MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2013

Nombre: **LAO GRUESO, OSCAR**
Referencia: RYC-2013-14797
Área Científica: Biología Fundamental y de Sistemas
Correo Electrónico: oscar.lao@gmail.com

Título:

From the largest continent to the smallest population: boosting detection of genetic population substructure and positive selection in the human genome for the mapping of complex diseases

Resumen de la Memoria:

The aim of my research is the detection and analysis of human genetic population substructure and genetic ancestry, with particular interest in genetic epidemiology applications.

I have concentrated my research in:

i) Description of population substructure of several human datasets:
1) Analysis of the population substructure and genetic - geographic association present in Dutch population by means of whole genome SNP data.
2) Analysis of the population substructure present in European populations for the first time using microarray SNP data. This study was highlighted by The New York Times (http://www.nytimes.com/2008/08/13/science/13visual.html?_r=0). I am currently collaborating with investigators from the Department of Obstetrics and Gynaecology and the Department of Internal Medicine (Erasmus MC) for detecting population substructure in samples from European ancestry.

ii) Inference of demographic parameters that shaped the genetic variation:
1) Quantification of the proportions of genetic ancestry from Han and Melanesian populations in the Polynesian population.
2) Estimation of demographic parameters in East Asian and Oceanian populations using genome whole SNP microarray data. This study was included in the PhD of a PhD student that I co-supervised.
3) Estimation of demographic parameters and geographic identification of the origin of the proto-Romani using whole genome SNP data. The study was commented at El Pais (http://sociedad.elpais.com/sociedad/2012/12/06/actualidad/1354809333_605563.html) and El Mundo (http://www.elmundo.es/elmundo/2012/12/06/union_europea/1354821995.html) newspapers. I am currently analyzing the consequences of these demographic characteristics in the health of the Romani people in collaboration with investigators from the Evolutionary Biology Institute (UPF-CSIC).

iii) Detection of the fingerprint of selective pressures in the human genome:
1) Analysis of the genetic variation of genes putatively associated to human pigmentation in order to detect positive selective sweeps.
2) Development of a new statistic for estimating phenotypic-genetic co-variation at a population level and application to the pygmy height. I was involved in the design of the project and the co-supervision of PhD student Isabel Mendizabal. This research is followed by a Master student under my supervision in collaboration with investigators from the Evolutionary Biology Institute. I am also collaborating with investigators from the Department of Internal Medicine in a phenotype with health implications.

iv) Development of new statistical methods / algorithms for detecting population substructure in the human genome:
1) Development of new algorithms for ascertaining ancestry informative markers in human populations. The statistical framework I developed is being applied in an international collaboration with investigators from the Natural History Museum of Denmark to be used in ancient DNA samples. Furthermore, I am currently extending the method in collaboration with investigators from the Evolutionary Biology Institute.
2) Analysis of the proportion of recent genetic ancestry in different recently admixed populations, such as Argentineans or U.S. population.
3) Development of new algorithms for detecting fine population substructure using any type of genetic variant.

Resumen del Currículum Vitae:

I completed my PhD at Universidad Pompeu Fabra in Barcelona with a thesis entitled Natural history of mendelian and complex diseases in human populations, during which time I also studied at the Dipartimento di Biologia ed Evoluzione of Università di Ferrara. For the past nine years, I have been involved in postdoctoral research in the Forensic Molecular Biology Department of Erasmus University Medical Centre, including the thesis co-supervision of two PhD students and one Master student. During this period I participated on a regular basis in teaching of Master and PhD courses related to Human Genetics, and I am the co-supervisor of a journal club for PhD medical students about evolution. I have been involved in different projects financed by the Forensic Genomics Center Netherlands (Netherlands Genomics Initiative), Schiedam Vlaardingen and University of Cologne.

My research has equipped me with considerable expertise in human population genetic data analysis and a strong basis on statistics and human population history. I am used to work with data from whole genome scans, applying and developing statistical techniques to infer population substructure, recover estimations of the demographic parameters and detect signals of positive selection in the human genome. My work at Forensic Molecular Biology has allowed me to develop my skills to implement, manage and supervise my own scientific projects.

In particular, during my postdoc I have analysed the genetic diversity present in SNP microarray data of non-Romani and Romani European populations (Cur Biol 2008 & 2012), the Dutch population (Inv Genet 2013) and Oceanic populations (Cur Biol 2010 & Am J Hum Genet 2008), applying the state-of-art of algorithms from the field of population genetics. I have also developed new techniques for ascertaining the most suitable sets of ancestry informative markers (Am J Hum Genet 2006), with direct applications in human population genetics (Hum Mut 2010), forensic genetics (Ann Hum Genet 2010) and genetic epidemiology (J Clin Endocrinol Metab 2011). Finally, I have been involved in the analysis of positive selection in the human genome with implications in visual traits such as skin pigmentation (Ann Hum Genet 2007) or the pygmy height (Hum Genet 2012).

I have collaborated in several international projects, whose results have been published in high impact factor journals. Nowadays I am collaborating with investigators from different departments of the Erasmus MC. At international level, I am involved (either supervising the project or providing statistical advice) in collaborations with investigators from the Evolutionary Biology Institute (UPF-CSIC) and the Natural History Museum of Denmark.

All these achievements qualify me as an expert in the field of human population genetics, as acknowledged by the invitations to writing chapters about the subject in different on-line Encyclopaedias (Enc. Life Scien. 2009, Enc. Social & Behav Scien. 2014), a chapter of book popularizing science (http://bwm.trefcon.nl/media/pdf/Evolutie%20zit%20in%20je%20genen.pdf) and interviews in scientific journals about published works by other scientists (http://www.newscientist.com/article/mg21729055.200-sweat-mutation-may-have-helped-us-colonise-asia.html#.Uu959fl5OiU, http://news.sciencemag.org/biology/2014/02/black-death-left-mark-human-genome?rss=1).

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2013

Nombre: **FRIGOLA MAS, JORDI**
Referencia: RYC-2013-12727
Área Científica: Biología Fundamental y de Sistemas
Correo Electrónico: jordi.frigola@cancer.org.uk

Título:

Mechanistic insights into genomic replication

Resumen de la Memoria:

The goal of my PhD was to find out epigenetic changes associated to colorectal tumorigenesis. The main DNA methylation changes associated to cancer are global hypomethylation and regional promoter hypermethylation. To evaluate their potential role in tumor progression, we developed a novel technique, called Amplification of InterMethylated Sites (AIMS). We found that global losses and local gains are independent processes and contribute in different ways to cancer progression. Specifically, global hypomethylation has a correlation with genomic instability, regardless of p53 status. Concerning the regional hypermethylation, previously was associated to local silencing of discrete genes. However, we showed that this loss of gene expression can occur through long range epigenetic silencing, with similar implications as loss of heterozygosity in cancer. My postdoc studies are on chromosome replication. In eukaryotes, DNA replication is a two-step mechanism. During G1 the replication origins are licensed and in S-phase replication starts. At the heart of this regulation lays the replicative helicase. During the first step, an inactive helicase is loaded onto origins and is not activated until S-phase. Using budding yeast, we showed that the recruitment of the helicase onto origins, arguably the earliest step in the loading reaction, it depends on an essential C-terminal domain of Mcm3. Interestingly, this domain is conserved from yeast to humans, suggesting similar roles in higher eukaryotes. In addition, we found that ATP hydrolysis is not only critical for the helicase loading, it also plays an important role on releasing abortive reactions that could compromise the integrity of the origins. Furthermore, if the licensing components have been inactivated by Cyclin Dependent Kinase, the helicase is also released in ATP dependent manner. This result reveals a novel ATPase-dependent quality control of origin licensing contributing to precise once per cell cycle replication.

