He became Miguel Servet Researcher from the National Institute of Health Carlos III in 2010. Since July 2013, Dr Real is Principal Investigator of Gene Regulation, Stem Cells and Development group in GENyO, Granada, Spain.

Dr Real has published 37 publications in international peer-reviewed journals in his scientific career, 9 as first author and 2 as senior author. The number of cites exceeds 1990 (Web of Knowledge 8/01/16) and the accumulated impact factor is almost 300. Current H-Index for Dr Real is 17 (Web of Knowledge 8/01/16). He has also contributed to 38 oral communications and posters in national and international meetings. From these researches he has generated 3 patents.

In the last 5 years, Dr Real has led 8 projects funded through competitive calls from public and private entities from Spain and Europe as Principal Investigator. In addition, he has mentored 6 Master students, 2 PhD students and 3 postdoctoral researchers.

Since last year Dr Real is an Invited Professor in the Máster Universitario de Biomedicina Regenerativa (Master Degree in Regenerative Biomedicine) and Máster Universitario en Investigación Traslacional y Medicina Personalizada (Master Degree in Translational Research and Personalized Medicine) at the University of Granada. Furthermore, he has participated in the organization of actions of scientific popularization such as the Second Edition of the Scientific Meeting at GENyO (2014) or the PIIISA project for the initiation to the Research and Development for high school students.

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Nombre: **MONTERO BORONAT, JUAN JOSE**
Referencia: RYC-2015-18357
Área Científica: Biomedicina
Correo Electrónico: jomobs@gmail.com

Título:

INTEGRATION OF CELL SIGNALING WITH APOPTOTIC CELL DEATH TO IMPROVE CANCER TREATMENT

Resumen de la Memoria:

One of the biggest problems that oncologist face when treating cancer patients is the lack of good biomarkers for chemotherapy response, which is often responsible for the poor prognosis. Despite all the new available technologies (including "omic" approaches) and chemical armamentarium for clinical oncology (mostly represented by targeted therapies and immunotherapy), there is a clear unmet need for predictive biomarkers to precisely assign the right therapy to the right patient.

As a scientist, I have been always interested in this process of programmed cell death because it can explain why some therapies are not effective to treat cancer patients. My work at Dana-Farber Cancer Institute consisted in understanding how cancer cells will respond to anticancer agents. I specifically studied cell signaling and how targeted therapies specifically inhibit oncogenic signaling pathways' addiction to induce apoptosis and eliminate the tumor. For instance, I developed a new functional test based on apoptotic sensitivity called Dynamic BH3 profiling (DBP) that can predict chemotherapy response in patient biopsies and personalize cancer therapy. DBP has already been successfully proved as an excellent binary predictor in vitro, in vivo models and different types of primary samples (Montero et al., Cell, 2015), and provides technical possibilities to test multiple chemotherapeutic options in newly diagnosed and recurrent cancer biopsies prior to treating the patient.

A multidisciplinary approach is devised by combining the rational analysis of signaling pathways with the predictive biomarker DBP. My aim is to analyze several intracellular proteins and membrane receptors using transcriptomic and proteomic approaches to find dominant kinases that are responsible for the tumor survival. By better understanding how signaling pathways are altered in cancer, we can identify druggable kinases and which therapeutic options are more likely to eradicate each individual tumor, and once recognized we will directly test the treatments using DBP. We will perform our analyses first in vitro using cell lines and then in vivo using PDX models, emphasizing in developing resistance mechanisms models to test new combinations of agents. With this acquired experience, we will aim to improve clinical treatment by identifying dominant signaling pathways in human tumors and test several therapies using DBP; and when possible also learn how to better treat resistant cancers. I believe that combining the predicting capacity of DBP with kinome analyses, we can accurately improve personalized cancer therapy and patients' clinical outcome.

Resumen del Currículum Vitae:

EDUCATION

PhD. in Biomedicine (Magna cum laude), University of Barcelona. 2008
Diploma in Advanced Studies - Biomedicine Program. Score: Excellent. 2005
BS. Biochemistry, University of Barcelona. 2003
BS. Chemistry, University of Barcelona. 2001

RESEARCH EXPERIENCE

Junior Faculty - Instructor at Dana-Farber Cancer Institute/Harvard Medical School. 2015-Present

Postdoctoral Research Fellow at Dana-Farber Cancer Institute/Harvard Medical School. Dr. Anthony Letai laboratory. 2009 – 2015

Research collaboration with Merrimack Pharmaceuticals. 2013

CIBERehd (Networked Biomedical Research Center-Hepatic and Digestive Diseases). 2008

PhD in Instituto de Investigaciones Biomedicas de Barcelona - CSIC /University of Barcelona. 2004 – 2008

AWARDS

Stand Up To Cancer/The V Foundation for Cancer Research Convergence Scholar Award. 2015

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Career Transition Award Beatriu de Pinós (BP-DGR 2014), co-financed by the European Union Marie Curie Actions Declined. 2015
Keystone Global Health Travel Award. 2014
Best Business plan proposal at Healthcare and Innovation at Harvard Medical School. 2013
Postdoctoral Fellowship Beatriu de Pinós, co-financed by the European Union Marie Curie Actions.2009
Pre-Doctoral FPU Fellowship from Spanish Ministry of Education and Culture. 2004
Collaboration Research Fellowship from Spanish Ministry of Education and Culture. 2000

PUBLICATIONS

Etchin J, Montero J, [...] Letai A, Look T. Activity of a Selective Inhibitor of Nuclear Export, Selinexor (KPT-330), Against AML-Initiating Cells Engrafted into Immunosuppressed NSG Mice. Leukemia. Jul 2015.

Wu S*, Li LS*, Kopp N*, Montero J, [...] Gaul Cǂ, Weinstock DMǂ. A novel type II JAK2 inhibitor in B-cell acute lymphoblastic leukemia. Cancer Cell. Jul 2015.

Montero J, [...] Letai A. Drug-induced death signaling strategy rapidly predicts cancer response to chemotherapy. Cell . Feb 2015.

Montero J, Dutta C, van Bodegom D, Weinstock D, Letai A. p53 regulates a non-apoptotic death induced by ROS. Cell Death and Differentation. Nov 2013.

Sarosiek KA, Chi X, Bachman JA, Sims JJ, Montero J, [...] Letai A. Molecular Cell, Sep 2013.

Etchin J, Sanda T, Mansour MR, Kentsis A, Montero J, [...] Letai A, Kung AL, Look AT. Br J Haematol, Apr 2013.

Ercan D, Xu C, Yanagita M, Monast CS, Pratilas CA, Montero J, [...] Wong KK, Jänne PA. Reactivation of ERK Signaling Causes Resistance to EGFR Kinase Inhibitors. Cancer Discov. Oct 2012.

Montero J, [...] Fernández-Checa JC. Cholesterol and peroxidized cardiolipin in mitochondrial membrane properties, permeabilization and cell death. Biochim Biophys Acta. Feb 2010.

Montero J, [...] Colell A, Fernandez-Checa JC. Mitochondrial cholesterol contributes to chemotherapy resistance in hepatocellular carcinoma. Cancer Research. Jul 2008.

TEACHING

Accreditation as Tenure-track Lecturer and Collaborating Lecturer by The Catalan University Quality Assurance Agency. 2015
Pedagogical Aptitude Certificate (Master Equivalent), University of Barcelona. 2008

SELECTED PRESENTATIONS

5 times invited as speaker to different international research centers, 1 lecture at an international university summer school, 2 oral presentations at international and 1 at a national meetings, and 9 posters at international meetings.

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Nombre: **VILLAR LOZANO, DIEGO**
Referencia: RYC-2015-17997
Área Científica: Biomedicina
Correo Electrónico: diego.villarlozano@cruk.cam.ac.uk

Título:

Experimental and computational whole-genome approaches to study the specificity and evolution of gene regulation in mammals

Resumen de la Memoria:

My research careers focuses on understanding global gene regulation responses, the mechanisms involved, and how perturbation of gene expression leads to disease. A major revelation in recent years has been the rapid evolution of gene regulation in mammals, a discovery that has been facilitated by chromatin immunoprecipitation sequencing approaches to interrogate in vivo locations of transcription factor binding or histone modifications across the human (or other mammalian) genomes.

My postdoctoral research at the University of Cambridge (2011-present) combined chromatin immunoprecipitation sequencing with computational comparative genomics to characterise the evolution of mammalian regulatory regions (such as promoters and enhancers) across a collection of twenty mammalian species. Our findings on how evolutionarily dynamic mammalian enhancers are has led to my current studies on how these patterns of evolution may inform (i) downstream gene expression, (ii) evolution of tissue-specific regulatory regions and (iii) phenotypic adaptations in mammals.

Previously, I conducted postdoral work on gene regulation perturbations in Huntington's disease (CNB, Madrid, 2010-2011), as well as graduate studies on gene regulation in hypoxia (Universidad Autónoma de Madrid, 2005-2010).

Outcomes of my research activity include:

- 9 primary research publications in international peer-review journals, including (i) 4 first author publications and one as corresponding author, and (ii) journals such as Cell and the Journal of Clinical Investigations.
- 4 review and opinion articles, including a review of my postdoctoral research area in Nature Reviews Genetics and two opinion pieces as a corresponding author.
- 9 invited talks to international conferences, workshops and special seminars.
- 462+ citations, H index = 9. Google Scholar: http://scholar.google.es/citations?hl=en&user=mJOptGQAAAAJ Research gate: http://www.researchgate.net/profile/Diego_Villar
- 5+ years of international research experience, including research visits to the US and Austria and extensive postdoctoral work in the UK. Establishment of productive international collaborations.
- A research patent.
- Successful research funding applications to EMBO and CRUK.
- Invited peer review, outreach and teaching activities.

Resumen del Currículum Vitae:

During my PhD at Universidad Autónoma de Madrid (2005-2010), I worked under the supervision of Dr. Luis del Peso Ovalle in gene regulation under hypoxia, employing biochemical, genomic and computational approaches. My most relevant contributions include (i) the identification of the substrate binding region in HIF prolyl hydroxylases (Biochemical Journal 2007), (ii) global identification of HIF target genes and HIF binding sites (Nucleic Acids Research 2010) and (iii) characterisation of transcription factor cooperation in HIF-bound enhancers (PLoS One 2012, corresponding author publication). This last contribution from my PhD involved independently-sought international collaborations (Ohio State University, USA, 2008 and Technische Universitaet Graz, Austria, 2009; the latter through an EMBO short-term fellowship).

After obtaining my PhD, I moved onto a short postdoctoral training (March 2010-July 2011) in Dr. Jose Ramón Naranjo laboratory at the National Biotechnology Centre (CNB, Madrid) to study gene regulation responses in the context of disease. Using biochemical, behavioural and gene expression profiling experiments, I discovered small molecules of the glinide family that could bind the neuronal transcriptional repressor DREAM in vitro and inhibit its transcriptional activity • these results led to registration of a research patent for these molecules as a potential treatment for Huntington's disease, and a publication in the Journal of Clinical Investigation in 2016.

Since September 2011, I am completing my postdoctoral training at the University of Cambridge (UK), in the laboratory of Dr. Duncan Odom. My current work investigates the mechanisms underlying evolution of regulatory regions in mammals and their functional implications. During this time, I have reviewed the antecedents of my postdoctoral work on evolution of transcription factor binding (Nature Reviews Genetics 2014), and published a detailed characterisation of the evolution of whole regulatory regions in mammals (in particular, promoters and enhancers; Cell 2015).

My work combines whole-genome functional genomics experiments (mostly ChIP-seq and RNA-seq) with computational comparison of genome sequences across species (comparative genomics) to study the evolution of gene regulation in mammals. My current interests include the elucidation of (i) how evolutionary stability of regulatory regions associates with downstream gene expression, (ii) mechanisms of tissue-specific regulatory evolution and (iii) regulatory adaptations in mammals.

My career ambitions focus on attaining research independence. To aid in this goal, during my postdoc in Cambridge I have developed

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preliminary data for an independent research project focusing on naked mole-rat enhancer activities. The naked mole-rat is an emerging mammalian model for hypoxia tolerance, longevity and cancer resistance, and I independently led (CRUK Travel Award, University of Illinois at Chicago, 2012) its incorporation into our investigation of regulatory evolution in mammals (Cell 2015). Currently, I am developing further collaborations to extend this project to investigation of other mole-rat species and derived hepatocyte cultures.

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Nombre: **GONZALEZ TRAVES, FRANCISCA**
Referencia: RYC-2015-18530
Área Científica: Biomedicina
Correo Electrónico: pgonzalez@salk.edu

Título:

Physiopathology of Inflammatory Processes

Resumen de la Memoria:

With a degree in Biology (Genetics) and a PhD in Biochemistry and Molecular Biology, I accumulate eight years of postdoctoral experience working as immunologist. I carried out my PhD Thesis under the supervision of Drs. L. Boscá and S. Hortelano at the Fundación Centro Nacional de Investigaciones Cardiovasculares (CNIC)(Madrid, Spain). After that, I performed a first postdoctoral stay at Dr. Boscás laboratory in the Instituto de Investigaciones Biomédicas Alberto Sols (IIBm-CSIC)(Madrid, Spain), and a second postdoctoral stay under the supervision of Dr. Greg E. Lemke at The Salk Institute for Biological Studies (La Jolla, California, USA).
Throughout my scientific career I have made another 3 short stays in different international laboratories (San Diego, London and Munich), attended national and international conferences, participated in the training of undergraduate students and co-directed a PhD Thesis. I have also received specialised training in International Research Project Management and perform management activities for a consortium of research laboratories. Finally, I have a wide expertise in basic laboratory techniques including in vitro and in vivo experimental approaches such as cell culture, isolation and culture of murine primary cells, immunoassays and imaging techniques as well as designing and handling mice models.
My main research line has been focused on the study of the signalling pathways involved in the resolution of inflammation as a mechanism to avoid the establishment of chronic inflammation. Particularly, I am interested in elucidating the role of macrophages during the inflammatory response and how macrophage-signalling mechanisms initially contribute to the onset of inflammation; while later on play a role in its resolution. In addition, during the last years I have analysed the role of TAM receptors in different tissue resident macrophages and I have also evaluated the anti-inflammatory and anti-tumoral effects of natural and synthetic terpenes, trying to identify novel molecules with potential use in therapeutic.

