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AGENCIA ESTATAL DE INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2018

Turno de acceso general

Nombre: AMBROGIO , CHIARA
Referencia: RYC2018-024232-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: chiara.ambrogio@gmail.com

Título:

Targeting the KRAS oncogene in lung cancer

Resumen de la Memoria:

During my PhD in Immunology and Cellular Biology at the Center of Research in Experimental Medicine (CeRMS) in Torino in the Chiarle s Lab (2004-2009) I studied NPM-ALK driven lymphoma both in vitro and in vivo (Ambrogio et al, Blood 2005; Ambrogio et al, Cancer Res 2008, Ambrogio et al, Cancer Res 2009). At the end of my PhD training I started a project on non-redundant roles of Cdc42 and Rac1 in ALK-rearranged lymphoma supported by a MFAG (My First AIRC Grant by the Italian Association for Cancer Research) (Choudari et al, Blood 2016, co-last and corresponding author).

My principal study during my postdoc in Mariano Barbacid s lab contributed to the understanding of K-Ras driven lung tumorigenesis by focusing on the early stages of tumor progression. We demonstrated that a gene expression signature corresponding to malignant tumors, at least in K-Ras-driven lung adenocarcinoma, is acquired much earlier than what is conventionally accepted, even at the stage of early lesions of few hundred cells.

Thanks to this approach I was able to identify DDR1/NOTCH targeted therapy as a novel treatment for K-Ras-driven lung adenocarcinoma (Ambrogio et al, Nature Medicine, 2016, co-corresponding author).

Moreover, during my last two years at the CNIO, I started an independent line of investigation to study the mutual regulation of K-Ras and EGFR oncogenes both in vivo and in vitro by generation of knock-in mouse models that express K-Ras and EGFR in the lung, either alone or in combination. My research data demonstrated that the expression of both oncogenes is detrimental for tumor progression, instead of conferring a selective advantage to lung tumor cells (Ambrogio et al, Oncogene, 2016, co-corresponding author).

Recently, I ve taken part to the exciting discovery of BRAF inactivating mutations as new driven oncogenes in lung adenocarcinoma (Nieto et al, Nature, 2017, second author). Our results suggest that patients carrying BRAF inactivating mutations could benefit from therapies based on selective CRAF inhibitors.

In the Jänne s lab, I continued my work on the biology of WT and mutant KRAS in in the context of lung cancer. I was able to demonstrate by different genetic tools that the WT KRAS acts as an onsuppressor in cells that have one copy of mutant KRAS. Remarkably, WT KRAS hampers the activity of mutant KRAS by a dimerization-dependent mechanism. These finding represent a real breakthrough as they solve a long-standing conundrum on the role of the WT KRAS in KRAS mutant adenocarcinoma (Ambrogio et al, Cell, 2018, co-corresponding author).

In the next few years of my independent career, I plan to understand unique features and biological liabilities of the oncogenic KRAS isoforms in terms of molecular signaling pathways, drug sensitivity and cell growth in vitro and in vivo. I will validate new mutation-specific therapeutic strategies in KRAS-mutant patient-derived cell lines and PDX models. Next, I will study the biological properties and therapeutic implication of RAS dimerization. Finally, I will study early mediators of KRAS-driven lung tumorigenesis in vivo. Through this work, I will broaden the current understanding of the biology of KRAS in cancer with comprehensive experiments from basic biology to mouse modeling with the ultimate goal of developing new therapeutic approaches for KRAS-driven cancers.

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Resumen del Currículum Vitae:

Education

2004-2008: Ph.D. in Immunology and Cellular Biology, University of Torino. Ph.D. thesis title: "NPM-ALK oncogenic kinase controls morphology and migration in Anaplastic Large Cell Lymphoma cells overcoming TCR signaling deficit by GTPase activation"

1999-2004: BS/MS Degree in Medical Biotechnology at University of Torino. Graduated summa cum laude. Thesis title: NPM-ALK MODIFIES CYTOSKELETON AND CELLULAR SHAPE BY THE ACTIVATION OF RAC1, CDC42 AND p130CAS .

Scientific training

April 2016-present: Senior Scientist, Dr Jänne Laboratory Medical Oncology Department, Dana Farber Cancer Institute, Boston, USA

Nov 2009 March 2016: Postdoc, Dr Barbacid Laboratory, Experimental Oncology Department, CNIO, Madrid, Spain

Dec 2008 - Nov 2009: Post Doctoral Fellow in Prof R. Chiarle laboratory, CeRMS (Center of Research in Experimental Medicine), University of Torino, Italy

2004-2008: PhD student in Prof R. Chiarle laboratory, CeRMS (Center of Research in Experimental Medicine), University of Torino, Italy

2000-2004: Research apprenticeship in the Dep. of Biomedical Sciences and Human Oncology, University of Torino, Italy

Scientific production

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As an overall summary of my scientific production, since 2005 I have contributed to 46 peer-reviewed manuscripts that have been cited more than 2000 times (h-index: 22). The independence acquired as a consequence of my experience as postdoc and senior scientist, where I conducted most of the projects as leading scientist, is reflected by my role as corresponding author in several recent publications, including papers in Nature Medicine and Cell.

Supervisory teaching and mentoring activity
2016: Marco Catalano, MS, Dana Farber Cancer Institute, Boston
2012-2013: Mattia Falcone, BS undergraduate student, CNIO, Madrid
2009-2013: Ramesh Choudari, PhD Student, University of Torino
2007-2009: Matteo Menotti, MS, undergraduate student, University of Torino
2005-2008: Cinzia Martinengo, PhD, post-graduate apprenticeship and PhD training, University of Torino

Awards
2018: Scientific Merit Award from the Lung Cancer Research Foundation (LCRF)
2014: Award Com.It.Es (Organization of Italians abroad), category University and Research .
2014: Best Poster presentation award EACR-23 meeting, Munich, Germany, (July 5-8, 2014).
2012: Proffered Paper Award EACR-22, Barcelona, Spain, (July 7-10).
2012: AECC (Spanish Association Against Cancer) Postdoctoral Award, personally conferred by the Queen of Spain
2009: Award "Silvia Fiocco" for Lymphoma and Leukemia Research, Accademia dei Lincei-Roma, personally conferred by the Italian President Giorgio Napolitano
2008: Award Fondazione Costa for cancer research
2007: SIBBM Prize (Italian Society of Biophysics and Molecular Biology)

Projects and Funding
2020-2023: Harvard-Armenise Career Development Grant, independent PI
2018-2020: Principal Investigator, LCRF (Lung Cancer Research Foundation), independent PI
2017-2018: Principal Investigator, Wong Funds in Translational Oncology (DFCI, Boston), independent PI
2012-2014: AECC (Spanish Association Against Cancer) Postdoctoral Fellowship
2009-2011: CNIO-Caja Navarra International Postdoctoral Program
2009-2012: Principal Investigator, MFAG-2009 funded by AIRC (Italian Association for Cancer Research), independent PI
2004-2008: four-years PhD Fellowship funded by Italian Ministry of Education and Research

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Turno de acceso general

Nombre: HERGUEDAS FRANCES, BEATRIZ
Referencia: RYC2018-025720-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: beatrizherguedas@gmail.com

Título:

Structural biology of synaptic ion channels

Resumen de la Memoria:

My interest in protein structure started being an undergraduate student at Ignacio Fita s group in Barcelona, where I spent the summer of 2005 working on the structure determination of the catalase-peroxidase KATG. During these two months I learnt crystal structure refinement and I found how atomic models can provide essential information on the mechanism of enzymes. Afterwards I pursued my PhD working with Milagros Medina and Marta Martínez-Júlvez at the University of Zaragoza, characterizing flavin-binding proteins by protein crystallography and kinetic measurements. My main project involved obtaining structural insights into bacterial FAD synthetase, the enzyme that synthesizes FMN and FAD cofactors, but I also collaborated with colleagues in the characterization of the photosynthetic electron transfer process between Flavodoxin and Ferredoxin NADP reductase. During this period I completed my training with research visits at Juan Hermoso¿s group in the Institute for Physical Chemistry Rocasolano and Angel Martinez¿s group in the Centre for Biological Research.

As a result of my predoctoral studies, I acquired a strong technical expertise in protein crystallography and enzymology, deciding to move to the molecular neurobiology field for my postdoc at Ingo Greger¿s group at the LMB in Cambridge. My current research is focused on the characterization of AMPA-type Glutamate receptors (AMPARs), cation channels involved in neurotransmission, synaptic plasticity and memory formation. AMPARs are tetrameric ion channels composed of four core subunits (GluA1-4) which also interact with auxiliary proteins. The composition of AMPAR complexes modulates receptor properties, and varies across different brain regions and neuronal sites (synaptic and extrasynaptic sites). During my postdoc I combined protein crystallography, electron cryo-microscopy, biochemistry (peptide arrays, unnatural aminoacids) and biophysical techniques (surface plasmon resonance, thermophoresis) to gain insights into the molecular mechanisms of AMPA receptors. I determined the first structures of AMPAR heteromers (the main population of AMPAR in the brain) by cryo-EM and crystallography (Herguedas et al, Science, 2016) and I mapped the interaction of AMPAR with one of its auxiliary subunits, stargazin (Cais, Herguedas et al, Cell Reports, 2014). My current aim is to determine the architecture of native AMPA receptors, combining different AMPAR subunits and auxiliary proteins to characterize a physiologically relevant receptor. In this line I have recently determined the cryo-EM structure of an AMPAR heterotetramer in complex with TARP8, which provides insights into the architecture of the pore in heteromeric channels, the binding of lipids in the transmembrane region of the receptor and the atomic details of the structural bases of the modulation of AMPAR function by TARP8.

I am also interested in developing new methods for the extraction and stabilization of membrane proteins, as current methods based in detergent extraction often lead to protein inactivation.

