# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

**Nombre:** KRIEG , MICHAEL
**Referencia:** RYC-2016-21062
**Área Científica:** Biología Fundamental y de Sistemas
**Correo Electrónico:** michael.krieg@icfo.eu

**Título:**

Neurophotonics and mechanical systems biology

**Resumen de la Memoria:**

My research at the interface between cell biology, biophysics and engineering sciences focuses on the study of cell mechanics in living organisms. My group uses novel genetic tools, optogenetic and emerging imaging techniques to non-invasively interrogate how protein and cell mechanics determines complex behaviors in freely moving animals. In addition, my group takes advantage of sophisticated nanotechnological metrology and modern computational models of cells and tissues to provide mechanistic insight how cell mechanics influences physiological processes (embryonic development, sensory function) and pathological transformation (cancer, neurodegeneration).

During my doctoral and postdoctoral work I acquired a solid experience in cell mechanics and have worked on several important lines in this field. My work as a PhD student culminated in a research article in Nature Cell Biology disrupting the differential adhesion hypothesis as a driving force for germ layer segregation during embryonic development in vertebrates. These results have implications beyond embryonic development but propose fundamental biophysical mechanism of cancer metastasis, in particular how cell separate and form new tissues. I collaborated with industry to develop an AFM suitable for measuring cell-cell adhesion forces with single molecule resolution and applied this instrument to previously technically intractable problems. The results of my PhD were disseminated in 12 peer-reviewed publications in some of the most prestigious magazines and contributed to a state-of-the-art commercial product for cell adhesion measurements (JPK Instruments, CellHesion). At the end I was awarded with one of the most prestigious science prices in Europe, the Studienpreis of the Koerberfoundation, which is annually given by the German President of the parliament to 3 visionary PhD theses.

For my postdoc, I moved to Stanford University where I worked in the interface between neurobiology and engineering to provide further insight in the fundamental aspects of mechanosensation and mechanoprotection. I recieved a prestigious HFSP Long-Term Fellowship and secured a highly competitive K99 Pathway to Independence award from the National Institute of health to pursue my science as a postdoc and a principle investigator. The tools I developed at Stanford sparked a wide interest, which I shared with 15+ groups in 10 different countries all over the world. With my unique focus in mechanobiology and understanding of biophysical principles of mechanosignaling, I had the opportunity to engage in many national and international collaboration. In total, I published 17 research article and 3 reviews in prestigious peer review journals (9 first and 3 corresponding author), which were cited more than 1400 times.

As a principle investigator at Stanford and with the support of NIH research grant, I assembled a team of engineers, physicists and biologists to develop and deploy new microfluidic devices to investigate mechanosensation. This device thus fills a gap in the current field allowing a precise micromanipulation of genetic model organisms.

At my own group at ICFO and the support of an ERC starting grant (Mechanosystems 715243) I will deepen our understanding how cells sense mechanical forces and how mechanics contributes to pathological changes of the nervous system during age and diseases.

**Resumen del Currículum Vitae:**

I studied biology at the University of Kassel with main subject cell biology and nanotechnology, where I enjoyed intensive, hands-on course works in various affiliated labs and internships at the MPI-Biophysics, the MPI for solid state research and the MPI of Cell Biology and Genetics. During my final master exams, I got tested in physics, cell biology and genetics as one of the best of my year.

During my Master's thesis at the Biotechnological center of the TU-Dresden, I collaborated with JPK Instruments to develop an atomic force microscope (AFM) that can be used to routinely perform cell adhesion measurements with single molecule resolution. Specifically, I tested the AFM prototype, developed strategies for substrate preparation and developed procedures to analyze experimental data. I applied this assay to the biophysical principles of zebrafish development. This led to a robust application of AFM in cell biology, publications in the Journal of Cell Sciences and Developmental Cell and a state-of-the-art commercial product for cell adhesion measurements with single molecule resolution.

With the support of a PhD fellowship of the Boehringer Ingelheim Fonds during my PhD at the MPI for Cell Biology and Genetics (MPI-CBG, Dresden), I modified this assay to measure cell-cell adhesion and cell mechanics to challenge a central paradigm in developmental biology: the differential adhesion hypothesis. Moreover, I was able to apply this assay to various other biological questions that were technically intractable at that time. I published 12 papers in total and counted two oral presentations at international conferences during that time.

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

My doctoral thesis was honored with a summa cum laude and were awarded by two postdoctoral fellowships (HFPS and Life Sciences Research Foundation, declined) and the German Study Award, annually given by the german president of the parliament to three visionary PhD theses.

For my postdoctoral research, I aimed to apply my expertise in mechanobiology to questions about the neurobiological mechanisms underlying physiology and behavior. I developed tools to measure forces on mechanosensory neurons in a multicellular organism, Caenorhabditis elegans. I used these tools to dissect the biomechanical processes mediating responses to touch and its foundations to neuronal mechanoprotection. This work constitutes the first example of a force measurement in a living organism. As a postdoc, I served on review committee and was an elected chair of the Stanford Postdoc committee. I organized the first BayArea Mechanobiology meeting and attracted sponsors and helped to assemble the scientific program. During my postdoctoral work I published 8 research papers and have given 18 oral presentations as an invited speaker at international meetings and conferences and received 8 awards in total including the best postdoc award from the American society of mechanical engineers.

My career culminated in an NIH K99 Pathway to Independence award, one of the most prestigious grants given to senior postdoc in the US with the aim to facilitate a streamlined transition into an independent research career. In 2017, I start my own lab at the ICFO  The Institute of Photonic Sciences as a tenure track group leader with the support of an ERC starting grant.

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

**Nombre:** MAESO MARTIN, IGNACIO
**Referencia:** RYC-2016-20089
**Área Científica:** Biología Fundamental y de Sistemas
**Correo Electrónico:** nacho.maeso@gmail.com

**Título:**

Cis-Regulatory Landscapes in Animal Development and Evolution

**Resumen de la Memoria:**

Since I started my scientific career, I have been investigating the complex interplay between the evolution of genomic organization and transcriptional regulation during development, aiming to understand the genetic changes responsible for the astonishing morphological diversity of the animal kingdom.

I started my career working as an undergrad at the Universidad Complutense, with a solid training in Molecular Biology, and then at the Aarhus Universitet in Denmark, where I acquired my first international research experience and knowledge on vertebrate development.

I then moved to the Universitat de Barcelona, obtaining a FPU fellowship to do my PhD under the supervision of Prof. Jordi García-Fernàndez. My studies showed that the evolutionary conservation of cis-regulatory elements can be much deeper than previously thought and that long-range regulatory interactions are major selective constraints for the evolution of genomic organization in animals. With these works I already started my main future research line and developed my own projects, with an article as co-corresponding and co-first author in Genome Res plus 4 other articles as joined first author, including a PNAS.

As a postdoctoral researcher in the lab of Prof. Peter Holland at the University of Oxford, I worked within an ERC-funded grant to study the evolutionary mechanisms underlying the origin and functional diversification of homeobox transcription factors. My findings uncovered novel homeobox transcription factors that are only active during early preimplantation stages, when cells are still totipotent. These genes are specific to placental mammals and by studying their origin I was able to investigate the asymmetric evolution of gene duplicates, an important but previously neglected phenomenon. This project, published in BMC Biology, allowed me to study the evolution of cis-regulatory elements from the perspective of the transcription factor proteins regulating them, complementing my previous work. Furthermore, I acquired experience in managing intellectual property rights and technology transfer, with a filed patent as a co-inventor.