Resumen del Currículum Vitae:

Summary of Qualifications

Molecular and cellular biologist, with a wide experience in designing and manipulating animal models and in vitro studies including cell culture, immunoassays, and statistical analyses to elucidate pathways underlying the pathophysiology of inflammatory processes. Excellent training in overall basic laboratory techniques and experienced in isolation and culture of murine primary cells. Active participant in productive collaborative teams that have generated high quality data, reflected in high-impact scientific journals.

Education

2006	PhD	Biochemistry and Molecular Biology	Universidad Complutense de Madrid (UCM), Spain
2003	MS	Biochemistry and Molecular Biology	Universidad Complutense de Madrid (UCM), Spain
2001	BS	Biochemistry and Molecular Biology	Universidad Complutense de Madrid (UCM), Spain

Complementary Education

2009 Specialist in International R+D+I Project Management Course. Universidad Politécnica de Madrid (UPM)
2007 Management of Science and Technology and Multinational Project Management Courses

Professional Development

2011 Present Postdoctoral Research Associate at The Salk Institute for biological studies. La Jolla, CA. Mentor: Prof. Greg Lemke, PhD.
2007 2011 R+D+I Project Manager at CIFRA consortium. Instituto de Investigaciones Biomedicas Alberto Sols (IIB) and Universidad Complutense de Madrid. Madrid, Spain.
2001 2006 Graduate Student at CNIC Foundation (Fundación Centro Nacional de Investigaciones Cardiovasculares) (CNIC-ISCIII), Physiopathology of Inflammatory Processes. Madrid, Spain. Mentors: Lisardo Bosca, PhD and Sonsoles Hortelano, PhD.

Mentoring Experience

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As a graduate student and postdoctoral fellow, I have managed and mentored 3 undergraduate summer students and a graduate student resulting in a PhD Thesis award.

Also, I volunteered for 4 years as teacher assistant for the Biochemistry Laboratory at the Veterinary Faculty, Universidad Complutense de Madrid.

Honors and Awards

Postdoctoral Fellowships awarded: Ramon Areces Foundation postdoctoral Fellowship (2011) and Marie Curie International Outgoing Fellowship (2012)

Twice awarded by the Royal Academy of Pharmacy, Spain. Annual Scientific Contest

Three short stays in international laboratories: Dr. Michael Palladino. Nereus Pharmaceuticals, Inc. (San Diego, CA) (10 weeks), Dr. Peter Parker. Cancer Reseach UK (London, UK) (12 weeks) and Dr. Thomas Miethke. Institute of Medical Microbiology, Immunology and Hygiene. (Munich, Germany) (8 weeks)

Predoctoral Fellowship awarded: BEFI (2006). Instituto de Salud Carlos III. Madrid. Spain

Publications
34 peer-reviewed articles, 28 of them in journals of the first quartile. 10 articles as first author and 24 articles as co-author.

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Nombre: **FERNANDEZ FUENTES, NARCISO**
Referencia: RYC-2015-17519
Área Científica: Biomedicina
Correo Electrónico: narcis.fernandez@gmail.com

Título:

Structural Bioinformatics in Biological and Clinical Research

Resumen de la Memoria:

Dr Fernandez-Fuentes scientific expertise lies within the realms of Structural Bioinformatics and Computational Biology. Dr Fernandez-Fuentes has long-standing interest in protein structure prediction and structure-to-function relationships and has developed a range of commonly used tools and resources for the scientific community. Through numerous collaborations, Dr Fernandez-Fuentes has been exposed to the work of multidisciplinary projects ranging from molecular immunology, virology, pharmacology, protein design, and drug discovery. Most of his recent research has been devoted to the study of protein complexes both at the level of understanding the dynamics and structural details of interactions and to computational modelling of orthosteric peptides to modulate protein-protein interactions. The study of genome-wide interaction maps, i.e. interactomes, to understand the underlying cause of diseases as well as linking the study of genetic changes, e.g. SNPs, or post-translational modification and the functional modelling of the impact both at protein and system level represents also an important part of his research portfolio.

Resumen del Currículum Vitae:

Narcis Fernandez-Fuentes received his B.Sc. degree in Biology from the University of Girona in 1997 and his B.Sc. degree in Biochemistry from the University Autonomous of Barcelona in 1999. Between 2000 and 2004 he did his Ph.D. studies at University Autonomous of Barcelona, supported by the Catalan Government with the FI-FIAP predoctoral fellowship, where he was awarded a Ph.D. in Computational Biology. During his Ph.D. he collaborated with several bioinformatic labs across Europe and USA: from Sep. 2001 to Feb. 2002 he was Marie Curie Training Fellow at the Structural Genomic Group in EMBL-EBI, Hinxton; Cambridge, U.K. where he worked with Prof. Liisa Holm on remote recognition of protein structures; from Oct. 2002 to Apr. 2003 he worked with Prof. Michael J.E. Sternberg, Imperial College of London, U.K., supported by EMBO and FEBS short term fellowships; finally, between Oct. 2003 and Mar. 2004 he was visiting fellow at Dr. Andras Fiser's Lab., Albert Einstein College of Medicine, NY, supported by Boehringer Ingelheim Fonds Fellowship. On August 2004 he was appointed Research Associate at Dr. Andras Fiser Laboratory at Albert Einstein College of Medicine, NY On September 2007 he was appointed Lecturer at the University of Leeds were he established the Computational Biology Group at the Leeds Institute of Molecular Medicine. From January 2012 to Dec 2013 he was Reader in Bioinformatics at the Institute of Biological, Environmental and Rural Science, University of Aberystwyth, position which currently holds. From Jan 2014 to Dec 2015 he was an incoming TECNIOSpring Fellow at the University Pompeu Fabra, Barcelona, Spain. On his relatively short scientific career Dr. Fernandez-Fuentes has published over 40 peer-reviews articles, most of them in highly impact journals, and contributed chapters to four books. He is an expert in Structural Bioinformatics, in silico Drug Discovery and Computational Biology.

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Turno de acceso general

Nombre: **ARANGUREN LOPEZ, XABIER**
Referencia: RYC-2015-17233
Área Científica: Biomedicina
Correo Electrónico: xlaranguren@unav.es

Título:

IntereXt

Resumen de la Memoria:

My experience in biomedical research extends to the last 13 years. This period can be divided in 3 stages: PhD training in CIMA ("Center for Applied Medical Research"), Navarra (September-2002-November 2006); international Postdoctoral training in KULeuven (Belgium) (January 2007-March 2014) and the current Principal Investigator activity in CIMA, Navarra, (April 2014-Today). During my PhD, my work focused on the study of a strategy to differentiate stem cells into vascular endothelium and on the application of such stem cells in mouse models of vascular disease, mainly limb ischemia. The results of this work have been published in Blood (2007 IF: 10.896), generated a patent, for which I am co-inventor (Vascular/lymphatic Endothelial cells. US-2009-0104159-A1) and earned me a PhD title with greatest distinction and also an award for the best PhD of the Biochemistry faculty of the University of Navarra. After the PhD, I performed my post-doc in the research group headed by Prof. Aernout Luttun, at KULeuven (Belgium). In the first period of my post-doctoral training, I continued the work started during the PhD, determining the therapeutic potential of AC133+ and MAPCs in a mouse model of limb ischemia. The results of this work were published in JCI and Cell Transplantation (Aranguren et al. JCI, 2008; Aranguren et al. Cell Transplantation, 2011). Later on, I drifted the focus of my investigation on the molecular basis of endothelial heterogeneity in physiological and pathological conditions and on the vascular system development in mouse and zebrafish models. This work resulted in the publication of several papers for which I am first author (Aranguren et al. Blood 2013; Aranguren et al. J Cell Sci 2013; Aranguren et al. BBRC 2011), one paper for which I am co-last author (Coppiello et al. Circulation 2015) and others, for which I am collaborator. Since April 2014 I'm the Principal Investigator of a new research line in the Cell Therapy Area of CIMA in Pamplona, where I was recruited as a Marie-Curie fellow. At the moment my group is composed by a postdoctoral fellow and a part time research assistant. My research aims to deliver proof of principle that the host versus graft rejection in organ xenotranplantation would be dramatically reduced by the presence of the host ECs on the transplanted xeno-organ. To that aim chimera mice harboring rat ECs will be generated by blastocyst complementation and the heart of these chimerae will be xenotransplanted in rat. If the proposed proof of principle will be demonstrated, we will further develop this strategy in a nonhuman primate-pig model. To sustain economically this project, as Principal Investigator I have obtained 2 R&D projects funding:
70278 Fundación Caja Navarra: January 2015-March 2016: 18.000€
031-2015 Gobierno de Navarra: December 2015-December 2018: 41.700€

Resumen del Currículum Vitae:

My experience in biomedical research extends to the last 13 years. This period can be divided in 3 stages: PhD training in CIMA ("Center for Applied Medical Research"), Navarra (September-2002-November 2006); international Postdoctoral training in KULeuven (Belgium) (January 2007-March 2014) and the current Principal Investigator activity in CIMA, Navarra, (April 2014-Today). I have participated in several international R&D projects including FP6 and FP7 calls and as principal investigator, I have been awarded with 3 R&D public call projects, 1 from FWO (Flemish research foundation), for one of my postdoctoral project and the other 2 from "Fundación Caja Navarra" and "Gobierno de Navarra" for my current research line. As a post-doc I was involved in the training of several lab technicians, as well as 1 master thesis students and 3 PhD students. I was officially the co-director of the master thesis student (defense date 24-5-2012) and one of the PhD students (defense date 29-9-2014). During my career I have published 16 articles in international journals, 7 of them as first author in JCI, Blood (two articles), Journal of Cell Science, Cell Transplantation, BBRC and Journal of Molecular Medicine (review). Furthermore, recently I have published a co-last author paper in Circulation. As result of these works I am co-author of two international patent applications. I have 2 years of teaching experience in the department of Biochemistry (from 2002 to 2004; University of Navarra). The teaching consisted in practical courses of biochemistry techniques. Furthermore, in October 2015, I have been the speaker of one class of the "Máster Universitario en Investigación Biomédica por la Universidad de Navarra". Awarded with IEF Marie-Curie Fellowship, I obtained a Principal Investigator position in the Centre for Applied Medical Research (CIMA), Pamplona in April 2014. During the last 2 years I have formed my own small group, at the moment composed by a postdoctoral fellow and a part time research assistant. Furthermore, I have obtained as principal investigator project grants from €Fundación Caja Navarra€ and €Gobierno de Navarra€ to sustain my own research line.

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Nombre: **DEL PINO YANES, MARÍA DEL MAR**
Referencia: RYC-2015-17205
Área Científica: Biomedicina
Correo Electrónico: mdelpino@ull.edu.es

Título:

Precision medicine of allergic diseases: genetic susceptibility and treatment response

Resumen de la Memoria:

My research career has focused on determining the genetic factors underlying complex diseases and traits. The main focus of my doctoral thesis was the analysis of genetic factors associated with asthma susceptibility. As a first approach, we evaluated the transferability of common variants of candidate genes for asthma susceptibility in the Spanish population. I demonstrated that some important genes for asthma are not well covered by most genotyping platforms and that genome-wide association studies (GWAS) of asthma have sub-optimally surveyed these genes (JACI 2012; 129:573-5). I also performed the first fine mapping of the human leukocyte antigen region for asthma susceptibility using imputation of classic alleles, identifying pleiotropic effects of associated alleles with autoimmune diseases and lipid traits (JACI 2014; 134: 1201-3). Furthermore, I performed a characterization of the North African admixture of Spanish populations using nuclear autosomal markers, showed its potential confounding effect in association studies and proposed methods to reduce it.

During my postdoctoral period, my knowledge in population genetics allowed me to assess the role of ancestry in asthma susceptibility and related outcomes. Firstly, I demonstrated that disparities in asthma prevalence among Latinos (highest in Puerto Ricans and lowest in Mexicans) could be explained by differences in genetic ancestry, independently of environmental and socioeconomic factors (JACI 2015; 135: 228-35). Secondly, I leveraged local ancestry to perform the first admixture mapping of immunoglobulin E (IgE) levels and revealed genomic regions where African, European and Native American ancestry contribute to this trait. I also performed the first GWAS of IgE levels in Latinos and co-lead the first GWAS of asthma in Spanish populations, discovering new genes associated with both traits (JACI 2015; 135: 1502-10, JACI 2015, in press). I have participated in numerous international GWAS meta-analyses to characterize the susceptibility to atopic dermatitis and allergic rhinitis, and to identify interactions of asthma genes with sex. I have also analyzed the contribution of rare variants in asthma susceptibility (Nat Commun 2015; 6: 5965) and IgE levels (JACI 2015; 135: 1502-10), using both exon chip and next generation sequencing data.

My current independent research line has moved towards precision medicine. I am co-PI of a project aiming to detect somatic mutations of metastatic renal-cell carcinoma involved in treatment resistance using exome sequencing. In addition, I am the PI of a grant co-funded by the Instituto de Salud Carlos III and the EU framework programme Horizon 2020 to study the role of genetic variation in the response to asthma medications. This is an international effort including 20 studies integrated in the Pharmacogenomics in Childhood Asthma (PiCA) consortium. My expertise in pharmacogenomics has also been recognized with an invited talk in the most prestigious meeting on pulmonary diseases (ATS, 2015). Since January 2016, I am leading the largest GWAS meta-analysis of asthma treatment response ever performed. My aim is to use a multi-omics approach to disentangle the molecular mechanisms underlying the large variability observed in asthma treatment response among children, allowing a better prediction of the response and an improved disease prognosis.

