



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

### Turno de acceso general

**Nombre:** GÜELL CARGOL, MARC  
**Referencia:** RYC-2015-17734  
**Área Científica:** Biología Fundamental y de Sistemas  
**Correo Electrónico:** marcguellc@gmail.com

#### Título:

Design of biologically inspired synthetic systems

#### Resumen de la Memoria:

Past research (From Systems to Synthetic Biology):

During my PhD, I acquired a deep knowledge in -omics technologies to accurately measure biological systems. We focused on describing one of the simplest microorganisms, *Mycoplasma pneumonia*, with unprecedented detail. I developed DSSS, the first method for strictly strand specific transcriptome genome-wide profiling (Vivancos\*, Güell\* (\*equally contributing) et al., Genome Research 2010), and generated the most comprehensive integrated dataset for a bacterium including quantitative transcriptomics, proteomics and metabolomics (Güell et al., Science 2009; Kühner, .., Güell et al., Science 2009; Yus, ◆, Güell et al., Science 2009; see commentaries by Glass, ..., Venter, MSB 2009; Ochman et al, Science 2009). Combining DSSS with tiling arrays, and microarrays, we characterized the transcriptome of *M. pneumonia*. We pioneered the observation of widespread occurrence of antisense transcription and alternative transcripts in bacterial genomes. For the first time, we reported the genome-wide identification of small RNAs associated with transcription initiation sites in prokaryotes (Yus\*, Güell\* (\*equally contributing) et al., MSB 2012), and analyzed the correlation between mRNA and protein (Maier, ..., Güell et al., MSB 2011).

During my postdoc and as a Wyss Technology Development Fellow, I have moved to completely synthetic projects. I created new synthetic systems to generate safe microorganisms, and create human compatible tissues.

Synthesis of a radically recoded *E. coli* genome (submitted): I co-led the synthesis of a radically recoded *E. coli* genome, reassigning more than 64,000 codons. RC2 will be resistant to viruses, and its DNA will not be able to be shared with other organisms, as it has a unique synthetic genetic code. RC2 will be able to be used as a safe and bio-contained microorganism.

Mammalian multiplex genome engineering: We have developed multiple CRISPR-based technologies that have been relevant for the development of mammalian genome engineering. (Mali, ◆, Güell et al., Science 2013; Yang, Güell et al., NAR 2013; Güell et al., Bioinformatics 2014).

◆Humanizing◆ the pig genome for xenotransplantation: We combined gene synthesis and CRISPR technologies to generate pigs with human physiological and immune compatibility. We recently reported the complete inactivation of all porcine endogenous retroviruses from the pig genome (Yang\*, Güell\* (\*equally contributing) et al., Science 2015; see commentary ◆No pig in a poke◆, The Economist 2015).

Future Research (Design of Synthetic Systems):

In my lab, I would like to leverage the synergism of the best principles of synthetic biology, and advanced fabrication to better understand biology and to create new biologically inspired systems. I am especially interested in three different levels:

Molecules: I will use synthetic biology techniques to investigate the evolution of small molecules, and to create new ◆synthetic◆ natural products with new properties.

Supra-cellular structures: Synthetic biology, 3D printing, and regenerative medicine have provided with the necessary foundations to design multi-cellular systems. I will create new personalized tissues with new properties

Integrated bionic systems: I would like to develop hybrid systems to carry out advanced functions such as cell-free systems for expression, and sensing.

#### Resumen del Currículum Vitae:

I have a solid multidisciplinary training with degrees in Chemistry (best grade in my class), Chemical Engineering, Telecommunications Engineering, a PhD in Biomedicine, and have international experience at multiple top institutions in the USA (Harvard University), Germany (European Molecular Biology Laboratory-EMBL), UK (Oackland & Calvert), and Spain (Center for Genomic Regulation-CRG, Consejo Superior de Investigaciones Científicas-CSIC). I have published manuscripts in computational, as well as in experimental research obtaining more than 3400 citations.

During my career I experienced excellent mentorship. I feel very fortunate to have trained in two extraordinary laboratories:

Systems Biology: PhD-Luis Serrano(2006/7-EMBL, 2008/10-CRG)

Synthetic Biology: postdoc/Wyss Technology Fellow-George Church(2011/current-Harvard)

I have had independent funding since my early career as an undergraduate at the CSIC. My PhD and postdoc were also funded by independent competitive fellowships and research grants (FPU, EMBO, HFSP, Amazon Research Grant). More recently, I became a Wyss Technology Development Fellow at Harvard University which is an intermediate position between postdoctoral researcher and principal investigator. Also, I am the cofounder and founding scientist of two biotech companies for which we secured independent funding:



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Sbiomedic([www.sbiomedic.com](http://www.sbiomedic.com)) is a startup company focused on developing therapies based on the skin microbiome. We have created therapeutic formulations for acne containing selected strains. The project was started in Santiago de Chile after receiving an award from the Chile Startup Competition in 2014. The company is currently located in Magdeburg, and we have received non-dilutive funds from the German government as well as private investments. We are currently running clinical trials and evaluating potential partnerships with established companies.

eGenesis([www.egenesisbio.com](http://www.egenesisbio.com)) is a startup focused on creating organs for transplantation using genetic engineering in pigs. The company is incubated at Dr. Church's laboratory (Harvard University). The founding team includes two of the co-inventors of CRISPR-cas9 in human cells, and we obtained licenses from Harvard University and Broad Institute to use CRISPR in our field. We obtained private investments and service contracts.

During my career I won several awards including

- 1) 2015 - Received from the King of Spain Felipe VI an award as South Summit 2015 winning team (Sbiomedic) in the Healthcare & Biotech category. Madrid, Spain
- 2) 2013 - Awarded with the distinction of Garrotxa's Embassador, Olot City Council, Olot, Girona, Spain
- 3) 2010 - P. Salvador Gil Award to the best final degree project in the Bioengineering Department, IQS, Barcelona, Spain
- 4) 2001 - Special award from the Catalan Government (top 10 grade) in the university admission exam

Finally, I would like to highlight that I envision teaching and student training as an important part of my research mission. I have participated as invited speaker in several workshops and courses worldwide (Japan, Argentina, Spain), and mentored numerous graduate and undergraduate students while being a postdoctoral fellow and a Wyss technology Development Fellow at Harvard University.



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**Nombre:** SUPEK , FRAN  
**Referencia:** RYC-2015-17853  
**Área Científica:** Biología Fundamental y de Sistemas  
**Correo Electrónico:** fran.supek@gmail.com

#### Título:

Genomic signatures of mutational processes and selection - from microbes to mammals

#### Resumen de la Memoria:

My research interests revolve around characterizing the mutational processes that generate genetic diversity, while learning how to distinguish the resulting DNA sequence variability from the subtle signatures of natural selection overlaid upon it. I investigated these issues by comparative genomics analyses of bacterial and archaeal genomes on the one hand, and of human cancer genomes on the other hand.

In the former case, my investigation has focused on synonymous variation in microbial genes and how the biased use of codons in mRNA can affect the efficiency of their translation into protein. (publications in PLOS Genetics, Genetics, and Genome Biology). Furthermore, we examined the evolution of compositional properties of microbial genomes and proteomes in pathogens and extremophiles (published in Cell Reports & Genome Biol Evol).

Next, I have investigated the signatures of selection acting upon somatic variants in human cells in carcinogenesis. Our work provides evidence that ~1 in 5 synonymous variants in oncogenes are selected due to effects on splicing. In addition, TP53 bears inactivating synonymous mutations (Supek et al, Cell 2014).