I then obtained a Juan de la Cierva fellowship to continue my career in the group of Prof. Gómez-Skarmeta in the CABD in Seville, where I conceived and I designed my current research projects. The research program I developed was awarded with a Marie Sklodowska-Curie Actions grant, within the highly competitive H2020-MSCA-IEF call. With this project I am investigating how changes in the 3D chromatin organization of the cis-regulatory landscapes of developmental genes have shaped the evolution of gene expression, developmental processes and animal morphology. The outcomes of this works will have a high impact, as I have recently shown with the publication of a Nature Genetics paper as co-corresponding author.

Finally, thanks to my solid multidisciplinary trajectory on genomics, developmental biology and gene regulation, I have been invited to give 11 conferences in different courses, meetings and institutions worldwide. Furthermore, since November 2016 I am supervising the PhD of David Ricote Hernández.

Thus, after 13 years of experience, I have attained a position of professional maturity that together with my current research lines and projects will set the grounds to continue my independent career as a Ramón y Cajal researcher.

**Resumen del Currículum Vitae:**

EDUCATION:
2010 PhD in Genetics by the Universitat de Barcelona, Spain.
2007 Master in Genetics (Diploma de Estudios Avanzados) by the Universitat of Barcelona, Spain.
2005 Degree in Biology, Genetics Speciality, by the Universidad Complutense de Madrid, Spain.

POSITIONS:
May/2014- present: MSCA IEF Post-doctoral fellow (1/2016-present), Centro Andaluz de Biología del Desarrollo (CABD), CSIC/UPO, Seville
May/2014-Dec/2015: Juan de la Cierva Post-doctoral fellow, Centro Andaluz de Biología del Desarrollo (CABD), CSIC/UPO, Seville
Jun./2011-Apr/2014: Post-doctoral research assistant in an ERC project, University of Oxford, Department of Zoology, Oxford (UK)
Nov./2005-Nov./2010 FPU PhD student at the Universitat de Barcelona, Department of Genetics, Barcelona
Dec./2003-Aug./2004 Undergrad Erasmus intern student at the Universidad Complutense de Madrid
Sep./2004-Jul./2005 Undergrad Erasmus intern student at the Aarhus Universitet (Denmark)

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

PUBLICATIONS & INDICATORS OF SCIENTIFIC PRODUCTION:
28 publications (18 articles, 9 reviews and commentaries, 1 book chapter), 12 of them as first or joined first author (including PNAS, Genome Res, Mol Biol Evol and BMC Biol) and in 5 of them as corresponding or co-corresponding author (in Nat Genet, Genome Res and 3 reviews in BioEssays, Curr Opin Genet Dev and Semin Cell Dev Biol).
Total citations: 601
h-index: 15
Publications in Q1: 26 out of 27
Impact Factor of the publications: 1 Nature Genet. (IF 31,6); 2 PNAS (IF 9,4) ; 4 Mol. Biol. Evol. (IF 13,6); 2 Genome Res. (IF 11,3); 1 Trends Genet. (IF 9,8); 1 Curr. Biol. (IF 8,9); 2 BMC Biol. (IF 6,9); 2 Phil. Trans. R. Soc. B-Biol. Sci. (5,8); 1 Curr. Opin. Genet. Dev. (IF 5,7); 2 Sci Rep (IF 5,2); 1 Semin. Cell Dev. Biol. (IF 5,1); 1 BioEssays (IF 4,7); 1 Wiley Interdiscip. Rev.-Dev. Biol. (IF 4,7); 2 Genome Biol. Evol. (IF 4,0); 4 publications in Heredity, EvoDevo, J. Exp. Zool. Part B, Int. J. Dev. Biol. (IFs 3,8 to 1,7)

PARTICPATION IN I+D+i PROJECTS
I have worked in 10 funded projects, including 5 international projects.

FELLOWSHIPS AND FUNDING:
FPU PhD fellowship of the Spanish Ministry of Science.
Juan de la Cierva Postdoctoral fellowship (Spanish Ministry of Economy and Competitiveness)
EMBO Short-Term Fellowship
Marie Sklodowska-Curie-IEF Fellowship, H2020-MSCA-IF-2014_ST call (158.122 )

SUPERVISION OF GRADUATE STUDENTS:

| | |
|---|---|
| Nov./2016  present | PhD supervisor of David Ricote Hernández. |
| Mar./2010-Nov./2010 | Co-supervision of the master student Stéphanie Correia de Matos David Bosne. |

PATENTS:
Co-inventor in the Patent application GB1613078.3, filed 28/7/16: Stem cells and cancer

CONTRIBUTIONS TO SCIENTIFIC MEETINGS AND INVITED TALKS
11 Invited Talks
14 contributions (10 posters and 4 oral contributions) in 15 national and international meetings

REFEREE WORK:
I have performed reviewer duties for the following journals: Genome Research, BioEssays, Molecular Biology and Evolution, Genome Biology and Evolution, Frontiers in Ecology and Evolution, PlosONE, Seminars in Cell and Developmental Biology, International Journal of Biological Sciences

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

**Nombre:** MARTINEZ MARTIN, NURIA
**Referencia:** RYC-2016-20173
**Área Científica:** Biología Fundamental y de Sistemas
**Correo Electrónico:** numarmar@gmail.com

**Título:**

Lymphocytes, polarity and autophagy.

**Resumen de la Memoria:**

Since 2007 I have developed an important knowledge in cell biology and immunology along two different stages, first as a PhD student in Dr. Alarcon¿s laboratory and second as a postdoctoral fellow in Dr. Batista¿s laboratory. Both groups offer an outstanding research environment that allowed me to gain expertise in a broad range of multidisciplinary techniques and to achieve important milestones such as the publication of papers in high impact journals as a first author in both stages and even as a co-corresponding author in the last one.
In my predoctoral stage, I worked with T lymphocytes and I published, among others, three peer-reviews papers (Nature immunology, Science Signalling and Immunity), in two of which I was first author. This successful period was recognized with two different awards to the Best Thesis in Molecular Biology (2010-2011) and later on with two important European grants (EMBO long-term fellowship and the Marie Curie Intra-European fellowship).
In my postdoctoral stage I continued in the immunology field but this time focusing my work in B lymphocytes. Some of my contributions were published in two papers (Science and Journal Experimental Medicine) in which I appeared as a co-author. However, my biggest effort was invested in leading a project focused on autophagy. The findings of this work are not only important for the immunology field, also revealed important aspects of autophagy, which are relevant for a broad range of areas. This work was published in Science and I am first and co-corresponding author
Furthermore, I am co-first author in two other manuscripts (under revision in Science Signaling and submitted to Nature Immunology) that will be potentially published this year.
My theoretical or technical contributions to the autophagy field are likely to be extrapolated to many other biological systems. In this regard, my next research stage will be focused on understanding the role of autophagy in a particular set of cells enrich in lysosomal degradation of the intestine (lysosome rich enterocytes, LRE). The role of autophagy in these cells, which are highly involved in the nutritive capacity of the intestine, is still unknown.