Resumen del Currículum Vitae:

I obtained my bachelor degree in Biology in 2007 from University of La Laguna (ULL), with the recognition of Extraordinary Award. During this period, I was the recipient of 4 collaborative fellowships: one from the Institute for Renewable Energy (ITER), two from the Spanish National Research Council (CSIC) to work in the Institute of Natural Products and Agrobiology, and one from the Spanish Ministry of Education and Science (MEC) to work in the Department of Genetics of ULL. In 2012, I obtained my PhD degree in Life and Environmental Sciences under the supervision of Dr. Carlos Flores and Dr. Mariano Hernández, working at the Hospital Universitario Nuestra Señora de Candelaria. My thesis was distinguished with the Extraordinary Doctorate Award in the area of Health Sciences by ULL. In 2012 I was awarded with two postdoctoral fellowships, from Fundación Canaria Dr. Manuel Morales and from Fundación Ramón Areces, to work with Dr. Esteban G. Burchard at the Department of Medicine at the University of California at San Francisco (UCSF) for a period of 28 months.

I am co-author of 33 papers published in international peer-reviewed journals (85% in the first quartile of its area), 12 of them as a first or co-first author and two of them as corresponding author. Sixteen of my articles (48% of the total) are within the first decile, including the first-ranking journals of specialized areas (J Allergy Clin Immunol and Am J Respir Crit Care Med), as well as other top ranking journals such as Nat Genet, Nat Commun, PLoS Medicine, and Proc Natl Acad Sci USA. My publications accumulate an impact factor of 272.6, 312 citations and an H-index of 11 (according to Google Scholar). I have 53 contributions to conferences or workshops (44 international and 9 national), 4 of them as invited speaker. I have contributed as a reviewer to 7 international journals. I have participated in 13 research projects (2 regional, 5 national, and 6 international), being the principal investigator in two of them involving pharmacogenomics. One of those grants was awarded by a private foundation and the other by the Instituto de Salud Carlos III (AC150015), as part of a complementary action to an ERA-Net project (EU framework programme Horizon 2020).

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I am a member of several national and international research networks and consortia, including The Biomedical Research Center Respiratory Disease Network (CIBERES, since 2009), The EVE Asthma Genetics Consortium (since 2012), the Consortium on Asthma among African Ancestry Populations in the Americas (CAAPA, since 2013), and the EArly Genetics & Lifecourse Epidemiology Consortium of atopic dermatitis (EAGLE, since 2013). I am a member of the scientific committee of the Pharmacogenomics in Childhood Asthma (PiCA, since 2014) consortium and also coordinate the largest meta-analysis of asthma treatment response ever performed, which includes 20 studies from all over the world.

My teaching experience includes 90 hours in the official Master of Biomedicine and Biotechnology and in the degrees of Pharmacy and Biology at ULL. I have the certification of "Profesor Ayudante Doctor" by the ANECA. I have mentored two graduate students in the laboratory of Dr. Burchard (UCSF) and the final degree project of an undergraduate student of Biology (ULL). I am currently supervising two students performing their final degree/master projects.

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Turno de acceso general

Nombre: **MENDEZ GARCIA, PABLO**
Referencia: RYC-2015-18545
Área Científica: Biomedicina
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Título:

Synaptic, cellular and network mechanisms of memory

Resumen de la Memoria:

My research career has focused on the study of brain physiology and pathology, and particularly, on the brain mechanisms of memory.

I graduated with a degree in Chemistry and obtained a Master in Biochemistry in the University Autonoma of Madrid where I received my first laboratory training as an undergraduate student. I pursued my career with a PhD in Neuroscience (2000-2005, Instituto Cajal, Madrid) focusing on the protective actions of sexual hormones in epilepsy and Parkinson's disease. During my postdoctoral stage at the University of Geneva, Switzerland (2006-2008), I investigated the cellular and synaptic basis of memory and their malfunctioning in cognitive disorders. At the European Brain Research Institute, in Rome, Italy (2008-2012), my research topic was the physiology of inhibitory neurotransmission and its involvement in depressive disorders.

Since 2012, I am a senior research assistant, a semi-independent position at the University of Geneva Medical Center. My research interest is the study of memory and its disease-related alterations using a system approach and a wide portfolio of techniques (from molecular biology to behavioral analysis and optogenetics). This position allowed me to develop my own research projects, supervise a small group of scientists and gain invaluable experience in scientific management, supervision and communication.

The impact of my work is supported by 28 publications (first, senior and corresponding author level) in peer-reviewed international journals, more than 2500 citations for an h-index of 22 and invitations to present my results in seminars and international congresses.

At this point of my career, my priority is to attain scientific independence in a Spanish institution and I truly believe that the Ramon y Cajal program is an excellent and timely opportunity to achieve it. It is my wish to bring to my home country my scientific experience and creativity and contribute to its reputation by developing a solid and innovative research project.

Resumen del Currículum Vitae:

- Degree in biochemistry and Doctor in Science (Universidad Autónoma de Madrid)
- Six years of international post-doctoral experience in neuroscience research
- Four years as a senior research and teaching assistant at the University of Geneva, Switzerland
- Remarkable knowledge of the state of the art technology for the study of brain function
- Excellent track of peer reviewed international publications (Senior, corresponding and first author levels)
- Extensive experience in scientific project management and scientific supervision and communication
- Participation in numerous national and international research projects
- Innovative and solid project to investigate synaptic, cellular and network mechanisms of memory

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Turno de acceso general

Nombre: **REDONDO MUÑOZ, JAVIER**
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Área Científica: Biomedicina
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Título:

How epigenetic changes influence on lymphocyte migration

Resumen de la Memoria:

I started my PhD studies with Prof. A. García-Pardo at Centro de Investigaciones Biológicas (awarded with Ramon-Areces PhD Fellowship). There I determined how cell adhesion through integrins regulates catalytic and non catalytic functions of MMP-9 in B-chronic lymphocytic leukaemia (B-CLL) cells. I also visited the group of Dr. Alison M. Michie at the University of Glasgow, where I used in vivo models of B-CLL to study the migration of these leukaemic cells (2008, awarded with a travel grant from Boehringer-Ingelheim Foundation).
In 2010 I obtained my PhD in Immunology with Hons (Universidad Complutense) and was awarded with a JAE Postdoctoral Fellowship, to take up the position of research associate with Prof. A.C. Carrera (Centro Nacional de Biotecnología). This allowed me to expand my research field from cell adhesion to transmitting signals into the nucleus and chromatin homeostasis. Subsequently I was awarded with a postdoctoral Juan de la Cierva Fellowship. During my postdoctoral studies, I determined how a catalytic isoform of PI3K (p110beta) localises to the nucleus and controls chromatin homeostasis and nuclear envelope integrity.
In 2014 I moved to Manchester, awarded with a Wellcome Trust Recruitment enhancement (£180000/3years) to join as Junior Group Leader the Wellcome Trust Centre for Cell-Matrix Research at the University of Manchester. Here, I started my own research group combining my expertise in lymphocyte migration and nuclear biology to explore the interplay between cell-matrix interactions and chromatin changes during lymphocyte migration.
Integrins are cell surface receptors critical for lymphocyte infiltration and tumour persistence in haematological disorders. Importantly, normal and malignant lymphocytes alter the physical properties of their nuclei to be more malleable to enable migration through tissues. My group has recently published a dual role of integrins in mediating lymphocyte cell attachment and in controlling nuclear physical properties (Zhang et al., 2015). However, the mechanisms linking integrins and nuclear chromatin and how they control nuclear deformability are unknown. This research line, using cutting-edge techniques and developing multidisciplinary approaches will discover novel molecular mechanisms that transduce signals from the cell surface into the nucleus during lymphocyte migration. These findings will define new potential therapeutic targets in inflammation and human pathologies where lymphocyte infiltration is crucial.

Resumen del Currículum Vitae:

The attached Curriculum Vitae (CV) shows my scientific and academic achievements.

PhD (with Hons) in Immunology (Universidad Complutense de Madrid, 2010) at the laboratory of Prof. A. García-Pardo (Centro de Investigaciones Biológicas).

Research associate (2010-2013) at the laboratory of Prof. A.C. Carrera (Centro Nacional de Biotecnología).

Junior Group Leader (2014-) in the Wellcome Trust Centre for Cell Matrix Research (University of Manchester).

I visited as PhD student the group of Dr. A.M. Michie at the University of Glasgow (2008) and more recently s visiting researcher the group of Dr. C. Zaph; University of British Columbia (2014).

My work has generated 15 research articles (9 as first author or co-author; and 1 as corresponding author) in the highest impact journals in the haematology, cancer and nuclear biology fields, such as Blood (2006, 2008a, 2008b), Cancer Cell (2010), Clinical Cancer Research (2010) and Nucleic Acids Research (2013, 2015). My key contributions were recognised by editorial comments in Blood, Clinical Cancer Research and Molecular of Cellular Biology and with a cover image in Molecular of Cellular Biology. My publications have 522 citations and an 8 h-index value (source and date: Google Schoolar, December 2015).

My honors and awards include:

Ramon Areces PhD Fellowship (2006-2010)
Travel grant Boehringer-Ingelheim Foundation (2008)
JAE Postdoc Fellowship (2010)
Juan de la Cierva (2011-2013)
Wellcome Trust Recruitment Enhancement (2014-2016)

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Best Spanish thesis of the year in Natural Sciences and Health from the Royal Academy of Doctors of Spain (2010)
Best paper of the year (Basic Research in oncology) by the National Cancer Network RTICC (2010).

I presented my findings in more than 30 national and international meetings, including Adhesion meeting, EMBO meeting, Keystone symposium and Gordon Research Conference. I have been involved as co-participant in more than 10 national and international research projects, such as CAM, SAF, Red temática de Cáncer and Wellcome Trust.

During my career I collaborated in the Academia, as research tutor supervising undergraduate student (Universidad Autónoma de Madrid, 2013), as guest lecturer on the Immunology course for undergraduate students in Medicine (Universidad Complutense, 2012) and as assistant professor in the Biochemistry Laboratory for undergraduates in Biology (Universidad Autónoma de Madrid, 2011) and in the Tutorial scheme (University of Manchester, 2014 and 2015). I found this training and experience rewarding and enjoyable. Additionally, I am member of the Society of Spanish Researchers in the United Kingdom, the Sociedad Española de Inmunología and the European Hematology Association.

In summary, over my research career I have acquired background and expertise to establish my independent career and a Ramón y Cajal Fellowship will allow me to establish my own research group in Spain.

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Nombre: **LLORENS MARTÍN, MARÍA VICTORIA**
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Área Científica: Biomedicina
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Título:

Physiological and pathological modulation of adult hippocampal neurogenesis. Importance for Alzheimer¿s disease therapeutics

Resumen de la Memoria:

María Llorens-Martín received her Ph.D. from the Complutense University of Madrid in 2009 for her research into the effects of physical exercise on the hippocampus, which was conducted under the supervision of Dr. José Luis Trejo at the Cajal Institute. Her PhD thesis addressed the mechanisms by which different subpopulations of hippocampal neurons are differentially affected by physical exercise. She studied the generation of newborn neurons in the dentate gyrus of the hippocampus (a process known as adult hippocampal neurogenesis (AHN)). Fascinated by this singular process occurring in the adult brain, María Llorens-Martín decided to devote her career to studying this phenomenon. The neuroprotective potential of AHN has been María Llorens-Martín&#65533;s focus throughout her research career, given that AHN is seriously impaired in Alzheimer¿s disease (AD).

In 2010, she then moved to the Center for Molecular Biology &#65533;Severo Ochoa&#65533; to undertake postdoctoral research on AD and AHN under the guidance of Prof. Jesús Ávila. During this time she addressed AHN alterations in the brains of murine models of AD and in patients with this disease. In particular, she studied the impairment of AHN caused by alterations in the activity of certain toxic proteins, in particular Glycogen synthase kinase 3 (GSK3) and Tau.

Special mention is given to the applicant&#65533;s study entitled &#65533;GSK3 overexpression causes reversible alterations on postsynaptic densities and dendritic morphology of hippocampal granule neurons in vivo&#65533;, published in Molecular Psychiatry. In this study, she described that granule neurons of AD patients display a particular shape (&#65533;V-shape&#65533;), which completely differed from that of control subjects (known as &#65533;Y-shape&#65533;). In addition, the overexpression of GSK3; (a protein whose activity is dysregulated in the brain of AD patients) caused granule neurons to acquire the same morphology as that observed in AD patients. Importantly, these alterations were reversed by restoring GSK3; expression levels and by exposing the mice to environmental enrichment.

Since 2012, she has been working on establishing an independent research line, combining her acquired expertise in neurodegenerative disorders with her extensive knowledge of AHN and neuroprotection. In 2015, she was awarded a prestigious &#65533;New Investigator Research Grant&#65533; by the Alzheimer¿s Association (USA) to develop, as Principal Investigator (PI), a research project on the neuroprotective properties of AHN to treat AD. The research project she is currently developing involves the use of physical exercise to counteract the deleterious effects of GSK3 Beta; and Tau on AHN and memory. In fact, in 2015 she directed a doctoral thesis on the involvement of Tau in the modulation of AHN exerted by external stimuli. In addition, at the beginning of January 2016, María Llorens-Martín started to direct a doctoral thesis focused on the neurotoxic actions of Tau on AHN and microglial activation.

The conceptual frame of her research as junior independent researcher has allowed her to focus on the translational aspects of biomedical research. In this regard, she has relentlessly pursued her research interests with the aim to contribute to our understanding of the cellular mechanisms that are dysregulated in an incurable neurodegenerative disease such as AD and thus pave the way to towards a cure for this disease.