Furthermore, we investigated somatic mutation rate variability across the human genome. The regional rate variability is tissue-specific, reflecting the change in the DNA replication timing program, and is generated by the differential activity of DNA mismatch repair pathway (Supek & Lehner, Nature 2015).

In addition to the above, I've been involved in chemoinformatics analyses related to new antitumor drug candidates - deducing their biological mechanism of action as well as cellular resistance via the P-gp efflux pump (publications in J Med Chem, Inv New Drugs and Eur J Med Chem).

My future work as a Ramon y Cajal fellow will further elucidate the mechanisms behind various mutational processes that shape the human genome, their consequences on carcinogenesis as well as the potential therapeutic opportunity they represent.

#### Resumen del Currículum Vitae:

**EDUCATION:** (1998 ♦ 2004) BSc/MSc in Molecular biology. Department of Biology, U of Zagreb, Croatia. Top 10% at graduation; overall grade: 4.88/5.00. (2004 ♦ 2010) PhD program at the Faculty of Science and Mathematics, U of Zagreb, Croatia. Supervisor: dr. Tomislav Smuc; Laboratory for Information Systems (LIS), Rudjer Boskovic Institute (RBI), Zagreb. Courses/schools: (2005) "ACAI Advanced course in knowledge discovery", JSI, Ljubljana, Slovenia. (2006) "Creating interdisciplinary research projects", MedILS, Split, Croatia. (2008) "Science and the Web: from theory to implementation" MedILS, Split, Croatia. (2014) "1st CRG Bio-business School" CRG, Barcelona, Spain.

**POSITIONS:** (2004 ♦ 2010) Early-stage researcher - PhD candidate; Division of Electronics, RBI, Zagreb. Funded by a fellowship of the Croatian Ministry of Science. (2010 ♦ 2012) Postdoctoral researcher/Marie Curie fellow, INTERPOD interdisciplinary postdocs program. Shared between the Computational Genomics and the Genetic Systems group, PIs: T. Gabaldón, B. Lehner, CRG, Barcelona. (2012 ♦ current) Postdoctoral researcher. Genetic Systems Group. PI: Ben Lehner, EMBL/CRG Systems Biology Unit, CRG Barcelona. (2013 ♦ current). Research associate, 20% time. Laboratory for Information Systems, Rudjer Boskovic Institute (RBI), Zagreb, Croatia.

**AWARDS:** (2003) Award from the Dean of Faculty of Science and Mathematics (U of Zagreb) for exceptional success in undergraduate studies. (2008) Croatian National Science Award ♦ Annual Award for Junior Researchers. (2010) Award of the Director of the RBI for excellence in research.

**SUPERVISION:** (2011-2015) supervised 3 master students/interns; two at RBI Zagreb and one at CRG Barcelona. Resulted in two publications where I'm senior author, and student is first author (in J Med Chem and in Genome Biol Evol); third publication is in preparation. (2014 ♦ current) co-supervision of one PhD student, and supervision of one postdoc at RBI Zagreb, as a part of MAESTRA FP7 FET project.



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TEACHING: (2004 – 2005) Teaching assistant – Computer science lab for molecular biology students, Faculty of Science and Mathematics, U of Zagreb, Croatia.

REVIEWED FOR: (2009 - 2015) PLOS One 5x, J Mol Evol 5x, Eur J Med Chem 3x, Genome Biol Evol 2x, Microbiology 2x, Gene (2x), J Med Chem, Genetics, Mol Genet Genomics, BMC Genomics, Sci Rep, PLOS Genetics. (2013) Referee for US NSF.

OUTREACH ACTIVITIES: (2007-2010) S3++ – Summer School of Science – for high-school students in Vinkovci, Croatia. Group leader - computational chemistry lab and microbiology lab; organizer of the school scientific program; volunteer work. (2007) Winner of the science communication contest – FameLab – Croatia; participant in the international FameLab. (2013 – 2015) Jury member for local/national FameLab, organized by British Council Croatia.

PUBLICATION SUMMARY, as of 22/12/2015: Total 24 journal publications, of that 11 first-author, 4 last-author. 2 publications from supervising students, where student is 1st author. Two book chapters. Citations: 1106 (Google Scholar); 778/748 (Scopus total/-self). h-index=13 (Google), 11 (Scopus). Impact factor of first & last-author publications: average IF=9.4; cumulative IF=140.4. Linked on Twitter 431x, saved 1836x to reference managers, FigShare data sets accessed 365x. Full list at <https://impactstory.org/FranSupek>



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

### Turno de acceso general

**Nombre:** ARIAS PALOMO, ERNESTO  
**Referencia:** RYC-2015-19059  
**Área Científica:** Biología Fundamental y de Sistemas  
**Correo Electrónico:** e.arias.palomo@gmail.com

#### Título:

Structural and functional studies of macromolecular machines involved in nucleic acids transactions

#### Resumen de la Memoria:

My career has focused on the development of structure-based mechanistic models to explain how macromolecular machines are assembled, regulated, and capable of transducing chemical energy into force and movement for supporting essential cellular processes. This interest drove me to join in the newly-founded laboratory of Prof. Óscar Llorca (CIB-CSIC, Spain), where I obtained my PhD in biochemistry and molecular biology. While being one of the founding members of this group was challenging, it also gave me the opportunity to play an active role in the organization and management of the laboratory. During my PhD I unraveled the activation mechanisms of essential nucleotide-dependent human protein complexes implicated in intracellular signaling regulation and nucleic acid quality control. Additionally, I became proficient in cryo-electron microscopy and numerous molecular biology techniques.

My growing interest in understanding how large multi-subunit assemblies control fundamental nucleic acid transactions led me to join the laboratory of Prof. James Berger at UC Berkeley (California, USA). As a postdoctoral fellow, I applied my experience in cryo-electron microscopy, in conjunction with X-ray crystallography and a host of biophysical techniques, to study the molecular mechanisms of ATP-fueled nucleic-acid machines that control DNA replication. In particular, I characterized the loading mechanism of the bacterial replicative helicase, DnaB, shedding light to a long-standing question in the field. In July of 2013, I moved with Prof. Berger's laboratory to Johns Hopkins University (Maryland, USA). Here, the striking similarity between some of the factors involved in DNA replication and those that regulate ATP-dependent transposases has drawn my attention to a particular streamlined class of transposable elements implicated in disseminating antibiotic resistance and virulence factors.

For the last ten years I have been interested in studying macromolecular complexes that regulate fundamental cellular processes. Now, I am keen to continue investigating the molecular mechanism underlying DNA transposition and genomic instability as an independent investigator.

#### Resumen del Currículum Vitae:

##### Positions and professional activity:

2015 - present Research Associate (Faculty). Johns Hopkins University, USA.  
2013 - 2015 Postdoctoral Fellow. Johns Hopkins University, USA.  
2010 - 2013 Postdoctoral Fellow. University of California, Berkeley, USA.  
2008 - 2010 Postdoctoral Fellow. CIB-CSIC, Spain.  
2004 - 2008 Graduate Student. CIB-CSIC, Spain.

##### Publications:

I have 15 publications in international journals such as Nature and Molecular Cell. I have published 6 first-author papers: two articles in Cell, one in EMBO J, one in Genes and Development, and two in Biochem and Biophys Acta.

##### Conferences:

I have presented my work in numerous international meetings such as the Keystone and the Gordon Conferences.

##### R&D Projects:

I have participated in six national and international scientific projects.

##### Research in international centers:

I have worked almost six years at international institutions, three at UC Berkeley, and three at Johns Hopkins University (USA).