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Resumen del Currículum Vitae:

EDUCATION:

2007-2011	PhD, University of Zaragoza (Premio Extraordinario de Doctorado).
2001-2006	Degree in Biochemistry (Premio Extraordinario and Tercer Premio Nacional de Licenciatura)

RESEARCH EXPERIENCE:

2011-2019	Postdoctoral Scientist. MRC Laboratory of Molecular Biology, Cambridge, UK (two periods of maternity leave, 1 year).
2007-2011	PhD student. University of Zaragoza.
2009	2 months research visit at Instituto de Quimica Fisica Rocasolano (CSIC)
2008	6 months research visit at Instituto de Quimica Fisica Rocasolano (CSIC)
2007	3 months research visit at Instituto de Quimica Fisica Rocasolano (CSIC)
2006	4 months research visit at Centre of Biological Research (CSIC)
2005	2 months research visit at Molecular Biology Institute of Barcelona (CSIC).

PUBLICATIONS:
8 first-author publications (including 2x Science, one as corresponding author).
4 second-author publications (including Cell Reports and Journal of Physiology)
10 co-author publications (including JBC, BBA, Biochemical Journal).
375 cites and H-index of 12.
3 book chapters.

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FELLOWSHIPS/GRANTS

2012-2013	MRC Centenary Award
2007-2011	FPU fellowship (Ministry of Education)
2007	FPI fellowship, Diputación General de Aragón.
2006	Fellowship for graduate students (CSIC)
2005/2006	Collaboration fellowship (Ministry of Education)
2005	Fellowship for undergraduate students (CSIC)

CONFERENCES:
5 talks, including invited and keynote speaker (Spanish Biophysical Society conference 2017, ESRF user meeting 2018), 15 posters and 3 specialization courses (crystallography).

TEACHING:
Day-to-day supervisor 2 master students (Part-III Natural Sciences program from the University of Cambridge)
100h Degree in Biochemistry (University of Zaragoza).

OTHER:
Referee International Journal of Molecular Sciences and Biomembranes
Selected to attend Young Scientist Forum (IBMB) and Lindau Nobel Laureate Meeting.
Member of SBE and SEBBM
Participation in science dissemination at the Programa Ciencia Viva in Aragon.
Positive evaluation ANECA (Profesor ayudante doctor)

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Nombre: GUARDADO CALVO, PABLO
Referencia: RYC2018-025038-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: pablo.guardado@gmail.com

Título:

STRUCTURAL VIROLOGY

Resumen de la Memoria:

My research career was being focused on understanding the molecular mechanisms of the viral life cycle. Particularly, I have focused on three important aspects of the virus-cell interactions: (1) The structural characterization of the proteins involved in viral attachment to cells, (2) the structural mechanism of viral assembly and, (3) the structural and molecular mechanisms of viral fusion. Related with viral fusion, I have studied the structural basis of the neutralization capability of some broadly neutralizing antibodies against enveloped viruses.
I started my research career at Universidad de Santiago de Compostela with a thesis entitled Crystallographic structures of proteins from animal viruses involved in the interaction virus-host under the supervision of Dr. Mark Johan van Raaij with an FPU Fellowship. During my Ph.D., I worked on several projects with viral proteins of the families Reoviridae and Adenoviridae. After my Ph.D., I moved to the Institut Pasteur in Paris, where I spent five years as a postdoctoral fellow under the supervision of Dr. Felix Rey with an EMBO Fellowship and later with a Sidaction Postdoctoral Fellowship. During these years I was involved in many projects: 1) I carried out structural studies of capsid proteins of viruses of the family Retroviridae, solving the structure of the CACTD domain of the Feline Immunodeficiency Virus (FIV), the structures of several HIV-CACTD mutants, and the complexes of the different capsid domains with several nanobodies. 2) I did structural studies of several class II fusion glycoproteins of bunyaviruses and 3) solved the structures of several broadly neutralizing antibodies in complex with the Dengue envelope glycoprotein. These structures led to the development of novel vaccine strategies, which was the object of different UK and US-based patents.
Afterwards, I have obtained a permanent position as a staff scientist in the Institut Pasteur, where I am leading a small team of 3 persons. I am expanding my postdoctoral research in bunyavirus. In 2016 I have obtained a 3-years grant as PI to develop novel viral antigens of bunyaviral proteins inspired on complexes with human neutralizing antibodies and in 2019 another grant to characterized a conserved lipid binding pocket in viral fusion proteins that can use as a target for the development of antivirals.
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Resumen del Currículum Vitae:

CURRENT POSITION

Staff scientist (grade CR1 in the French system). Institut Pasteur, France.

Previous positions and professional activity:

2015 - 2017: Staff scientist (grade CR2 in the French system). Institut Pasteur, France.
2010 - 2014: Postdoctoral Fellow. Institut Pasteur, France.
2005 - 2010: PhD student. University of Santiago de Compostela, Spain

PUBLICATIONS:

I have 21 publications in international journals such as Nature, Science, and Nature Communications. 13 of them are in the first quartile (Q1).

I have published 13 first-author papers: one in Science (IF 37.2 and co-corresponding author), one in Nature (IF 41.4), one in Nature communications (IF 12.1), one in Plos Pathogens (IF 7.7), two in Journal of Virology (IF 4.7), two in Journal of General Virology (IF in 2008 was 3.2, one of the papers was selected for the cover), one in Journal of Molecular Biology (IF in 2005 was 4.8), two in Act. Cryst. F (IF 0.7), and one in Advances in Virus Research (IF 4.2).

In addition, I am co-author in 8 additional publications: one in Nature, one in Nature Communications, one in Journal of Virology, one in Journal of Structural Biology, one in Journal of Immunology Research, one in Journal of Medicinal Chemistry, and two in Act. Cryst. F.

PATENTS:

2014: Dengue subunit vaccine and antibodies binding the virion dependent epitope of dengue virus (UK 1413086.8)

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2014: Anti-SAMHD1 monoclonal antibody:clone I19-18 (2014-62). Commercialized by EMD Millipore.
2018: Engineered spike proteins of hantaviruses and uses thereof (US 62/642429)

CONFERENCES:

I have presented my work in several international meetings: 9 oral communications and 7 posters.

R&D PROJECTS:

I have participated in 7 national (Spain and France) and European scientific projects. Currently, I am principal investigator of two three-years grants from ANR: one finishing at the end of 2019 and one starting in the beginning of 2019.

RESEARCH IN INTERNATIONAL CENTERS:

I have worked nine years at the Institut Pasteur in Paris. I have made a three months stay in the Hellenic Institut Pasteur in Athens (Greece), a 2-months stay at ESRF in Grenoble (France), and a 1 month stay in the University of Creete (Greece).

FELLOWSHIPS:

2005-2006: PhD Fellowship from Diputacion de La Coruña
2006-2010: FPU Fellowship from the Spanish Ministry of Education
2010-2012: EMBO Long Term Postdoctoral Fellowship from European Molecular Biology Organization (EMBO)
2013: ANRS postdoctoral Fellowship (Rejected in favour of Sidaction Fellowship)
2012-2014: Sidaction Fellowship from Fundation Sidaction.

AWARDS:

2006: Award to the best communication in the XVII Symposium of the GEC (Grupo especializado de cristalografia).

TEACHING:

2008-2009: I have taught in the Department of Biochemistry and Molecular Biology in the University of Santiago de Compostela.

During my career I have assisted numerous graduate students and postdoctoral fellows. Actually, I am in charge of one PhD student and two postdoctoral fellow.

OTER SCIENTIFIC ACTIVITIES:

I have reviewed articles for the International Journal of Molecular Sciences, Journal of Virology and Nature Microbiology.
I develop Python modules for the analysis of proteins in Pymol. One of them has been cited 3 times.

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Nombre: GARCIA NAFRIA, JAVIER
Referencia: RYC2018-025731-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: javier7462@hotmail.com

Título:

Structural mechanisms of neuronal membrane proteins and their therapeutics

Resumen de la Memoria:

During my last year of the Biochemistry degree at CNIO (2006-07) and later during PhD in York, UK (2007-2011) I gained wide experience in protein sciences, biochemistry and structural biology. During this time I worked on structural mechanisms of DNA replication and proteins involved in DNA damage prevention.

During my two postdocs I got stablished in my current field of research - structure and mechanism of neuronal membrane proteins and their therapeutics (MRC LMB, 2012-2019). I first worked on AMPA receptors (AMPARs), which are primary mediators of cognitive functions and memory formation. I used biochemistry, biophysics and structural biology (crystallography and state of the art cryo-EM) to perform major breakthroughs in the field including the description of the architecture of heteromeric receptors (Science 2016), and understanding regulation by auxiliary membrane proteins (Science 2019,accepted in principle). I also worked with industry, first with the MRC-T to develop the first subunit-specific drug against AMPARs (patent drafted) and then obtaining funding from AstraZeneca to develop monoclonal antibodies against AMPARs.

I then worked in general structural and functional mechanism of G protein coupled receptors (GPCRs) (Chris Tate s laboratory). My initial work obtaining the structure of the human adenosine A2A receptor (A2AR) in complex with heterotrimeric G-proteins showed that high-resolution structural information of GPCR complexes could be obtained using single-particle electron microscopy. This was also the first comparison on a real case scenario where the Volta phase plate had a significant effect in electron cryo-microscopy single-particle data (eLife 2018). Using this technology I then described how the human serotonin 5-HT1B receptor couples to the GO heterotrimer, starting to understand how different GPCRs discriminate between different G-proteins (Nature 2018).

I have independent work where I simplified all molecular cloning protocols (Sci Reports 2016), and collaborated carrying structural work in the field of clathrin dependent endocytosis (Cell 2018). I now perform my own research on dopamine receptors and their complexes with other types of receptors.