Resumen del Currículum Vitae:

María Llorens-Martín received her Ph.D. from the Complutense University of Madrid in 2009. She developed her Ph.D. thesis under the supervision of Dr. José Luis Trejo at the Cajal Institute. She received an Extraordinary Award for her Ph.D. work, which also received the highest grade of &#65533;Sobresaliente Cum Laude&#65533;. During her Ph.D., she made international and national stays, and she published 18 articles in scientific journals such as Molecular Psychiatry (IF 15.1) and Neuropsychopharmacology (IF 7.05). She also presented her work at 9 international and national congresses, both as posters and as invited speaker.

In 2010, she joined Prof. Jesús Ávila¿s lab at the CBMSO as a postdoctoral researcher. She was awarded two post-doctoral fellowships (JAEDoc-2009 and &#65533;Juan de la Cierva-2012&#65533;). During the postdoctoral period, she has published 21 scientific articles in journals such as Molecular Psychiatry or Human Molecular Genetics. She has presented her work at 22 international and national congresses and has participated in 6 Research Projects. She has also been featured in two press releases and several interviews for Spanish TV and radio media. Of particular relevance is the first-authorship study published in Molecular Psychiatry in 2013. This achievement contributed to her obtaining two National Young Investigator Awards, in 2013 and in 2014 respectively.

Of particular international relevance is her participation in the select Route28 symposium on adult neurogenesis in 2012. Organized by the most important European researcher in the field, Gerd Kempermann, this symposium gathers distinguished researchers in the field of adult neurogenesis and 30 pre- and post-doctoral students. María Llorens-Martín participated in the team that received the Symposium Award for the best scientific proposal.

María Llorens-Martin has been awarded (as Principal Investigator) an international &#65533;New Investigator Research Grant&#65533; from the Alzheimer¿s Association (USA), one of the most prestigious research organizations worldwide. This achievement constitutes one of the most important milestones in the development of the applicant¿s career as an independent researcher, not only due to financial

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independence but also to the international visibility, recognition and prestige that this grant has conferred. In 2015, she was the recipient of a prestigious international fellowship from the Japan Society for the Promotion of Science (JSPS) to develop part of her research at the University of Tsukuba (Japan). María Llorens-Martín has already directed a doctoral thesis, which was defended in July 2015, obtaining the highest mark ⁄Sobresaliente Cum Laude⁄ from the Universidad Autónoma de Madrid. The work resulting from this Ph.D. is currently being submitted to EMBO Journal and awaiting final acceptance.

Importantly, she has been invited to participate as a senior speaker in the Eurogenesis Congress, (Bordeaux, 2016), considered to be one of the most prestigious international gatherings in the field of Neurogenesis.

As a result of her research trajectory, María Llorens-Martín is external reviewer for 23 international journals, and Reviewer panelist for two international and one national (ANEP) evaluation agencies. She has published a total of 39 scientific articles. These studies have been cited a total of 791 times and she has an H-index of 16.

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Nombre: **GARAUDE , JOHAN**
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Área Científica: Biomedicina
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Título:

Innate Immune Regulation of Mitochondrial Electron Transport Chain for Immunotherapies

Resumen de la Memoria:

I am puzzled by the dual capacity of the immune system to either protect us from infections or to directly promote life-threatening processes such as autoimmune disorders and cancer development. While I was a Ph.D. student, the fundamental basis for the ﷺcancer immunoeditingﷺ theory, which proposes that constant attack of cancer cells by the immune system modulates the nature of emerging tumors, was being expanded. Interestingly, my own published observations were in line with this theory. It was thus clear to me that innate immune cells were at the cornerstone of the decision made by the immune system to promote or counteract tumor development. I was convinced that for developing potent immunotherapies it was necessary to better understand the molecular mechanisms governing activation of myeloid cells that initiate immune responses. Therefore, I focused my postdoctoral studies towards understanding innate immune receptor-mediated regulation of myeloid cell capacity to activate T cells. This work, which is now reaching a clinical trial stage, demonstrated that controlling the ﷺassociative recognitionﷺ of tumor antigens with a dual-ligand for complementary innate receptors triggers a potent anti-tumor immune response. At the same time, the preponderant role of T helper 17 cells (Th17) in immune-related disorders, including cancer, was becoming obvious. Yet, a natural stimulus for their differentiation was missing. Our work uncovered a natural Th17 inducer defined by myeloid cells that have engulfed infected-dying cells. While developing these investigations, I made the preliminary observations that innate immune sensing of various threats could modulate mitochondrial respiratory chain organization and function, which in turn influences the nature of the adaptive immune responses generated. As an independent principal investigator, I am currently exploring the mechanisms that control myeloid cell metabolism and how this impacts T cell fate. This research is used to develop new immunotherapies and improve emerging therapies that target tumor metabolism and bacterial infection.

Resumen del Currículum Vitae:

I have contributed to 17 scientific publications. I am first author on 6 research articles (one as co-corresponding author) published in high impact journals including Science Translational Medicine or The Journal of Immunology. I am lsecond author on a Nature Letter. I have contributed to 7 review articles, being the corresponding author of 3. I have filled 2 patents. My H-index is 11.

6 relevant achievements in my CV are:

1- My first manuscript as independent Principal Investigator is currently in a second revision round in Nature (Garaude et al., Nature, in revision, Corresponding author). I am listed as first author and as the only Corresponding author.

2- In 2011, I was ranked 1st at the highly competitive selection process for Principal Investigator (Chargé de Recherche de classe 2; 7th commission ﷺ commission scientifique specialisée 7) from the French governmental biomedical research agency (INSERM). This demonstrates my capacity as young principal investigator as well as the quality of my research project and its strong orientation toward biomedical applications. In addition, this project is covered by several funding, including a Marie Curie-CIG grant, an EMBO short-term fellowship and a grant from the French association ﷺLa Ligue Contre la Cancerﷺ.

3- Part of my postdoctoral work at the Mount Sinai School of Medicine (MSSM, New York, USA) specifically described a new approach for cancer immunotherapy that appeared to have an important impact. The data summarizing these finding were published in Science Translational Medicine (Garaude et al., Science Translational Medicine, 2012; cover article), and was accompanied by several comment and opinion articles. More important, this research is protected by a patent and a clinical trial (Phase I/II) is going to be developed in collaboration with Drs. J. Brody and A. Sikora at the Mount Sinai School of Medicine as well as Pr. G. Cartron at the University-Hospital of Montpellier, France.

4- During my postdoc at MSSM, I closely participated to the discovery of a natural stimulus for T Helper 17 cells (TH17) differentiation. This work, for which I am listed as second author, was published in Nature (Torchinsky et al., Nature. 2009). The study described dendritic cells that have engulfed infected-apoptotic cells as potent inducers of TH17. It is considered as cornerstone study in the field of immunology and is largely cited. In addition, this constitutes a strong base for my current research project.

5- My pre-doctoral studies were centered on the role of ERK5 in leukemogenesis. These studies were published in several high quality journals including the Journal of Immunology, and a patent was also published. Of note, this work constituted the pedestal of an important part of the investigation currently led by M. Villalbaﷺs group in Montpellier.

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6- During my pre-doctoral studies, I self initiated a research project investigating the posttranslational control of the transcription factor JunB, a member of the Activating Protein-1 (AP-1) family. A part of this study was published in the Journal of Immunology (Garaude et al., JI. 2008; co-corresponding author). Importantly, I am listed as co-corresponding author on this article. This underlines my ability to undertake new and innovative projects and demonstrates that I rapidly acquired the capacity to lead a line of investigation.

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Nombre: **JIMÉNEZ SCHUHMACHER, ALBERTO**
Referencia: RYC-2015-17622
Área Científica: Biomedicina
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Título:

Mouse models, target modulation, imaging and drug discovery.

Resumen de la Memoria:

I completed my PhD at the CNIO in Dr. Barbacid¿s laboratory. My main goal was to generate a knock-in mouse strain that expressed endogenous H-Ras in the germ line, a model that recapitulates most of the defects observed in Costello Syndrome patients. We discovered that these mice developed hypertension in an angiotensin II-dependent manner, and that this can be prevented with the inhibitor captopril (JCI 2008 & Genes, Br. & Behav. 2009). I generated another mouse model with a germline mutation in K-Ras that reproduces the main alterations found in Noonan syndrome patients and we prevented part of their symptoms via prenatal treatment with MEK inhibitors (PNAS 2014 and Rare Dis. 2015). My other main PhD work focused on the study of pancreatic ductal adenocarcinoma (PDA). We demonstrated that classical pancreatic "ductal" neoplasia can be induced by oncogenic K-Ras in non-ductal exocrine cells and that K-Ras mediated tumorigenesis in mature exocrine pancreas requires pancreatitis (Cancer Cell 2007). The pancreatitis-induced inflammation contributes to pancreatic cancer by inhibiting oncogene-induced senescence (OIS) (Cancer Cell 2011). We showed that EGFR signaling is essential for K-Ras driven PDA (Cancer Cell 2012). I collaborated in the demostration that OIS occurs in vivo (Nature 2005).

I moved Dr. Joyce¿s lab at the MSKCC (USA) to explore the role of the tumor microenvironment in brain tumors. The main focus of research was understanding the role of tumor associated macrophages and microglia (TAMs) in gliomagenesis and evaluating CSF-1R inhibition as a novel target for these tumors. CSF-1R inhibition dramatically increased survival in mice and regressed established GBMs. Surprisingly, TAMs were not depleted upon treatment. Instead, analysis of gene expression in TAMs isolated from treated gliomas revealed a decrease in alternatively activated/ M2 markers, consistent with impaired tumor-promoting functions (Nat. Med. 2013). In a follow up study we investigated whether long-term CSF-1R inhibition results in stable regression of GBM and mechanisms of resistance (2nd revision in Science). These inhibitors are currently in clinical trials.

In 2013 I joined the new Brain Tumor lab at the CNIO lead by Dr. Squatrito. I follow 2 main lines of research:

A) To understand and overcome glioma cell resistance to current therapies we have performed in vitro genetic screenings with customized shRNA libraries including one against the DNA repair machinery and one vs genes encoding known drug targets. We are currently validating the findings in vivo, in xenografts and the RCAS:Tva mouse model of gliomagenesis.

B) Development of new diagnostic tools for brain tumors to improve diagnostic imaging of GBM by Immuno-Positron Emission Tomography (ImmunoPET) which combines the high resolution and quantitative capabilities of PET with the specificity and selectivity of antibodies against a given tumor marker. We identified MT1-MMP as a suitable target and identified a highly specific monoclonal antibody that we labeled with the radioisotope 89Zr and whose immunogenicity and specificity was evaluated in mouse orthotopic xenografts and "avatar" models of primary tumors. . However, for its application in medical clinic we will address antibody engineering and labelling with isotopes whose output does not depend of a cyclotron and has a lower economic cost.

Resumen del Currículum Vitae:

I studied my B.Sc. in Biochemistry at the U. of Zaragoza (1998-2003). During this time I got experience in several labs including the slaughterhouse and the U. of Geneva (Switzerland). I completed my PhD at the Spanish National Cancer Center (CNIO, 2003-2009), in Dr. Mariano Barbacid¿s lab where I developed and characterized several mouse models to address the role of H-Ras and K-Ras oncogenes during tumorigenesis and several developmental disorders. I moved to the lab of Dr. Johanna A. Joyce at the Memorial Sloan Kettering Cancer Center (MSKCC, 2009-2012) in the USA to explore the role of the tumor associated macrophages and microglia in gliomagenesis and evaluating CSF-1R inhibition as a novel target for brain tumors. In 2013 I joined the newly established Seve-Ballesteros Foundation-CNIO Brain Tumor Lab lead by Dr. Massimo Squatrito. First as Staff Scientist and then trough a Madrid-MIT M+Visión program. Since I joined I follow 2 main lines of research:1) Identification of mechanisms of resistance to the current treatments in gliomas and 2) Development of new diagnostic tools for brain tumors.

I autored a total of 10 publications in journals as Nature, Nature Medicine, Cancer Cell (x4), Journal of Clinical Investigation, Genes, Brain and Behaviour and the Proceedings of the National Academy of Sciences. I have 3 papers currently under revision in Science, Journal of Nuclear Medicine and Journal of Pathology as well as others still in preparation. I received several awards. I have participated in multiple conferences and regularly teach in many courses and contribute to many popular science magazines. I have mentored several students in

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Spain and the USA, more than 9 internship technicians. I have directed 2 Bachelor Theses.

I have always been supported with different fellowships among my career including a FPU (MEC) for my PhD and Ramón Areces Foundation, Ibercaja Foundation and M+Visión Consortium for my postdoctoral research. I have been participant in several national and international grants. I was successful to obtain a prestigious BBVA Foundation Grant from which I am Principal Investigator.

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Nombre: **GIL SANZ, CRISTINA**
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Área Científica: Biomedicina
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Título:

CORTICAL DEVELOPMENT STUDIES: FROM STEM CELLS GENERATION TO NEURONAL MIGRATION

Resumen de la Memoria:

The Central Nervous System is an extremely complex and organized biological system. My curiosity to understand the mechanisms that regulate this extraordinary system, from the generation of the neural cells to the establishment of specific connections, directed my interest to carry out my PhD research in Neuroscience. During my PhD in the laboratory of Alfonso Fairén, at the Instituto de Neurociencias de Alicante, I characterized the role of a metabotropic glutamate receptor (mGluR1) regulating associative learning and synaptic plasticity in the hippocampus. This work was published at the renowned journal Cerebral cortex. Additionally I collaborated in other projects leading to additional publications.