##### Fellowships:

2006 FPU fellowship from the Spanish Ministry of Education  
2007 CPI contract from the Autonomous Region of Madrid  
2009 Postdoctoral Fellowship from the Ramon Areces Foundation  
2010 Postdoctoral Fellowship from the Spanish Ministry of Education



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**Awards:**

2009 Juan Abelló I award to the best thesis in biochemistry from the Real Academia de Doctores de España.

**Teaching and mentorship:**

I have taught in the ♦Topics in Macromolecular Structure and Function♦ Post-graduate course from the Biophysics and Biophysical Chemistry Department. Johns Hopkins University. Moreover, during my career I have assisted numerous graduate students and postdoctoral fellows.

**R&D management:**

I played an essential role implementing single-particle electron microscopy in Prof. James Berger♦s laboratory (UC Berkeley). Additionally, I am currently implementing high-resolution cryo-EM at Johns Hopkins University, which had a significant contribution to my recent appointment as Research Associate (Faculty) in the Department of Biophysics and Biophysical Chemistry (Johns Hopkins University).



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

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**Nombre:** CARVAJAL GONZÁLEZ, JOSÉ MARÍA  
**Referencia:** RYC-2015-17867  
**Área Científica:** Biología Fundamental y de Sistemas  
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#### Título:

Cell biology of epithelia polarity

#### Resumen de la Memoria:

In the last 11 years, I have been working on 3 main topics, the Dioxin receptor physiology, apical-basal polarity and planar cell polarity.

As predoctoral fellow with Pedro Fernandez Salguero in Extremadura, we examined the physiological role of the transcription factor Aryl hydrocarbon Receptor(AhR) or Dioxin receptor (9 articles, 1 review and 1 book chapter published). My thesis work was focused on the role of AhR in cell migration using immortalized fibroblast (MBoC, 2009) and keratinocytes during wound healing in mice skin (JCS, 2009). Also in several collaborative studies, we looked at the role of AhR in carcinogenesis (Carcinogenesis 2006), angiogenic and cardiovascular functions (JBC, 2009 and JBC, 2011) or the AhR transcriptional regulation of a new retrotransposon (PNAS, 2008).

During my first postdoctoral training at Cornell University, we looked at clathrin adaptors and polarized sorting in epithelial cells (8 articles and 1 review published). The discovery in 2008 that clathrin is a key regulator of basolateral polarity, offered me during the last seven years an opportunity to search for clathrin adaptors and sorting signals in epithelial cells in vitro. This was the idea when I joined Enrique's Rodriguez-Boulan group in New York as an EMBO long term postdoctoral fellow in 2009. In 3 years we were able to show that AP-1A was a key basolateral adaptor in epithelial tissues (Dev Cell, 2012 and PNAS, 2012), including those lacking AP-1B (Kidney Int, 2010) and described the mechanism of sorting for several sorting signals including YxxPhi (PNAS, 2012) motif or dileucine motifs (MBoC, 2015). Furthermore, we established new methods to study polarity in polarized cells using biochemical assays (Dev Cell, 2012; PNAS, 2012 and MBoC 2014) or time-lapse confocal microscopy (PNAS, 2014).

More recently in my second postdoctoral with Marek Mlodzik at Mount Sinai, I studied planar cell polarity (PCP) biology to find new effectors and regulators of planar cell polarity (2 articles, 1 review published). In 2013 using loss-of-function studies, we revealed that Wg and dWnt4 act redundantly in PCP determination providing directionality to the PCP process (Nat Cell Biol, 2013). Furthermore, combining my experience in trafficking and clathrin adaptors, we were able to show the clathrin adaptor AP-1 complex and Arf1 regulation of planar cell polarity in vivo (Nat Comm, 2015).

Now as junior group leader (1 manuscript under second review in Nat Comm NCOMMS-15-22433) at University of Extremadura combining my research experience, I continue my research in two lines funded within the Plan Nacional-Excelencia 2014 call: 1) to characterize the trafficking processes used by planar cell polarity core complexes during development and 2) to find new effectors and regulators of PCP.

Overall my career has been focus on understanding the contribution of trafficking pathways and cytoskeleton to polarity, which is a fit for the ANEP area in Biología Fundamental y de Sistemas.

#### Resumen del Currículum Vitae:

##### CURRENT POSITION

Sept2014- Junior group leader at University of Extremadura. Department of Biochemistry, Molecular Biology and Genetics.

##### PREVIOUS POSITIONS

2012-2014 Postdoctoral Associate, Mount Sinai School of Medicine, New York, (USA) with Prof. Marek Mlodzik.

2009-2012 EMBO Long-Term Postdoctoral Fellow and Postdoctoral Associate, Weill Cornell Medical College, New York, (USA) with Prof. Enrique Rodriguez-Boulan.

##### ACADEMIC EDUCATION.

2004-2008 PhD Thesis: The Aryl Hydrocarbon Receptor regulates signaling pathways that control cell migration. University of Extremadura, Supervisor: Prof. Pedro Maria Fernandez-Salguero

1999-2004 B.Sc. Degree (Biology), University of Extremadura, Badajoz, Spain.

##### FELLOWSHIPS AND AWARDS

- Fellowship/Contract: "Ayudas destinadas a la retención y atracción de talento investigador para su incorporación en los centros de





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investigación de la comunidad autónoma de Extremadura" awarded by the regional government (Junta de Extremadura). (I ranked first position among dozens of candidates).

-EMBO Long Term postdoctoral Fellowship. Of note, only 20% of the EMBO postdoctoral fellowship are awarded to work in non-member states like USA.

-Best PhD Thesis in Biomedicine award in 2009 by University of Extremadura.

-FEBS travel award: Workshop ◆Understanding Transient Molecular Interactions in Biology◆.

-FEBS travel award: EMBO Plenary lecture.

-EACR travel award: 20th Meeting of the EACR.

-Predoctoral Fellowship (FPU) awarded by Regional Government of Extremadura.

#### PUBLICATIONS SUMMARY

-Number of publications: 21 in peer-review journals, 1 under second review in Nature Communications and 2 book chapters.

-First author position in 6 publications and 1 under review: Carcinogenesis 2006 (Impact factor-IF- 5,4), MBoC 2009(IF 5,98), JCS 2009 (IF 6,1), PNAS 2012 (IF 9,7), Nature Comm 2015(IF 11,5 and co-corresponding author), F1000 PR 2014, and Nature Comm 2016 (under second review, co-corresponding author)

-Second author position in 6 publications: Bioch Phar 2009 (IF 4,3), JBC 2009 (IF 5,3), JCB 2009 (IF 9,6), JBC 2011 (IF 4,8), Dev Cell 2012 (IF 12,9) and book chapter 2011.

-Co-author position: Among other 11 publications, PNAS 2008 (IF 10,3), PNAS 2014 (IF 9,7), NCB (IF 20,1), EMBO J 2013 (IF 10,7), Kidney Int 2010(IF 6,1).

-Number of citations: Scopus 462; Google Scholar 590

-H-index: Scopus h-13; Google Scholar h-14

#### AWARDED GRANTS AND CONTRACTS AS PRINCIPAL INVESTIGATOR:

-Title: Novel effectors and regulators of PCP.

Funding: Plan Nacional Excelencia 2014.

-Title: ◆Viabilidad científica◆ Agrotech◆

Funding: Ixiolabs S.L.

#### OTHERS:

-ORGANIZER COMMITTEE of the III Membrane Trafficking and Polarity Interest Symposium (METRAPOLIS) 2014.

-REVIEWER FOR GRANT PROPOSALS for ANEP 2015 in Plan Nacional 2015.