**Resumen del Currículum Vitae:**

I started my research career after accomplishing my B.S in Biochemistry at the University of Valencia. Since then, I have mainly gained experience in two of the most pre-eminent immunology laboratories such as Dr. Alarcon¿s laboratory (2007-2011) and Dr. Batista¿s laboratory (2011-2016) as a PhD student and as a postdoctoral fellow respectively. Along these years I have been granted with different important scholarships and grants such as the predoctoral fellowship from the Spanish Ministry of Education (2006-2010), EMBO long-term fellowship (2012-2014) and Marie Curie Intra-European fellowship (2014-2016).
Along this time I have developed and lead different projects focused on how the immune system works. I have done this from a cell biology point of view but also analysing the physiology of the immune response in murine models. All the projects necessitated a multidisciplinary experimental approach, involving a wide range of biochemical and molecular biology techniques, culture/cell isolation techniques, flow cytometry, confocal and electron microscopy and animal handling to study T and B cell development and activation in vivo.
The publication of my research in a number of high impact publication such as Nature Immunology, Immunity and Science among others, in both of my stages as a researcher, provides an excellent illustration of my capacity for rapid acquisition of new knowledge and the ability to apply this to address pertinent and interesting scientific questions effectively.

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

**Nombre:** FORESTI , OMBRETTA
**Referencia:** RYC-2016-20919
**Área Científica:** Biología Fundamental y de Sistemas
**Correo Electrónico:** OmbrettaForesti@gmail.com

**Título:**

Molecular Mechanisms of the Secretory Pathway

**Resumen de la Memoria:**

My main research interest is to elucidate the molecular mechanisms of essential processes of the secretory pathway. While completing a Biotechnology degree in Milan (Italy), I worked in the laboratory of Dr Alessandro Vitale at the CNR. There, I studied the recognition properties and activity of the chaperon BiP, an essential component of the protein quality control system of the endoplasmic reticulum (ER) (Foresti et al., Plant Cell, 2003; Foresti et al., Molecular Plant, 2008).
To continue to investigate the secretory pathway, I joined the group of Prof Jürgen Denecke at the University of Leeds (UK). My PhD was supported by a Marie Curie Fellowship and the project was part of a European Research Training Network. My research focused on the process of protein delivery to the vacuole. First, I identified the SNARE protein SYP21 as an essential element for this branch of the secretory pathway and I characterized its role in the process of vesicle targeting to the prevacuolar compartment (Foresti and Denecke Traffic, 2008; Foresti et al., Plant Cell, 2006). Then, as a post-doctoral fellow funded by BBSRC, I identified the signals that mediate the anterograde and retrograde transport of the plant vacuolar sorting receptor BP80 (DaSilva, Foresti et al., Plant Cell, 2006; Foresti et al., Plant Cell, 2010).
In 2011, I joined the group of Dr Pedro Carvalho at the Centre for Genomic Regulation (CRG) in Barcelona, Spain. My work was supported by an International Early Career Award from the Howard Hughes Medical Institute (HHMI) and a grant of the Spanish MCCIN. My project focused on the elimination of damaged or unwanted proteins from the gateway of the secretory pathway, through ER associated degradation (ERAD). This process can also promote degradation of folded functional ER proteins in a highly-regulated manner (Ruggiano, Foresti et al., J Cell Biol, 2014). Indeed, I showed that a key enzyme in the sterol pathway, squalene monooxygenase, is selectively degraded by ERAD in response to an evolutionarily conserved feedback system (Foresti et al., eLife, 2013). Moreover, I identified a new branch of the ERAD pathway that had not been characterized before. This branch, mediated by the Asi ubiquitin ligase complex, specifically degrades proteins in the inner nuclear membrane and helps maintaining the specialized proteome of this ER subdomain (Foresti et al. Science, 2014).

**Resumen del Currículum Vitae:**

EDUCATION
2006 PhD Cell Biology - University of Leeds, Leeds, UK
2001 Bachelor□s degree Biotechnology, summa cum laude - University of Milan, Milano, Italy

WORK EXPERIENCE
2011 □2016
Senior Researcher - Centre for Genomic Regulation (CRG) Barcelona, Spain.
HHMI & MINECO funded project □ Supervisor: Dr Pedro Carvalho.
Molecular mechanisms of endoplasmic reticulum-associated protein degradation (ERAD).

2010-2011
Researcher - Institute of Molecular and Cell Biology (IMCB), University of Leeds.
Wellcome Trust fellowship - Supervisor: Dr Eric Hewitt.
The Cell Biology of Natural Killer Cells.

2006-2010
Researcher - Institute of Integrative and Comparative Biology (IICB) - University of Leeds, Leeds,UK.
BBSRC fellowship - Supervisor: Prof Jürgen Denecke.
Anterograde and retrograde transport of the plant vacuolar sorting receptor BP80.

2002-2006
PhD in Cell Biology - Faculty of Biological Sciences, University of Leeds, Leeds, UK.
Marie Curie Post-Graduate Fellowship - Supervisor: Prof Jürgen Denecke.
Characterisation of the vesicle-fusion machinery at the prevacuolar compartment in plants.

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

2001-2002
Research trainee - Faculty of Agricultural Sciences, University of Milan, Milano, Italy.
Supervisor: Prof Giuseppe Gavazzi.
Characterisation of genes involved in maize embryo development.

1999-2001
Research trainee  Istituto di Biosintesi Vegetali, CNR, Milan, Italy.  Supervisor: Dr Alessandro Vitale.
BiP recognition properties and activity in the endoplasmic reticulum.

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

**Nombre:** LUCAS GAY, MARIA JESUS
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**Correo Electrónico:** mlucas@cicbiogune.es

**Título:**

Structural biology of macromolecular complexes

**Resumen de la Memoria:**

My research activity is focused in the study of macromolecular complexes by X-ray crystallography. In order to understand the function of protein complexes is vital to know its molecular structure. Crystallography provides this precious atomic level knowledge that offers splendid insights into the molecular mechanism of action of macromolecular complexes and allows the designing of drugs that modify, activate or inhibit proteins involved in pathological processes.

Throughout my scientific career I have worked in several fields with different protein families. Thanks to excellent mentors, I have gained a solid expertise in the integrated use of macromolecular X-ray crystallography, small-angle X-ray scattering, protein biochemistry, and molecular biology. This has allowed me to have a good scientific production in all the projects I have been involved.

My research career began in the research group of Dr Fernando de la Cruz in the University of Cantabria (2000-2006) in the field of bacterial conjugation that has an important role in the spread of antibiotic resistances, in the dissemination of virulence factors and in bacterial symbiosis. I studied the structure and function of the relaxase TrwC of plasmid R388, responsible for the initiation and termination of DNA transfer in bacterial conjugation.

My enthusiasm for structural biology led me to carry out my first postdoctoral work in CIC bioGUNE in the laboratory of Dr. Alfonso Martínez (2006-2008). I worked in the crystallization and functional characterization of CBS domains that regulate the activity of associated enzymatic and transporter domains in response to binding to adenosyl molecules.

I continued my scientific career abroad in the laboratory of Dr. Karl-Peter Hopfner in the University of Munich LMU (2009-2012). I worked with the Mre11-Rad50 complex, an evolutionarily conserved protein complex fundamental for genomic stability. This complex functions in the detection and repair of DNA double strand breaks, highly genotoxic lesions linked to cancer development.