After graduation I joined the Müller laboratory at The Scripps Research Institute in California. In the Müller laboratory I have been working on multiple projects aimed to understand the roles of certain adhesion molecules regulating neuronal migration and stem cell proliferation in the developing neocortex and how stem cells contribute to neuronal diversity and ultimately circuit formation. We addressed a long-term unsolved question, the specific role of an old know protein involved in cortical development, the reelin protein. We found that reelin controls, a specific type of migration called somal translocation, regulating the function of the adhesion molecules cadherins. Additionally we identified a second family of adhesion molecules, the nectin proteins that connect reelin and cadherin molecular pathways. This connection occurs via the specific interaction of migrating neurons with a second type of cells present at the surface of the brain, the Cajal-Retzius cells, using a particular nectin-adhesion code to recruit cadherins to the adhesion site. The conclusions of these two works were published at the prestigious journal Neuron. These new insights in the role of these molecules during neocortical development are remarkable because mutations in reelin and cadherins genes have been linked to neurodevelopmental disorders like autism and schizophrenia. Recently we found that these adhesion molecules have additional roles regulating stem cell proliferation and defects in its expression mimic a human syndrome, the Double Cortex syndrome, whose symptoms include intellectual disability, epilepsy and behavior problems in humans beings. This work was published at the renowned Journal of Neuroscience.

Regarding to the stem cell diversity studies we have described for the first time the existence of heterogeneity in the cortical stem cells pool. We found that a particular type of progenitors, fated to produce the cortical cells involved in the cortico-cortical communication, is specified since very early embryonic ages. The conclusions of these works have been published at the prestigious journals Science and Neuron.

My current and future interest is focused in determine the molecular mechanisms involved in the regulation of cortical stem cell proliferation mediated by adhesion molecules, and the study of the origin of the progenitor cells that give rise to a different type of nerve cells, the astrocytes. Astrocytes are essential for many processes in the brain and recently alterations in this type of cells have been related with the onset of neurodegenerative and neurodevelopmental diseases, including Rett Syndrome or autism.

Resumen del Currículum Vitae:

I obtained a degree in Biology from the University of Valencia in June 2001. I received the special award for degree. Due to my high marks as undergraduate I was granted a Collaboration Fellowship and an Introduction to the Research Fellowship from the Spanish Council of Research during my final year of degree.

I completed my PhD at the Instituto de Neurociencias de Alicante in May 2008, under the supervision of Dr. Alfonso Fairén. I focused in the study of the role of a metabotropic glutamate receptor (mGluR1) regulating associative learning and synaptic plasticity in the hippocampus. Additionally I collaborated with other members of the lab in different projects. During my predoctoral training I obtained 3 publications, and I was granted a predoctoral fellowship and 3 predoctoral travel fellowships from the Generalitat Valenciana.

In August 2008 I joined the Müller lab at the Scripps Research Institute in California as a postdoctoral fellow, where currently I hold a Staff Scientist position after 2 promotions. During this time I have been working elucidating the role of some adhesion molecules regulating cortical development and I have been studying the diversity of cortical stem cells in the neocortex. During my postdoctoral period I have obtained 6 publications in top-tier journals and I have obtained independent funding from institutions from Spain (Generalitat Valenciana and Ministerio de Educación) and USA (California Institute for Regenerative Medicine).

During my scientific career I have participated in several international and national I+D projects. As part of my training, I have often helped Prof. Müller in peer-reviewing manuscripts and I have actively participated in the design and writing of NIH grant proposals awarded to him that had supported my research while not in fellowships

I have presented more than 20 communications in national and international meetings and conferences, including several invited oral presentations.

I have also experience supervising students, technicians and other postdocs. Currently as a Staff Scientist I have 2 people under my direct

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supervision and exclusively working for me. Note that the American system does not provide opportunities for postdoctoral researchers to direct or co-direct graduate students in their PhD theses, so we cannot compete in this aspect with people trained in Europe.
*Updated list of publications (475 citations)
-Gil-Sanz and Müller (2015) Neuron (Corresponding author)
-Gil-Sanz et al (2015) Neuron
-Gil-Sanz et al (2014) J.Neurosci.
-Gil-Sanz et al (2013) Neuron
-Franco, Gil-Sanz et al (2012) Science
-Franco, Martinez-Garay, Gil-Sanz et al (2011. Neuron
-Gil-Sanz, Martinez-Garay (2009) Mol Reprod Dev.
-Espinosa, Gil-Sanz et al (2009). Front Neuroanat.
-Gil-Sanz et al (2008) Cerebral Cortex
-Girós, Morante, Gil-Sanz et al (2007) BMC Developmental Biology
-Alcaide, Gil-Sanz et al (2001) Journal of Fish Diseases

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Nombre: **PARDO SAGANTA, ANA**
Referencia: RYC-2015-18580
Área Científica: Biomedicina
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Título:

Defining the role of lung stem cells in lung homeostasis, regeneration and disease

Resumen de la Memoria:

My scientific career includes an outstanding intellectual and technical training built over the last 12 years. My 5 years long of postdoctoral training has been performed in the most relevant and innovative field (Regenerative Medicine in the lung) in the best institution worldwide (Massachusetts General Hospital (MGH)/Harvard University) and it culminated with my Faculty appointment (MGH, Harvard Medical School). As a result of my hard and constant work, my findings have been published in high profile journals (Nature, Cell Stem Cell), reaching a profound impact on the scientific community. Consequently, I have been invited to present these findings at the NIH (March 2015) and at the Cold Spring Harbor meeting ﷺStem Cells in Biologyﷺ (October 2015). Many other of my findings have been also published in first-author articles or as a co-author in multiple collaborations demonstrating the relevance and high quality of our research. Importantly, I have established very valuable collaborations that are allowing me to initiate a promising and relevant line of investigation following a unique approach to address important scientific questions with significant clinical applications for respiratory diseases that have no cure.

During my postdoc, I have greatly expanded my expertise moving from analyzing the role of molecules (molecular biology and biochemistry) to the study of the identity, regulation and function of cells (cell biology) in a different tissue. Particularly, I have identified a novel mechanism of cell regulation to keep tissue homeostasis, I have defined the functional segregation of the airway stem cell population involved in airway regeneration, and I have described the role of airway stem cells in the initiation of the allergic-immune response and the molecular mechanism underlying mucous metaplasia in asthma, COPD and CF. As an independent investigator, I would like to focus my research on the study of the role of lung stem cells, their regulation and their cellular interactions in actual human respiratory diseases, particularly IPF and lung cancer, with the ultimate purpose of, once we understand the behavior of lung stem/progenitor cells after damage, developing promising cellular therapies to restore a proper regenerative response to cure the disease. The line of investigation I propose to inititate is of paramount importance in respiratory diseases for which there is no cure. There is a lack of investigation in respiratory Regenerative Medicine in Spain and I think this is a good opportunity to begin this research, focused on a translational application of our findings. I truly believe that my investigations will make a difference in the understanding, diagnosis and treatment of respiratory diseases.

The experience that I gained in the last twelve years has provided me with a very complete, broad, diverse but deep, excellent and unbeatable training, that allow me to carry out my own investigations independently. My experience includes not only a huge variety of techniques but an intellectual understanding of different fields such as inflammation, tissue regeneration, cancer biology, development and stem cell biology, and immunology. My unique and exceptional trajectory demonstrates my ability to reach and re-enforce a position of professional maturity to carry out relevant findings making the difference with my research.

Resumen del Currículum Vitae:

My name is Ana Pardo Saganta and I was born in Jaca (Huesca, Spain) on December
1981. I got my Bachelor in Science (Biology) from University of Navarra on July 2003
(1999-2003). My first experience in research was as an undergraduate student when I joined the Department of Genetics (2001-2003). After graduation I joined the Department of Gene Therapy and Hepatology at the Center for Applied Medical Research (Pamplona, Spain) to carry out my doctorate (2003-2008). In August 2009, I joined Dr. Ragagopalﷺs lab at the Center for Regenerative Medicine of Massachusetts General Hospital (MGH) (Boston, USA) as a postdoctoral fellow (2009-2014). In November 2014, I obtained my first Faculty position as an Instructor in Medicine (Harvard Medical School) and got my appointment as an Assistant in Biology in the Department of Pulmonology at MGH.

During my PhD my main project was focused on the study of the molecular mechanisms underlying liver regeneration and inflammation and the development of new therapeutic strategies to treat hepatic disorders including hepatocellular carcinoma, liver fibrosis and cirrhosis. As a result of my PhD I acquired a broad expertise in the field of molecular and cell biology, handling cell culture and molecular techniques, and in vivo animal models.

Additionally, I worked as an assistant teacher of Genetics in the Faculty of Biology, Pharmacy and Medicine at the University of Navarra (2003-2007). My postdoctoral research has focused on the study of adult airway stem cells, their regulation and their role in airway homeostasis and regeneration and in the pathologic mechanisms underlying airway diseases like asthma, COPD and CF. As a result of my postdoctoral work three first-author articles have been published, two of them in high profile journals (Pardo-Saganta et al, Nature, 2015; Pardo-Saganta et al, Cell Stem Cell, 2015; Pardo-Saganta et al, Am J Resp Cell Mol Biol, 2013).

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Two additional first-author manuscripts are in preparation (five first-author articles in total).
Additionally, I have contributed as an author in another ten articles. My postdoctoral experience also includes the learning and use of a huge variety of techniques of cell biology, mouse genetics, molecular biology and microscopy and imaging. I have established collaborations with top-notch investigators, and gained experience in communicating my findings and writing grants as Principal Investigator (ERC Starting Grant, Marie Curie), including NIH grants (RO1). Importantly, I have also supervised two undergraduate students, one of them awarded with the Best Thesis Award from the Department of Stem Cell and Regenerative Biology (Harvard University).

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Nombre: **SANJUAN PLA, ALEJANDRA**
Referencia: RYC-2015-17534
Área Científica: Biomedicina
Correo Electrónico: asanpla13@hotmail.com

Título:

Regulation of normal and malignant hematopoiesis

Resumen de la Memoria:

During my predoctoral training, I studied the transcription factor hypoxia-inducible factor-1 (HIF-1). I dissected the role of mitochondrial reactive oxygen species (ROS) on HIF-1 alpha subunit (HIF-1α) stabilization using novel mitochondria-targeted antioxidants developed by our collaborator Dr. M. Murphy (FEBS Lett, 2005). In the time of my stay at his laboratory, I contributed to the characterization of the antioxidant MitoLipoic Acid (Free Radic Biol Med, 2006). I also studied the impact of mitochondrial ROS as signaling molecules involved in the etiology of mitochondrial diseases caused by SURF1 mutations.

During my postdoctoral research, I centered on hematopoietic transcription factors, mouse genetics and hematopoietic stem cells (HSCs). I worked with Prof. Claus Nerlov at the European Molecular Biology Laboratory (EMBL) in Italy and subsequently at the Institute of Stem Cell Research (ISCR) in UK. My project on normal hematopoietic stem cells (HSCs) studied the role of HSC lineage priming in specifying HSC fate. BAC transgenic Vwf-eGFP mice were generated to label the expression of the platelet-specific von Willebrand factor (Vwf) in the HSC compartment. This model allowed us to define a specific subset of long-term vWF+ HSCs that at the molecular level was primed for megakaryocytic-associated genes. This molecular signature functionally correlated with an increased platelet output upon in vivo transplantation. Importantly, these platelet-biased HSCs were able to generate myeloid- and lymphoid-biased HSCs in serial transplantations, demonstrating a hierarchical organization of self-renewing HSCs (Sanjuan-Pla et al. Nature, 2013). Later on, we uncovered the changes in vWF- and vWF+ HSC populations during aging. We interrogated single cell transcriptomes using mRNA-Seq. We identified an increased molecular and functional platelet bias of HSCs as a key feature of hematopoietic aging and this could contribute to the age-associated imbalance between myeloid and lymphoid cell production. The paper on aged vWF- and vWF+ HSCs has been recently resubmitted (Grover*, Sanjuan-Pla* et al. - *equal contribution; Nature Communications, 2016).

In late 2013, my research activity continued at Josep Carreras Leukemia Research Institute in Barcelona. Using different approaches, I am assessing if embryonic/fetal HSCs are more susceptible to leukemic transformation than adult HSCs in the context of infant acute leukemias with prenatal origin. From the mouse and human angles, we study the secondary hits and mutational landscape (using genomic omic approaches) of the infant MLL-AF4+ acute lymphoblastic leukemia (Sanjuan-Pla, et al., Blood, 2015).

For my independent scientific career, I plan to exploit mouse models to assess the implications of HSC heterogeneity in leukemia, the most prevalent pediatric cancer. It manifests predominantly as a lymphoid disease during childhood and as myeloid disease in the adulthood and elderly. My long-term goal is to investigate on HSC heterogeneity and molecular targets in hematological diseases using mouse models.

Resumen del Currículum Vitae:

I obtained my degree in Pharmacy at University of Valencia (2002). Supported by a FPU fellowship, I conducted my predoctoral research on hypoxia signaling and mitochondrial metabolism at Unidad Mixta de Investigación CNIC-Universitat de València. I got my PhD degree in 2007 with European Doctorate distinction. My work resulted in a first-author publication (FEBS Lett, 2005) and three co-authorships (Cancer Lett, 2006; Cell Death Diff, 2006; Free Radic Biol Med, 2007). I participated in teaching courses at Nursery University and carried out a predoctoral stage at MRC Mitochondrial Biology Unit (Cambridge, UK).

After my PhD, I got interested in stem cells biology and moved to the laboratory of Prof. Claus Nerlov at European Molecular Biology Laboratory (EMBL) (Monterotondo, Italy). Funded by a MEC Postdoctoral BEOI Fellowship (2008-2010), I worked on genetically engineered mouse models of hematopoiesis. In May 2010, together with Prof. Nerlov&#65533;s group, we moved to the Institute of Stem Cell Research (ISCR) at University of Edinburgh. My postdoctoral work was focused on studying platelet-primed hematopoietic stem cells (HSCs) in young and aged mice. I published a first-author publication (Nature, 2013) and a revised shared first-author paper has just been resubmitted (Nature Communications, 2016). Always in close collaboration with Prof. Sten Eirik Jacobsen group (WIMM, Oxford), I participated in several research projects and contributed to other publications (EMBO J, 2011; Nature Immunology, 2012). I also presented my work in several international conferences: EHA, EMBO, etc. (oral and poster presentations).