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Resumen del Currículum Vitae:

Current position
Investigator Scientist at the MRC LMB, Cambridge, UK. Chris Tate s group.

Education
2002-2007 Degree in Biochemistry Universidad Autónoma de Madrid.
2007-2011 PhD in Chemistry. The York Structural Biology Laboratory, York, UK.

Research experience
2006-2007 Research student at CNIO.
2007. Summer Trainning program at CNIO.
2007-2011 PhD in Chemistry. The York Structural Biology Laboratory, York, UK.
Jan-Apr 2012 Post-doc at The York Structural Biology Laboratory, York, UK.
2012-2016. Post-doc at the MRC LMB, Ingo Greger s group.
2017-2019. Investigator Scientist at the MRC LMB, Chris Tate s group.

Publications (2010-2018)
All my work is published in international peer-reviewed journals adding a total of 17 publications, where 13/17 as first/co-first author and one of them as the only corresponding author. I have four publications in top-tier journals (2xScience, Nature and Cell), two of them as first author. Most of the journals are positioned in the first quartile ranked by impact factor including eLife, Structure, J. of Physiology and Scientific reports. My average impact factor is 13.48 and H index of 7, but most of my citations come from the later years and show a dramatic progression. My work has been highlighted twice as paper of the month by the Sociedad de Biofísica Española (Biofísica - Magazine) (May and June 2018).

Research projects, translational work and industry collaborations
-Industrial Funding by Heptares as main investigator in performing structural determination of G-protein coupled receptors by cryo-

electron microscopy.
-Industrial funding by AstraZeneca as main investigator in the project Development of monoclonal antibodies for AMPA receptors .
-MRC-Technology Transfer Unit Developmental gap funding. Main researcher in the project Developing subunit-specific drugs against the N-terminal of AMPA receptors.
-Researcher in the European TRYPOBASE project. 2012
-Researcher in the European SPINE2Complexes project. 2007-2010.

Conferences
I have presented my work in 19 conferences in the form of oral presentations and posters. I have been invited twice as speaker for conference and a workshop.

Teaching
I have supervised 4 summer students, 3 undergraduates and 2 master students in their laboratory projects. I have also led practical classes for first-year students in Chemistry and Biochemistry (Kinetics course). The University of York, York, UK, 2008-2009.

Other
Positive evaluation from ANECA for Profesor Ayudante Doctor.
Reviewer for Scientific Reports and JBC.

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Nombre: MARCOS BENTEO, ENRIQUE
Referencia: RYC2018-025295-I
Área Temática: **Biociencias y biotecnología**
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Título:

Molecular modelling and de novo design of proteins

Resumen de la Memoria:

My research started focusing on the use of computational methods to understand the mechanisms of action of natural proteins. My PhD in Computational Chemistry, under the supervision of Dr. Ramon Crehuet (IQAC-CSIC), involved the multi-scale modelling of the reactivity, dynamics and thermostability of phosphoryl transfer enzymes from different metabolic pathways, and culminated in studies rationalizing former controversial experiments. During my PhD I did research stays at the University of Pittsburgh (USA) for studying large conformational changes in proteins and at the Institut de Biologie Structurale (Grenoble, France) for modeling enzyme active sites. The work from my PhD led to 8 journal articles (7 as first author) and a book chapter. For my first postdoc I shifted my focus to the design of artificial proteins and joined the laboratory of Prof. David Baker at University of Washington (USA) with a Marie Curie fellowship (IOF). I successfully transitioned from computational to multidisciplinary research integrating theoretical predictions with experimental verification; and developed an approach for the computational design of proteins from scratch (de novo) with structures and interfaces suited for custom-designing ligand-binding and enzymatic functions (Marcos E. et al. Science, 2017), which now opens up new avenues into biosensors and biocatalysts not found in nature. For my second postdoc, at IRB, I developed methods for the de novo design of beta-sheet proteins for the first time, which allows custom-engineering novel ligand-binding proteins and antibodies (Marcos E. et al. Nature Struct. Mol. Biol., 2018). During this time I was also awarded with a second Marie Curie fellowship (Reintegration) at the group of Prof. Modesto Orozco for a project on the design of proteins binding nucleosomal DNA for developing new chromatin research tools and epigenetic therapeutic approaches.
My career goal is to lead a multidisciplinary research group using computational protein design and experimental testing to engineer novel molecular sensors, therapeutics, and catalysts for medical and biotechnological applications in collaboration both with academic groups and industry. Under the RyC programme, I would undertake the challenge of designing protein conformational switches de novo triggered by small-molecules; with the aim of regulating biological functions and developing biosensors and smart therapeutic strategies through regulated enzymes.
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Resumen del Currículum Vitae:

I obtained my degree in Chemistry at the Instituto Químico de Sarriá (IQS) in 2005 and completed the IQS s Chemical Engineer thesis in 2007. Then I started my PhD in Theoretical and Computational Chemistry at the IQAC-CSIC, as a JAE-CSIC pre-doctoral fellow (FPU was obtained, but declined). During that time I obtained travel fellowships to visit groups of different institutions: University of Pittsburgh (USA) for 3 months, Institut de Biologie Structurale in Grenoble (France) for 3 months and University of Washington (USA) for 1 month. In 2012 I completed my PhD with a total of 8 publications (7 as first author) and 1 book chapter. During that time I mentored 1 PhD student, 2 undergraduate students, co-organized seminars in the institute and wrote most of the manuscripts.
For my postdoc, I shifted my focus to de novo protein design and in 2012 I joined the laboratory of Prof. David Baker at the University of Washington (USA), first with a university research contract and later with a Marie Curie fellowship (IOF panel). My work on de novo design of proteins with cavities suited for ligand-binding and catalytic sites resulted in a first-author publication in Science. During that time I mentored two PhD students, coordinated collaborations with structural biology groups, and gained hands-on experience on experimental biochemistry and structural biology techniques for protein characterization.
In 2015 I moved to the group of Prof. Modesto Orozco at IRB Barcelona for the return phase of the IOF Marie Curie fellowship where I focused on the de novo design of beta-sheet proteins for custom-engineering ligand-binding proteins and antibodies; leading to a publication in Nature Struct. Mol. Biol., both as first and corresponding author. In 2017 I was awarded with a second Marie Curie research contract (Reintegration Panel) to set a new research line on the design of proteins binding chromatin (also obtained Juan de la Cierva-Incorporación , but declined in favor of Marie Curie Reintegration). During my postdoc I have also co-authored two publications in Nature on the de novo design of proteins for ligand-binding and anti-cancer therapeutics, and been invited to write a review in WIREs Comput. Mol. Sci.
Throughout my scientific career I have carried out diverse projects involving a broad range of computational and experimental techniques both for understanding and engineering proteins, which has resulted in a total of 17 publications (4 in high-impact journals such as Science, Nature and Nature Struct. Mol. Biol.) from which 13 are as first author (one in Science), 4 as corresponding author (one in Nature Struct. Mol. Biol.) and 8 without the doctoral advisor. I have presented 19 contributions in international meetings, including 8 oral communications. I have peer-reviewed for different journals and have acquired wide experience in writing grants, as I have secured my own funding across all stages of my career with very competitive fellowships, including two independent Marie Curie postdoctoral actions and others I had to decline. I have also mentored 3 PhD and 2 undergraduate students, and also taught at university and workshops. My

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publication track record (mostly as first author), capacity to obtain funding and leadership qualities demonstrate my independence to lead research.

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Nombre: FLORIAN , MARIA CAROLINA
Referencia: RYC2018-025979-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: cflorian@cmrb.eu

Título:

Epigenetics of stem cell aging

Resumen de la Memoria:

I am a highly motivated and innovative scientist and I am strongly committed to further develop my research to contribute to the translation of stem cell therapies into clinically applicable treatments. My research focuses on understanding cellular and molecular mechanisms of somatic stem cell aging, supporting the development of new therapeutic strategies to preserve the regenerative capacity of stem cells over time. In addition, since aging is the primary risk factor for many diseases, it is likely that the application of these strategies will extend also to limit or prevent the development of several age-related disorders. I initiated my scientific career as PhD student at the University of Milan (Italy), investigating mechanisms of neuroblastoma migration and invasion and the involvement of microRNAs in reducing tumor aggressiveness. During the PhD training, I acquired solid bases for my scientific work, I learnt to work in a team to respect diversities and to organize my ideas and my practical laboratory work to optimize their outcome.
Afterwards, I moved as post doc to the University of Ulm (Germany). My post-doctoral education in Ulm gave me the possibility to dramatically extend my technical and scientific skills and also to experience training periods in extremely competitive environments, as the Department of Experimental Hematology at Cincinnati Children s Hospital (USA). Overall, the results of my post-doctoral work strongly challenged the concept that aging is an irreversible process. I demonstrated that an intrinsic autocrine Wnt5a signaling drives the alterations of hematopoietic stem cell (HSC) polarity establishment, underlying the decrease in regenerative potential of aged stem cells. Moreover, I showed that it is possible to pharmacologically target the aged-dependent alteration of stem cell polarity and functionally rejuvenate aged HSCs in vivo. My work was finalized with outstanding publications in eminent scientific journals like Nature and Cell Stem Cell and offered me the possibility to present my work in international meetings.
In 2016, I was awarded an extremely prestigious grant from the German Research Foundation (DFG, Emmy Noether Grant) dedicated to outstanding early-career researchers to establish of my independent research team.
In 2018, I was appointed by the Center for Regenerative Medicine in Barcelona (CMRB) as group leader. Within my team, we are committed to further grow our understanding of alterations affecting aged somatic stem cells and we are investigating changes of the epigenetic architecture that drive stem cell aging. This represents a completely novel and exciting field of research to develop new therapeutic strategies and foster clinical translation of stem cell based therapies to improve tissue attrition with age (as for sarcopenia) or even to prevent aging-associated diseases (leukemia, cardiovascular diseases and neurodegeneration).
The support of the Ramón y Cajal subprogram would provide a critical and prestigious recognition of my scientific career and enable me to continue along my trajectory as an innovative and independent investigator.