Resumen del Currículum Vitae:

Bachelor degree in Biology, Universitat de Girona (1997), bachelor degree in Biochemistry, Universitat Autònoma de Barcelona (1999). PhD degree in genetics, Universitat de Barcelona (2005). Awarded with special doctorate (2006). Thesis title: Epigenetic alterations in colorectal cancer. Supervisor: Miguel Angel Peinado. From my thesis I published five different papers, all as a first author. Nucleic Acids Research (2002), Oncogene and Human Molecular Genetics (2005) and Cancer Research and Nature Genetics (2006). This last paper deserved news and views on the same journal and was recommended by Faculty 1000. During my PhD studies, I decided to visit professor Susan Clark (Sydney, Australia). I stayed for a year on her laboratory and it was the beginning of a long collaboration between her and Dr.Peinado. Furthermore, based on the published results (Nature Genetics, 2006), we submitted a US-based patent, which I am the first author. My postdoc studies are on chromosome replication in S. cerevisiae at the London Research Institute with Dr. John diffley. So far, my work has resulted in two published papers, one review in Current Opinion in Cell Biology (2012) and an article format paper in Nature (2013), both as a first author. The Nature article has been cited in Faculty 1000 and it was highlighted in Nature Review in Molecular Cell Biology and Molecular Cell. Both of my PhD and postdoc studies have been presented in several international meetings and they have been cited 473 times. From my thirteen years of research experience, eight have been abroad (Sydney and London). During this time I have established successful collaborations with other scientists and I have gained experience with both, mammalian cells and yeast. My scientific background spans from epigenetics in humans to biochemistry in yeast, complementing my degrees in Biology and Biochemistry, respectively. Consequently, I feel highly qualified and confident to establish my own research group.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2013

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

Nombre: **CARBALLO GONZALEZ-CORROTO, JESUS**
Referencia: RYC-2013-13950
Área Científica: Biología Fundamental y de Sistemas
Correo Electrónico: jac56@sussex.ac.uk

Título:

Investigating the essential functions of the DNA Damage Response during Gametogenesis and Cancer

Resumen de la Memoria:

Most of my research experience has been focussed in trying to understand how cells maintain genome stability after DNA damage or in natural developmental processes like gametogenesis. Defects in the second one can lead to disorders like infertility or cancer. During gametogenesis a specialized cell division known as meiosis takes place. Meiosis is required to reduce the number of chromosomes to half. Two key processes are essential during meiosis: 1) to swap genetic information between parental chromosomes without introducing mutations and 2) to accurately segregate homologue chromosomes and sister chromatids respectively to avoid aneuploidies in gametes. These two processes require meiotic recombination to occur and this is initiated by the catalysis of programmed Double Strand Breaks (DSBs) on the DNA. This is a hazardous process that can lead to genome instability if unregulated. DSB repair is monitored by a network known as the DNA damage response (DDR). During my years as PhD student and postdoc I extensively studied the DDR and how it is critical for checkpoints and maintenance of genome stability. I have shown the implication of the DDR in monitoring meiotic DSB repair and how it actively promotes homolog recombination by ensuring repair using the right DNA template. The DDR is also critical in modulating the amount of DSBs catalysed. With this solid experience my future research will be based on the identification of novel components of the meiotic DDR and to understand their molecular mechanisms and possible implications in cancer. These are may aims for the future:

1. I am developing a SILAC based phospho-proteome wide screen method to identify in vivo meiotic phospho-proteins. I will use this method as a tool to acquire high quantity of data that will be developed in several projects in the future.
2. I have shown that phosphorylation of the synaptonemal complex (SC) is required for meiotic checkpoints. In my preliminary studies, I observed that mutations that prevent interaction of SC proteins with ATR kinase fail to trigger checkpoint response. I have identified the relevant regions in human and yeast SC proteins required for such interaction. With this project I aim to identify the molecular mechanism that differentially activates the DDR in meiosis in yeast and humans.
3. Initiation of meiotic DSBs happens only in selected regions in the genome called hotspots. Whereas most of these hotspots have been mapped, little is known of how their expression is regulated. I have shown that ATM/ATR modulates meiotic DSBs at hotspots via phosphorylation. I have been able to predict the existence of two different populations of DSB-hotspots that are regulated and expressed in a timely manner, but most importantly, their expression is likely controlled by the meiotic DDR. In collaboration with a group in Japan, I will be able to work on my hypothesis using ChIP-Seq methodology.
4. Several meiotic genes have been identified as oncogenes recently. Identification of meiotic-DDR genes with oncogenic potential could be a key in finding new targets to fight against some cancers.

Altogether, the study of meiosis can offer numerous advantages and complementary analyses to those extensively performed in somatic cells. Furthermore, the approach from a different angle to classic problems in biomedicine could yield a more synergistic contribution to the current advance in those areas.

Resumen del Currículum Vitae:

I currently hold a New Investigator Research Grant research fellowship awarded by the Medical Research Council (MRC) working at the Genome Damage and Stability Centre part of the University of Sussex' campus in UK. There I perform independent research endowed by Prof. Anthony Carr, the director of this prestigious institute. Currently I have my own budget for research consumables and equipment that will fund the 36 months that this fellowship lasts.

During the first 15 months I have successfully directed a student for his MsC thesis as part of the of university MSc. program. I have also authored two manuscripts during that period and a third one is currently in preparation. Among those publications, I was the first and co-corresponding author of a paper published in PLoS Genetics where I identified a new target of ATR, Rec114, required to meiotic recombination (Carballo et al. 2013). I was also second author in a paper published in PLoS ONE in collaboration with Eva Hoffmann's group. There, I assessed the implication of Aurora kinase during meiotic checkpoint arrest (Newnham et al. 2013). I am currently finalizing a third manuscript that will be submitted this month.

Earlier I held two postdoc positions at the prestigious National Institute for Medical Research in London.. My research focused on the DNA damage response (DDR) in yeast and mouse. There I published my main work as lead author in the prestigious journal Cell. In that work I discovered the first meiosis specific DDR adaptor which was phosphorylated by ATM/ATR kinases. (Carballo et al. 2008). This manuscript has been extensively cited by my peers in the field due to its high relevance, not just in yeast, but also in humans. During my postdoc I focused my research on the meiotic functions of ATM/ATR kinases. A summary of this was published in a review in Chromosome research (Carballo and Cha, 2007).

In collaboration with Luis Aragon&#65533;s group from Imperial College we published a paper in the Journal of Cell Biology about CDC14 phosphatase and rDNA segregation (Machín et al. 2006).
During my postdoc training I visited Luis Aragon&#65533;s group in London and also visited Professor Marco Foiani&#65533;s group at the IFOM institute located in Milan, Italy to learn new techniques relevant to my research.
During my PhD studies, I learnt how ionizing radiation affects cell cycle proliferation. My optimization of the irradiation to analyze DNA damage and cell cycle progression in plant cells was used as part of four publications (Gimenez-Abian et al. 2002, Perez-Talavera et al. 2003a, Perez-Talavera et al. 2003b and Gimenez-Abian et al. 2004). One of the highlights of my PhD research was the identification of apoptosis-like death in plants in response to severe DNA damage (Carballo et al. 2006).
I was accepted to present my work to an international audience in 5 Gordon Research Conferences in US and 5 EMBO conferences. I also participated as invited speaker in several meetings in UK.
I have extensive experience in many molecular, biochemical, cytological, and immunohistochemical techniques required for running a multidisciplinary lab. I have experience in plants, yeast, bacteria, and cell lines. I have basic training in bio-statistics and knowledge of most of the commonly used bioinformatics tools. I have also training in areas involving systems level techniques like ChIP-CHIP/Seq.
With my experience I'm now in an excellent position to create quality research and attract funding.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2013

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

Nombre: **SANCHEZ RODRIGUEZ, CLARA**
Referencia: RYC-2013-13933
Área Científica: Biología Fundamental y de Sistemas
Correo Electrónico: c.sanchez@mpimp-golm.mpg.de

Título:

Plant cell biology during development and in response to stress

Resumen de la Memoria:

Cells continually perceive signals from other cells and from their environment, which is essential for the organism to respond to stress and for correct cell division and differentiation. Plants have evolved particular mechanisms to adapt to their ecosystem, many of which are still under investigation. In my research career I apply multidisciplinary approaches to shed some light on the plant cell biology: the interconnections of its structures and pathways, and the similarity to other eukaryotes.
During my PhD I identified and characterized prominent players in plant response to necrotrophic non-adapted and adapted fungi. Among them, I leaded new areas of research with the aim of elucidating the role of the cell wall as one of the first barriers of the plant cell against pathogens. Moreover, in collaboration with a colleague, I started a new study on plant vaccines from fungi origin.
My work as postdoctoral researcher is mainly focused on elucidating how plant cell walls are synthesized and remodelled. One of my projects aims to understand the cellulose production and assembly in muro. At the same time I investigate the trafficking pathways involved on cell wall arquitecture. This work has led to the identification of a unique evolutionary adaptation of the canonical eukaryotic pathway for clathrin-mediated endocytosis in plants, which is being published in Cell. I am currently evaluating the role of this process on plant development and its evolutionary significance in eukaryotes. In addition, I have brought new areas of research into the lab connecting hormone signaling and cell wall synthesis, and am currently pursuing this topic in more detail.

Resumen del Currículum Vitae:

PUBLICATIONS
1.- Sánchez-Rodríguez C¥, Gadeyne A¥, et al. Accepted in Cell (Tentatively: 156/4;Feb 14). ¥Equal contribution
2.- Sanchez-Rodriguez C¥, Krishnamoorty P¥, et al. Accepted in Annals of Botany. ¥Equal contribution
3.- Sánchez-Rodríguez* and Persson S. Book chapter. Under edition (Wiley-Blackwell). *Corresponding author
4.- Wu XN, et al. (2013) Mol Cell Proteomics. Oct 12(10):2856-73
5.- Torres MA, et al. (2012) Mol Plant Microbe Interact. Jun; 26(6):686-94
6.- Ramos B, et al., (2013) Mol Plant Pathol., Jan;14(1):44-57
7.- Sánchez-Rodríguez C, et al. (2012) Plant Cell, Feb;24(2):589-607
8.- Sánchez-Rodríguez C¥, Delgado-Cerezo, M¥, et al. (2012) Mol. Plant, Jan;5(1):98-114. ¥Equal contribution
9.- Endler A., et al. (2010) Nature chemical biology, Dec; 6(12):883-4
10.- Sánchez-Rodríguez C, et al. (2010) Trends Plant Sci., May;15(5):291-301
11.- Sánchez-Rodríguez C, et al. (2010) Book chapter. ISBN 978-0-9654625-6-3
12.- Sánchez-Rodríguez C, et al. (2009) Mol Plant Microbe Interact., Aug;22(8):953-63
13.- Llorente F, et al. (2008) Mol. Plant., May;1(3):496-509
14.- Molina A, et al. (2008). Phytoma, 192: 43
15.- Hernández-Blanco C, et al. (2007) Plant Cell, Mar; 19(3):890-903.
16.- Stein M, et al. (2006) Plant Cell, Mar; 18(3):731-46.
17.- Llorente F, et al., (2005) Plant Journal, Jul;43(2):165-80
Patents
1.- Method for Increasing pathogen resistance in plants. Ref. Nm: PCT/EP2013/077076

GRANTS AND AWARDS
- Postdoctoral Contract "Programa Nacional de Recursos Humanos de Investigación, subprograma de estancias de movilidad postdoctoral en el extranjero". Ministerio de Ciencia en Innovación, Spain. Nov 2008
- Postdoctoral Fellowship "Becas de investigación en universidades o centros en el extranjero 2008". Fundación Alfonso Martín Escudero, Spain. Dec 2008
- Postdoctoral Fellowship. Fundación Ramón Areces, Spain. Jun 2008
- Fellowship for short term research at Carnegie Institution of Washington, Stanford, USA. Ministerio de Ciencia y Tecnología. Spain. Jan 2006
- Academic Award (First Class Honors) 1998-2003. Universidad Politécnica de Madrid, Spain. May 2004

- PhD Fellowship. Ministerio de Ciencia y Tecnología, Spain. May 2004
- Research Student Collaborator Fellowship. Universidad Politécnica de Madrid, Spain. Sep 2002
- Academic Award:best academic national record. Instituto de la Ingeniería de España and Asociación Mutualista de Ingeniería Civil,Spain. May 2002
- Academic Award: the best academic faculty record. Fundación General de la Universidad Politécnica de Madrid, Spain. Jan 2002

PROFESSIONAL EXPERIENCE
- Since 2008: Postdoc. Max-Planck Institute for Molecular Plant Physiology, Golm-Potsdam, Germany. Plant Cell Walls lab
- Mar 2013: Visiting scientist. Carnegie Institution. Department of Plant Biology,Stanford, USA. Plant cell biology lab
- 2007-2008: Postdoc.UPM, Madrid, Spain. Plant innate immunity lab
- 2003-2007: PhD student. UPM,Madrid,Spain. Plant innate immunity lab
- Jul-Oct 2006: Visiting scientist.Carnegie Institution. Department of Plant Biology,Stanford,USA. Plant-pathogen interaction lab
- 2002-2003: Research collaborator. UPM,Madrid,Spain. Plant innate immunity lab

EDUCATION
- PhD at Universidad Politécnica de Madrid (UPM), Madrid,Spain. Dec 2007. Sobresaliente cum laude
- Degree in Agricultural Engineering at UPM,Madrid,Spain. Sep 2003; Sobresaliente cum laude

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2013

Nombre: **MUÑOZ ESPIN, DANIEL**
Referencia: RYC-2013-14471
Área Científica: Biología Fundamental y de Sistemas
Correo Electrónico: dmunoz@cnio.es

Título:

Viral DNA replication - Cellular Senescence in Development

Resumen de la Memoria:

I am a PhD researcher with over 10 years' experience in the fields of DNA replication and Cell Biology trained in Spain and the United Kingdom. I have published sixteen research articles (including first author papers in Cell, PNAS, EMBO J, and JBC) and two reviews (including Nat Rev Mol Cell Biol), experience directing PhD students, and leadership potential.

1. PhD training. My doctoral thesis was carried out in Margarita Salas' group, at the CBMSO, and was focused on viral DNA replication studies. From that period (2002 to 2006), I published a total of 7 articles, 4 of them as first (or co-first) author in The EMBO Journal (2003) and The Journal of Biological Chemistry (2004, 2005 and 2007). My main discovery during this period was a bacteriophage homeodomain-related DNA-binding protein that organizes viral DNA replication in bacteria.

2. International stay. In 2005, I moved to the Sir William Dunn School of Pathology (University of Oxford) as a final PhD training. From this stay in the Jeffery Errington's laboratory (member of the Royal Society) I published an article in PNAS as first author (2009). In this work, I reported for the first time that, similar to some eukaryotic viruses, prokaryotic viruses are able to exploit the cytoskeleton of their hosts to promote efficient viral DNA replication, and this functional property is widespread in bacteriophages infecting gram-positive and -negative bacteria.

3. Postdoctoral period. I did a first postdoctoral stay (from 2007-2011) working in virology and bacterial cell biology at Margarita Salas' group (CBMSO). From this stage, I would like to highlight two articles in PNAS as a first author (2010 and 2012) and a review manuscript (2012). These papers describe that phage terminal proteins contain a DNA-binding domain to attach the viral DNA replication machinery to the bacterial nucleoid and, unexpectedly, a functional nuclear localization signal (NLS). Based on this work, we developed a patent on a novel gene delivery system that has been licensed to Sygnis AG Pharma. Moreover, I have co-directed the research projects of two PhD students that are defending their doctoral theses in the first half of 2014 (one of them on February 28th). From this research on the interaction between viruses and their hosts, two papers were additionally published in PNAS (2012 and 2013), and an extra one in Molecular Microbiology (2013), where I participate as senior (or co-senior) and as corresponding author.