In September 2013, I joined the Josep Carreras Leukemia Research Institute in Barcelona as contracted researcher in Dr. Menéndez laboratory. Soon after, I was awarded by Marie Curie Actions with a Career Integration Grant (FP7-PEOPLE-2013-CIG). Using the mouse as a model, I studied the influence of cell ontogeny on leukemia initiation in infant ALL with MLL rearrangement. From this period I got several

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publications (Sanjuan-Pla et al., Blood, 2015; Sanjuan-Pla et al., Stem Cells & Dev, 2016) and one co-authorship (Bueno, et al., Leukemia, 2016). I actively participated in research projects funded by national and international funding bodies (ERC Consolidation grant, MINECO-Plan Nacional SAF, José Carreras Leukämie-Stiftung, etc). Regarding teaching experience, I supervised one Biomedicine Master thesis at University of Barcelona (2014-2015). I also hold the ANECA Acreditation for Profesor Ayudante Doctor.

Overall, I consolidated comprehensive expertise in mouse models of hematopoiesis and competence in the state-of-the-art approaches required for studying HSC biology. My international mobility facilitated my development into an independent researcher and allowed me to obtain extensive experience in embryonic and adult hematopoiesis that will be instrumental in my own laboratory.

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Nombre: **WIMMER , KLAUS**
Referencia: RYC-2015-17236
Área Científica: Biomedicina
Correo Electrónico: wimmer.klaus@gmail.com

Título:

Neural network dynamics underlying cognitive function

Resumen de la Memoria:

A key question in systems neuroscience is how the brain processes incoming sensory stimuli, giving rise to perception and action. The neural basis of the computations that underlie cognitive function has been studied extensively with decision making and working memory tasks in humans and monkeys. In my work, I have developed computational models of neuronal circuits to pin down the physiological mechanisms underlying an animal's behavior during these elementary cognitive tasks. I have complemented the study of the dynamics of these circuits with quantitative analysis of psychophysical and electrophysiological data (single and multi-unit recordings, local field potentials). A tight interaction between theory and experiment, based on active collaborations with experimental groups has been the basis of my work (e.g. T. Pasternak, Rochester Univ.; C. Constantinidis, Wake Forest Univ.; M. Sur, MIT).

My research in computational neuroscience started out with an investigation of the computational principles underlying "lower-level" sensory processing during my PhD at the Technische Univ. Berlin, Germany (2004 – 2009). In particular, I investigated the generation and adaptation of orientation selectivity in primary visual cortex, which led to the publication of several papers, three of them in top-tier journals (Cereb. Cortex 2009, PLoS Comput. Biol. 2008, Front. Neurosci. 2007).

As a postdoc at IDIBAPS, Barcelona (2010 – 2015), I extended the scope of my research towards biophysical models of cognitive functions. In particular, I was interested in the relationship between trial-to-trial variability of neural activity ("neuronal noise") and behavioral responses. In a first project, I used a neural attractor model together with data from monkey experiments to reveal for the first time the neural basis of working memory precision in prefrontal cortex (Wimmer et al., Nat. Neurosci., 2014). In a second project, I developed a hierarchical model of perceptual decision making which prompts for a reformulation of the current standard framework (Wimmer et al., Nat. Commun., 2015). Moreover, I obtained research funding in competitive international calls (Marie Curie fellowship, research fellowship from the German Research Foundation), I acquired experience in teaching and supervising students, and I organized local and international scientific meetings.

I initiated a successful collaboration with T. Pasternak, Univ. of Rochester, NY, USA, and examined local field potentials recorded from prefrontal cortex of monkeys performing motion comparison tasks (Wimmer et al., J. Neurosci., 2016). Since 07/2015, I am a postdoctoral fellow at the Univ. of Rochester and at IDIBAPS, focusing on the analysis of neurophysiological data to uncover the substrates of working memory for visual motion.

The results of my work, and the collaborations that I have established, open the door to a new stage in my career as an independent investigator, with a research line aimed towards a better understanding of the neural mechanisms of cognitive function, with the ultimate goal of understanding the link between cortical neuronal activity and behavior. Specifically, I plan to investigate the mechanisms underlying confidence in perceptual decisions by developing a biophysical model and studying their dysfunction in psychiatric diseases.

Resumen del Currículum Vitae:

CURRENT POSITION:
Since 07/2015: Postdoctoral fellow, Dept. of Neuroscience, Univ. of Rochester, NY and IDIBAPS, Barcelona (joint appointment at both institutions).

RESEARCH EXPERIENCE:
07/2010 – 06/2015: Postdoctoral fellow, IDIBAPS, Barcelona. From 06/2011 to 05/2014 funded by a research fellowship from the German Research Foundation (DFG).
11/2004 – 03/2010: Research and teaching assistant (pre-doctoral), Technische Universität Berlin, Germany.
10/2007: Research stay in the laboratory of Mriganka Sur at MIT, USA.

EDUCATION:
2009, Dr. rer. nat. (Ph.D.) in Computational Neuroscience, "summa cum laude"; Technische Universität Berlin and Bernstein Center for Computational Neuroscience, Berlin, Germany. Supervisor: Klaus Obermayer.

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2004, Dipl.-Ing. (eq. M.Sc.) in Information and Computer Engineering, with highest honors, Technische Universität Graz, Austria.

RESEARCH ARTICLES:
7 journal papers (6 as first author); 1 article under revision.
3 conference papers and 1 book chapter.
Total number of citations: 150 (42 in 2015), h-index: 7 (source: Google Scholar).
Recent publications in high-impact journals: Nature Neuroscience, 2014 (IF: 16.1) and Nature Communications, 2015 (IF: 11.5), both as first author.

CONFERENCES: more than 30 oral and poster presentations at international conferences and workshops.

TEACHING:
2005 – 2010: Computational Neuroscience, Computer Science and Programming Methods, Machine Intelligence; Technische Universität Berlin, Germany.
2011: Neurophysics, Universitat Autònoma de Barcelona.
2014: Summer School in Theoretical and Computational Neuroscience, CRM, Barcelona.

THESIS SUPERVISION:
I have co-supervised 4 master thesis (Genis Prat Ortega, 2014; Marc Ramon, 2013; Gidi Farhi, 2010; Thorsten Dietzsch, 2008).

AWARDED GRANTS / FELLOWSHIPS:
2013: ESF exploratory workshop (EW12-019), European Science Foundation, 14.000 EUR.
2011: Research Fellowship (Wi3767/1-1), German Research Foundation, 125.000 EUR.
2010: Marie Curie Inter-European Fellowship (PIEF-GA-2010-275800), REA-European Commission, 167.181 EUR.

SCIENTIFIC ACTIVITIES:
Ad-hoc reviewer for Neural Computation, Frontiers in Computational Neuroscience, Cerebral Cortex.
Associate Faculty Member of F1000.
Organizer of the ESF workshop –Noise and decision making: theory meets experiment–, Sant Fruitós de Bages, 2013 (www.crm.cat/2013/DecisionMaking).

SELECTED PUBLICATIONS:
1. K Wimmer, M Ramon, T Pasternak, A Compte (2016). Transitions between multiband oscillatory patterns characterize memory-guided perceptual decisions in prefrontal circuits. J. Neurosci. 36, 489–505.
2. K Wimmer, A Compte, A Roxin, D Peixoto, A Renart, J de la Rocha (2015). Sensory integration dynamics in a hierarchical network explains choice probabilities in cortical area MT. Nat. Commun. 6, 6177.
3. K Wimmer, DQ Nykamp, C Constantinidis, A Compte (2014). Bump attractor dynamics in prefrontal cortex explains behavioral precision in spatial working memory. Nat. Neurosci. 17, 431–439.
4. M Stimberg*, K Wimmer*, R Martin, L Schwabe, J Mariño, J Schummers, DC Lyon, M Sur, K Obermayer (2009). The operating regime of local computations in primary visual cortex. Cereb. Cortex 19, 2166–2180. * equal contribution.
5. K Wimmer, KJ Hildebrandt, RM Hennig, K Obermayer (2008). Adaptation and selective information transmission in the cricket auditory neuron AN2. PLoS Comput. Biol. 4, e1000182.

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Turno de acceso general

Nombre: **LÓPEZ-ATALAYA MARTÍNEZ, JOSÉ PASCUAL**
Referencia: RYC-2015-18056
Área Científica: Biomedicina
Correo Electrónico: jose.lopez@umh.es

Título:

Transcriptional and Epigenetic Mechanisms in Memory and Cognitive Disorders

Resumen de la Memoria:

My scientific career focuses on the molecular basis of learning and memory formation and its dysfunction in neurological disorders.

During my PhD studies in Cellular and Molecular Neuroscience at INSERM U919 (France), I acquired a solid knowledge in the molecular and cellular processes leading to neuronal death in neurodegenerative disorders and ischemic brain disease. My work led to the identification of the molecular mechanism underlying pro-neurotoxic effects of the clot-busting drug tPA (JBC, 2004; Stroke, 2007) and the development of new tools aimed at improving thrombolytic therapy for acute ischaemic stroke (J Cereb Blood Flow Metab, 2008; International patent: WO2011023249 A1, 2011).

In 2006, I joined the laboratory of Ángel Barco at Instituto de Neurociencias (Spain), interested in the transcriptional and epigenetics mechanisms that govern learning and memory storage and how the malfunction of these mechanisms may lead to pathological situations. I showed that (1) protein acetylation governs maladaptive learning behavior underlying substance abuse disorders and identified a genetic program involved in the development and maintenance of addictive behavior (Neuropsychopharmacology, 2009). (2) I identified a critical role of CBP in the improvement in learning and memory and enhanced neurogenesis induced by environmental enrichment and voluntary exercise (EMBO J, 2011). (3) I showed, for the first time, that histone acetylation is impaired in individuals affected by Rubinstein-Taybi syndrome (RSTS), and demonstrated the reversibility of such deficits paving the way to therapeutic intervention (J Med Genet, 2012). (4) I identified a genomic signature of Hungtinton's disease that may constitute new biomarkers useful in prognosis as well as therapeutic targets for early intervention (J Neurosci, 2013). (5) I unravelled the genomic targets of the memory booster drug HDACis and showed that they preferentially target NF-kB-regulated genes (Nucleic Acids Res, 2013).

Last year, I was awarded a grant from the Spanish Ministry of Economy and Competitiveness (MINECO) to establish my independent research program, which I am currently developing as Principal Investigator at Instituto de Neurociencias (Alicante) (Severo Ochoa Centre of Excelence),. Overall, it offers an energetic, interactive and fast-paced environment at the forefront of neurosciences research and therefore, constitutes the ideal place to develop my research and advance my career. My current line of research aims to identify the neuronal specific NF-kB-dependent gene regulatory network and its regulation by NF-kB subunits posttranslational modification, during memory formation. This project has the potential to identify new targets to treat age-related memory loss and cognitive impairment in neurological condition. In summary, I perform fundamental research and have also demonstrated my ability to build bridges of collaboration with clinical research scientists to give it a focus and emphasis on translational science. With the support of the Ramon y Cajal program, I aim to consolidate my group and develop an ambitious research program in functional and integrative genomics of neurological disorders and aging.

Resumen del Currículum Vitae:

I did my PhD in Cellular and Molecular Neuroscience at INSERM U919, France (2006). My research focused on neurodegeneration and cell death caused by acute ischemic stroke. I published 10 articles (3 first-author and 2 corresponding author). I was co-Principal Investigator of 2 projects sponsored by biopharma PAION GmbH (Germany) on the development of novel stroke therapeutics and co-authored a patent granted on international application (WO2011023249 A1, 2011).

In 2006, attracted by the emerging field of neuroepigenetics and its potential to explain many key features of memory formation and its dysfunction in neurological disorders, I moved to Alicante (Spain) to join Angel Barco's group, an internationally recognized pioneer in the field. I developed a number of projects aimed to elucidate how epigenetic mechanisms operate during memory formation under both normal and pathological conditions. I published 15 articles (first author of 5 papers, 1 review, and 1 book chapter; 1 publication as corresponding author).

I am currently Principal Investigator at Instituto de Neurociencias (Spain). I seek to elucidate the neuronal specific gene regulatory network driven by NF-kB transcription factors during long-term memory formation. I also want to understand how NF-kB-dependent transcriptional activity associated to neuronal activation is fine-tuned by specific posttranslational modifications of its components. This work aims to identify critical aspects of the molecular underpinning of memory formation and contribute to understanding memory impairments, one of the greatest health problems among the ever-aging population. The project is funded by a grant awarded by the Spanish Ministry Economy Competitiveness (MINECO).

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To date, I have co-authored 25 articles that have received over 980 citations (h-index 17). I have a strong track of publications as first (10) and corresponding author (3) in top ranked journals (EMBO J, Nucleic Acids Res, J Neurosci, Trends Genet). A number of these papers have been highlighted and also received coverage in the media. I have obtained funding based on national competitive calls leading to research independence (MINECO). I have co-directed 2 industry-funded projects (PAION GmbH) and co-authored an international patent (WO2011023249 A1, 2011). I regularly serve as a reviewer for international journals (Neuropharmacology, Molecular Brain, Neuroscience) and I am a reviewer for the Spanish national funding agency ANEP (Biomedicine). I participate as organizer, chairman, speaker and poster presenter in numerous national and international scientific conferences. I am professor at the Master in Neurosciences organized by the Miguel Hernández University. I have been invited to serve as professor at the XIV Curso Nacional en Neurociencias. I have supervised many undergraduate students and I am currently co-Director of a Doctoral Thesis. I have been awarded several prestigious fellowships (Juan de la Cierva (2007, MINECO); JAE-DOC (2010, CSIC)). In addition, I have ample international experience (stays, collaborations, funding).