-INVITED TALKS: IV Workshop mechanisms of cell adhesion, migration and invasion (SEBC) June 2015, Seville.

-SUPERVISOR: I have directed three Trabajos fin de Master two of them defended in 2015 and one currently under development.





## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

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**Nombre:** MANZO , CARLO  
**Referencia:** RYC-2015-17896  
**Área Científica:** Biología Fundamental y de Sistemas  
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#### Título:

QUBIC: QUantitative Biolmaging of Cellular processes

#### Resumen de la Memoria:

The scientific career of Dr. Carlo Manzo follows an international and multidisciplinary path. He obtained his PhD at the University of Naples, defending a dissertation on the molecular interaction between liquid crystals and organic molecules in relation to nonlinear optics effects and the transfer of spin-to-orbital angular momentum of light. His work led to the invention of the  $\diamond$ q-plate $\diamond$ , a liquid crystal device largely used for photonics and quantum optics applications.

From 2006 to 2008, he was a postdoctoral fellow at the Emory University (Atlanta, USA). There, he developed methods for single-molecule manipulation, imaging and quantification of DNA-protein interactions and studied the effects of mechanics and kinetics of DNA looping in the regulation of the lambda-phage epigenetic switch and the induction of virulence.

Between 2008 and 2011, he worked as a Postdoctoral Fellow at IBEC (Barcelona, Spain), where he studied the spatiotemporal organization of cell membrane components by means of state-of-the-art nanoscopy techniques. His studies contributed to the understanding of the mechanism of lipids and receptors compartmentalization.

In 2011, he joined ICFO (Barcelona, Spain), where he is working as a Research Fellow within the Single-Molecule Biophotonics group. His research line, based on cutting-edge optical approaches (nanophotonics, super-resolution nanoscopy, multicolour single particle tracking), the development of analytical tools (Bayesian inference, machine learning) and the application of these methods to study biological problems related to health, such as the molecular mechanisms of transport, the dynamics and organization of components of stem cell nuclei (chromatin) and the plasma membrane (pathogen recognition receptors).

His independent research line  $\diamond$ QUantitative Biolmaging of Cellular Processes $\diamond$  aims at determining how fundamental processes underlying cell function are controlled by the dynamic interplay of molecular components. The accurate description of these molecular mechanisms in cells is still challenged by instrumental limitations and intrinsic properties of the system under investigation, in spite of the recent development of groundbreaking techniques. His research simultaneously faces these challenges from three different angles: i) the implementation of dedicated state-of-the-art photonics tools for nanoscopy; ii) the design and application of analytical approaches allowing extraction of quantitative information at the molecular level; iii) the use of numerical simulations and analytical modeling to complement experimental data and provide falsifiable predictions. The combination of these approaches has already been successful in providing a complete picture and a comprehensive understanding of two investigated topics, such as the nucleosome organization in stem cells (Cell, 2015) and the dynamics of membrane receptor (Phys. Rev. X, 2015).

Besides impacting fundamental aspects of science, his research provides insights on the mechanisms of immunological response and applications for the identification of stem cells, along the  $\diamond$ Health, demographic change and wellbeing $\diamond$  Societal Challenge of the H2020 program, and includes the development of new technology in photonics (considered as one of the key emerging technologies by the H2020 program).

#### Resumen del Currículum Vitae:

Dr. Carlo Manzo obtained his Master in Science ( $\diamond$ Laurea $\diamond$  degree) in Physics in 2001 and his PhD degree in Physics in 2005 at the University of Naples (Italy) with top honors.

He has worked from 2006 to 2008 as postdoctoral fellow at the Emory University (Atlanta, USA) and from 2008 to 2011 at IBEC (Barcelona, Spain) on topics at the interface between physics and cell biology in health and disease. From 2011, he is working as Research Fellow at ICFO (Barcelona, Spain).

He is largely experienced in implementing single molecule techniques and optical diagnostic tools aimed at the investigation of fundamental mechanism in cell biology. His experimental skills cover super-resolution imaging, mechanical nanomanipulations and fluorescence microscopy. His technical expertise is complemented by skills in computer and data science, modeling and data analysis, theoretical and statistical physics.

His research interests include the study of fundamental processes underlying cell function and how they are regulated by the dynamic interplay of molecular components.

Dr. Manzo has authored 27 peer-reviewed papers in leading journals including Cell, PNAS, Phys. Rev. X, Nucl. Acids Res., Nanoletters, Phys. Rev. Lett. and Biophys. J., as well as 5 book chapters. His work has made a big impact with about 800 citations and an h-index of 12 as of January 2015 (Google Scholar). He has presented his work in about 30 international events and delivered 7 invited lectures and colloquia.

He is also involved in the technology transfer of his research results for both scientific and commercial interest. He is the author of a patent application and wrote a software algorithm currently being evaluated by a company for potential commercial purposes.

He has extensive teaching experience in physics and biophysics. He has taught the bachelor courses PHYS380 and ECFS190 at the Emory University (Atlanta, USA); he has been lecturer and teaching assistant for the course in  $\diamond$ Structure of Matter $\diamond$  at University of Naples



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(Italy) and he has imparted several demonstrative and hands-on courses in biophysics and nanoscopy at the master level (Emory Univ., IBEC, ICFO). He is also involved in outreach activities to promote science to the general public.

He has supervised about 10 students, including 1 PhD and 1 master thesis, several master and undergraduate projects. Currently, he is supervising 2 PhD students.

He has participated in several international projects financed from the European Community, the Human Frontiers Science Program and the NIH in highly interdisciplinary areas, demonstrating capabilities in attracting independent funding and establishing a world-wide network of collaboration with experts in the fields of biophysics, immunology and experimental and theoretical physics.

He has received prestigious fellowships and awards including a Marie Curie experienced researcher fellowship and a Howard Hughes/Emory University scholarship.

He is a member of the American Biophysical Society and of the Spanish Biophysical Society, referee of several scientific journals (Scientific Reports, Biophysical Journal, BMC Bioinformatics, Molecular Crystals and Liquid Crystals) and has been invited to be vocal in a PhD defense tribunal.

He is currently the Community Manager of the Spanish Biophysical Society.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

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**Nombre:** VALLE ROSADO, IVAN  
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**Área Científica:** Biología Fundamental y de Sistemas  
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#### Título:

Papel de la ruta de la Anemia de Fanconi en la reparación del DNA causada por compuestos metabólicos endógenos.

#### Resumen de la Memoria:

Mi carrera científica comenzó en 2001, como alumno interno en el Dept. de Genética, estudiando la falta de función del gen *qid74*, mediante recombinación homóloga en el hongo *T. harzianum*. En 2002, atraído por la potencia predictiva de la genética, llevé a cabo mi tesis doctoral en las bases genética y bioquímica del ensamblaje de partículas prerribosómicas usando como modelo la levadura *S. Cerevisiae*. Este periodo me permitió adquirir un conocimiento excepcional sobre genética y bioquímica, del proceso de síntesis de ribosomas, y me permitió establecer colaboraciones con grupos nacionales e internacionales del campo. En 2007 defendí mi tesis doctoral, y expandí mis conocimientos y mi experiencia en biología molecular y genética usando líneas celulares humanas mediante una estancia posdoctoral en el laboratorio del Dr. José Antonio Pintor-Toro en CABIMER, en el que diseñamos y testamos librerías de shRNA en líneas celulares tumorales. Tras este periodo de formación, quise dedicarme al campo de los defectos en la reparación del DNA asociados a condiciones patológicas en humanos. Obtuve una beca posdoctoral FEBS para unirme al laboratorio del Dr. Patel en el LMB en Cambridge, UK. Mi proyecto se basó en descubrir el papel biológico en líneas celulares de la helicasa de DNA FANCM que es defectuosa en la enfermedad Anemia de Fanconi. En 2009, obtuve la beca "Career Development Fellowship" del Medical Research Council, destinada a la formación de "group leaders" para estudiar los efectos de los aldehídos tóxicos en la Anemia de Fanconi, usando modelos genéticos celulares y murinos. Estos trabajos han sido publicados en Nature, Nature Genetics, Nature Structural and Molecular Biology, Science o Molecular cell.