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Resumen del Currículum Vitae:

Dr. M. Carolina Florian holds a PhD from the University of Milano (Italy). She pursued postdoctoral training at the Institute of Molecular Medicine in Ulm University (Germany) from 2009 to 2015. During this period, she trained as visiting scientist in the Experimental Hematology Department at Cincinnati Children s Hospital (USA). In 2015, she was awarded an extremely prestigious grant from the German Research Foundation (DFG, Emmy Noether Grant) dedicated to outstanding early-career researchers. This grant supported the establishment of her independent research team on Epigenetics of Stem Cell Aging. In 2018, she moved as group leader to CMRB (Spain).
Her research in the past 5 years strongly challenged the concept that aging is an irreversible process and showed that it is possible to pharmacologically target the aged-dependent alteration of stem cell epigenetic polarity and functionally rejuvenate aged HSCs in vivo. Somatic stem cells are central for tissue homeostasis and regeneration. Their age-dependent functional decline constitutes a hallmark of tissue attrition upon aging, eventually limiting health-span and lifespan. She demonstrated that an intrinsic autocrine Wnt5a signaling drives the alteration of hematopoietic stem cell (HSC) polarity establishment, underlying the decrease in regenerative potential of aged stem cells. Moreover, she showed that it is possible to pharmacologically target the aged-dependent alteration of stem cell polarity and functionally rejuvenate aged HSCs in vivo. Her work was finalized with excellent publications in eminent scientific journals like Nature and Cell Stem Cell. Now, she s committed to further grow the understanding of alterations affecting aged somatic stem cells and she is investigating changes of the epigenetic architecture that drive stem cell aging. This represents a completely novel and exciting field of research to develop new therapeutic strategies and foster clinical translation of stem cell based therapies to improve tissue attrition with age (as for sarcopenia) or even to prevent aging-associated diseases (leukemia, cardiovascular diseases and neurodegeneration).

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CONVOCATORIA 2018

Turno de acceso general

Nombre: LOPEZ AVILES, SANDRA
Referencia: RYC2018-024273-I
Área Temática: **Biociencias y biotecnología**
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Título:

Principles of cell cycle control by protein kinases and phosphatases

Resumen de la Memoria:

Throughout my research career I have been interested in the study of fundamental questions in cell biology, particularly regarding the control of cell cycle progression and the cellular responses to environmental cues. Already during my PhD I became interested in the regulation of cell cycle and its implications in cancer progression. During that time my main focus was on protein kinases (Stress and checkpoint kinases, and Cyclin-Dependent Kinases), and it was not until I started my post-doc that I became aware of the importance of regulated phosphatase activity for cell cycle regulation. During my post-doc, I mainly studied the role of the Cdc14 phosphatase in the regulation of budding yeast mitotic exit. However, although Cdc14 is clearly essential for mitotic progression in budding yeast, its role in other organisms seems less critical. For this reason, during the last years of my post-doc I started analysing mitotic exit in the fission yeast Schizosaccharomyces pombe, which in many regards is closer to higher eukaryotes than budding yeast. This project was the starting point for the research program that I have developed at the Norwegian centre for Molecular Medicine (NCMM) since my recruitment in late 2011 as group leader. During these years I have worked intensively in understanding the role of protein phosphatases belonging to the PP2A family in cell cycle progression and cell fate decisions. In this time we have achieved: (1) a proven track record with 4 publications (Current Biology, JCS) and 3 manuscripts in preparation, (2) successfully established national and international research collaborations and (3) attracted significant external funding from multiple sources.

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Resumen del Currículum Vitae:

In 2002 I started my scientific career at the Department of Cell Biology of the School of Medicine (University of Barcelona), where I did my PhD. There, under the supervision of Prof. Rosa Aligue I investigated the role of Stress-responsive kinases in the regulation of cell cycle progression in response to environmental stress. During this time I developed my work using the fission yeast Schizosaccharomyces pombe as model organism. In 2007, I moved to the London Research Institute (currently part of the CRICK institute) for my post-doctoral training. In London I joined the laboratory of Dr. Frank Uhlmann and initiated a project aimed at understanding the implications of regulated phosphatase activity during mitotic exit. This resulted in a total of four publications (i.e. Nature). Moreover, the work I developed in London on protein phosphatases belonging to the PP2A family was the starting point when I established my research group at NCMM (previously the Biotechnology Centre of Oslo, part of the University of Oslo) in late 2011. After five years holding this group leader position, in 2016 an international panel of experts evaluated my research activity satisfactorily and my research program was renewed for five additional years.

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Turno de acceso general

Nombre: SANCHEZ GURMACHES, JUAN
Referencia: RYC2018-025202-I
Área Temática: **Biociencias y biotecnología**
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Título:

Developmental and Molecular Mechanisms of Obesity

Resumen de la Memoria:

How tissue homeostasis is achieved in vivo is a long-standing scientific question. Usually, this features a refined crosstalk between tissue resident stem cells or precursor cells and functionally differentiated cells. Within adipose tissue, adipocytes show cellular, molecular, and functional heterogeneity between and also within fat depots. The origins of this heterogeneity are not understood. However, it is key in determining the pathophysiological effects of an accumulation of fat (a.k.a. obesity) because an increase in visceral fat is associated to an increase in heart disease and mortality while an increase in subcutaneous fat is protective. During my postdoctoral work, I used mouse genetics to identify the origins of adipocyte heterogeneity. For this, I developed innovative lineage tracing techniques that allow me single cell resolution at the adipocyte precursor and mature adipocyte levels.

My postdoctoral research delineated a whole new conceptual framework in adipose tissue development that now is used and accepted by the field. This work made new implications between developmental clues and adult metabolic homeostasis and it demonstrates a possible cause of different fat pattering between healthy humans and in obese-lipodystrophic patients. This new field of study I created is now expanding and it has been proposed to be of key importance moving the field forward toward treatments against obesity and other adipose tissue related diseases.

Since July 2017, I hold a tenure track faculty position at the Cincinnati Children s Hospital Medical Center (CCHMC), the second children s hospital of USA with more than 1000 faculty, and 2000 peer reviewed publications and $223 millions in extramural grants and contracts over the last fiscal year. My lab is in the Division of Endocrinology and the Division of Developmental Biology. CCHMC made available to me over $1.4 million as start-up package to cover the first years of my independent research as well as laboratory and office space for up to 10 people. On this short period of time as a fully independent researcher, I successfully obtained competitive extramural funding and published peer reviewed papers as corresponding author. Additionally, I play a strong role in the activities of CCHMC including mentoring students and postdocs, been part of several committees for students and grant review panels at the institution levels and also at the national and international levels.

In the next years, I want to move my lab back to Spain and recreate the same type of lab I have successfully created in Cincinnati. A lab where critical thinking, hard-work, accepting challenges and productivity is encouraged, not only by me, but by all the members of the lab as a way to achieve our long-term goals. I want to be a productive member of the field setting the path for future research, in my lab and others, through new ideas, concepts and collaborations. My demonstrated work ethics and capacity for teamwork, my research vision and capacity to generate and follow up productive projects, my competence to adapt and develop methodological approaches to my experimental needs will help me accomplish these goals.

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Resumen del Currículum Vitae:

Honors
2003 Research fellowship, University of Barcelona
2006 - 2010 University of Barcelona Pre-doctoral fellowship, University of Barcelona
2007 Iberian Endocrinology Society meeting scholarship award, Iberian Endocrinology Society
2008 Research travel fellowship, University of Barcelona
2009 Iberian Endocrinology Society meeting scholarship award, Iberian Endocrinology Society
2010 Thesis award, University of Barcelona
2012 - 2014 Marie Curie Postdoctoral Fellowship (Beatriu de Pinós), European Union and Government of Catalunya.
2012 Sanchez-Gurmaches (2012) Cell metabolism paper is selected for the cover of the September issue of Cell metabolism, Cell Metabolism
2013 Keystone Symposia Scholarship Award- Adipose Tissue Biology, Keystone Symposia
2013 Sanchez-Gurmaches (2012) Cell metabolism paper is selected as one of Cell metabolism: Best of 2012 publications, Cell Metabolism
2013 Sanchez-Gurmaches (2012) Cell metabolism paper is selected for the One year ago section of Cell metabolism., Cell Metabolism
2014 Keystone Symposia Scholarship Award - Obesity: A multisystems perspective. Keystone Symposia

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2014 Sanchez-Gurmaches (2014) Nature Communications paper is selected by Nature Reviews Endocrinology for the August Research highlights section., Nature Reviews Endocrinology
2015 - 2017 American Heart Association Postdoctoral Grant (15POST25550079). American Heart Association. American Heart Association
2016 Sanchez-Gurmaches (2016) Trends in Cell Biology paper is selected for the cover of the May issue of Trends in Cell Biology, Trends in Cell Biology
2017 Beatriu de Pinós Program Fellowship. Government of Catalunya. (Declined), Government of Catalunya
2017 Excellence in science award, Diabetes Center of Excellence, University of Massachusetts Medical School.
2018 - 2021 Career Development Award (18CDA34080527), American Heart Association

Ongoing Research Support
Career Development Award (18CDA34080527), American Heart Association
Sanchez Gurmaches (PI)
07/01/18-06/30/21
Developmental and Molecular Mechanisms of Obesity
Role: PI
Start-Up, Cincinnati Children's Hospital Medical Center
Sanchez Gurmaches (PI)
01/01/17-01/01/22
Research Start-Up Funds
Role: PI

Completed Research Support
Postdoctoral Grant (15POST25550079), American Heart Association
Sanchez Gurmaches (PI)
01/01/15-01/01/17
Preventing Cardiovascular Disease by Targeting its Greatest Risk Factor - Obesity
Role: PI
Marie Curie Postdoctoral Fellowship (Beatriu de Pinós) 2010 BP-A 00108, European Union and Government of Catalunya
Sanchez Gurmaches (PI)
01/01/12-01/01/14
Signaling Pathways Controlling Lipid Metabolism and Thermoregulation in Brown Adipose Tissue
Role: PI
Pre-doctoral fellowship, University of Barcelona
Sanchez Gurmaches (PI)
01/01/06-01/01/10
Pre-doctoral fellowship
Role: PI
Research travel fellowship, University of Barcelona
Sanchez Gurmaches (PI)
01/01/08-01/01/08
Research travel
Role: PI

Total publications: 31
First author publications: 12
Corresponding author publications: 6
Total number of citations: 1276
h-index: 21
i10-index: 25

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CONVOCATORIA 2018

Turno de acceso general

Nombre: GALLEGO BARTOLOME, JAVIER
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Área Temática: **Biociencias y biotecnología**
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Título:

Regulation of gene expression in plants

Resumen de la Memoria:

I have focused my research career on the regulation of gene expression in plants at three different levels: (i) post-transcriptional regulation by small RNAs, (ii) transcriptional regulation by hormones and (iii) epigenetic regulation by DNA methylation.