All of the above described indicates my research skills, independency and capability to lead my research career. I believe that a Ramon y Cajal grant will have a great impact on my scientific career and will definitely constitute a major further step towards the consolidation of my research group.

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Nombre: **GELLER , RON**
Referencia: RYC-2015-17517
Área Científica: Biomedicina
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Título:

Interaction of RNA Viruses with the Host Cell

Resumen de la Memoria:

My scientific interests focus on understanding the interaction between viruses and their hosts. This field provides an exciting interface that allows for basic science discoveries and holds great potential for identification of therapeutics that can have broad impact on public health. In particular, I have focused on RNA viruses, which are responsible for numerable diseases plaguing our society and are the principle threat for emerging infections. Few treatments are available to combat viral infections, underscoring the need for novel approaches to combat these pathogens. Two nearly universal aspects of RNA virus biology are small genomes and an extreme capacity for rapid evolution, which enable their escape from antiviral drug therapy, the immune system evasion, and effective vaccination strategies. In my research career, I have investigated these fundamental aspects of RNA viruses. First, I have studied how the proteins of multiple RNA viruses interact with the cellular protein production, folding, and degradation machinery. Viral proteins are of particular interest in this context as they present unique challenges to cellular proteostasis machinery due to being multifunctional, complex, highly expressed, and frequently mutated. Indeed, results from my studies led to insights into both basic aspects of cellular protein folding and to the discovery of a broad-spectrum antiviral therapy. The diversity of viral proteins, the breadth of the cellular proteostasis machinery, and the scarcity of studies in this field, promises a great deal of discoveries lie ahead.

Second, I have investigated the consequences and drivers of RNA virus evolution. I examined the ability of different viruses to gain drug resistance to antiviral agents and studied the mutation rate and spectrum of HIV and HCV using computational and laboratory studies. Gaining a better understanding of the mechanisms underlying viral evolution is critical for understanding the biology of RNA viruses and for combating them, as it is directly related to the success of antiviral and vaccination strategies as well as immunological responses. In the future, I plan to combine these research lines to address both basic and applied questions involving the interaction of viral pathogens with their hosts, both on a cellular level and an organismal/systems-biology level.

Resumen del Currículum Vitae:

I obtained my Bachelor of Science in Biopsychology (2000) from the University of California Santa Barbara with high honors. Subsequently, I worked as a research associate at the Structural Biology and Immunology department at Stanford University in the Parham lab (2000-2001). Following this, I did my PhD at Stanford University (2002-2008), working between a protein folding laboratory (Frydman lab, Stanford University) and a virology laboratory (Andino lab, University of California San Francisco, UCSF). During this time, I was a teacher assistant for two undergraduate courses and a fellow at the Summer Institute for Entrepreneurship at the Stanford University School of Business (2007). After graduation, I did my first postdoctoral fellowship in the Frydman lab at Stanford University (2008-2012). At the same time, we filed a patent application for the use of Hsp90 inhibitors to treat viral with Stanford University and UCSF and I cofounded a biotechnology startup together with my advisors (Avira Therapeutics LLC; 2008-2009). I next did a postdoctoral stay at the University of Valencia in the Sanjuan lab (2012-2015). During this time, I co-advised a Master's Thesis project, carried out two stays in the Alcami laboratory at the Instituto de Salud Carlos III, and became an associate editor for the Journal of Human Virology and Retrovirology (April 2015 - current).

Throughout my research career I have gained a broad-spectrum of skills and techniques that help me now tackle complex biological questions using a multidisciplinary approach. I have worked with numerous viral systems, in both primary and tumoral cells systems, as well as in vivo pathogenesis models. I have extensive biochemistry, molecular biology, and cell biology expertise, as well as knowledge in bioinformatics and next-generation sequence analysis. Working both independently and collaboratively, I have successfully combined these skills across multiple projects to produce high impact findings in both the USA and Spain, with the vast majority of my publications in top journals, including 3 such publications in 2015. This is further evidenced by my invitation to present my work in international conference both in the USA and in Europe. Finally, I have had experience leading a biotechnology startup, and hence have first hand knowledge in translation of laboratory findings to the public sector. I now look forward to starting an independent research group to continue my investigation at the host-pathogen interface.

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Nombre: **PERUGORRIA MONTIEL, MARÍA JESÚS**
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Área Científica: Biomedicina
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Título:

Búsqueda de nuevas dianas terapéuticas en Enfermeadades Hepáticas Crónicas.

Resumen de la Memoria:

I performed my PhD at the University of Navarra (Spain) which was awarded with a Doctoral Extraordinary Prize. I focused on the mechanisms involved in the progression of chronic liver disease, fibrosis and cancer. Specifically, I worked on a transcription factor called Wilms¿ tumor 1 (WT1) and we found that WT1 contributed to the dedifferentiation of liver cancer cells. Importantly this work uncovered a novel potential therapeutic target in liver cancer [Perugorria MJ, et al. Can Res 2009]. We also demonstrated that Amphiregulin (AR), which is a target of WT1, is a survival and proliferative factor for fibrotic cells [Perugorria MJ, et al. Hepatology 2008] and also that AR is involved in the acquisition of neoplastic traits in the liver [Castillo J, et al. Can Res 2006; Castillo J, et al. Gastroenterology 2009].

From 2009 to 2012, I performed my Postdoctoral training in Prof. Derek A Mann¿s laboratory at Newcastle University (UK). During this time I developed my interest in liver fibrosis and my independent thinking as well as project management skills. I decided to work on the fibrogenic signalling of Toll like receptors (TLRs), focusing on Tpl2 kinase [Perugorria MJ, et al. Hepatology 2013]. At Newcastle University I established very productive collaborations that gave me the opportunity to broaden my knowledge in liver fibrosis [Perugorria MJ, et al. Hepatology 2012; Ebrahimkhani MR, et al. Nat Med 2013; Wilson CL, et al. Plos One 2014].

Additionally, moved by my growing interest in TLR signalling, innate immunity and liver fibrosis, I decided to establish a very productive collaboration with Dr. Sylvia Knapp, based at CeMM (Austria). This involved studying the role of a negative regulator of innate immunity and inflammation called TREM-2 in liver injury. This collaboration has proved to be very fruitful and the preliminary data obtained have formed the basis for my grant application in 2014 (PI14/00399).

After 3 years of postdoctoral training I returned to Biodonostia Research Institute (Spain) and joined the Group of Hepatic Diseases, which has a deep and broad expertise in the field of Biliary Pathophysiology. This group has provided an ideal environment to broaden my knowledge in other types of liver diseases [Perugorria MJ, et al. Nat Rev Gastr Hepat 2014; Banales JM, et al. Nat Rev Gastr Hepat 2014; Santos-Laso A, et al. Curr Drug Targets 2015 (In press); Uribarri AD, et al. Gut 2014; Munoz-Garrido P, et al. J Hepat 2015].

In 2013 I started my independent research line and I obtained an IKERBASQUE Research Fellowship. This programme has allowed me to consolidate as Principal Investigator and to be able to apply for my own research projects funded by competitive calls; Carlos III Institute, Basque Government, IKERBASQUE and CIBERehd.

As Principal Investigator I have recently co-directed a Master&#65533;s Degree Student which obtained the maximum qualification and was selected as the best project and currently I am directing another Master&#65533;s Degree student and Co-directing another 3 Ph.D. students. With the aim of discovering new targets in the progression of chronic liver diseases I have also started my own research line which is focused on the negative regulation of TLR mediated cytokine production called TREM2 and its implication in acute liver injury, liver fibrosis and hepatocellular carcinoma development.

Resumen del Currículum Vitae:

After obtaining the Bachelor Degrees in Biology and Biochemistry (1998-2004) in the University of Navarra I started my scientific career in the Department of Hepatology and Gene Therapy of CIMA, University of Navarra. My PhD was focused on elucidating the mechanisms involved in the progression of chronic liver disease including liver fibrosis and cancer. Importantly, we uncovered two novel therapeutic targets in liver cancer. These results were published in top peer reviewed journals and I received the Extraordinary Award of Doctorate from the University of Navarra in 2009. From 2009 to 2012, I performed my Postdoctoral training in Newcastle University (UK). The dynamic environment in Newcastle provided me with the opportunity to broaden my knowledge in liver fibrosis, which in turn resulted in several important publications.

Mobility and International collaborations during my scientific career have been crucial for the success of various projects. Thus, during my PhD, I obtained a short term FPI fellowship that was awarded by the Spanish Ministry of Education and Science (MEC) and worked for 3 months in the laboratory of Dr. Sophie Lotersztajn in Paris. During my postdoctoral training in Newcastle University I was on the lead on proposing my scientific goals. Thus, I have done several stays in Vienna and established a very productive collaboration with Dr. Sylvia Knapp, based at the Center for Molecular Medicine (CeMM), Vienna (Austria).

AYUDAS RAMÓN Y CAJAL
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Turno de acceso general

After 3 years of postdoctoral training at Newcastle University (UK), I returned to Biodonostia Health Research Institute (Spain) in November 2012 to create and lead a new research line in my area of expertise. In 2013 I obtained an IKERBASQUE Research Fellowship. This programme has allowed me to consolidate as Principal Investigator and to be able to apply for my own research projects funded by competitive calls. In this regard, now I am Principal Investigator in active research projects funded by the Carlos III Institute (FIS PI14/00399: 109,626 €), Department of Industry of the Basque Government (SAIOTEK Programme: 10,535 €), IKERBASQUE (4,000 €) and CIBERehd and Associate Investigator in projects funded by Regional Institutions (DFG015/010: 70,200 €).

All along my scientific career I have pursued the excellence in research. A good example of this is that my work has always been published in top International Journals. I have published 22 manuscripts in top international journals (15 original articles, 6 reviews and a book chapter) that accumulate a JCR impact factor of 180.199, 556 citations and a Hirsch Index of 10. In most of the articles I am first, second or third author. During my scientific career I have also presented my work in several National and International Congresses (Please see CV) and obtained predoctoral and postdoctoral fellowships to cover my salary as well as to carry out short stays abroad. On the other hand, I have always taken great care and pride in training students and believe that excellent mentorship and leadership are of great importance to begin a good scientific career. I have recently co-directed a Master¿s Degree Student in the University of Navarra (2014-2015), which has obtained the maximum qualification of €Matrícula de Honor€. Currently, I am directing another Master¿s Degree student and Co-directing another 3 Ph.D. students.

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Turno de acceso general

Nombre: **NEVZOROVA , YULIA A.**
Referencia: RYC-2015-17438
Área Científica: Biomedicina
Correo Electrónico: nevzorovaj@googlemail.com

Título:

MOLECULAR MECHANISMS DRIVING CELL PROLIFERATION AND CELL DEATH IN ACUTE AND CHRONIC LIVER DISEASE

Resumen de la Memoria:

During the last decade my research has been focused on the mechanisms of hepatic cell proliferation with the main goal to address the functional relevance of cell-type specific pathways of cell cycle regulation. My first publications defined unknown functions of E-cyclins for hepatocyte proliferation during liver regeneration (using 2/3 partial hepatectomy) and identified Cyclin E1 as a novel and unexpeted key factor (Nevzorova et al., 2009). Additionally, we recently showed that Cyclin E1 also mediates kinase-independent functions during cell cycle control (Hu, Nevzorova et al., 2014).

Next, I aimed to define the relevance of Cyclin E1 for hepatocarcinogenesis progression using two experimental models. After chemical-induced carcinogenesis, Cyclin E1-deficient animals were mostly resistant to hepatocellular carcinoma (HCC) induction. Consistently, we found that Cyclin E1 deficiency alters both tumor initiation and progression in a novel mouse model of c-myc-driven HCC, where the proto-oncogene c-myc (myctg) is overexpressed in hepatocytes (Moro, Nevzorova et al., 2016). Notably, this indicates that targeting Cyclin E1 in HCC can be a potential therapeutic approach.

My next goal was to identify the specific role of Cyclin E1 and c-myc in precancerous stages such as liver fibrosis. I provided strong evidence that Cyclin E1 is essential for proliferation and survival of hepatic stellate cells (HSCs) and thus represents not only a novel key mediator and potential therapeutic target of hepatic fibrosis (Nevzorova et al. 2012), but also its overexpression can be a useful as a novel marker for the diagnosis of liver fibrosis (Nevzorova et al., 2013). Finally, my current research interest is focused on the relationship between cell proliferation, tissue regeneration and common alcohol-induced liver injury (ALD). For this purpose, I actively collaborated with related research lines in my Department exploring the pathophysiology of chronic liver injury (Cubero FJ, 2013; Zhao G, 2014; Cubero FJ, 2015; Schaefer FM, 2015; Hatting M, 2015; Cubero FJ, 2016). In recent studies, I found that hepatic c-myc is strongly up-regulated in human patients with advanced ALD and in mice fed with an ethanol (EtOH)-diet. Thus, c-myc is a new potential marker for the early detection of ALD and identification of risk patients (Nevzorova et al, 2015).

For my independent career with a Ramon y Cajal Fellowship, I aim to extend the current knowledge of hepatic proliferation in the progression of various chronic and acute liver diseases with a special focus on chronic alcoholic liver disease (ALD) with the ultimate goal to define new treatment options, by (a) investigating the impact of the Cyclin E1/Cdk2 interphase complex for initiation and progression of chronic ALD (b) further characterize the mode of liver injury (extrinsic versus intrinsic apoptosis; necrosis) in acute and chronic alcoholic liver intoxication; (c) identify hepatic cell types (hepatocytes, stellate cells, macrophages, T-cells) that rely on proliferation and, thus on cyclins, to contribute to liver disease and (d) evaluate cell-cycle regulation in immune cells in animal models of acute liver injury.