En 2013 obtuve un contrato Miguel Servet para PI emergentes en investigación biomédica que sufraga mi salario, para el estudio del papel del formaldehído en modelos animales que recapitulen enfermedades humanas que cursen con fallo medular debido a la muerte selectiva de las células madres hematopoyéticas. Además, el proyecto asociado a este contrato financia el salario de un técnico durante 3 años y un presupuesto limitado para material consumible. En 2014 se me concedió un proyecto del MINECO como PI, para el estudio del papel que juega el ácido tetrahidrofólico en la toxicidad por formaldehído en líneas celulares y en animales murinos deficientes en la ruta AF. En 2015, me han concedido un proyecto de la Acción Estratégica en Salud, para el estudio de las modificaciones epigenéticas causadas por el formaldehído. Llegar a ser investigador principal en España es un proceso muy largo. Desde 2013 he sido aceptado en el laboratorio del IBiS, dirigido por el Dr. José Antonio Pérez Simón.

Durante mi carrera investigadora, he llevado a cabo proyectos que implican un alto grado de adaptación a los cambios, y he tenido que adaptarme al uso de modelos de estudio de diversa índole. Mi implicación intelectual y técnica me ha permitido llevar a cabo una investigación responsable. He supervisado estudiantes de distinta índole, durante el último año de mi etapa predoctoral y posdoctoral. En IBiS, he explotado todo mi conocimiento para dirigir tanto personal técnico del laboratorio, como estudiantes de doctorado y a un postdoctoral, los cuales han adquirido toda la formación necesaria ser competentes en este campo de investigación.

#### Resumen del Currículum Vitae:

##### Currículum Vitae

##### Research experience

March 2013- Present Miguel Servet (IBiS). HUVR.  
Aug 2007-March 2013 Postdoctoral post n at the LMB Cambridge, UK.  
Feb 2007-Jul 2007 Postdoctoral post at the CABIMER CSIC.  
Apr 2002-Feb 2007 Ph.D. student (University of Seville).  
Sep 2000-Sep 2001 Research student (University of Seville).

##### Publications

- García-Rubio ML, Pérez-Calero C, Barroso SI, Tumini E, Herrera-Moyano E, Rosado IV, Aguilera A. (2015). PLoS Genetics.
- Rosado IV\*, Pontel LB\*, Burgos-Barragan G, Garaycochea JI, Yu R, Arends MJ, Chandrasekaran G, Broecker V, Wei W, Liu L, Swenberg JA, Crossan GP, Patel KJ. (2015). Molecular Cell.
- García-Gómez J.J., Fernández-Pevida A., Lebaron S., Rosado I.V., Tollervy D., Kressler D. and de la Cruz J. (2014). PLoS Genetics.
- Rosado I.V., Langevin F., Crossan G.P., Takata M., Patel K.J. (2011) Nat. Struc. Mol. Biol.
- Langevin F., Crossan G.P., Rosado I.V., Arends M.J., Patel K.J. (2011) Nature.
- Crossan G.P., van der Weyden L., Rosado I.V., Langevin F., Gaillard P.H., McIntyre R.E.; Sanger Mouse Genetics Project, Gallagher F.,



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

### Turno de acceso general

Kettunen M.I., Lewis D.Y., Brindle K., Arends M.J., Adams D.J., Patel K.J. (2011). Nat. Genetics.  
7. Pace P., Mosedale G., Hodkinson M.R., Rosado I.V., Sivasubramaniam M., Patel K.J. (2010). Science.  
8. Rosado I.V., Niedzwiedz W., Alpi A. F. and Patel K. J. (2009). Nucl. Acid. Res.  
9. Rosado I.V., Kressler D. & de la Cruz J (2007). Nucl. Acid. Res.  
10. Rosado I. V., Rey M., Codón A.C., Govantes J., Moreno-Mateos M.A. & Benítez T (2007). Fungal Genet. Biol.  
11. Rosado I.V., Dez C., Lebaron S., Caizergues-Ferrer M., Henry Y. & de la Cruz J (2007). Mol. Cell. Biol.  
12. Rosado I.V., & de la Cruz J. (2004). RNA.  
13. Codón A.C., Rincón A.M., Moreno-Mateos M.A., Delgado-Jarana J., Rey M., Limón C., Rosado I.V., Cubero B., Peñate X. & Benítez T (2003). Journal of Agricultural and Food Chemistry.

Nr. of publications in D1: 9/13  
Nr. of publications in Q1: 13/13  
Nr of First author publications: 7/13

#### Proyectos recientes:

- El formaldehído como agente causante de modificaciones epigenéticas en enfermedades neoplásicas hematológicas (PI15/01409). AES2016-2018. IP: IV Rosado.
- Descifrando el papel genotóxico del formaldehído en la Anemia de Fanconi. (BFU2013-41457-P). 2014-2015. IP: IV Rosado.
- Cannabinoides como potenciales agentes terapéuticos en el Mieloma Múltiple (PI-0335-2013). Junta de Andalucía 2016-2018.

#### Patents

- Methods and kits to generate transcriptome-specific siRNAs libraries by convergent transcription
- JA Pintor Toro; MÁ Moreno Mateos; I Valle Rosado
- WO 2009071722 (A1)

#### Invited speaker in conferences

First CABIMER Genome Biology Meeting, Seville Spain. Keynote Speaker.  
14th Fanconi Anemia Network, Barcelona Spain. Invited Speaker.  
IBiS Oncohematology Dept seminars, Seville Spain. Invited Speaker.  
SEBBM, Valencia, Spain. Invited Speaker.

#### Teaching experience

Practical lectures (Molecular biology, Dept. of Genetic, U. Seville: 20 hours/year, 2002-2005).  
Lecturer (Biología Molecular del Cancer, Dept. of Medicine, U. Seville: 2 hours/term, 2014-present).

#### Awards and Fellowships

- Miguel Servet Contract (2013).
- Career Development Fellowship from Medical Research Council (2010)
- Long term Fellowship from FEBS (2007)
- Student Fellowship from the Spanish Ministry of Education (2001).



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

### Turno de acceso general

**Nombre:** NOGALES ENRIQUE, JUAN  
**Referencia:** RYC-2015-19251  
**Área Científica:** Biología Fundamental y de Sistemas  
**Correo Electrónico:** jnogales@cib.csic.es

#### Título:

Systems Biotechnology

#### Resumen de la Memoria:

My research career spans multidisciplinary approaches whose common goal is the understanding of microbial systems, from the molecular characterization of their fundamental components (gene, proteins) and their interrelationships, to their systems properties (phenotype, robustness), towards biotechnological applications.

My predoctoral stage covers my Thesis Degree (Univ. Extremadura, 2003, Premio extraordinario de licenciatura), and my PhD (Univ. Complutense of Madrid, 2004-2009). During my PhD I worked in several research projects covering fundamentals and biotechnological aspect of aromatic acids degradation. I published five journal articles, (four of them as first author in top journals like JBC and Molecular Microbiology) and a book chapter.