After graduating as Agronomical Engineer (UPV, Valencia, Spain), I joined in 2005 Dr. Voinnet¿s lab (IBMP, Strasbourg, France) with a short-term postgraduate fellowship to study the role of small RNAs in antiviral defense and development. Part of this work resulted in a publication in Science.

To continue my studies on transcriptional regulation I decided to pursue a PhD in Drs. Blázquez and Alabadí lab at the IBMCP (Valencia, Spain) to study how different plant hormones interact to regulate gene expression, in particular during differential growth processes, such as apical hook development or tropisms. Several publications in top journals (PNAS, Mol Biol Evol, and Plant Phys) came out from my thesis work (PhD degree in 2011). As a result I was awarded UPV Extraordinary Doctoral Thesis Award and SEFV award and FESPB award to young plant scientist.

Then I decided to explore the contribution of epigenetics to gene expression by joining in 2013 the Jacobsen lab (UCLA, Los Angeles, US), which is pioneer in the study of DNA methylation and gene silencing in plants. Here I am mostly focused on developing genetic tools to manipulate DNA methylation levels in plants in a locus-specific manner. Part of these studies has been recently accepted in Cell and PNAS. Moreover, the genetic tools generated have been patented. Also, different collaborative projects have been published in top journals (Cell, Science, Molecular Cell, PNAS).

During my training, I have obtained funding through the CSIC I3P Program (PhD), EMBO and HFSP Postdoctoral Fellowship. This RyC contract will allow me to expand my career back in Spain where I plan to continue working on epigenetics in plants. I would like to understand (i) how environmental signals modulate chromatin architecture to control gene expression and (ii) developing genetic tools to study chromatin dynamics.

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Resumen del Currículum Vitae:

I graduated as Agronomical Engineer at the Polytechnic University of Valencia (UPV) in 2004. For my Master Thesis, I joined the lab of Drs Domingo and Talón (IVIA, Moncada, Spain), to study the expression profile of a stress-response gene in rice. After graduating, I moved with a short-term fellowship for postgraduates to the Voinnet lab (IBMP, Strasbourg, France), to study post-transcriptional gene silencing in plants. Part of this work resulted in a publication in Science. Afterward, I decided to continue studying other aspects of transcriptional regulation in plants and decided to join the lab of Drs Blázquez and Alabadí (IBMCP, Valencia, Spain), where I centered my studies on the molecular mechanisms by which the plant hormone Gibberellins (GAs) interacts with other hormones to control gene expression. During this time I did 3 short term internships in the labs of Dr. Fankhauser (UniL, Lausanne, Switzerland), Drs Friml and Benkova (PSB, Ghent, Belgium) and Dr. Bennett (CPIB, Nottingham, UK), that led to joined projects and publications. From my thesis work, we published 8 publications in top journals like PNAS, Mol Biol Evol, Plant Physiology and Plant Journal, of which I am a first author in 7. Also, I was awarded Extraordinary Doctoral Thesis Award from the UPV. Once I defended my Ph.D. in 2011, I did a short postdoc in the Chory lab (The Salk Institute, La Jolla, USA), where I initiated a project to study cell-type specific transcriptional responses to changes in light and temperature. During this time I was awarded the prestigious EMBO and HFSP postdoctoral fellowships. For personal reasons I decided to move in 2013 to the Jacobsen lab (UCLA, Los Angeles, US) where I have been mostly dedicated to the development of genetic tools to manipulate DNA methylation levels in a locus-specific manner using artificial zinc fingers and CRISPR/ Cas9. One of the projects that I lead, where we developed genetic tools for

targeted DNA demethylation in plants, has been published in PNAS. Importantly, my main project, focused on the study of components able to target DNA methylation in plants, just got accepted for publication in Cell. Besides, the genetic tools developed in these two projects have generated 3 patents. Also, collaborative work with other members of the lab has resulted in various publications in top journals like Science, Cell, Molecular Cell, PNAS and Nature Plants. During my postdoc, I had the opportunity to train 9 undergraduates and 2 full-time technicians that provided technical support to my projects, as well as participate as teaching assistant in an undergraduate Epigenetics course taught by Dr. Jacobsen at UCLA. Moreover, during this time I have been awarded the prestigious Sabater Award from the Spanish Society of Plant Physiology (SEFV) (2013) and Young Plant Scientist award from the Federation of European Societies of Plant Biology (FESPB) (2014). Both awards gave me the chance to present my work in a plenary talk in the SEFV meeting in Lisbon, Portugal (2013) and FESPB meeting in Dublin, Ireland (2014). I am currently a member of the Society of Plant Physiology (SEFV) and of the board of reviewers of Journal of Experimental Botany. In the future, I hope to become an independent researcher and continue working on the epigenetic regulation of gene expression in plants.

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CONVOCATORIA 2018

Turno de acceso general

Nombre: BALSA MARTINEZ, EDUARDO
Referencia: RYC2018-024342-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: eduardo_balsamartinez@dfci.harvard.edu

Título:

MITOCHONDRIAL BIOLOGY AND METABOLISM: IMPLICATIONS IN PHISYOLOGY AND DISEASES.

Resumen de la Memoria:

During my career I have built experience in studying the molecular mechanisms that drive mitochondrial function and how its dysregulation can underlie human diseases.
As a PhD student, under the mentorship of Dr. Manuel O. de Landazuri at the Hospital de la Princesa, my research was devoted to understanding how cellular metabolism is reprogrammed under hypoxic conditions. My main interest was to get further insights in the mitochondrial changes that occur under hypoxia and try to uncover new players involved in controlling metabolic adaptations to low oxygen tensions. I elegantly demonstrated how electron transport chain complex I is downregulated in a HIF-1 dependent fashion, and pinpoint NDUFA4L2 as a major player in hypoxic adaptation. This way, I add further elements to the strategic armory used by HIFs to ensure that mitochondrial oxygen consumption is repressed in mild hypoxic conditions, highlighting the biological relevance of the regulation of this cellular response. During my PhD studies I moved to the laboratory of Prof. Enriquez at the Centro Nacional de Investigaciones Cardiovasculares (CNIC), where as a visiting researcher, I continued my quest to gain further understanding of mitochondrial biology. I was able to challenge the perception of Complex IV structure and subunit composition showing that NDUFA4, formerly considered a constituent of NADH Dehydrogenase (Complex I), was instead a component of the cytochrome c oxidase (Complex IV). Furthermore, I significantly contributed to several articles describing the role of the electron transport chain supercomplexes in controlling physiological flexibility to different food substrates and identified COX7A2L, as the first assembly factor that promotes the superassembly of complex III and IV.

During my current postdoctoral endeavour, in Pere Puigserver s lab at Dana-Farber Cancer Institute and Harvard University, I am seeking to apply my knowledge to find novel genes and pathways governing mitochondrial function. I performed a high-throughput chemical screen in combination with a genome wide- CRISPR/Cas9 screen to discover genes and chemical compounds that rescue bioenergetic defects caused by mitochondrial disease mutation. These experiments yield BRD4 protein as a molecular target. I convincingly demonstrated that BRD4 inhibition, either chemically or genetically, remodeled the mitochondrial proteome to increase the levels and activity of OXPHOS protein complexes, leading to rescue of the bioenergetic defects and cell death caused by mutations or chemical inhibition of CI. In addition to my personal leading research, I have been closely collaborating with members of my lab investigating cancer metabolism in melanoma. We found that ERRα selectively mediates the growth-supporting bioenergetic functions of PGC1α in these types of cancers.
My latest investigations are focused on the regulatory mechanisms and components that drive mitochondrial respiration under conditions of nutrient stress. I found that ER stress and glucose deprivation stimulate mitochondrial bioenergetics and the formation of respiratory supercomplexes (SCs) through the eukaryotic translation initiation factor 2-alpha kinase 3 (PERK).