In 2011, I obtained a "Juan de la Cierva" contract to work in the group of Dr. Manuel Serrano, at the CNIO. Recently, I published my main research project in Cell (2013), which describes for the first time that cellular senescence promotes tissue remodelling during embryonic development. The scientific community has received this paper enthusiastically and it has been the topic of commentaries in Nature, Cell, Nature Reviews Molecular Cell Biology and EMBO Journal. In addition, we have written a review covering this novel field in Nature Reviews Molecular Cell Biology, which is currently in press (2014).

My long-term goal is to further characterize and understand the role of cellular senescence during embryonic development and in pathological disorders, and I consider that a "Ramón y Cajal" contract would provide the necessary continuity to develop this outstanding research.

Resumen del Currículum Vitae:

PUBLICATIONS

1. Authorship: First Author. Review: Nat Rev Mol Cel Biol (2014). Impact Factor: 37.162
2. Authorship: First Author. Journal: Cell (2013). Impact Factor: 31.957
3. Authorship: Senior and Corresponding Author. Journal: Mol Microbiol (2013). Impact Factor: 4.961
4. Authorship: Second Author. Journal: Mol Microbiol (2013). Impact Factor: 4.961
5. Authorship: Senior and Corresponding Author. Journal: PNAS (2013). Impact Factor: 9.737
6. Authorship: Second Author. Journal: Commun Integr Biol (2013). Impact Factor: -
7. Authorship: Co-First Author. Journal: PNAS (2012). Impact Factor: 9.681
8. Authorship: Co-Senior and Corresponding Author. Journal: PNAS (2012). Impact Factor: 9.681
9. Authorship: First Author. Review: Adv Virus Res (2012). Impact Factor: 3.971
10. Authorship: First and Corresponding Author. Journal: PNAS (2010). Impact Factor: 9.771
11. Authorship: First Author. Journal: PNAS (2009). Impact Factor: 9.380
12. Authorship: First Author. Journal: J Biol Chem (2007). Impact Factor: 5.581
13. Authorship: Second Author. Book Chapter: Bacteriophage (2007). Impact Factor: -
14. Authorship: Second Author. Journal: The EMBO Journal (2006). Impact Factor: 10.086

15. Authorship: Second Author. Journal: J Biol Chem (2005). Impact Factor: 5.854
16. Authorship: Co-First Author. Journal: J Biol Chem (2005). Impact Factor: 5.854
17. Authorship: Second Author. Journal: J Neurooncol (2004). Impact Factor: 1.968
18. Authorship: First Author. Journal: J Biol Chem (2004). Impact Factor: 6.355
19. Authorship: Co-First Author. Journal: The EMBO Journal (2003). Impact Factor: 10.698

DOCTORAL THESES
PhD Student: David Ballesteros Plaza.
Title: Estudios funcionales de la proteína p1 y de la proteína p17 del bacteriófago phi29.
Reading Date: February 28th, 2014.

PhD Student: Isabel Holguera Álvarez.
Title: Estudios funcionales de la proteína p6 y de proteína terminal del bacteriófago phi29.
Estimated Reading Date: June, 2014.

PATENTS
Patent presented at the 'Oficina Española de Patentes y Marcas' (2012).
Application Number: P20231107
Title: Utilización de Señales de Localización Nuclear de Proteína de Bacteriófagos como Vehículos para Transferencia de Genes.
Licensed: Sygnis AG Pharma (2013).
PCT stage: PCT/ES2013/070498

INTERNATIONAL STAYS
Centre: Sir William Dunn School of Pathology, University of Oxford
City, Country: Oxford, UK
Period: 7 months, from 20th February 2005 to 20th September 2005.

FELLOWSHIPS AND PROJECTS
2002-2006. Fellow of the Fund for Health Research (FIS), ISCIII.
2007-2010. I3P contract of the 'Consejo Superior de Investigaciones Científicas' (C.S.I.C.) for young PhD.
2011-Present. 'Juan de la Cierva' contract of the 'Spanish Ministry of Science and Innovation'.
I have participated as a Collaborator Researcher in 19 projects by national and international funding bodies.

CONFERENCES
I have participated as a speaker, with a poster presentation or as a co-author in a total of 25 congresses.

ACCREDITATIONS
2010. Accreditation for Assistant Professor by ANECA.
2012. Certificate of Competency on Laboratory Animal Sciences for Researchers: Category C.

HONOURS AND AWARDS
2006-2007. PINP prize to the best doctoral thesis performed in the 'CBMSO' and presented at the 'UAM'.
2006-2007. Special doctorate award in biology of the 'UAM'.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2013

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

Nombre: **ORTEGA DE LA O, FELIPE**
Referencia: RYC-2013-13290
Área Científica: Biología Fundamental y de Sistemas
Correo Electrónico: felipeortega80@gmail.com

Título:

Role of purinergic signaling on neuronal survival/Study of the mechanisms regulating adult neurogenesis and oligodendrogliogenesis in the subependymal zone

Resumen de la Memoria:

During my PhD in the laboratory of Prof Maria Teresa Miras Portugal, I focused on the study of the signaling pathways activated and the neuroprotection exerted by nucleotide receptors on cerebellar granule neurons. As a result of my PhD research I published a total of 7 publications (4 as first author and one as second). In addition, I contributed to the development of 7 research projects funded by governmental institutions and one project funded by the Marcelino Botin Foundation. Moreover I actively participated in teaching activities of the department of Biochemistry and Molecular Biology IV at the University Complutense of Madrid (80 hours Biochemistry in 2007-2008 and 45 hours of Pharmacological Biochemistry in 2008).
Subsequently I moved to the laboratory of Magdalena Götz at the Ludwig Maximilians Universität of Munich. There, I studied the lineage progression of the neural stem cells and the mechanisms regulating the neurogenesis and oligodendrogenesis that takes place in the adult murine subependymal zone under the supervision of Prof Benedikt Berninger, with whom I moved afterwards to the Johannes Gutenberg Universität of Mainz. In addition I could also contribute significantly to the field of cellular reprogramming, the other main line of research studied in my host laboratory.
As a consequence of our findings, a total of 8 publications were obtained (4 of them as first author, 2 of them as a second author (3 of them currently submitted/in revision) including highly prestigious Journals as Development (1st author), Nature Protocols (1st author), Cell Stem Cell (Co-author), Nature Cell Biology (1st and co-corresponding author) and Cell (second author, under review). Moreover, I was involved in 6 international projects funded by the German government/European Agencies (5 as a collaborator and one as a co-cordinator). In addition I was selected as speaker and teacher to several international meetings and courses in order to share results and our self-developed techniques (including the LMU-Harvard young scientists forum (2011) and the RIIP International course (55 hours) at the Helenic Pasteur Institute of Athens in 2013). I also obtained the Positive evaluation of the National Agency for Evaluation of Quality and Accreditations (ANECA) For the title "PROFESOR AYUDANTE DOCTOR" (February 2012) and positive evaluation of the agency of Quality, Accreditation and Prospective of the Universities of Madrid for the title of "PROFESOR AYU¬DANTE DOCTOR", "PROFESOR CONTRATADO DOCTOR" and "PROFESOR DE UNIVERSIDAD PRIVADA" (August 2012). Furthermore, I could establish a widespread network of worldwide contacts that resulted in several international collaborations with renowned laboratories. All these collaborations were based on the results and scientific tools/protocols developed during my postdoctoral period. Likewise I also contributed to the teaching activities in the Ludwig Maximilians Universität of Munich (150 hours in the subject of Praktikum Physiologie I für Humanmediziner (7M0408) for the Medicine degree in the academic years 2009-2012).