At the beginning of 2012 I returned to the research center CIC bioGUNE as a postdoctoral researcher to the group of Dr. Aitor Hierro. I studied how virulence factors are regulated within host cells and how their activity is directed toward a particular host cell compartment. We elucidated the precise link between the catalytic activity of a phospholipase from Legionella pneumophila and its endosomal localisation during infection.

Nowadays, my main research line is the study of protein complexes involved in endosomal trafficking. I am currently leading a subgroup in the laboratory of Dr Aitor Hierro that studies the recycling of cellular receptors by the retromer complex. We have recently reported the structural mechanism of cargo recognition and membrane recruitment of retromer that has been published in the renowned journal Cell. In the future I plan to apply my expertise on a new line of research focused on the role of retromer in Alzheimer's disease. Retromer plays a central role in controlling the localization and processing of the amyloid precursor protein via interaction with sortilin and SorLA. Understanding the mechanisms of such selective recruitment should facilitate the development of new drugs, such as chemical chaperons, that stabilize this recycling pathway.

**Resumen del Currículum Vitae:**

After getting a Master□s Degree in Biochemistry from the University of the Basque Country (1994-1999) I did my PhD in the Molecular Biology program from the University of Cantabria in the research group of Dr. Fernando de la Cruz (2000-2006). During my doctoral studies I undertook a research visit of three months to the laboratory of Dr. Joel Schildbach in the Johns Hopkins University (Baltimore, USA). After graduating with a distinction cum laude as a doctorate I did my first postdoctoral work in CIC bioGUNE in the laboratory of Dr. Alfonso Martínez (2006-2008). I continued my scientific career abroad in the laboratory of Dr. Karl-Peter Hopfner in the University of Munich LMU (2009-2012). At the beginning of 2012 I returned to CIC bioGUNE. Since then I have been working as a postdoctoral researcher in the group of Dr. Aitor Hierro.

The results I have obtained up to now have given rise to 15 articles in JCR indexed journals and 11 communications to scientific meetings, 3 of them as invited speaker. In total, my articles have been cited 398 times and my H-index is 10. I would like to point out that I have published in high impact journals such as Cell and PNAS as first author, and Nature Structural and Molecular Biology and EMBO Journal as second author.

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

My most relevant publications are:

Guasch A, Lucas M, Moncalian G, Cabezas M, Perez-Luque R, Gomis-Ruth FX, de La Cruz F & Coll M. Recognition and processing of the origin of transfer DNA by conjugative relaxase TrwC. Nature Struct Biol. 2003; 10:1002-10.

Gonzalez-Perez B, Lucas M, Cooke LA, Vyle JS, de la Cruz F, Moncalián G. Analysis of DNA processing reactions in bacterial conjugation by using suicide oligonucleotides. EMBO J. 2007; 26:3847-57.

Lammens K, Bemeleit DJ, Möckel C, Clausing E, Schele A, Hartung S, Schiller CB, Lucas M, Angermüller C, Söding J, Sträßer K and Hopfner KP. X-ray structure of a bacterial Mre11:Rad50 complex reveals an ATP dependent molecular clamp in DNA double-strand break repair. Cell 2011; 145:54-66

Lucas M, Gaspar AH, Pallara C, Rojas AL, Fernández-Recio J, Machner MP, Hierro A. Structural basis for the recruitment and activation oft he Legionella phospholipase VipD by the host GTPase Rab5. PNAS, 2014; 111:E3514-23.

Lucas M, Gershlick DC, Vidaurrazaga A, Rojas AL, Bonifacino JS, Hierro A. Structural Mechanism for Cargo Recognition by the Retromer Complex. Cell. 2016;167:1623-1635

Throughout my scientific career I have participated in 5 R+D+I international projects and 6 R+D+I national projects funded in competitive tenders by public bodies. My research career has been funded with 3 research contracts and I have been granted with the following fellowships:

- PhD fellowship FPU from the Spanish Ministry of Education and Culture
- PhD fellowship from the Marqués de Valdecilla Foundation.
- Postdoctoral fellowship of the Basque Government.

After ten years of postdoctoral experience I am considered a senior postdoctoral researcher. I am able to write articles and grants independently. I have mentored rotation and graduate students, technicians and junior postdoctoral fellows. Besides, I am codirecting a final year thesis project. Due to my expertise I have been asked to review articles in international journals as Plasmid and Acta Crystallographica, to be part of a PhD thesis committee and also to teach in a Master of Molecular Biology and Biomedicine.

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

**Nombre:** LECONA SAGRADO, EMILIO
**Referencia:** RYC-2016-20705
**Área Científica:** Biología Fundamental y de Sistemas
**Correo Electrónico:** elecona@cnio.es

**Título:**

UBIQUITIN AND SUMO IN CHROMATIN AND CANCER

**Resumen de la Memoria:**

Throughout my career I have tried to understand the mechanisms of regulation of chromatin metabolism by post-translational modifications. During my PhD in the laboratory of Prof. Mª Antonia Lizarbe I studied how butyrate and histone deacetylase inhibitors induce differentiation and apoptosis in colon adenocarcinoma cells. I described new mechanisms of transcriptional regulation by these agents and I identified new acetylation sites regulated by butyrate. Following my interest on chromatin and epigenetics I moved to Prof. Danny Reinberg¿s lab where I carried my postdoctoral studies on the functions of Polycomb protein SCML2. During this time, I unveiled a role for SCML2 in the cell cycle progression and I dissected how SCML2 modulates the targeting and transcriptional repression exerted by the Polycomb Repressive Complex 1 (PRC1). Further, I found that SCML2 brings the protein deubiquitinase USP7 to PRC1 and induces its stabilization. Next, I joined the laboratory of Oscar Fernandez-Capetillo as part of my International Outgoing Fellowship. In the last years I have contributed to the research in the lab while I have also started my independent projects. Studying the action of USP7 as a deubiquitinase for SUMO2/3 during DNA replication, I have discovered a role for the collective SUMOylation and ubiquitination of the replisome.

In the near future I will build on these results to understand how the ubiquitination and SUMOylation of protein complexes regulate transcription, replication and repair. The analysis of the roles of ubiquitin and ubiquitin-like modifers has been hampered by the lack of good methods for their study. The development of new proteomics and the use of CRISPR has set the right conditions to approach these questions. Further, these pathways are frequently altered in cancer and constitute potential therapeutic targets to develop new anti-cancer drugs. My background in biochemistry and chromatin biology together with my expertise in cancer are a perfect match to succesfully complete this project. I propose three main lines of research:

1. Analysis of the termination of DNA replication and the role of ubiquitin and SUMO in this process.
While the initiation and the elongation of DNA replication have been widely studied, our knowledge of the mechanisms that govern termination and disassembly of the replisome is very limited. I aim to understand how this process is controlled and linked to the entry into mitosis.
2. Establishment of a system to study enzymes of the ubiquitin and SUMO pathways in vivo, leading to the identification of their substrates and functions.
New proteomic tools allow a better analysis of the modification of proteins by ubiquitin and SUMO. However, we do not have the right systems to directly explore the targetome of individual enzymes. I will develop a system to induce the fast degradation of enzymes, mimicking their inhibition by small molecules, in order to identify their substrates and real functions.
3. Identification of new potential therapeutic targets for cancer treatment in these pathways.
There are many alterations of the ubiquitin and SUMO pathways in cancer. I will try to exploit these alterations to identify potential targets and design new cancer treatments, also taking into account the new functions discovered in the previous experiments.