After my PhD I joined to Prof. Bernhard Palsson's group, first at University of Iceland (Iceland, 2010) and later at University of California, San Diego (USA, 2011-2012). My post-doctoral stage provided me with a deep knowledge on the basic foundations of the cutting-edge field of systems biology. I published six research papers, (5 of them as first author including two in high impact journals such as Nature Biotechnology and PNAS).

After my postdoctoral I joined to CIB-CSIC (2013- present). During this stage I have worked in several projects focused on systems metabolic engineering. I have developed my own metabolic modeling platform. I have worked in the establishment of an independent research line focus on systems biotechnology, a growing field poorly developed in Spain. In this step, I have published nine papers, three of them as corresponding author, and I have been invited as speaker to nine national and international conferences. In addition, I have co-advised three Doctoral Thesis (one already presented, 2014) and one Thesis degree. I have contributed to the design and writing of five funded grants in which I act as Principal Investigator in two of them, one funded by the EU and other by the MINECO.

#### Resumen del Currículum Vitae:

##### PUBLICATIONS

Co-Author. Mol Syst Biol. Oct 14;11(10):831 (2015)  
Co-Author. Syst Appl Microbiol. Oct;38(7):462-71 (2015)  
Co-Author. Appl Environ Microbiol. Aug 15;81(16):5477-85 (2015)  
Co- Author. Environ Microbiol. Sep;17(9):3362-78 (2015).  
Senior and Corresponding Author. Book Chapter: Hydrocarbon and Lipids Microbiology Protocols (2015).  
Senior and Corresponding Author. Mol Biosyst 11(1), 60-70 (2015).  
Co-author. Genome announcements Feb 13;2(1) (2014)  
Senior and Corresponding Author. Book Chapter: Hydrocarbon and Lipids Microbiology Protocols (2014).  
Co-First Author. Nature Biotechnology 32 (5), 447-452 (2014).  
Co-author. Genome announcements 2 (1), e01248-13 (2014).  
Co-author. Microbial Cell Factories 12, 118 (2013).  
Co- author. Current Opinion in Biotechnology 24 (3), 4311-442 (2013).  
Co-First Author. Bioengineered. 3 (3), 158-163 (2013)  
First Author. International Journal of Hydrogen Energy 37 (17), 12205-12218 (2012)  
First Author. PNAS 109 (7), 2678-2683 (2012)  
First Author. Molecular Microbiology 9 (2), 279-551 (2011)  
Co-First Author. Book Chapter Handbook of Hydrocarbon and Lipid Microbiology, 1297-1325 (2010)  
First Author. BMC Systems Biology, 2 (1), 79 (2008)  
First Author. Microbiology, 153 (2), 357-365 (2007)  
Co-Author. Environ Microbiol 8 (1), 165-177 (2006)  
First Author. JBC, 280 (42), 35382-35390 (2005)  
First Author. Planta, 219 (2), 325-331 (2004)

##### DOCTORAL THESES

1. PhD Student: Loreine J. Agulló Carbajal

Title: Nuevos aspectos del control del metabolismo en Pseudomonas putida KT2440: metabolismo del ácido fenilacético y papel del gen *apaH*

Reading Date: February, 2014. Sobresaliente "cum laude"



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

### Turno de acceso general

2. PhD Student: Lucía Agudo Algibe

Title: Mejoramiento de las capacidades nutricionales de la Spirulina mediante abordajes de Biología de Systemas

Reading Date: In progress

3. PhD Student: María-Tsampika Manoli

Title: Bioingeniería a nivel de sistemas de la producción de PHA funcionalizados en P. putida

Reading Date: In progress

#### MASTER THESES

Student: Lucía Agudo Algibe

Title: Reconstrucción y análisis a escala genómica del metabolismo de la bacteria modelo en degradación anaeróbica de compuestos aromáticos Azoarcus sp. CIB.

Reading Date: September, 2014. Matricula de Honor

#### INTERNATIONAL STAYS

Center. Department of Bioengineering, University of California at San Diego

City: San Diego, California, USA

Period: 2 Years. From November 2010 to November 2012

Center. Center for Systems Biology, University Iceland

City: Reykjavic, Iceland

Period: 7 Months. From April 2010 to November 2012

Center. Department of Bioengineering, University of California at San Diego

City: San Diego, California, USA

Period: 4 Months. From June 2007 to October 2007

#### PROJECTS

1. Systems analysis of the metabolic robustness in bacteria (RobDcode). IP: J Nogales. Spanish Ministry of Economy and Competitivity. Ref: BIO2014-59528-JIN. Funding: 200,860 €. Duration: 2016-2019.

2. Living (LIAR). Coordinator, Rachel Armstrong (U. Newcastle). PI CIB Team: J Nogales. EU H2020. Ref. FET-OPEN-686585. Funding: 975,151.25 €. Duration: 2016-2019.

#### FELLOWSHIPS

2010-2012. Fellow from the Programa de Ayudas Postdoctorales en el extranjero MEC/FULBRIGHT

2005-2009. I3P Predoctoral Fellowship from the Consejo Superior de Investigaciones Científicas

2007. I3P Short-stay fellowship from the Consejo Superior de Investigaciones Científicas

#### CONFERENCES

Author in a total of 30 national or international conferen





## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

### Turno de acceso general

**Nombre:** ARENAS BUSTO, MIGUEL  
**Referencia:** RYC-2015-18241  
**Área Científica:** Biología Fundamental y de Sistemas  
**Correo Electrónico:** miguelmmmab@gmail.com

#### Título:

Molecular Evolution and Population Genetics in Biological Systems that are relevant for Biomedicine

#### Resumen de la Memoria:

In 2003 I graduated at the University of Santiago de Compostela. I also obtained a Ms degree in 2005, which derived in a publication on binding affinities of HIV-1 protease inhibitors.

In 2010 I obtained my PhD degree -European Doctorate, sobresaliente cum laude, Best Thesis Award- in the University of Vigo under the supervision of Prof. David Posada. My thesis derived in 9 publications, 7 as first author, on molecular evolution and applications to biomedicine of HIV-1. During my PhD I also worked in the institutions: Brigham Young University (USA), University of Reading (UK) and Instituto de Salud Carlos III.

In 2010 I moved to the University of Bern (Switzerland), lab of Prof. Laurent Excoffier, as a postdoc to participate in the European FP7 project **SCALES**, where I studied the influence of range contractions, range shifts and habitat fragmentations on genetic diversity through the analysis of genome data. 6 publications were produced, 4 as first author.

In 2012 I obtained a Juan de la Cierva fellowship and I moved to the Centre for Molecular Biology Severo Ochoa (CSIC) with Prof. Ugo Bastolla. There I was involved in the analysis of NGS data, genome-wide and protein structure evolution. 12 publications were produced, 9 as first/last author.

In 2014 I received a European EMBO fellowship and I spent some months in the University of Wyoming (USA), lab of Prof. David Liberles, to investigate ancestral reconstruction accounting for structural constraints.

In 2015 I obtained a FCT Starting Grant and I moved to the Institute of Molecular Pathology and Immunology of the University of Porto (IPATIMUP, Portugal). Here I investigate the molecular evolution and population genetics of HIV-1 and cancer tumor cells. So far 4 publications have been produced, all of them as first/last author.