Resumen del Currículum Vitae:

During my PhD in the laboratory of Prof Maria Teresa Miras Portugal, I focused on the study of the signaling pathways activated and the neuroprotection exerted by nucleotide receptors on cerebellar granule neurons. As a result of my PhD research I published a total of 7 publications (4 as first author and one as second). In addition, I contributed to the development of 7 research projects funded by governmental institutions and one project funded by the Marcelino Botin Foundation. Moreover I actively participated in teaching activities of the department of Biochemistry and Molecular Biology IV at the University Complutense of Madrid (80 hours Biochemistry in 2007-2008 and 45 hours of Pharmacological Biochemistry in 2008).
Subsequently I moved to the laboratory of Magdalena Götz at the Ludwig Maximilians Universität of Munich. There, I studied the lineage progression of the neural stem cells and the mechanisms regulating the neurogenesis and oligodendrogenesis that takes place in the adult murine subependymal zone under the supervision of Prof Benedikt Berninger, with whom I moved afterwards to the Johannes Gutenberg Universität of Mainz. In addition I could also contribute significantly to the field of cellular reprogramming, the other main line of research studied in my host laboratory.
As a consequence of our findings, a total of 8 publications were obtained (4 of them as first author, 2 of them as a second author (3 of them currently submitted/in revision) including highly prestigious Journals as Development (1st author), Nature Protocols (1st author), Cell Stem Cell (Co-author), Nature Cell Biology (1st and co-corresponding author) and Cell (second author, under review). Moreover, I was involved in 6 international projects funded by the German government/European Agencies (5 as a collaborator and one as a co-cordinator). In addition I was selected as speaker and teacher to several international meetings and courses in order to share results and our self-developed techniques (including the LMU-Harvard young scientists forum (2011) and the RIIP International course (55 hours) at the Helenic

Pasteur Institute of Athens in 2013). I also obtained the Positive evaluation of the National Agency for Evaluation of Quality and Accreditations (ANECA) For the title "PROFESOR AYUDANTE DOCTOR" (February 2012) and positive evaluation of the agency of Quality, Accreditation and Prospective of the Universities of Madrid for the title of "PROFESOR AYU¬DANTE DOCTOR", "PROFESOR CONTRATADO DOCTOR" and "PROFESOR DE UNIVERSIDAD PRIVADA" (August 2012). Furthermore, I could establish a widespread network of worldwide contacts that resulted in several international collaborations with renowned laboratories. All these collaborations were based on the results and scientific tools/protocols developed during my postdoctoral period. Likewise I also contributed to the teaching activities in the Ludwig Maximilians Universität of Munich (150 hours in the subject of Praktikum Physiologie I für Humanmediziner (7M0408) for the Medicine degree in the academic years 2009-2012).

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2013

Nombre: **MOREY RAMONELL, LLUIS**
Referencia: RYC-2013-14098
Área Científica: Biología Fundamental y de Sistemas
Correo Electrónico: lluis.morey@crg.eu

Título:

Epigenetic events in cancer and development

Resumen de la Memoria:

During my PhD (2003-2008) in the laboratory of Luciano Di Croce (CRG, Barcelona) I discovered that in leukemic cells the NuRD complex (Nucleosome Remodeling and Deacetylase complex) facilitates the recruitment to chromatin of two of the main epigenetic factors, the Polycomb Repressive complex 2 (PRC2) and the DNA methyltransferase DNMT3A. Importantly, this epigenetic mechanism is essential for leukemogenesis, since depletion of several members of the NuRD complex resulted in spontaneous differentiation of leukemic blasts (Morey et al. MCB, 2008). Therefore, loss-of function of the NuRD complex could be exploited for therapeutic intervention.

I then moved to Copenhagen as a postdoctoral fellow in the laboratory of Kristian Helin (Centre for Epigenetics and BRIC, University of Copenhagen), where I became interested in the epigenetics mechanisms that regulate embryonic stem cell (ESC) pluripotency and differentiation. Profound analysis of the pluripotency loci, like Oct4 and Nanog, revealed that long non-coding RNAs (ncRNAs) are specifically expressed in pluripotent ESC, but not in differentiated cells. Interestingly, these ncRNAs are nuclear, expressed anti-sense of the coding mRNA of these genes, bind to the active histone modification H3K4me3, and their depletion resulted in loss of ESC identity, suggesting a new mechanism involved in ESC pluripotency (manuscript under preparation). In 2010 moved back to Luciano Di Croce¿s laboratory, to do my second postdoc. I embarked on a broader direction to understand the epigenetic mechanism involved in ESC pluripotency and differentiation. I am paying particular attention in characterizing the function of the canonical PRC1 complex in ESC identity. I discovered that the PRC1 complex architecture is not static, but rather dynamic. Importantly, this subunit composition switch not only confers distinct target selectivity of the PRC1 complex during ESCs differentiation, but also achieves the balance between pluripotency and differentiation of ESCs (Morey et al. Cell Stem Cell, 2012). Moreover, I dissected the function of the canonical and non-canonical PRC1 complexes in ESC. Canonical and non-canonical PRC1 complexes are defined by the presence of either Cbx or RYBP polypeptides. I found that PRC1 complexes containing either Cbx7 or RYBP have specific biological functions, their genomic localization it is mutually exclusive in certain genes, which confers specific biological function, and enzymatic activity, of these two PRC1 complexes (Morey et al. Cell Reports, 2013).
I strongly believe that my studies summarized above open new paths and questions that prompted me to investigate the function of Polycomb complexes in a broader direction, to better understand the function of these complexes in development, but also in cancer progression.

Resumen del Currículum Vitae:

Publications: I have published a total of 17 peer-reviewed articles in top-tier journals. As first author I published in Cell Stem Cell (2), Cell Reports, MCB and TiBS. Moreover, I am second author in several papers, and I have been actively involved in studies, which were published in journals like Nature, Molecular Cell, Cancer Cell, EMBO J and Genes and Development (see CV for details). I am also corresponding author of an article published in Cell Reports in 2013.

Reseach experience:
- Staff scientist: Centre for Genomic Regulation. Differentiation and Cancer Program. Supervisor: Dr. Luciano Di Croce. 2012-present 
- Post-doctoral research: Centre for Genomic Regulation. Differentiation and Cancer Program. Supervisor: Dr. Luciano Di Croce. 2010-2012 
- Post-doctoral research: Biotech Research and Innovation Center (University of Copenhagen). Gene Regulation, Epigenetics, stem cells, cancer biology. Supervisor: Dr. Kristian Helin. 2008-2010 
- Pre-doctoral research: Centre for Genomic Regulation. Differentiation and Cancer Program. Supervisor: Dr. Luciano Di Croce. 2003-2008 
- Erasmus fellowship: Department of Microbiology. Thesis Director: Dr. Jan Tommassen. Utrecht Universiteit. 2002-2003..

Mentoring: I have experience in supervising master and PhD students. I am currently co-supervising a doctoral thesis.

Awards:
- Post-doctoral fellowship (4DCellFate-Funded by the European Commission 2012 FP7) 
- Post-doctoral fellowship (Novartis-CRG) 2010
- Post-doctoral fellowship (Beautriu de Pinós) 2010
- Post-doctoral fellowship (Biotech Research and Innovation Center, University of Copenhagen) 2008
- Pre-doctoral fellowship (Centro de Regulación Genómica, Barcelona) 2003
- Erasmus fellowship (Universitat de Barcelona) 2002

Participation in conferences: I have participated in many national and international meetings (see CV for details); here I just mention the ones I was invited as a speaker.