My future research will be dedicated to understanding the molecular components that regulate mitochondrial energy metabolism, in the context of physiology and disea
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Resumen del Currículum Vitae:

My scientific higher education began at Universidad de Leon, from which I received my bachelor's degree in Biología fundamental. Later, I obtained a position as Biólogo Interno Residente (B.I.R) to start the immunology residency program at Hospital Universitario de la Princesa. During this period, I started my PhD studies with Dr. Manuel O. de Landazuri focusing on the metabolic reprogramming that take place when cells have to face with low oxygen conditions.
I established a collaboration with Prof. J. Antonio Enriquez, and I moved to the Centro Nacional de Investigaciones Cardiovasculares (CNIC) to continue my scientific research. I competed my PhD (Excellent Cum laude) in Bioquímica, Biología Molecular y Biomedicina by Universidad Autonoma de Madrid in 2012. These studies yield two first-author publication in Cell Metabolism. Additionally, I took part in a breakthrough work characterizing the function of the respiratory chain function supercomplex published in Science. During my PhD, I also participated in scientific meetings presenting my data with posters at Keystone symposia and Euromit.
I moved to Boston to join Dr. Pere Puigserver s laboratory at the Dana Farber Cancer Institute and Harvard Medical School for my postdoctoral training; here, using a combination of chemical and CRISPR/Cas9 genome-editing screenings, I identified BRD4 as a potent transcriptional regulator of OXPHOS-related genes. This work led to a first-author publication in Molecular Cell. Based on these studies our lab has been awarded with an RO1 grant (Metabolic and bioenergetic control in mitochondrial diseases-R01 GM121452) and more importantly, I was awarded a Muscular Dystrophy Association (MDA) Development Grant, with myself as the principal investigator. MDA

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Development Grants are awarded to senior postdoctoral researchers on the brink of becoming independent investigators and are intended as seed money to help launch the scientific programs of promising new researchers. Development grants total $70,000 per year, for three years. Thanks to this funding I have been able to initiate my independent line of research, with full support of my mentor Prof. Puigserver. Furthermore, I have stablished ongoing collaboration with groups at Harvard University and Broad Institute at M.I.T. and published co-author papers. My latest first-author manuscript (under revision in Molecular Cell) reports on the regulatory mechanisms and components that drive mitochondrial respiration under conditions of nutrient stress.

During my postdoctoral studies, I was awarded several prestigious fellowships, including the Alfonso Martín Escudero Postdoctoral Fellowship and the EMBO Long-Term Fellowship.

I have participated in numerous scientific meetings including oral presentations at the Cell Symposia: Multifaceted mitochondria in San Diego and EMBO Fellow s meeting in New York, 2018. In addition to my research interest, I also value mentoring and teaching young students and scientists. I have trained a number of residents, students and technicians, and I have been engaged in active teaching at the BBS program in Cell Biology and Harvard-Amgen Scholars Program at Harvard university.

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CONVOCATORIA 2018

Turno de acceso general

Nombre: OROZ GARDE, FRANCISCO JAVIER
Referencia: RYC2018-026042-I
Área Temática: **Biociencias y biotecnología**
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Título:

Structural Biology in Neurodegenerative Diseases

Resumen de la Memoria:

The incurable neurodegenerative diseases (NDs), which have vast socioeconomic implications, primarily result from the aberrant misfolding and subsequent gain-of-toxic function and aggregation of the so-called amyloid proteins (1). Remarkably, the structural basis of these critical misfolding events triggering NDs remains unclear (1). My research career is focused on deciphering the structural and mechanistic basis of these pathogenic molecular events in order to develop future therapeutics for NDs. To achieve my aims, I have obtained great expertise in structural and biophysical techniques at prestigious International Institutes. During my career, I revealed common toxicity-related structural transitions in several amyloid proteins (2), as well as the structure of inflammasome proteins, which play critical roles in NDs (3). Using NMR spectroscopy, I also characterized complexes of neurotoxic proteins with molecular chaperones at atomic resolution (4), and screened for active chaperones against fatal tauopathies (5). More importantly, I elucidated the structure and pro-toxic mechanism of the Hsp90/FKBP51/Tau complex, critical for the onset of Alzheimer s disease (6). This milestone study establishes novel disease-triggering roles for chaperone complexes in Alzheimer s, and postulates that they may play similar fatal roles in other NDs.
I aspire to establish my independent career in Spain in the Protein NMR Group at the Rocasolano Institute (IQFR/CSIC, Madrid). There, I will be able to mesh my expertise with that group s experience and facilities to create powerful synergies, to further test my hypotheses that aberrant chaperone/client interactions trigger pathogenic cascades at the onset of Amyotrophic Lateral Sclerosis (ALS). I will explore new translational premises to understand the molecular mechanisms triggering disease progression and search for effective therapeutics. Based on the grave costs of NDs, my recent discoveries and the feasibility of my projects, I expect that my proposed work will have a strong scientific and social impact.
By mid 2019, I expect to have a total of eighteen publications and one patent. My work has been funded by competitive international fellowships such as the Marie Curie Fellowship and, thanks to the importance of my discoveries, I have been invited as Keynote Speaker at International Conferences. All these merits position me as an expert in the Structural Biology of NDs and enable me to postulate revolutionary hypotheses regarding molecular mechanisms in NDs that constitute the mainstays of my future independent career. To achieve my aims, I have submitted several international grant applications as PI that are currently under review. I have been lecturer in several Master Courses and been involved in communication initiatives to the lay public. I have been invited to write a review on my field of expertise by mid 2019. I started my lines of research in my former labs, developed the projects, helped to secure funds for their execution, supervised masters and doctoral students, and performed all the necessary experiments. I have attended courses in team-leadership skills, conflict resolution and risk management by the Max Planck Society.

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Resumen del Currículum Vitae:

In April 2018 I joined as a young independent researcher the Protein NMR Group at the Rocasolano Institute of Physical Chemistry (IQFR, Madrid, Spain). My main area of expertise is Structural Biology in neurodegenerative diseases. I have become an expert in solution NMR spectroscopy of intrinsically disordered amyloidogenic proteins and molecular chaperones in the context of Alzheimer's disease, and now have recently started to work on ALS. I have acquired a long multidisciplinary experience in the biophysical analysis of proteins involved in neurodegeneration. Other methodologies that I have largely employed are single-molecule force spectroscopy, small-angle light scattering, circular dichroism, fluorescence spectroscopy and calorimetry. This broad and unique background allows me to carry out my research in multiple aspects that converge in my main scientific interest, which is to understand molecular mechanisms underlying neurodegeneration and to develop targeted therapeutics to cure these diseases by means of structure-based drug design. During my career, I have produced all my samples, acquired all my experiments and analyzed all my data.
I have obtained important findings in the relevant field of molecular mechanisms of neurodegenerative diseases. The most innovative and relevant findings are: 1) I demonstrated that several amyloidogenic proteins undergo similar monomeric conformational transitions that trigger their toxicity, 2) I described an octapeptide, QBP1, that inhibits these monomeric conformational transitions and consequently, their neuronal toxicity,

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3) I described for the first time the atomic structure of the toxic conformation of the protein transthyretin, responsible for familial cardiac amyloidosis, 4) I characterized the dynamic structure and binding mechanism of the Tau-Hsp90-FKBP51 ternary complex, critical for the development of Alzheimer's disease and 5) I found regions in Hsp90 chaperone responsible for the recognition of toxic misfolded substrates, making Hsp90 an attractive target for targeted therapeutics.
I have published THREE first-author articles in high profile journals (PLoS Biol., Nat. Struct. Molec. Biol. and Nat. Commun.). I have contributed to other studies published in high impact journals such as Nat. Struct. Molec. Biol., PNAS and Angewandte Chemie, among others.
My first article as corresponding author was published in J. Biol. Chem.;
currently I have two other papers as corresponding author under review. I have produced a patent approved in 2011 (CSIC/CIBERNED). In total, I have published 17 articles. My articles have been cited 337 times (h=8, source Google Scholar). I have produced first-author scientific papers from all the laboratories where I have worked. In January 2014, I was awarded with a Marie Curie IEF Fellowship (180 k) as PI. I have participated in two ERC projects. I have an ample experience in teaching after co-supervising one master student during my PhD, and two PhD students and four master students during my second postdoc, and I have been lecturer in several master courses. I have been invited as Keynote Speaker in International Conferences.
I have worked in TWO Institutes abroad (Max Planck Institute and U. Southern Denmark).
I have established my own independent hypothesis, nurtured collaborations and applied for funds as PI to develop my lines of research.

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AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2018

Turno de acceso general

Nombre: BARCA MAYO, OLGA
Referencia: RYC2018-026293-I
Área Temática: **Biociencias y biotecnología**
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Título:

ASTROCYTE RHYTMHYC REGULATION OF BRAIN FUNCTION

Resumen de la Memoria:

The applicant pursued a PhD in Neuroendocrionology (2008) at the University of Santiago de Compostela (Spain). The results of her PhD were published, as first author, in seven international journals of Neurophysiology, presented at major International Conferences and allowed her to graduate Cum Laude. Moreover, she was awarded with four competitive fellowships and a prize for innovative and technological ideas.

After obtaining her PhD degree, she moved as postdoctoral researcher at the Laboratory of Dr. Roy Weiss at the University of Chicago (2008-2011) where she expanded her research and focused on thyroid hormone action and metabolism in physiological and pathological conditions. She identified a target gene of thyroid hormone specifically regulated by the Thyroid Hormone Receptor alpha isoform, and characterized its mechanism of regulation in vivo. This study, published in Molecular Endocrinology as first author, was rated Exceptional in Faculty 1000. She had been also studying a paradigm of the role of thyroid hormone in critical illness. To develop this second project, she was awarded with a grant from the CTSA-ITM Genomics Core (UoC). She also contributed to the characterization of the first mouse model with constitutive deletion of both DuoxA1 and DuoxA2, the maturation factors of Dual oxidases (DUOX1 and DUOX2). Remarkably, the findings of the three studies were further translated to human patients with Thyroid Hormone Receptor alpha isoform and DuoxA1/DuoxA2 mutations and allowed the identification type 2 Deiodinase as a novel candidate gene which confers susceptibility to acute lung injury and ventilation induced lung injury in humans.