**Resumen del Currículum Vitae:**

Since I began my degree in Biochemistry I wanted to follow a career in research. I had an outstanding academic record (2nd National Award in B. Sc. Biochemistry) and I started my career in the laboratory of Prof. Mª Antonia Lizarbe in July 1999 as an undergraduate student. From that moment I have developed an internationally oriented career, I have made important contributions and achieved a very strong publication record. Recently, I have started the transition to carry out my independent research, with two papers as corresponding author and a Young Investigator Grant from the Spanish Ministry of Economy. My CV shows my potential to become fully independent.

My career has been shaped by the different environments I have been working in. First, I obtained my PhD under the supervision of Mª Antonia Lizarbe and Nieves Olmo in the Complutense University of Madrid . This was a small lab focused on the formation of PhD students, where I learnt all the basic knowledge to design, carry out and analyze my experiments. For my postdoctoral training I moved to the laboratory of Prof. Danny Reinberg at NYU School of Medicine in New York, one of the best groups in the fields of transcription, chromatin and epigenetics, where I acquired a strong expertise in biochemistry. This is a very competitive lab, institution and field, where I started to gain independency in my research. During this time I was awarded an International Outgoing Fellowship (IOF) from the European Union, with a return phase in the group of Oscar Fernández-Capetillo in the Spanish National Cancer Research Centre. This lab has constituted the perfect environment for my transition to become an independent researcher and also to complement my biochemistry background with

**AYUDAS RAMÓN Y CAJAL**
**CONVOCATORIA 2016**

**Turno de acceso general**

an expertise in cancer and DNA replication.

I have been very productive at all the stages of my career, publishing 26 papers (10 first author, 2 corresponding author, 428 citations and h-index: 12) and making important contributions in different areas of chromatin metabolism. During my PhD, I described a new mode of regulation of gene transcription by histone deacetylase inhibitors. In my postdoctoral studies I revealed, for the first time, an interplay between the Polycomb machinery and the cell cycle, and I also described how non-coding RNA bind to SCML2 and regulate the action of the Polycomb Repressive Complex 1. After my return to Spain, I discovered a role for USP7 as a SUMO deubiquitinase acting in DNA replication, and I have proposed a function for the collective SUMOylation in the termination of DNA replication. I have given several talks at international meetings and seminars at research institutions. I have received 2 awards for my academic track and 3 awards for my PhD work. I have secured my own funding for most of my career, obatining very competitive Fellowships, including the IOF from the Marie Curie Actions. I have developed a very international career, working in the laboratory of Prof. Flower in London during my PhD, staying for 5 years in the Reinberg lab, and through the International Outgoing Fellowship from the Marie Curie Actions. I have been involved in teaching and outreach activities, I have supervised two students in the past and I am currently supervising two more students. Finally, I have a Young Investigator Fellowship as a Principal Investigator and I have another application to the AECC Ideas Semilla under review, supporting my potential to become a PI.

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

**Nombre:** GONZALEZ GUZMAN, MIGUEL
**Referencia:** RYC-2016-19325
**Área Científica:** Biología Fundamental y de Sistemas
**Correo Electrónico:** migonguz@cib.csic.es

**Título:**

Hormone signalling steering plant stress tolerance

**Resumen de la Memoria:**

My research interests are focused on understanding molecular mechanisms steeringl plant stress adaptive responses. These plant stress responses are controlled by the fine tuning interaction of plant hormones as abscisic acid (ABA) or jasmonic acid derivates (JAs). Understanding how hormones steer plant adaptive responses to stresses will allow us to enhance plant survival and productivity under a predicted worldwide scenario of food security alert.

During my PhD, I identified new mutant alleles of the ABA biosynthesis pathway in Arabidopsis thaliana. Indeed, we were the first worldwide group to clone the ABA2 gene and characterized their enzymatic activity. Our data confirmed ABA hormone as a pivotal target on future plant biotechnology to increase plant survival and productivity under abiotic stress conditions and we showed that ABA functions not only in plant stress responses but also in plant growth of non-stressed plants. I published as first author these results in top journals of plant science as Plant Cell and Plant Physiology

During my postdoctoral in Gent, I was focused on JA-dependent reprogramming of plant secondary metabolism under plant biotic stress conditions. We identified an ERAD -type RING membrane-anchor E3 ubiquitin ligase controlling the activity of 3-hydroxy-3-methylglutaryl-CoA reductase (HMGR), showing that JA recruits the ERAD quality control system to manage the production of plant defence metabolite synthesis (published in Nature). This project increased my versatility skills since I was studying Medicago truncatula and several medicinal plants from Asia and Africa.

As postdoctoral of the ABA signalling group of Dr. Pedro Rodriguez, I actively participated in the characterization of the molecular mechanism of the ABA perception by PYR/PYL/RCAR receptors and their connection with PP2Cs and SnRK2s leading to drought stress tolerance in Arabidopsis and tomato plants. Moreover, I have found new ABA signalling players including two regulatory proteins of the ABA PYR/PYL/RCAR receptors involved in ABA signalling membrane-delimited events As a result, I published 21 scientific papers in top journals as Plant Cell, Plant Physiology, PNAS, and EMBO journal.

In collaboration with several Europeans groups, I have found hormonal crosstalk between ABA signalling and others signalling pathways which show high potential biotechnological application. Specially promising was the crosstalk between biotic and abiotic plant stress responses I found since many times crops have to survive to a combination of both stresses. To increase my knowledge of stress combination I moved in 2015 to Plant-Insect Interaction group headed by Prof. Pedro Castañera and Dr. Felix Ortego where I have obtained a JIN project to develop a research line to understand hormonal signalling mechanisms steering plant stress tolerance under biotic and abiotic stress combination.

During my scientific career I published 33 scientific papers in high impact journals including Nature, EMBO journal, Plant Cell, and PNAS among others. In addition I have been involved in 13 R&D&I projects one of them as PI, I have been granted with a Juan de la Cierva and JAE-DOC contracts, I am co-director of one PhD thesis and two end-of-course projects, and I taught several university and master courses.

**Resumen del Currículum Vitae:**

Education:
1992-1997: degree on Biology, speciality of Biochemistry (University of Valencia).
1999-2005: PhD thesis on Plant Biotechnology (Department of Biotechnology, Polytechnic University of Valencia) being supervisors Prof. Ramon Serrano Salom and Dr. Pedro Luis Rodriguez Egea.
Grants and contracts:
1999: FPI fellowship founded by CSIC-Bancaja foundation.
2000-2002: FPU founded by MEC (IBMCP, CSIC-UPV).
2002-2004: Technician of Research and Laboratory (INIA).
2004: UPV fellowship (IBMCP, CSIC-UPV)
2005-2009: Postdoctoral Researcher at Plant Systems Biology Department (VIB-Gent University, Belgium).
2009-2012 Juan de la Cierva (JCI-2008-2050).
2012- 2014 JAE-DOC postdoctoral contract (IBMCP, CSIC).
2015-2016 Postdoctoral contract (CIB, CSIC).
2017-present Junior Principal Investigator (AGL2015-73235-JIN).
Publications:
H index: 19 (20/01/2017). 39 scientific contributions being 31 out of 33 papers published in the Q1 of their category (WOS) with an impact factor average of 7.7. 1344 citations, 40.7 citations per paper. Top 5 publications:
1- González-Guzmán M et al., Plant Cell.;14:1833-46 (2002) Impact factor: 10.751.