So far my work has resulted in 32 peer-review publications (28 articles in journals and 4 book chapters; 21 articles in the Q1) and where I am the first/last author of 25 publications. These include prestigious journals such as: Mol Bio Evol (x7 articles; x6 as first author with IFs: 9.10, 9.10, 9.10, 14.31, 10.35, 7.28, sum 59.2 that is higher than any journal; x1 as second author), Mol Ecol, Bioinformatics, Retrovirology, Genetics (x2 articles), Heredity (x2 articles), Mol Phylogenet Evol, Infect Genet Evol, PLoS Comput Biol, PLoS ONE, BMC Bioinformatics (x2 articles), J Comput Chem, Curr Genomics, Curr HIV Res, J Mol Evol, among others.

I worked in a variety international and national research Projects (including European FP7 program), currently I am the Principal Investigator of one.

I contributed to 35 international and national congresses and seminars (some upon invitation). I organized an international research congress and I also performed science divulgation to non-scientists.

I am Associate Editor of 3 journals, I reviewed 57 articles for 24 different journals and I am Referee of research grants for the DC CFAR (USA).

I taught in Bs, Ms and PhD programs of diverse universities and I supervised a variety of students.

#### Resumen del Currículum Vitae:

- European Doctorate, highest score **sobresaliente cum laude** and best Thesis award of the University of Vigo in 2010.

- Research work in a variety of internationally recognized research centres. Abroad: Brigham Young University (USA), University of Wyoming (USA), University of Reading (UK), University of Bern (Switzerland), University of Porto (Portugal). In Spain: University of Santiago de Compostela, University of Vigo, Instituto de Salud Carlos III (ISCIII), Centre for Molecular Biology **Severo Ochoa** (CSIC).

- 32 publications (28 research articles and 4 book chapters). Importantly, first/last author of 25 publications. The journals are the following: Molecular Biology and Evolution (x7 articles; x6 as first author with IFs: 9.10, 9.10, 9.10, 14.31, 10.35, 7.28, sum 59.2 that is higher than any journal; x1 as second author), Molecular Ecology, Bioinformatics, PLoS Computational Biology, Retrovirology, Genetics (x2 articles), Heredity (x2 articles), Molecular Phylogenetics and Evolution, Infection Genetics and Evolution, PLoS ONE, Journal of Computational Chemistry, BMC Bioinformatics (x2 articles), Current Genomics, Current HIV Research, Journal of Molecular Evolution, Computational and Mathematical Methods in Medicine, Frontiers in Genetics (x3 articles).

The publishers list of the book chapters is the following: Oxford University Press, Pensoft Publishers, CRC Press/Taylor & Francis, Wiley.

Number of publications in the first quartile (Q1): 21.

- I participated in international and national I+D+I research Projects, including from the European FP7 program. Currently I am the Principal Investigator (PI) of an active research Project.

- 35 international and national contributions to congresses and seminars (some of them upon invitation).

I organized an international research congress, the XVII Portugaliae Genetica. I also performed divulgation of science to non-scientists





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ADMINISTRATIVA

## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

### Turno de acceso general

(article in the newspaper "Faro de Vigo", 2015).

- Concerning scientific responsibilities:

I have reviewed 57 articles for the following 24 journals.

I am Associate Editor of three Journals: American Journal of Computational Biology; American Journal of Molecular Evolution; Frontiers in Evolutionary and Population Genetics (specialty sections: Frontiers in Genetics, Frontiers in Ecology and Evolution, Frontiers in Plant Science).

I am Referee of Research Grants for the DC CFAR program (USA).

- I participated in a variety of international and national workshops and courses such as the ♦Workshop on Molecular Evolution (MBL, Boston, USA)♦, ♦Molecular Markers and Population Genetics (Gulbenkian Institute of Science, Lisbon, Portugal)♦, ♦Phylogenetics and Genealogies of DNA: Reconstruction and Applications (University of Barcelona, Spain)♦, ♦Structural Bioinformatics: Modeling and Simulation of Biological Molecules (University of Santiago de Compostela, Spain)♦ and ♦Workshop on Coalescent Theory (Gulbenkian Institute of Science, Lisbon, Portugal)♦.

- Teaching activity at all Bs, Ms and Doctoral programs in the University of Santiago de Compostela, University of Vigo, University of Bern, University of Lausanne, University of Geneva, University Autonoma of Madrid and University Complutense of Madrid.

I supervised the final research projects of several students.

- I am a member of a variety of research societies and research networks.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

### Turno de acceso general

**Nombre:** JIMENO GONZÁLEZ, SILVIA  
**Referencia:** RYC-2015-17246  
**Área Científica:** Biología Fundamental y de Sistemas  
**Correo Electrónico:** silvia.jimeno@cabimer.es

#### Título:

Transcription elongation, a coordinated process with pre-mRNA processing and chromatin

#### Resumen de la Memoria:

Since I started my PhD I have been interested in how the RNA polymerase II (RNAPII) is able to coordinate transcription elongation with other processes like pre-mRNA processing and the remodeling of chromatin structure.

During my PhD studies at Sebastián Chávez's laboratory I was focused on the study of the influence of chromatin structure on transcription elongation in *Saccharomyces cerevisiae*. I isolated histone mutants with a defect in transcription elongation and I studied the function of FACT complex in transcription elongation in vivo. I set up a system to downregulate FACT to measure the effect on transcription elongation of genes with different chromatin structure. FACT complex was more necessary in those genes with a strong chromatin positioning. I also did a stay at José E. Pérez Ortín's laboratory where I performed Genomic Run-On and Chromatin Immunoprecipitation experiments. The main contribution I made to the field of transcription was the idea of having different factors regulating elongation of different genes.

In my first postdoctoral stay at Torben Heick Jensen's laboratory in Aarhus University (Denmark) I decided to study about the quality control of the pre-mRNA. My research was focused on the protein Rat1, a 5'-3' exonuclease mainly implicated in transcription termination. I discovered a completely new function of the 5'-3' exonuclease Rat1 in degrading uncapped RNA during transcription promoting RNAPII premature transcription termination and a role of Rat1 regulating transcription termination through the modification of the RNAPII CTD. In this period I made relevant contributions to the field of transcription and mRNA processing as I demonstrated for the first time a mechanism to control the quality of the pre-RNA at the 5' end.

After my postdoctoral stay abroad I joined José Carlos Reyes's laboratory in the CABIMER where I changed from yeast as a model organism to human cells and I went back to my interest in chromatin structure and transcription elongation. I studied the relationship between the first (+1) nucleosome inside the gene and promoter proximal pausing in vivo. With the system that I developed I found that when the +1 nucleosome is very strongly positioned the pause is favored. Interestingly, an increase in the pause improves the quality of the pre-mRNA. I also worked on the function of chromatin on transcription rate and pre-mRNA processing. Using a cell line in which histones levels could be downregulated I discovered that having a normal histone supply is essential to maintain the normal transcription rate. I also analyzed the effect of the faster transcription on the pre-mRNA quality and I found that splicing was defective in those conditions. In this period I made important contributions to understand the function of chromatin as a structure on transcription not being just an obstacle but a regulator of the speed and the pauses of the RNA polymerase II for the proper function of processes associated to transcription, like pre-mRNA processing.

In the last months I have been working in the group of Felipe Cortés Ledesma initiating a project about the regulation of transcription through DNA double strand breaks (DSB). The preliminary results indicate that the Topoisomerase II regulates transcription at the level of early elongation and we are trying to unravel the mechanisms and factors implicated.

#### Resumen del Currículum Vitae:

2000: Internship from the Ministry of Culture and Education at Sebastián Chávez's laboratory, Department of Genetics, Seville University

2001: FPU fellowship from the Ministry of Education and Culture for a PhD in Sebastián Chávez's laboratory to investigate about the influence of chromatin structure on transcription elongation in *Saccharomyces cerevisiae*.