Her long-term interest in Neuroscience prompted her to pursue a second postdoc experience at Dr. Richard Lu lab (University of Texas Southwestern, Dallas, USA) to investigate glia development and physiology (2011-2012). She identified several DNA and RNA binding factors by performing high throughput techniques (Chip-seq and RNA-seq) and functionally validated the selected candidates in glia cell fate specification and physiology. She had also leaded a project aimed to study the role of microRNAs in oligodendrocyte differentiation and myelin formation.

In 2013 she moved to the Italian Institute of Technology. In 2014, she was awarded with two Marie Curie Fellowships (FP7-CIG and FP7-IEF) to explore the contribution of astrocyte circadian rhythms to the timekeeping system. One year later, she was awarded as Co-Principal Investigator, with a Cariplo Research Grant. She identified a crucial role of astrocytic Bmal1, a core clock gene, for the coordination of neuronal clocks and published two papers as corresponding author, including a study in Nature Communications, which was rated Exceptional in F1000. She was an invited speaker at 10 international conferences including a Hot Topic speaker at the Gordon Conference Chronobiology and awarded at 4 major international conferences. The results of her studies are currently in revision in Developmental Cell, Cell Metabolism and Nature Methods (she is corresponding author in two of them). She has three more papers in preparation (she is corresponding author in two of them) and a patent of invention in revision.
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Resumen del Currículum Vitae:

1) Main scientific contributions:
The indicators of quality of the applicant include:
- 14 publications in JCR journals (10 Q1, 3 Q2, 1 Q3)
- 2 peer-reviewed book chapters
- 2 publications rated as "Exceptional" at Faculty 100
- 1 publication as Co-corresponding author and 1 publication as Corresponding author
- 3 papers currently in revision and 3 manuscripts in preparation
- 34 papers published in peer-reviewed conference proceedings (30 in international conferences, 4 in national conferences)
- 10 additional works presented on seminars or conferences either with assessment committee or upon invitation by the organizers.
- Participation in 19 R&D funded projects (8 extra-European projects: 7 from USA and 1 from Japan); 7 European projects; 3 National projects; 1 Regional project)
- Participarion in 1 project of technology transfer with Industry
- 3 Technological results derived from specialized activities
- 1 patent of invention in revision

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2) Main international activities
- Participation in 15 European and extra-European R&D projects
- 4 research stays (1 predoctoral and 3 postdoctoral stays) in top universities and research centers worldwide: University of Wales (United Kingdom), University of Chicago (USA), University of Texas Southwestern (UTSW, USA), Italian Institute of Technology (Italy)
- 2 international competitive grants as Principal Investigator (Clinical and Translational Science Awards (University of Chicago) and Cariplo Research Grant (Italy)
- 38 publications with international collaborations (7 in JCR journals, 1 book chapter, 30 in conference proceedings).
- 10 additional participations in seminars or workshops outside Spain upon invitation or through assessment committee.
- 17 contributions as external reviewer in JCR journals and grant proposals

3) Other merits:
- 7 competitive fellowships (5 national and 2 international FP7-Marie Curie fellowships)
- 5 awards at international conferences
- 1 award for Technological and Innovative ideas
- Multiple mentions of research quality at magazines (The Scientist, Popular Science, Genova Today, elmundo.es, etc)
- Member of multiple national and international Societies (Society for Neuroscience, Japan Neuroscience Society, Endocrine Society, etc)
- Evaluator for the Spanish State Research Agency
- Extensive experience supervising doctoral thesis and research projects
- 6 years of official teaching at the Schools of Biology and Pharmacy (University of Santiago de Compostela)
- 35 training courses (14 courses for technical and specialized studies; 8 courses for specialized healthcare studies; 10 courses for specialized healthcare studies in R&D; 3 teacher training courses)
- Participation in multiple dissemination activities (manager of the group "Circadian Rhythms" in LinkedIn; media interviews; organizer and manager of focus groups targeting shift workers aimed to establish a dialog with sociaty about the detrimental effect of night shifts), etc.

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Nombre: PEREZ LARA, FRANCISCO ANGEL
Referencia: RYC2018-023837-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: angelpl77@gmail.com

Título:

Molecular mechanism of protein-protein and membrane-protein interactions in cellular processes.

Resumen de la Memoria:

My primary research interest is to study the molecular basis of the membrane-protein and protein-protein interactions involved in different cellular processes, such as signaling, vesicle trafficking, exocytosis, autophagy, etc., because of dysfunction of these networks lead to many human diseases.
During my PhD at the University of Murcia, I studied the molecular mechanism of the protein kinase C (PKC) membrane binding in the presence of different lipid effectors which results were published in seven research articles (three as the first author).
Then, I moved to the MPI for Biophysical Chemistry (Göttingen, Germany) where I was granted with a Max Planck Society two year fellowship. Here, I focus on the study of the molecular mechanism of the synaptic vesicle exocytosis and recycling, in collaboration with several German and American groups. The outcomes of this work were published in nine research articles (two first author and, two last and corresponding author).
Since 2014, I have been a Researcher Associate in the MPI for Biophysical Chemistry and, together with the study of molecular exocytosis and vesicle trafficking, I established my own research line in the study of molecular mechanism of the autophagy in the neuron. I have supervised two Bachelor and one Master theses; given method courses at The Göttingen Graduate School for Neurosciences, Biophysics, and Molecular Biosciences (GGNB) and I am currently supervising one Master and two PhD theses. Additionally, I have established an active network of collaborators in different fields and reviewed for prestigious journals.
In summary, after 12 years of scientific career I have published 16 scientific articles; collaborated in international and national projects; supervised Bachelor, Master and PhD theses; organized and given summer and method courses. Everything described above confirms my leadership role and supports my candidature to the Ramon y Cajal programme in order to establish my own group in Spain.

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Resumen del Currículum Vitae:

EDUCATION
2011 PhD in Molecular Biology and Biotechnology by the University of Murcia, Spain.
2011 Degree in Biochemistry by the University of Granada, Spain.
2008 Master in Molecular Biology and Biotechnology (DEA) by the University of Murcia, Spain.
2002 Degree in Biology by the University of Málaga.

POSITIONS
Oct./2006-Dec./2011: FPI PhD Student at the University of Murcia, Dep. Biochemistry and Molecular Biology A, Spain.
Apr./2012-Apr./2014: Max Planck Society fellow, MPI for Biophysical Chemistry, Göttingen, Germany.
Apr./2014-present: Researcher associate, MPI for Biophysical Chemistry, Göttingen, Germany.

PUBLICATIONS AND INDICATOR OF SCIENTIFIC PRODUCTION

Total publications 16
h index 7
Average citations per item 9.68
Sum of Times Cited 184 (177 without self-citations)
Citing articles 165 (159 without self-citations)
16 publications, 5 of them as first authors and 2 last and corresponding author.

5 year Impact Factor of the publications (2018):

3 Nat Commun. (IF 13.691); 1 Nat Str Mol Biol (IF 12.816); 2 PNAS (IF 10.359); 1 eLife (IF 8.508); 1 Haematologica (IF 7.012); 1 Biochim Biophys Acta (IF 4.916); 1 Sci Rep (IF 4.609); 2 Biophysical J. (IF 3.711); 2 PloS One (IF 3.352); Arch Biochem Biophys. (IF 3.210) and J Phys Chem B (IF 3.101).

PARTICIPATION IN R+D PROJECTS

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I have worked in 7 funded projects, including 4 international projects.
FELLOWSHIPS AND FUNDING
FPI PhD fellowship of the Spanish Ministry of Education and Science.
Max Planck Society fellowship

SUPERVISION OF GRADUATE STUDENTS
Jan. 2019-present PhD supervisor of Tobias Grothe.
Jun. 2017-present PhD supervisor of Sonja Pribicevic.
Jun.2017-Jan 2018 Bachelor Thesis co-supervisor of Jennifer Struck.
Feb.2015-Aug 2016 Bachelor Thesis co-supervisor of Ina Ott.
Jun.2015-Mar 2016 Master Thesis co-supervisor of Ana Buvac.

TEACHING
Laboratory lectures and method courses.

CONTRIBUTIONS TO SCIENTIFIC MEETING
18 Congress contributions (2 oral communications) and 2 Congress organizations.

REFEREE WORK
I have performed reviewer duties for Nature Communications, Biophysical Journal and Journal of Structural Biology.

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Turno de acceso general

Nombre: COLOM DIEGO, ADAI
Referencia: RYC2018-024686-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: adai.colom@gmail.com

Título:

Cell membrane biophysics and trafficking

Resumen de la Memoria:

During my thesis with Dr.Simon Scheuring, I studied the membrane proteins dynamic with molecular and sub-second resolution of aquaporin-0 (AQP0) and connexin (Cx) in lens cells. Malfunction in any of them result in the opacity of the eye lens or cataract, using what was, one of the first prototypes of high-speed atomic force microscopy:
1- I determined the interaction energy of AQP0-AQP0 and its sensitive to the energetic term of the interaction.
2- We found that actin and microtubules from the cytoskeleton does not affect the measured the stiffness of lens cells.
3- We found that the protein-associated lipids are stiffer.
4- I developed a hybrid HS-AFM/Optical Microscopy to study the lens cells membrane proteins in living cells. Overall, my work pointed out that the free displacement of junctional microdomains has importance in the context of the tissue integrity during lens accommodation.
The scientific activity as a postdoctoral researcher with Dr.Aurélien Roux was mainly focused in two topics: 1-on the role of membrane remodelling proteins (ESCRT machinery and dynamin). 2- lipid membrane physics quantification, developing a new methodology to quantify lipid membrane tension in vitro and in living cells:
1- Dynamin only moves (torsion and contract) on GTP presence, and GTP does not produce dynamin depolymerisation.
2- GTP-induced dynamic rearrangements of the dynamin helix turns.
3- We found that once lipid bilayers are fully covered by the Snf7 spirals, they stop to grow and engage a polygonal shape, most likely as a result of the lateral pressure produced by the membrane curvature.
4- I developed a new methodology, which shows a probe that can monitor changes in membrane tension by changing its fluorescence lifetime, and showing than membrane tension and membrane phase are related.
Actually, I am applying the technique to study the cell membrane properties from cells and embryos. Recently, we adapted the probe and we are studying ER, mitochondria and lysosomes organelles.