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

2- P. Lackman*; M. Gonzalez-Guzman*; et al., PNAS 108(14):5891-6 (2011) Impact factor 9.681. *Equal contribution.
3- Gonzalez-Guzman M*, Pizzio GA*, et al., Plant Cell. 24:2483-96 (2012) Impact factor 9.251. *Equal contribution
4- Rodriguez L*, Gonzalez-Guzman M et al., Plant Cell 26:4802-20 (2014). Impact factor: 9.575. *Equal contribution.
5- Pollier J*, Moses T*, Gonzalez-Guzman M et al., Nature Dec 5;504 (7478):148-52 (2013) Impact factor: 42.351 *Equal contribution
Congress: 32 contributions to national and international congress
Projects: Participation in 3 International projects, 8 Spanish projects one of them as Junior Principal Investigator, and 2 regional projects.
Funding: 372.591 euros from Spanish competitive calls Juan de la Cierva, JAEDOC and JIN.
Guiding: Co-director of a PhD student qualified as Sobresaliente Cum Laude and of two Polytechnic University (UPV) research projects (qualification of 9).
Teaching: Teaching at UPV, Biotechnology Department in the Biotechnology degree and the Master course Bioinformática aplicada en Biotecnología de plantas in the UPV Master in Molecular Biotechnology and Cellular of Plants.
Awards/accreditations: Premio extraordinario de doctorado de la UPV 2005.ANECA accreditations Profesor Ayudante Doctor, Profesor de Universidad Privada and Profesor Contratado Doctor.
Peer-review of Functional Plant Biology, J. Exp. Bot., Span. J. Agric. Res. and Science Reports.

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

**Nombre:** RINCON PADILLA, SERGIO
**Referencia:** RYC-2016-20652
**Área Científica:** Biología Fundamental y de Sistemas
**Correo Electrónico:** sarpadilla@gmail.com

**Título:**

Molecular mechanisms of polarized cell growth and cell division

**Resumen de la Memoria:**

The aim of my PhD was the identification of novel Cdc42-effectors controlling polarized growth. To do this, two approaches were taken:
- A two hybrid screen on the novel Cdc42 GEF Gef1 to find effectors in this pathway. The BAR domain protein Hob3, was one of the positive hits. My work established this membrane-interacting protein as key factor in the activation and recruitment of Cdc42 to the division site. (Coll*, Rincon* et al., 2007; Rincon et al., 2007).
- I also produced a collection of Cdc42 thermosensitive mutants, which showed delocalized actin patches and almost absent interphasic actin cables, suggesting a defective formin function. In collaboration with the lab of Dr. Fred Chang, (Columbia University, NYC), we determined that Cdc42 activates the mDia-like protein For3, responsible for actin cable formation (Rincon et al., 2007; Martin et al., 2007). In a multicopy plasmid suppression screen, I found that ectopic expression of the SH3 protein Pob1 rescued the ability of the Cdc42 mutants to produce actin cables. I determined that Pob1 is an adaptor protein that contributes to Cdc42-dependent activation of the formin For3 (Rincon et al., 2009). Further characterization of the polarity defects of Cdc42 mutants implicated it in membrane trafficking events, such as exocyst-mediated secretion or endosome to vacuole transport (Estravis*, Rincon* et al., 2011).
During my first post-doctoral training in the lab of Anne Paoletti, I studied the mechanisms of division plane positioning dependent on the SAD kinase Cdr2. I identified a cryptic C-terminal KA-1 domain responsible for membrane anchoring. In collaboration with the lab of Sophie Martin (Lausanne University), we determined that the tip kinase Pom1 phosphorylates Cdr2 next to the positively charged region, downregulating its membrane attachment at the cell tips and promoting medial cortex localization (Rincon et al., 2014). We also found that Pom1 controls Cdr2 kinase activity to control the cell cycle progression. (Bhatia et al., 2014).
I also found that Cdr2 completely detaches the medial cortex upon mitotic entry in a SIN pathway-dependent manner. I determined that the SIN promotes Cdr2 interaction with a 14-3-3 protein, triggering its cortical dissociation. Analysis of the phospho-inhibit Cdr2 mutants allowed the proposal of a model in which SIN-dependent Cdr2 dissociation from the cortex resets the cortical cues from the mother cell to ensure proper medial division in the next cell cycle (Rincon et al., 2017).
During my second postdoc training I have deciphered the molecular mechanisms that cells require for of a bipolar spindle assembly in the absence of kinesin-5. I have shown that fission yeast lacking any molecular motor are capable of assembling a bipolar spindle with a very short length at metaphase and a prolonged metaphase-to-anaphase transition. In these conditions, the antiparallel microtubule bundling protein Ase1/PRC1 becomes essential, due to its own bundling activity and because it contributes to microtubule stability through the recruitment of the CLASP protein Cls1. These results are supported by computational simulation, which show that mitotic spindle can be assembled in the absence of motor activity if an antiparallel microtubule bundler (Ase1) organizes and stabilizes the structure (Rincon et al., in favorable revision).

**Resumen del Currículum Vitae:**

Name: Sergio RINCÓN

Date of birth: 03/07/1979

Gender: Male

Nationality: Spanish

Work: Institut Curie, 12 rue Lhomond 75005 Paris

e-mail: sergio.rincon@curie.fr

Current position: Post-doctoral fellow

Education

2007 PhD (cum laude), Microbiology, University of Salamanca, Spain

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

Thesis: Screening and Analysis of Novel Effectors of the Rho GTPase Cdc42 in S. pombe
Advisor: Prof. Pilar Pérez

2004 MA (cum laude), Microbiology, University of Salamanca, Spain.
Project: Study of the Rho GTPase Rho5 in the fission yeast S. pombe
Advisor: Prof. Pilar Pérez

2002 BS, Biology, University of Salamanca, Spain

Research Experience

2009 – now Post-doctoral Fellow, Institut Curie, France
Project 1: Spatial regulation of cell polarity and cell size Advisor: Dr. Anne Paoletti
Project 2: Mechanisms of spindle formation Advisor: Dr. Phong Tran

2008 Post-PhD, University of Salamanca, Spain
Project: Cdc42 function in fission yeast Advisor: Prof. Pilar Pérez

2003 – 2007 PhD student, University of Salamanca, Spain
Project: Cdc42 function in fission yeast Advisor: Prof. Pilar Pérez

2005 Visiting PhD student, Edinburgh University, Scotland
Project: Mto1 and microtubule nucleation Advisor: Dr. Ken Sawin

Honors & Awards
2009 Post-doctoral fellowship / Fundacion Ramon Areces, Spain (accepted)
2011 Post-doctoral fellowship / Marie Curie Action, EU (accepted)
2011 Post-doctoral fellowship / EMBO (declined)

Teaching

Microbiology / University of Salamanca
Practical course for university students / 2005, 30 hrs; 2006, 90 hrs

Experimental Methods in Cell Biology / Master AIV, Universities Paris Diderot & Paris Descartes
M1 course / 2012, 20 hrs; 2013, 20 hrs; 2014, 20 hrs; 2015, 20 hrs; 2016, 20 hrs.