- IV CRG-Postdoc symposium. 19th November 2013. "What are the molecular mechanisms that drive embryonic stem cell differentiation?"
- IMB Conference: Chromatin Dynamics & Stem Cells- 17th-20th October 2013. "Role of different PRC1 complex subunits in mouse ESC pluripotency and differentiation".
- Herrenhausen Symposium on Stem Cells and Regenerative Medicine - October 8-10, 2013 Hanover Germany. Invited delegate.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2013

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

Nombre: **POSE PADILLA, DAVID**
Referencia: RYC-2013-12699
Área Científica: Biología Fundamental y de Sistemas
Correo Electrónico: dpose@uma.es

Título:

Abiotic stress tolerance and floral transition and development in Arabidopsis

Resumen de la Memoria:

During my scientific career my research has been focused on understanding how plants perceive environmental signals and how this information is translated into developmental outcomes. Particularly, I have focused on two important aspects of the plant-environment interaction: (1) The identification and characterization of genes involved in abiotic stress tolerance, and (2) the study of transcription factors (TFs) involved in the regulation of the floral transition and fruit ripening.

As a doctoral student at the University of Málaga I worked on the identification and characterization of Arabidopsis mutants that displayed impaired development under drought stress. As part of my PhD thesis, I isolated a drought hypersensitive mutant (dry2) and could demonstrate that the gene was involved in sterol biosynthesis. This worked revealed an unexpected connection between root sterol composition and drought tolerance through the regulation of the production of reactive oxygen species (ROS). The production of ROS regulated stomata opening/closure and root development (Posé et al. 2009; Plant J, 59(1):63-76) (Posé and Botella 2009; Plant Signal Behav, 4(9):873-874). I also generated second-site suppressors mutations of dry2. Characterization of one of these suppressors highlighted similarities but also important mechanistic differences among components involved in the regulation of the key enzyme of the mevalonate pathway in plants, yeast and animals (Doblas et al. 2013; Plant Cell, 25(2):728-743).
After my PhD, I was involved in the molecular characterization of Arabidopsis mutants of the TETRATRICOPEPTIDE THIOREDOXIN-LIKE (TTL) gene family. This work revealed that TTL genes are specific for land plants and play a regulatory role in different aspects of plant development, such as male gametophyte development, and in abiotic stress tolerance (Lakhssassi et al. 2012; Plant Phys, 158(3):1252-1266).

During the postdoctoral period I spent at the Max Planck Institute (Tübingen, Germany), I investigated the complex regulatory network that controls floral transition and flower development in Arabidopsis. In particular I studied the role of key TFs in these processes, focusing mainly on understanding the molecular mechanisms by which temperature regulates flowering time. In this study, we identified a new mechanism of regulation based in two functionally antagonistic splice variants of the MADS-Box TF FLOWERING LOCUS M (FLM). This work has been recently published in Nature (Posé et al. 2013; 503(7476):414-417) and Science (Lee et al. 2013; 342(6158):628-632), which were reviewed in a Science "Perspective" article (Nilsson 2013; 342(6158):566-567).
In addition, I established several collaborations during this period that led to the publication of the following articles:
-Immink*, Posé* et al. 2012; Plant Phys, 160(1):433-449 (*Equal contribution).
-Galvao et al. 2012; Plant J, 71(3):517-526.
-Moyroud et al. 2011; Plant Cell, 23(4):1293-1306.

My current interest is to translate the expertise gained on the analysis of TFs in Arabidopsis to understand developmental programs in crop species such as strawberry. In particular, I am working on the identification of key TFs involved in the control of strawberry fruit ripening and the determination of the regulatory networks controlled by these TFs.

Resumen del Currículum Vitae:

I obtained a degree in Biology from the University of Málaga (UMA) in August 2003. Due to my high marks as undergraduate (2,9) I was granted a Collaboration Fellowship for lab training during my final year of the Degree and a predoctoral fellowship (FPU).

I completed my PhD in the Department of Biología Molecular y Bioquímica at the UMA in October 2008, under the supervision of Profs. Miguel A. Botella and Victoriano Valpuesta. I focused on the physiological and molecular characterization of genes involved in abiotic stress tolerance. Particularly I studied the following Arabidopsis genes:
-The DRY2 gene, which links sterol biosynthesis and the generation of reactive oxygen species, which in turn controls stomata regulation, root development and drought tolerance (Posé et al. 2009; Plant J, 59(1):63-76) (Posé and Botella 2009; Plant Signal Behav, 4(9):873-874). The study of a dry2 suppressor identified a positive regulator of HMGR activity, the key enzyme of the mevalonate pathway (Doblas et al. 2013; Plant Cell, 25(2):728-743).
-The TTL genes, which are involved in osmotic stress tolerance and male sporogenesis (Lakhssassi et al. 2012; Plant Phys, 158(3):1252-1266).

During my predoctoral period I spent 4 months at the Cell and Developmental Biology Department, John Innes Centre (Norwich, UK), under the supervision of Prof. Liam Dolan, where I gained experience in cell biology and confocal microscopy techniques.

After obtaining my PhD, I worked as a postdoctoral researcher in the group of Dr. Markus Schmid at the Molecular Biology Department of the Max Planck Institute (MPI) (Tübingen, Germany), from September 2009 until May 2013. During this period I focused on the analysis of transcription factors (TFs) involved in the regulation of floral transition and flower development. This work resulted in the publication of five peer-reviewed research articles and a review. Of particular importance are the following publications, that include reports in the two most important journals of multidisciplinary science, i.e. Nature (Posé et al. 2013; 503(7476):414-417) and Science (Lee et al. 2013; 342(6158):628-632). These papers report the temperature-dependent regulation of flowering, focusing on the role of several MADS-Box TFs. I also characterized the role of the TF SOC1 in flowering by the identification of its up- and downstream regulators (Immink*, Posé* et al. 2012; Plant Phys, 160(1):433-449. *Equal contributors).

In May 2013 I moved to the IHSM-UMA-CSIC, funded by a JAE-DOC postdoctoral fellowship. I am currently interested in translating the molecular background and technical skills learned using Arabidopsis to a crop species such as strawberry. In particular, I am working on the identification and analyses of TFs involved in strawberry fruit ripening.

During my scientific career I have participated in several international and national I+D projects, and I have presented my work in more than 30 national and international conferences. I have been involved in the teaching of several practical courses: (1) UMA (120 hours) and (2) MPI and University of Tübingen (20 hours). I have been appointed as a professor in the Master de Biotecnología Avanzada provided by the UMA and Universidad Internacional de Andalucía in 2014. I have also supervised several undergraduate and PhD students and I am currently supervising a master thesis student.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2013

Nombre: **DI MEGLIO MARTELLY, THOMAS**
Referencia: RYC-2013-14018
Área Científica: Biología Fundamental y de Sistemas
Correo Electrónico: thomasdimeglio@yahoo.fr

Título:

Hox mediated control of neuronal diversity within the rhombic lip lineage and its possible consequences in medulloblastoma formation

Resumen de la Memoria:

My research career has been focused in understanding the molecular mechanisms that orchestrate neuronal migration in vertebrates, focusing on the rhombic lip (RL). The RL span the entire dorsal hindbrain and is composed of precursor cells that give raise to a stream of rostro-caudally and tangentially migrating cell populations, fated to become, within a defined sequence, cerebellar, cochlear, and precerebellar neurons. During my thesis I worked on the migration of precerebellar population revealing that the spatial origin of restricted pools of RL progenitors is maintained in the migrating post-mitotic neurons by the combinatorial expression of specific classes of Hox transcription factors (TFs). These TFs in turn confer the precerebellar neurons with the appropriate response to environmental cues, controlling at the same time the expression of guidance molecules and their receptors. Spatio-temporal integration of these intrinsic and extrinsic mechanisms controls neuronal migration along stereotyped pathway.
During my postdoctoral training, we demonstrated that Ezh2 dependent epigenetic regulation orchestrates the complex migratory behaviour of RL derivatives by differentially regulating the expression of the Hox transcriptional code. Indeed we showed that Ezh2, a histone methyl-transferase at Lysine 27 (H3K27me3) belonging to the Polycomb Repressive Complex (PRC) 2, restrict the spatial expression of Hox paralog groups (PG) 4 and 5 of posterior precerebellar RL precursors. This restriction impacts on the migratory behaviour of their derivative by changing their signalling properties.
The leading hypothesis for my on-going project, based on strong preliminary results, is that PRC2-dependent regulation of a transcriptional program implicating the TF Otx2 could be responsible of restricting the late expression of Hox PG2 to precerebellar RL. This regulation in turn should directly influence the differential response of RL derivatives to Shh mitogenic activity. In this context, Hox PG2 activity should have an anti-tumoral role in the different Otx2 or Shh dependent medulloblastomas that are among the most aggressive types of juvenile tumors.