2005: Three months stay at José E. Pérez Ortín's laboratory in the University of Valencia to learn about Genomic Run-On and ChIP experiments.

2006: Publication of an article in the journal *Molecular and Cellular Biology* as first author about the function of FACT in transcription elongation through chromatin templates.

2007: PhD thesis defense and postdoc position in Torben H. Jensen's laboratory, Aarhus University. My research was focused on the quality control of uncapped pre-mRNAs during transcription elongation in yeast.

2009: Publication of three articles from the research I developed in my PhD thesis; one in *PLoS Genetics* as second author, another one in *EMBO Journal* as sixth author and the last one in *PLoS Genetics* as sixth author.

2010: Publication of a paper in *Molecular Cell* as a first author describing a new step to control the quality of the pre-mRNAs in transcription elongation. I also directed the work of the Master Student Henriette Eenberg. Maternity leave for 1 year.

2011: Juan de la Cierva fellowship to work at José C. Reyes's laboratory, CABIMER, CSIC, to investigate about chromatin and transcription elongation in human cells.

2013: Direction of two Master Thesis, of Paula Aguilera and Laura Payán.

2014: Publication of an article in *RNA* as first author with the research describing a function of the exonuclease Rat1 in the regulation of RNA polymerase II CTD phosphorylation. Maternity leave for 5 months.



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ADMINISTRATIVA

## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

### Turno de acceso general

2015: Publication of two articles both as first and co-corresponding author, one in Nucleic Acids Research about the function of the +1 nucleosome in promoter proximal pausing in human cells and another one in PNAS about the role of chromatin regulating transcription elongation rate and pre-mRNA splicing. I also started working as a postdoc in Felipe Cortés Ledesma's laboratory. My project deals with the regulation of transcription through DNA Double Strand Breaks.



## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

### Turno de acceso general

**Nombre:** GASCÓN JIMÉNEZ, SERGIO  
**Referencia:** RYC-2015-19185  
**Área Científica:** Biología Fundamental y de Sistemas  
**Correo Electrónico:** sergio.gasc@googlemail.com

#### Título:

Brain disease and reprogramming

#### Resumen de la Memoria:

In my first contribution I addressed the molecular mechanisms responsible for a fast, efficient and irreversible down-regulation of the subunits of the N-Methyl-D-Aspartate type of glutamate receptors (NMDARs) and the interacting proteins PSD-95, Kidins220/ARMS and TrkB during the delayed neuronal death occurring in cerebrovascular diseases. Since these are fundamental molecules for the normal synaptic function and neuronal survival, this might have a crucial impact in ischemic disorders of the Central Nervous System (CNS). Additionally, we found that the protease calpain has a major role in this process. This discovery will help to design new therapeutic strategies improving neuronal survival (see Garmir-Morralla et al., 2015). Papers published in regard to this are Gascón et al., 2007a, Lopez-Menendez et al., 2009, Vidaurre and Gascón et al., 2012.

My internship in the previous laboratory of Prof. Peter Scheiffele (Columbia University, New York) and in collaboration with Prof. Francisco Gómez Scholl (IBiS, Sevilla) allowed me to obtain a valuable expertise in the design/application of lentiviral vectors for expression of recombinant proteins. This was crucial for the development of 2 papers in collaboration, showing that adult Neural Stem Cells (aNSCs) from the Sub-ventricular Zone (SVZ) can generate glutamatergic neurons (Brill et al., 2009) and that neuronal and oligodendroglial progenies are generated from two different pools of SVZ-resident aNSCs (Ortega et al., 2013).

As part of my postdoctoral work, I had the opportunity to collaborate with Prof. Benedikt Berninger, heading the group of neuronal reprogramming in Prof. M. Götz's laboratory. During this collaboration I investigated a fundamental question in the neuronal reprogramming field, namely whether cell division is or is not a prerequisite for neuronal conversion. By using video time-lapse analysis I found that non-proliferative astrocytes transfected with neuronal fate determinants could move towards neuronal identity. These data are collected in the articles Heinrich et al., 2009 and Heinrich et al., 2010, where I contributed as second author.

In parallel to my work on neuronal reprogramming of glial cells, I established a new model of reactive glia culture from injured cerebral cortex. This methodology corroborated that neurospheres with stem cell (NSC)-like properties isolated from the injured cortex (Buffo et al., 2008) derive from aNSCs migrating from the SVZ and not resident cortical astrocytes as previously believed. This concept is highly relevant for the scientific community working in the field of stem cells and produced an article published in "Cell Stem Cell" (Faiz et al., 2015), where I contributed as third author.

My last and more important contribution has been published in Cell Stem Cell (Gascón et al., 2015), where I am first and co-corresponding author. Here, we addressed for the first time the basic cellular and ultimately metabolic mechanisms during direct reprogramming from either astrocytes or fibroblasts into induced neurons. We identify crucial metabolic constraints blocking the conversion process into neurons by boosting oxidative stress, lipid peroxidation and finally ferroptosis. Treatments with antioxidants and/or co-transduction with Bcl2 result in unprecedented efficiency of direct neuronal reprogramming in the adult injured cerebral cortex.

#### Resumen del Currículum Vitae:

I started my research career in 2002, and since then I have been consistently producing scientific contributions that have been internationally recognized. I have authored an international patent and 16 original papers which have been cited a total of 696 times. My scientific background includes training in 3 different countries (Spain, USA and Germany) and 4 different institutes (IIB in Madrid, Columbia University in New York and LMU/HMGU in Munich). The significance of my research is corroborated by the fact that my work was selected for international scientific meetings such as the XII European Meeting on Glial Cells, for which I have been organizer, and the Conference-Debate "Regenerative medicine" from the Nature Publishing Group. Additionally, I successfully supervised the PhD work of the student Elisa Murenu and the internship of the Master's student Anna Katarzyna Marciniak.

After being trained as a biologist at the Complutense University of Madrid, I got exposed to the field of brain disease during my PhD work under the supervision of Prof. M. Diaz-Guerra, in which I analysed the role of glutamate NMDA receptors and other interacting postsynaptic proteins in cerebrovascular disease. My findings produced 5 original papers from which I am first author of 4 including renowned journals such as "Molecular Psychiatry". In addition, during my PhD work I moved to the lab of Prof. P. Scheiffele (Columbia University) to develop lentiviral vectors for the efficient expression of recombinant proteins in neurons producing an additional article from which I am also first author.



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Y GESTIÓN ECONÓMICA Y  
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SUBDIVISIÓN DE  
PLANIFICACIÓN Y GESTIÓN  
ADMINISTRATIVA

## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2015

### Turno de acceso general

Driven by my strong interest in brain disease, after my PhD training I moved to Munich to the lab of Prof. M. Götz where I focused in the field of neuronal direct reprogramming. I actively participated in one of the first two worldwide articles demonstrating that neuronal direct reprogramming is feasible. My active contribution in the field is corroborated by an international patent with a 70% of participation and my co-authorship in 5 publications in the field, being first- and co-corresponding author of the last publication in "Cell Stem Cell". However, my scientific contribution was not restricted to the reprogramming field, as I also participated in 4 papers addressing fundamental questions in regard to adult neurogenesis and the stem cell potential of reactive glia. Therefore, I authored papers in journals with the reputation of "Molecular Psychiatry" (1<sup>o</sup> author), "Nature Neuroscience" (5<sup>o</sup> author), "Nature Cell Biology" (2<sup>o</sup> author) and 3 "Cell Stem Cell" papers (1<sup>o</sup>/corresponding, 3<sup>o</sup> and 6<sup>o</sup> author), among others, with the impact factor in the range of 14.5-22.27.