EMBO Course - Molecular Genetics with Fission Yeast Schizosaccharomyces pombe / Institut Curie
Imaging course for PhD students / 2012, 1 day; 2014, 1 day

Publications

Original Reseach

13. Rincon SA et al. (2017). Nat Commun. (positively reviewed and resubmitted).
12. Estravis M, Rincon SA, et al. (2017). Microbiology (resubmitted).
11. Rincon SA*, ... , Paoletti A*. (2017). Curr Biol 27, 1-9. (* co-corresponding authors; in press).
10. Guzmán-Vendrell M, Rincon SA et al. (2015). J Cell Sci 128, 2842-53.
9. Rincon SA et al. (2014). J Cell Biol 206, 61-77.
8. Bhatia P, Hachet O*, Hersch M*, Rincon SA* et al. (2014). Cell Cycle 13, 538-52. (*equal contribution)
7. Estravís M*, Rincón SA* et al. (2011). (*equal contribution).
6. Samejima I, Miller VJ, Rincon SA et al. (2010). Curr Biol 20, 1959-65.
5. Rincón SA et al. (2009). Mol Biol Cell 20, 4390-9.
4. Pinar M, Coll PM, Rincón SA et al. (2008). Mol Biol Cell 19, 1727-38.
3. Martin SG, Rincón SA et al. (2007). Mol Biol Cell 18, 4155-67.
2. Coll PM*, Rincon SA* et al. (2007). EMBO J 26, 1865-77. (*equal contribution)

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

1. Rincón SA et al. (2006). Eukaryot Cell 5, 435-46.

Invited Reviews

6. Rincon SA et al. (2016). Semin Cell Dev Biol 53, 28-38.
5. Rincón SA et al. (2014). Biochem Soc Trans 42, 201-5.
4. Rincon SA, et al. (2012). Cytoskeleton 69, 764-77.
3. Estravis M, Rincón S et al. (2012). Comm Int Biol 5, 370-3.
2. Perez P, Rincón SA. (2010). Biochem J 426, 243-53.
1. Rincon S, et al. (2007). Cell Cycle 6, 1687-91.

Book Chapters

1. Rincon SA et al. (2016). Methods Mol Biol 1369, 379-92.

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

**Nombre:** SERRANO SAIZ, ESTHER
**Referencia:** RYC-2016-20537
**Área Científica:** Biología Fundamental y de Sistemas
**Correo Electrónico:** es2754@columbia.edu

**Título:**

Transcriptional Dynamics of Glutamatergic Identity

**Resumen de la Memoria:**

My doctoral dissertation was conducted in the laboratory of Prof. Fernando Valdivieso at Centro Biologia Molecular Severo Ochoa/Universidad Autonoma (Madrid, Spain) and dealt with the characterization of a mouse model of infection by Herpes Simplex Virus type 1 to study the etiology of Alzheimer's disease. Right after I completed my PhD, I started my postdoctoral studies at Columbia University in the laboratory of Dr. Carol Troy where I continued my research in neurodegeneration but where I took a more molecular approach focusing in the involvement of caspases in ischemic stroke.

Being exposed to the neuroscience community at Columbia University, I discovered my passion for studying gene regulatory programs in the nervous system and, hence, I decided to join the laboratory of Dr. Oliver Hobert. My research established fundamental regulatory mechanisms for the initiation and maintenance of glutamatergic neuronal identity. Using C. elegans as a model organism, I unraveled the highly modular architecture of the eat-4/VGluT locus, and I showed that the glutamatergic identity is controlled predominantly by homeodomain transcription factors. Importantly, I provided preliminary evidence that these mechanisms may be phylogenetically conserved in vertebrates (Serrano-Saiz et al, Cell 2013).

Recently, I have focused on the sexually dimorphic mechanisms that control the post-mitotic transformation of a sensory neuron into a hub neuron. This transformation results in axonal remodeling and the transcriptional scale up of pre-synaptic proteins, including the glutamate transporter eat-4/VGluT. Moreover, I showed that these molecular and anatomical transformations are controlled by the phylogenetically conserved Doublesex homologue transcription factor dmd-3 (Serrano-Saiz et al, Curr Biol 2017).

My primary research focus is the elucidation of the regulatory mechanisms required for the maintenance of glutamatergic neurons and the dynamic developmental plasticity of neurotransmitter systems. The correct specification and maintenance of neuronal identity is fundamental to achieve the proper function of a neuron within a neuronal circuit. Dysfunctional neurons could lead to detrimental situations including mental diseases or neurodegeneration. My expertise in C. elegans and mouse genetics, allows me to follow an approach by combining the specific strengths of the two model systems: (i) C. elegans as a gene discovery tool to identify the regulatory mechanisms for the dynamic developmental plasticity of neurotransmitter systems, (ii) conditional mouse genetics to translate my findings to vertebrates to pursue the phylogenetic conservation of such mechanisms.

**Resumen del Currículum Vitae:**

I obtained my bachelor in Biochemistry at the UAM in 2002. Following my interest in neuroscience, I decided to join Prof. Valdivieso's lab to obtain my PhD in 2007. During my thesis, I characterized a mouse model of infection by HSV-1 to study the etiology of Alzheimer's Disease (AD). In 2006, we published our findings in J. Neurovirology where we presented a remarkable finding that implied that HSV-1 infection induces the over-expression of TAP. Interestingly, TAP polymorphisms have been implicated as risk factors of AD. I, therefore, developed transgenic mice carrying the two human polymorphisms that I presented at the international 6th Transgenic Technology Meeting (2005).

In 2007, I started my postdoctoral studies at Columbia University in Dr. Troy's laboratory. I continued my research in neurodegeneration but I took a more molecular approach focusing in the involvement of caspases in stroke. In 2011, we published in J. Neuroscience how caspase-6 is involved in axonal degeneration in stroke.

In 2009, after being exposed to the neuroscience community at Columbia, I joined the laboratory of Prof. Hobert at Columbia University. At that time I was awarded with the postdoctoral Spanish Fellowship from the Ministry of Education and Science of Spain that allowed me to fund my research.

Using C. elegans as a model organism, I established fundamental regulatory mechanisms for the initiation and maintenance of the terminal glutamatergic neuronal identity and I showed that glutamatergic identity is controlled predominantly by homeodomain transcription factors. Additionally, I provided preliminary evidence that these mechanisms might be phylogenetically conserved in vertebrates (Serrano-Saiz et al, 2013. Cell).