Recommended reference: Constantino Sotelo

Resumen del Currículum Vitae:

After the two first years at the Paris VII University studying general cellular biology, I enroll in the Master of the "Ecole Nomale Supérieure de Paris", a highly selective and advanced program comprehensive of biochemistry formation, a research program in developmental biology (first year) and neuroscience (second year). During this period, I had the opportunity of performing a rotation in different labs that gave me a flavor of different research topics. This convinced me to pursue my career in Developmental Neurobiology.
I joined Dr Alain Chédotal's laboratory at the UMR7102 (Paris VI, France) and soon after was awarded with a Fellowship from the French Education Minister (three years) to undertake my Ph.D. The outcome of my PhD research developed in three years and three months was published in 6 papers (Plos Biology, J. Neuroscience; Cerebellar cortex) and a review published in a French Journal. In parallel, to my PhD research, I was appointed as an Assistant Professor at the University Paris VI to teach Cellular biology and Genetic regulation (License level, 50 h /year).
Following this period I joined Prof. F. Rijli's lab at the FMI (Basel, Switzerland) and I undertook a project on the epigenetic and transcriptional control of neuronal migration with the support of an EMBO Postdoctoral Fellowships (two years) obtained in a competitive call. The bulk of my postdoctoral work has been recently published in Science. I also co-authored two other studies, one of which is already published (J. Neuroscience) whereas the other is in preparation.
I recently joined the laboratory of Prof. P. Bovolenta (CBMSO, Madrid), who gave me the opportunity to lead my own research project within her group. During this period I already accumulated very encouraging preliminary data that are at the basis of the project I present in this call and that will give me the opportunity to begin my independent research carrier.
During my training period I had the opportunity to acquire technical skills in embryology applied to genetically engineered mouse lines, including immunohistochemistry and in situ hybridization, axon tracing (Dye and viral vectors), in utero electroporation, co-cultures in collagen matrix or organotypic cultures of the brain, confocal, bi-photon and time-lapse microscopy. I also acquired knowledge of epigenetic and transcriptional regulation applied to neuronal specification, migration and connectivity, which gave me the opportunity to co-author a book chapter on "Transcriptional regulation of tangential neuronal migration" (Elsevier).
The additional skills I acquired during my eight years of research experiences include the capacity of initiating research projects from scratch, defining the hypothesis and specific goals, analysing the results with a broad perspective and undertaking relevant international

collaborations when needed. I also acquired written, editorial and public speaking skills. This aspect was particularly favoured by my experience in teaching to students at different levels (undergraduate to doctorate) and presenting results at international conferences. I am a hard working person with a great enthusiasm, persuasive force and excellent communication skills. I therefore consider that I have all the technical and intellectual expertise needed to successfully undertake the research program presented in this application.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2013

Nombre: **CABRERA SOLA, MARGARITA**
Referencia: RYC-2013-12858
Área Científica: Biología Fundamental y de Sistemas
Correo Electrónico: margarita.cabrera@t-online.de

Título:

Regulación del tráfico intracelular de proteínas

Resumen de la Memoria:

I pursued my undergraduate studies (1994-1999) in the Faculty of Biology, University of Seville. During the last two years of my studies, I was intern student in the Department of Microbiology, where I had the opportunity to learn the basic techniques in molecular biology and microbiology.

After obtaining my Biology degree in 1999, I joined the group of Prof. Josefina Hidalgo and Angel Velasco in the Department of Cell Biology of the University of Seville. During the PhD period my research was focused on the study of protein quality control mechanisms, in particular the protein retrieval from the Golgi complex and the biogenesis of this organelle. The results associated with this study indicated that protein kinase A (PKA) plays a crucial role in both processes. The retrograde transport between Golgi and endoplasmic reticulum (ER) depends on the transport vesicle coat (COPI) and the KDEL receptor, which recognizes the escaped ER proteins (chaperones and misfolded proteins). My first study showed that the KDEL receptor is a substrate of PKA that requires phosphorylation for interaction with COPI and transport to ER. My second work was focused in the association of PKA with Golgi membranes and how this kinase controls Golgi architecture. We found that PKA is required for maintaining the characteristic Golgi structure and for its reassembly upon Golgi disruption.

After my thesis dissertation and my work as assistant professor, I decided to extend my knowledge in the protein trafficking field and joined in 2006 the group of Prof. Christian Ungermann in the Department of Biochemistry, University of Osnabrück. During my postdoc period, I examined the protein complexes and Rab GTPases involved in membrane tethering and fusion. These processes are essential in the transfer of proteins and lipids between organelles. Using yeast as eukaryotic model system I first studied the regulation of the tethering complex HOPS that mediates the fusion of late endosomes with the vacuole, the equivalent to the mammalian lysosome. My work showed that the phosphorylation of the HOPS subunit Vps41 controls its localization to endosomes and therefore the timing of membrane fusion. In the next study we identified a membrane curvature sensor motif within the phosphorylation site of Vps41 linking for first time membrane curvature sensing and phosphorylation.

A second focus of my postdoc work was the transition from early to late endosomes during endocytosis. This process is triggered by the Rab GTPase conversion from Vps21- to Ypt7-positive endosomes. Our findings uncovered two novel players involved in endosome maturation: the BLOC-1 complex required for the release of Vps21 from maturing endosomes and the Mon1-Ccz1 complex that is able to activate Ypt7, the next Rab along the endocytic pathway.

Recently we identified a novel contact site between mitochondria and vacuoles, which is mediated by the Rab Ypt7 and its binding partner the HOPS subunit Vps39. The assembly of this contact site is controlled by phosphorylation of Vps39 and depends on the growth conditions. Future studies are necessary to reveal the entire composition and functions of these membrane contacts in yeast and higher eukaryotes.

Resumen del Currículum Vitae:

I obtained my Biology degree with special award in 1999 (Faculty of Biology, University of Seville). I received a collaboration fellowship by the Spanish Ministry of Education and Culture during the last year of my undergraduate studies and a FPI fellowship by the Spanish Ministry of Education and Science during my PhD period. My postdoc research was initially supported by two fellowships from Ramon Areces and German Research foundations.

The results of my PhD work are included in two publications: Cabrera et al. 2003; Mol Biol Cell 14: 4114-25 and Bejarano*, Cabrera* et al. 2006; J Cell Sci 119:3764-75 (*equal contribution).

The findings of my initial postdoc research are part of three articles: Cabrera et al. 2009; Mol Biol Cell 20:1937-48, Cabrera et al. 2010; J Cell Biol 191:845-59, Nordmann*, Cabrera* et al. 2010; Curr Biol 20:1654-9 (*equal contribution). Last year I published three articles as corresponding author: Cabrera et al. 2013; J Biol Chem 288:5166-75, John Peter et al. 2013; J Cell Biol 201:97-111 and Cabrera and Ungermann 2013; J Biol Chem 288:28704-12. My last research work has been accepted for publication recently: Cabrera et al. J Cell Sci, in press.

I published two article reviews: Cabrera and Ungermann, 2010; Cell 141:404-6 and Peplowska, Cabrera and Ungermann 2008; Nat Cell Biol. 10:759-61, a methods review: Cabrera and Ungermann 2008; Methods Enzymol 481:177-96 and a book chapter as last author: Nordmann, Ungermann and Cabrera 2012; Bentham e Books 10:132-143.