Resumen del Currículum Vitae:

CURRENT PROFESSIONAL SITUATION:
2015, Research Group Leader and Medical Assistant, Internal Medicine III Department, University Hospital RWTH Aachen, Germany

EDUCATION:
2003, Degree in Medicine (M.D.) with Honors (Northern State Medical University, Archangel, Russian Federation)
2009, Ph.D. (Dr. nat. med.), University Hospital RWTH Aachen, Germay. Doctoral Thesis: ﷺCell cycle regulation in the liver: Differential functions of E-type Cyclins E1 and E2 for G1/S-phase transition and endoreplication in miceﷺ; Magna Cum Laude
RESEARCH AND MEDICAL EXPERIENCE
2014-present, Group Leader and Medical Staff, Internal Medicine III Department, University Hospital RWTH Aachen, Germany
2014-present, Assistant Professor, Department of Human Morphology and Physiology, Northern (Arctic) Federal University, Russia
2009-2014, Postdoc and Research Associate, Internal Medicine III Department, University Hospital RWTH Aachen, Germany
2005-2009, PhD Student, Internal Medicine III Department, University Hospital RWTH Aachen, Germany
2004-2005, DAAD Predoctoral Grantee, Medical University Hannover, Germany
2003-2005, Medical Intern/Resident, Infectious Diseases, Northern State Medical University, Archangel, Russia

TEACHING EXPERIENCE
2015 Abdominal Ultrasound Scanning Techniques (Seminars, Medical Students), University Hospital RWTH Aachen, Germany
2015, Endocrine Physiology (Lectures, Physiology Students), Northern (Arctic) Federal University, Archangel, Russia
2014, Molecular and Experimental Pharmacology (Lectures, Biotechnology Students), University Hospital RWTH Aachen, Germany
2014, Molecular Biology (Lectures, Physiology Students), Northern (Arctic) Federal University, Archangel, Russia

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Turno de acceso general

HEALTHCARE EXPERIENCE
2015, Abdominal Ultrasound (Liver, Gut, Kidney, Spleen, Uterus, Prostate, Thyroid Gland), Fine needle liver biopsy, Doppler Ultrasound, Fibroscan, Ascites punction, Internal Medicine III Department, University Hospital RWTH Aachen, Germany
2005,Daily examination of patients, blood withdrawal, Medical University Hannover, Hannover, Germany
2003-2005 Patient examination, Diagnosis of Infectious Diseases, order and interpretation of laboratory tests and X-rays, provide treatment, lumbar puncture and liver ultrasound for in- and outpatients, Northern State Medical University, Archangel, Russia

THESIS SUPERVISION:
2016, Master Thesis, Anna Ostroginskaya: ‘The incidence and epidemiology of ALD-associated liver cancer in Northern Russia’; Departments of Human Morphology and Physiology, Northern (Arctic) Federal University, Russian Federation
2016, Doctoral Thesis, Fengjie Hao: ‘The role of the pro-apoptotic protease Caspase-8 for initiation and progression of alcoholic liver disease: Mechanisms and therapeutic options’, University Hospital RWTH Aachen, Germany
2013, Doctoral Thesis, Wei Hu: ‘Inhibition of hepatic cell proliferation through the systematic dissection of Cdk2/cyclin E complexes in mice’, University Hospital RWTH Aachen, Germany

FUNDED GRANTS:
2016-2019, German Research Agency of Research (DFG), Principal Investigator; 280,000 EUR
2013-2015, Wilhelm-Sander Foundation, Principal Investigator; 100,700 EUR
2012-2014, Initium Pharma, Principal Investigator; 80,000 EUR
2011-2013, Faculty of Medicine, RWTH Aachen, Germany. START Package, Principal Investigator; 80,000 EUR
2004-2005 DAAD Grant for Scientific Training in Germany, Medical University Hannover. 10,000 EUR

AWARDS AND HONORS
2015, European

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2015

Turno de acceso general

Nombre: **CASO FERNANDEZ, JAVIER RUBEN**
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Área Científica: Biomedicina
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Título:

Estudio del papel del microbioma, de la traslocación bacteriana y de las vías del Nrf2, Inflammasomas y la IDO en la fisiopatología de las enfermedades neuropsiquiátricas.

Resumen de la Memoria:

Since 2002 when I started my scientific career as a pre-doctoral student, I have spent a total of 14 years working in neuropsychoimmunology, neuroinflammation and stress-related diseases as well as in stress-induced intestinal dysfunction and bacterial translocation.

As a result, one of the main objectives of my research has been to study the mechanisms through which the stress can be an inductor of neuroinflammation and to find the origin of the neuroinflammation and its signaling pathways as well as alterations in the inflammatory mechanisms in the periphery and brain in animal models of mental disorders and biological samples from patients (main achievements described above).

Consequently, all the experience accumulated during my research career in the realm of innate immunity (TLRs), neuropsychoimmunology, mental diseases and intestinal microflora is allowing me to study a very promising new field, which is the role of the microbiota (and the microbiome) on different pathologies, and specifically in the ones with a neuroinflammatory component such as mental disorders (e.g. depression, schizophrenia, autism, anorexia nervosa) as well as the role played by nuclear factors (e.g. Nrf2), enzymes (e.g. IDO) and Inflammasomes in their pathophysiology.

It seems pretty established nowadays that there is an inflammatory component in the mental diseases. However, it still does not seem clear the origin of that inflammation. One of the proposed mechanisms responsible for the inflammation is the bacteria translocation which has been already detected in some conditions such as depression. The research that I have been running the last years has provided results supporting this line of thought that clearly deserves further investigation.

Furthermore, one of the more cutting-edge areas of research in the next years will be the microbiota/microbiome and its effects on different pathologies, including the CNS-related ones. In view of that, the line of research that I've been carrying out encompasses three different areas: the brain, the microbiology and the digestive system. Importantly, I have years of expertise in the 3 realms, as it can be seen in my CV and the description of my professional trajectory.

The innovative nature and the originality of this line of research are based in establishing a new link between stress, bacteria translocation, neuroinflammation and mental disorders. Concretely, the possibility that stress (an agent involved in the origin of the many mental conditions) could be inducing an intestinal dysfunction and thus, it would be an intestinal dysfunction also in patients. This would allow to hypothesize that, in a depressive status (for example), it is possible an intestinal dysfunction leading to bacterial translocation and passage into the blood of immune activators in both brain and periphery. Some of these components, such as bacterial LPS would initiate an inflammatory response (through the innate immune system receptors, between others) which would participate in the neurotransmitter and neurogenesis alterations observed in depression. Even more, a different type of microbiota could have different effects (inducing a stronger or a weaker inflammatory response) and consequently, the type of microbiota/microbiome could be used as a biomarker and as a tool for helping in the selection of the kind of treatment.

Resumen del Currículum Vitae:

Since I began my scientific career I have obtained an FPU predoctoral fellowship, a postdoctoral fellowship MICINN/Fulbright program to continue my studies at Stanford University and a Juan de la Cierva Contract in order to return to Spain.
My Thesis received the Premio Extraordinario de Doctorado. I was awarded with the Young Investigator Award 2009 from the European Society for Neurochemistry (ESN), recognizing my professional trajectory and my achievements in the realm of neurochemistry.
Also, I have received Travel Awards for international meetings, a Basic Science Poster Award and an Award to the best Oral Communication in a national meeting.
Once I obtained my PhD degree, I moved to the United States, to the laboratory of Prof. Robert Sapolsky (Stanford University) where I also received a postdoctoral contract from the former MICINN/Fulbright program.

After 3 years in the USA, I obtained a Juan de la Cierva Contract to return to Spain, at the Psychiatry Department of the School of Medicine.

AYUDAS RAMÓN Y CAJAL
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Turno de acceso general

Since I returned I have been the coordinator of the line of research about depression and affective disorders in the Laboratory of Molecular Neuropsychopharmacology of Stress-related Pathologies at the UCM, directing the research and the researchers involved in this line. Importantly, I�m Principal Investigator of an Intramural Project from the CIBERSAM network coordinating 10 researchers/physicians from 5 different research groups.

Finally, as the role of every researcher is not only to generate knowledge but also to teach it and share it, I have been director of a Doctoral Thesis (graded with Sobresaliente cum laude) and I am currently directing another one (it is in the beginning of its fourth year). Also, I have been director of 4 Master�s Theses and I am directing other two Master�s Theses at this moment.

I have experience in the assessment and review of R&D activities; in particular, I've been reviewer of manuscripts in 13 different journals and I have been member of the organizing and scientific committee of a scientific meeting about the staging in schizophrenia hold by the Cerebro y Mente Foundation at the Hospital 12 de Octubre.

I am involved in the teaching activities of different subjects at the School of Medicine and other Master programs and I have been member of an evaluation tribunal analyzing the Master�s Theses of the students from the Master in Mental Health organized by the CIBERSAM.

Moreover, I�ve been invited as lecturer and/or guest speaker to Conferences and Symposia and I have participated in activities of science popularization, dissemination of the scientific knowledge and awareness sessions (including webs, interviews in mass media, etc.).

I've achieved a total number of 33 publications, 9 of them as a first author (6 in first decile, top 10% Impact Factor journals) and I�m Corresponding Author of 2 articles in a first decile (top 10% impact factor) journal. I�ve reached an Accumulated Impact Factor of 212.2, and a Mean Impact Factor of 6.43. This Mean Impact Factor is in the top 5% in the Pharmacology category, top 8% in Psychiatry and top 10% in Neurosciences. Importantly, all these publications have been well accepted by other researchers being cited by different groups, producing an H-index=16, an amount of Times Cited Without Self-citations of 1075, and a total of Citing Articles Without Self-citations of 911.

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2015

Turno de acceso general

Nombre: **COSCOLLÁ DEVÍS, MIREIA**
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Área Científica: Biomedicina
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Título:

Population genetics and evolution of microbial pathogens integrated with molecular epidemiology

Resumen de la Memoria:

My main line of work has been conducting transdisciplinary research combining evolution and population genetics of Legionella pneumophila and Mycobacterium tuberculosis (Mtb) with molecular epidemiology using cutting edge technologies and analyses. The line that unifies all my research is the study of the genetic diversity and the population structure of bacterial pathogens. This line includes the study of the impact of horizontal gene transfer on L .pneumophila evolution. We have shown, that contrary to early views, that Legionella populations are not clonal and that 30% of the genes seen in available genomes have been transferred horizontally. During my postdoc I have studied the genetic diversity and evolution of Mtb. One of the main findings has been an Mtb strain isolated from a wild chimpanzee in Côte d'Ivoire that was shown by comparative genomic and phylogenomic analyses to belong to a new Mtb lineage, closer to the human-associated lineages than to the other classical animal-associated strains. This result showed that the general view of the genetic diversity of Mtb was limited at that time and supports the possibility that other MTBC variants exist, particularly in wild mammals. Finally, the study of the evolution of M. tuberculosis is central in my research. I collaborated with Dr. Comas in analyzing 270 Mtb genomes to find that humans and TB bacteria have emerged in the same region of the world, in Africa, and they have also migrated out of Africa together and expanded all over the globe. But the previous study did not consider what happened in America, which was very controversial. We analyzed 1,000-year-old mycobacterial genomes from Peruvian human skeletons together with contemporary strains revealing that a member of the Mtb complex caused human disease before contact. The ancient strains are distinct from known human-adapted forms and are most closely related to those adapted to seals and sea lions. One of my main research lines have been Tuberculosis Vaccines. The current vaccine, BCG, renders no protection against adult pulmonary tuberculosis, the most frequent form of the disease. We have analyzed the genomic variation of the different strains used to vaccinate against TB and we have reported evidence that epitope sequence variation potentially affects human T cell recognition. Additionally, we used comparative genomics of Mtb strains to show that although most epitopes are conserved, variable epitopes exist. This identification of two sets of antigens with opposing evolutionary processes might have an important impact on TB vaccine strategy and design. Another main research topic has been Outbreak Investigation of bacterial pathogens. We discovered that a paving machine was the source of one legionellosis outbreak. This result pointed for the first time the device as a potential source of infections. Regarding Mtb, we utilized genomic sequencing to understand the establishment and dispersion of multi drug resistant Mtb within an immigrant group to the United States. Finally, we have studied the first reported case of resistance to the most recent approved drugs against resistant Mtb. The implication of our work is that although new drugs are approved, extensively drug resistance treatment is still a challenge.

Resumen del Currículum Vitae:

I started my research career during my last course of the Bachelor as research collaborator student in the evolutionary genetics department in University of Valencia. During my PhD I studied population genetics of Legionella pneumophila that led to develop molecular epidemiological tools to address relevant public health problems. I further developed the same research niche when moving to tuberculosis (TB) research 6 years ago, increasingly addressing evolutionary and ecological questions that contributed to public health applied research in tree fields 1) molecular epidemiology, 2) vaccines and 3) drug resistance. Finally, between my PhD studies and my postdoc abroad, I worked as a scientist in the University Pompeu Fabra with Dr. Calafell studying the microbial metagenomics of the skin for four months.

During the 10 years of my scientific career I have co-authored 31 papers including 15 as first author. In addition to publishing in high-impact journals (e.g. Nature, Cell Host and Microbe, New England Journal of Medicine or Nature Genetics), several aspects of my scientific work have been picked up by the general media (BBC, ABC, Pennsylvania Borough News. I was awarded with 2nd prize in the 1st International Legionella Prize from the company ALCORA SA in 2006 for my PhD work. I managed to acquire funding for my PhD and my postdoc through competitive process. I have attended and presented my work in 13 congresses, six of them selected by scientific committees to be presented as oral presentations. I have been invited to oral presentations in a congress in France and in the University of Navarra. Finally, I am a reviewer for Plos One, Epidemics and Infectious Genetics and Evolution.

I have been able to do productive research but also establishing and coordinating the bioinformatics platform in the Gagneux's Lab. In addition, I have participated in teaching activities at bachelor and master level, both during my PhD studies in Valencia and later as a postdoc in Switzerland. Considering my career trajectory and research experience to date, I see myself at consolidating an independent research by starting my own group.