Neurotransmitter identities are not as static as it was formerly thought, which reflects the intrinsic plasticity of a neuron to respond to external and internal cues. Recently, I have become very interested in the dynamics of glutamatergic neuron identity during sexual maturation. We have described a neurotransmitter switch from glutamatergic to cholinergic during sexual maturation (Pereira L, Serrano-Saiz E et al, eLife. 2015). Furthermore, I found a neurotransmitter-scaling phenomenon in a sensory neuron that occurs when this neuron remodels during sexual maturation to become a hub neuron in the male neuronal circuit. This scaling allocates distinct, sex-specific functions to PHC. Interestingly, I demonstrated how this remodeling is orchestrated by the coordination of two phylogenetically conserved TFs, a LIM homeodomain TF controlling the hard-wired identity of this sensory neuron, and a Doublesex TF that orchestrates the

**AYUDAS RAMÓN Y CAJAL**
**CONVOCATORIA 2016**

**Turno de acceso general**

remodeling after sexual maturation (Serrano-Saiz E et al, Curr Biology, 2017).
During my postdoctoral training, I have developed total independence and gained experience in leading projects. I have been mentoring several rotation students having a principal role in the design of their projects as well as mentoring the students in the execution of them.
Finally, I have recently been awarded a Young Investigator Grant from the Brain and Behavior Research Foundation that will allow me to partially fund my research for the next two years and I have recently applied for the 2017 ERC-Starting Grant.

# AYUDAS RAMÓN Y CAJAL
# CONVOCATORIA 2016

## Turno de acceso general

**Nombre:** FERNANDEZ ALVAREZ, ALFONSO
**Referencia:** RYC-2016-19659
**Área Científica:** Biología Fundamental y de Sistemas
**Correo Electrónico:** aferalv78@gmail.com

**Título:**

Chromosomal Instability in Meiosis

**Resumen de la Memoria:**

I started my scientific career in Ibeas lab. At that time, he was interested in opening a new line of research to explore how fungal pathogens use protein glycosylation to modulate the activity of their virulence factors. After an extensive comparative analysis of different pathogenic species, we decided to introduce the phytopathogen Ustilago maydis into the lab.
During my PhD, using a combination of molecular biology and proteomic approaches as well as confocal, high-resolution and electron microscopy, we identified the O-mannosyltransferase Pmt4 as a key factor for U. maydis virulence (AFA, et al., 2009 Plant Cell); we characterized the Pmt4 target proteins (AFA, et al., 2012 PLOS pathogens); and the interaction between Pmt4 with the N-glycosylation pathway (AFA, et al., 2013 Plant Cell).
My fascination about spindle formation and chromosome segregation began during my PhD, when I became familiar with the work from other labs at my institute. For this reason I decided to move to London to join the Cooper lab where I worked on an area which has been a long-standing mystery in this field: how the telomere bouquet, a specific and conserved chromosome conformation during meiotic prophase, controls formation of the meiotic spindle. The first question which I was interested in answering is how a population of bouquet-deficient cells retains any capability to form spindles. We employed high-resolution time-lapse imaging to discover that bouquet-mutant cells use centromeres to induce the spindle formation (AF* & AFA*, et al., 2015 Journal of Cell Biology).
Ever since I joined the Cooper lab, I have been interested in answering one major question: what is the mechanism by which the telomeres/centromeres are controlling the spindle formation? This has been an ambitious project for which we have found an answer: the mechanism behind this new layer of cell cycle control is to promote the nuclear envelope (NE) disassembly, thus allowing the chromosomes to access the spindle (AFA, et al., 2016 Developmental Cell).
Advanced maternal age greatly increases the probability of experiencing miscarriages. This occurs because with advancing age, oocytes have more chances to distribute unfaithfully the number of chromosomes; in most of these cases, the resulting embryos fail to develop and in others, children will be born with developmental conditions like Down□s syndrome or Turner syndrome. My research program addresses the fundamental processes by which chromosome state is coordinated with cell cycle progression during meiosis, a problem of enormous clinical significance. I will utilize the experimental advantages of model systems (Schizosaccharomyces pombe) to gain insights to drive understanding of human meiosis.
How might telomeres control chromosome segregation in meiosis? The capability of specialized regions of chromosomes to recruit enzymes like CDK1 and PLK1 raises the possibility that the spatial cues for meiotic progression are provided by enzymatic activity at positions where chromosomes interact with the nuclear envelope. An exciting challenge for the future is to uncover the relevance of interphase chromosome organization for communicating the state of the genetic information to the cell cycle control devices that regulate nuclear division.

**Resumen del Currículum Vitae:**

Upon completing my degree in Pablo de Olavide University, I was awarded prizes for □Mejor Expediente de Licenciatura (2005)□ in Pablo de Olavide University and □Primer Premio Nacional Fin de Carrera (2005)□ by Ministerio de Educacion y Ciencia. I started my scientific career in Jose Ignacio Ibeas□ lab at the CABD (UPO/CSIC). I was supported by a FPU fellowship (2005-2009) awarded by Spanish government to investigate the role of protein glycosylation in Ustilago maydis virulence. During my DEA (2006) and PhD (2011), I published four first author research papers (2 Plant Cell, 1 PLOS pathogens and 1 Plant Signaling & Behavior), one first author review paper (Fungal Genetics and Biology) and three second author research papers (2 PLOS pathogens and 1 Plant Cell). Upon completing my PhD, I was awarded prizes for the best PhD thesis in science in 2012 by both the Seville city council and Pablo de Olavide University (□Premio Extraordinario de Doctorado□). I was also awarded with the □Premio Real Maestranza de Caballeria□ in Science (2012).
Through my PhD training I learnt about scientific writing by writing all my manuscripts. During my last year in the Ibeas lab, I was teaching in Biotechnology degree as □Profesor Ayudante□ and I mentored a □proyecto fin de Carrera□ student and a PhD student, who is currently expanding upon my research and we are writing a manuscript together, which I will sign as corresponding author.
After my PhD in 2011, I renounced to my position as □Profesor Ayudante□ in Pablo Olavide University to do a postdoc and improve my knowledge about spindle formation and chromosome segregation. For this reason I decided to move to London to join Julie Cooper□s lab at London Research Institute (Cancer Research UK). I was working in the project □telomeres in meiosis□ awarded by an ERC consolidator grant. Then, I was awarded with a long-term EMBO fellowship (2012-2014) to explore the function of the telomere bouquet. In 2014, my supervisor, Julie Cooper, decided to move the lab to the National Cancer Institute at NIH in USA and she emploied me as senior postdoc in her lab (2014-currently). During my postdoc, I have published two first author research papers (1 Journal of Cell Biology and 1

**AYUDAS RAMÓN Y CAJAL**
**CONVOCATORIA 2016**

**Turno de acceso general**

Developmental Cell) and one first author review paper (Trends in Cell Biology). I have also actively collaborated in other research paper in the lab about centromere assembly (Nature Cell Biology). Through my postdoc training I have written all my manuscripts and I have signed as corresponding author my last work in Cooper lab (Developmental Cell).
My work has been well received by the field at international meetings. Through my postdoc I have given four oral communication in international meetings (EMBO Meiosis Conference, UK, 2015; The Eighth International Fission Yeast Meeting, Japan, 2015; Chromosome Dynamics (GRS), Italy, 2013; Meiosis (GRS), USA, 2012). I have reviewed manuscripts for Journal of Cell Biology, Developmental Cell, Cell Reports, Nature Communications and PLOS genetics with my mentor. I have also mentored two master students and learnt how a lab is managed in terms of recruiting people and using money sensibly. The fact that Cooper lab moved from London to USA has facilitated me to build relationships with researchers in USA and Europe.