I had the opportunity to discuss my findings in several meetings organized by the European Life Science Organization (ELSO), the European Molecular Biology Organization (EMBO), the American Society for Cell Biology (ASCB) and the Federation of European Biochemical

Societies (FEBS) among others.
During my PhD in the Department of Cell Biology of the University of Seville I supervised practical courses and after my thesis dissertation I worked as assistant professor. During my Postdoc in the Department of Biochemistry of the University of Osnabrück I supervised two practical, two Bachelor and three Master students in their end of course projects.
My publications were crucial for obtaining a significant support from the Collaborative Research Center (SFB 944) that started in 2011. This program provided 8,5 million euro funding for 15 research groups at the University of Osnabrück and Münster. This action enabled the collaboration between groups of different disciplines (genetics, biophysics, cell biology) and faculties (Physics and Biology) with a common interest in the assembly and functions of proteins and lipids microcompartments.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2013

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

Nombre: **GUTIERREZ GUTIERREZ, LAURA**
Referencia: RYC-2013-12587
Área Científica: Biología Fundamental y de Sistemas
Correo Electrónico: l.gutierrez@me.com

Título:

Hematopoietic lineage differentiation in health and disease.

Resumen de la Memoria:

During my PhD period at the ErasmusMC I developed interest on hematopoietic lineage differentiation with an emphasis on transcriptional regulation. I was then focused on Gata1 function on erythroid and dendritic cells (DC), research that gave rise to my first independent project, which was awarded with a VENI grant. In particular, after describing that Gata1 is expressed in DC, we discovered in collaboration with Anna Rita Migliaccio that the transcription of Gata1 in DC is regulated by different hypersensitive sites at the Gata1 promoter, depending on the DC subtype/maturation stage. We have identified interleukins that affect Gata1 expression in human and mouse DC, and characterized the Gata1 and PU1 interactome and transcriptome by using mass spectrometry analysis, ChIPseq and RNAseq technology coupled to in vivo loss of function studies, material that is being prepared for submission. A number of projects arose as a result of fruitful collaborations with a number of researchers, who contacted me for my expertise on erythro/hematopoiesis. Examples are my contribution to a very important study that identified KLF1 as a regulator of haemoglobin switching (Prof. J. Philipsen, Prof. G. Patrinos) and derived studies that confirmed another potential regulator, which is being prepared for submission. Another study highlighted the importance of orchestrated protein degradation during erythroid differentiation (W. Vermeulen, J. Mitchell, S. Bergink). In collaboration with Dr. N. Galjart, we defined the requirement of CLASP2 for HSC homing, turnover and commitment and differentiation. Derived from these studies and my own observations I have started a new project in which we study the CLASP2-dependent mechanisms of cKit and cMpl receptor trafficking. I have contributed to the study originated in Dr. Nolte's lab, where we have identified the transcriptional axis leading to a erythropoietic defect in CD70Tg mice, a mouse model of chronic sterile inflammation. At Sanquin, I am in charge of developing the platelets group. Since 2010 we have developed a novel flow cytometry based platelet aggregation test, that can be used to assess the function of platelets using very low numbers and in a receptor-wise manner, which has been successfully applied to study the function of platelets in transgenic mice and patients. We have built in our lab expertise on the characterisation of platelet function and megakaryopoiesis (mouse and human) and these resources allow us to engage into new studies, a number of them are currently being submitted for publication or in preparation. I am currently interested on megakaryopoiesis and platelet function in health and disease, and pathophysiology of platelet transfusion.

Resumen del Currículum Vitae:

Positions:
1 Junior group leader, Sanquin Research, Amsterdam - since 2010.
2 Postdoc, ErasmusMC, Rotterdam - 2005-2010.
3 PhD student, ErasmusMC, Rotterdam - 2000-2005.
4 Master student, ErasmusMC, Rotterdam - 2000, 6 months.
5 PhD student, Faculty of Biology, Oviedo - 1998, 1 year, not finished.
6 Master student, Asturias Transfusion Centre (Centro Comunitario de Transfusion del Principado de Asturias) - 1998, 3 months.
7 Predoctoral student, Faculty of Biology, Oviedo - 1997, 9 months - part time.

Thesis defence: 29th June 2005

Publications:
1 Sabrina Zeddies; Iris M. De Cuyper; Pieter F. van der Meer; Brunette B. Daal; Dirk de Korte; Daphne Thijssen-Timmer; Laura Gutiérrez. Pathogen reduction treatment using riboflavin and ultraviolet light impairs platelet reactivity towards specific agonists in vitro. Transfusion, in press. 2014.
2 I.M. De Cuyper; M. Meinders; E. van de Vijver; D. de Korte; L. Porcelijn; M. de Haas; J.A. Eble; K. Seeger; S. Rutella; D. Pagliara; T.W. Kuijpers; A.J. Verhoeven; T.K. van den Berg; L. Gutiérrez. A novel flow cytometry-based platelet aggregation assay. Blood. 2013.
3 S. Bergink; A. Theil; W. Toussaint; T. Clapes; R. van der Linden; J.A. Demmers; J.A. Marteijn; I.M. De Cuyper; T. van Gent; C. Robin; S. Philipsen; W. Vermeulen; J. Mitchell; L. Gutiérrez. Erythropoietic defect associated with reduced cell proliferation in mice lacking the 26S proteasome shuttling factor Rad23b. Mol Cell Biol. 2013.
4 R. Fujita; M. Takayama-Tsujimoto; H. Satoh; L. Gutiérrez; H. Aburatani; S. Fujii; A. Sarai; E.H. Bresnick; M. Yamamoto; H. Motohashi. NF-E2 p45 Is Important for Establishing Normal Function of Platelets. Mol Cell Biol. 2013.

5 P. Papadopoulos; L. Gutiérrez; R. van der Linden; J. Kong-A-San; A. Maas; D. Drabek; G.P. Patrinos; S. Philipsen; F. Grosveld. A Dual Reporter Mouse Model of the Human b-Globin Locus: Applications and Limitations. Plos One. 2012.

6 E. van de Vijver; I.M. De Cuyper; A.J. Gerrits; A.J. Verhoeven; K. Seeger; L. Gutiérrez; T.K. van den Berg; T.W. Kuijpers. Defects in Glanzmann thrombasthenia and LAD-III (LAD-1/v) syndrome: the role of integrin b1 and b3 in platelet adhesion to collagen. Blood. 2012.

7 L. Gutiérrez; K. Drabek; M. Vermeij; T. Clapes; S.R. Patel; J.C. Boisset; J. van Haren; A.L. Pereira; Z. Liu; U. Akinci; T. Nikolic; W. van IJcken; M. van den Hout; M. Meinders; C. Melo; C. Sambade; D. Drabek; R.W. Hendriks; S. Philipsen; M. Mommaas; F. Grosveld; H. Maiato; J.E. Italiano Jr; C. Robin; N. Galjart. The microtubule plus-end tracking protein CLASP2 is required for hematopoiesis and hematopoietic stem cell maintenance. Cell Reports. 2012.

8 L. Gutiérrez; S.F. Libregts; A.M. de Bruin; F.M. Wensveen; P. Papadopoulos; W. van IJcken; Z. Ozgür; S. Philipsen; M.A. Nolte. Chronic IFNgamma production in mice induces anemia by reducing erythrocyte lifespan and inhibiting erythropoiesis through an IRF1/PU1-axis. Blood. 2011.

9 J. Borg; P. Papadopoulos; M. Georgitsi; L. Gutiérrez; G. Grech; P. Fanis; M. Phylactides; A.J.M.H. Verkerk; P.J. van der Spek; C.A. Scerri; W. Cassar; R. Galdies; W. van IJcken; Z. Ozgür; N. Gillemans; J. Hou; M. Bugeja; F.G. Grosveld; M. von Lindern; A.E. Felice; G.P. Patrinos; S. Philipsen. Haploinsufficiency for the erythroid transcription factor KLF1 causes Hereditary Persistence of Fetal Hemoglobin. Nature Genetics. 2010.