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Resumen del Currículum Vitae:

Along the past years, my research activities have been focused mostly on the field of cell membrane biophysics and cell trafficking. I finished my doctoral thesis in Structural biology between the Institute Curie (Paris) and Aix-Marseille University (Marseille) in France, under the supervision of Dr.Simon Scheuring. Later, I moved for my postdoc to the University of Geneva with Dr. Aurélien Roux, where I am still working as postdoc . During these years, I have mastered and set-up a number of techniques and methodologies with the purpose of studying the mentioned research topics from different perspectives.
My research career started with a hospital research group during my period as lab technician in the University of Barcelona with Dr.Jordi Alcaraz, where I designed experiments to study extracellular matrix gel properties and fibroblast viability (JBMR 2014, CSB 2014, Resp. Res. 2015).
During my PhD thesis with Dr.Scheuring , I succeeded in developing one of the first High-Speed Atomic Force Microscopes (HS-AFM) with an optical setup to study membrane processes (IOVS2012, JMB 2012 Soft Matter 2013, Cell 2015, PNAS 2017), which provided the first molecular movies of membrane proteins on living cells (Nature Comm. 2013). My work pointed out that the free displacement of junctional microdomains has an importance in the context of tissue integrity during lens accommodation.

Later, during my postdoc with Dr.Roux, I developed new methods for the study of cell trafficking and membrane mechanics in cellulo and in vitro, which I applied in my own projects as well as through collaborations comprising different biological models like yeast (Nature Cell Biology 2017), a wide range of mammalian cells, hydra and zebrafish (3 papers will be out soon as a result of these collaborations), confirming the polyvalence of the technique .
The most remarkable achievement during my postdoc has been the new methodology I developed, which shows a probe that can monitor changes in membrane tension by changing its fluorescence lifetime as a function of the twist between its fluorescent groups (JACS 2015, Chem Commun 2016 and Helv. Chim 2017), allowing an easy quantification method of membrane tension. I showed that membrane tension and membrane phase are related (Nature Chem 2018). Today, I am applying this technique in combination with other microscopy approaches (Cryo-TEM, SEM and Light-Sheet Microscopy) to study cell membrane properties from cells to embryo models, passing through the study of organelle lipid membrane properties (JACS minor revision).
The scientific activity performed during these years has led to 17 research articles and 16 contributions in international and national conferences.

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However, the most important has been the opportunity to work, learn and grow as a scientist working in such an interdisciplinary environment. This has given me a wide perspective of the different topics that my work has focused on. Importantly, it has also been an opportunity to create a broad international and national network.

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Nombre: RODRIGUEZ BOTIGUE, LAURA
Referencia: RYC2018-024770-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: laura.botigue@cragenomica.es

Título:

Ancient genomics for the study of the domestication process

Resumen de la Memoria:

Throughout my career as a population geneticist, I have specialized in genomic analyses with the goal of making demographic inferences and finding evidence of selection. As a career track fellow at the Centre for Research in Agricultural Genomics since January 2018, I investigate one of the milestones of human evolution, plant domestication, from a new perspective: by using my expertise in population genetics and incorporating the genomes of ancient specimens. The study of plant domestication can also provide results of great value in other fields. For instance, in a scenario of climate change and depletion of Earth s natural resources, there is a growing interest towards sustainable agriculture. To that end, the characterisation of ancient variation and the identification of the wild populations that were directly involved in the domestication process can contribute to finding the genetic basis of traits of interest in agriculture and the identification of multiple variants associated with these traits. This information, in turn, can ultimately be used towards crop improvement, by generating more diverse crop varieties that are better adapted to a certain environment. This line of research is particularly relevant because at the moment few research groups in Spain work on ancient DNA, and none of them focus on plant domestication. My first work on this topic is on ancient Egyptian emmer wheat, which has been recently submitted to Nature Genetics. We describe details surrounding the dispersal of domestic emmer wheat and observe that overall the ancient sample shares the same domestication history of that of modern emmer landraces. Interestingly, though, we also find evidence of a unique history of gene flow from certain wild emmer populations to the ancient domestic emmer, a gene flow that is not present in modern emmer landraces and therefore should be studied more in depth.I My research in the field of population genetics spans from classical theory to modern coalescence. I published on the increase in genetic burden in human populations as distance from Africa increases (Henn, Botigué et al. 2016 PNAS, Henn et al. 2015 Nature Reviews: Genetics), rebutting recent publications on that topic, and on the genetic architecture and gene flow of understudied North African populations (published in PNAS and PloS Genetics), determining for the first time that modern North Africans are descended from a back to Africa migration that took place 18,000 years ago. I also have experience in palaeogenomics, a valuable skill since degraded DNA from ancient specimens requires the implementation of a specific set of filters when processing the raw sequenced data. I developed and led a study on Neolithic dog remains (Botigué, Song, Scheu et al. 2017 Nature Communications), where we narrowed down the onset of dog domestication and built a demographic model of canid evolution. During my five years of postdoctoral activity abroad, I also gained mentoring experience by supervising four data analysts to study novel and rare genetic variation for the H3Africa Consortium. The skillset I have developed throughout my career enables me to successfully carry out this novel line of research, which I anticipate can lead to major breakthroughs in the understanding of many aspects surrounding the plant domestication process.
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Resumen del Currículum Vitae:

Dr. Laura Botigué started her own lab at the Centre for Research in Agricultural Genomics as a Group Leader in 2018 after five years of scientific career abroad. She will use her background in population genetics and bioinformatics to study the domestication process of plants from a new prism: through the genomic analysis of both modern and archaeological specimens. She has recently submitted her first piece of work on this subject to Nature Genetics: the genomic analysis of a 3,000 year-old emmer wheat sample from Egypt. This is a collaborative project with peers from University College London and a proof of concept of a more ambitious project tackling wheat domestication. She has also two ongoing projects on domestic animals following her past experience.

Dr Botigué has continuously worked in the field of population genetics and developing her bioinformatic skills as a tool to analyse them. As a Postdoc at Stony Brook University (NY) she led three projects. One of them consisted in analysing the genomes of two Neolithic dogs from Germany in the context of other canid data. She estimated that dog domestication began between 40,000 and 20,000 years ago by inferring a demographic model. Dr. Botigué also found that Neolithic dogs were already very similar to modern European dogs, as genomic continuity was observed since the early Neolithic until present. This work has received great attention from public media and peers prior and after its publication in Nature Communications. The second project was more theoretical. She analysed genomic data from seven worldwide human populations to observe that genetic load (the burden of deleterious mutations) increases with distance from Africa, in agreement with what was described in classic population genetics theory. She published this work in PNAS in a shared first authorship and participated in a review on that topic for Nature Reviews: Genetics. During her postdoc she was invited to collaborate with the H3Africa Consortium and led a team of data analysts to investigate rare and novel variation in a genomic dataset of African populations. The resulting manuscript, a joint effort of five team leaders and the coordinator of the project, has recently been submitted to Nature.

During her PhD in the Institute of Evolutionary Biology in Barcelona Dr. Botigué became familiar with the fundamental concepts of population genetics and evolutionary theory. She worked closely with renowned population geneticists from Universitat Pompeu Fabra and Stanford University. The analysis of a North African dataset of human populations was carried out in collaboration with the

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Bustamante Lab (Stanford University) and was discussed in two papers published in PLoS Genetics and PNAS.
On 2017 she worked as a Bioinformatician at Kew Gardens for the Plant And Fungal Tree of Life project, and participated in a publication in Systematic Biology. Dr. Botigué raised her bioinformatic skills to a higher level, giving her the necessary knowledge to develop complex software that can be used by the scientific community. Finally, Dr Botigué contacted Herbarium curators to include Herbarium samples in her research and set the basis for a project on apple domestication.

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Nombre: PLASS , MIREYA
Referencia: RYC2018-024564-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: miriplass@gmail.com

Título:

Systems biology approaches to the study of eukaryotic gene regulation

Resumen de la Memoria:

My main research interest is to study the mechanisms that regulate gene expression in eukaryotic cells and in particular to understand what is the contribution of post-transcriptional gene regulation to cellular phenotypic diversity. During my PhD, the main focus of my research was to understand how alternative splicing is regulated. Eventually I became more interested on RNA binding proteins (RBPs) and during my first postdoc I investigated the role of RNA binding proteins in the regulation of mRNA stability.
More recently, I have taken advantage of single-cell transcriptomics methods to study gene regulation and cell differentiation. I have used this technology to reconstruct for the first time the cellular differentiation pathways of stem cells in vivo and identify the gene sets involved in this process (Plass et al. Science 2018). Currently, I am developing a new computational method to quantify individual isoforms from single-cell transcriptomics data and investigate its role in the regulation of mRNA stability during cell cycle progression.
In the coming years, I will exploit this new computational method to study the role of post-transcriptional regulation, and specially, alternative polyadenylation, in neural differentiation and degeneration processes. The results obtained from this research will provide an in-depth analysis of the changes in gene expression and APA in neuronal cell types at single cell resolution. Additionally, it will allow the characterization of thousands of genes specifically regulated by RBPs, many of them with key functions in the nervous system such as Nova, HuR or MBNL.

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Resumen del Currículum Vitae:

My main research interest is to study the mechanisms that regulate gene expression in eukaryotic cells and in particular to understand what is the contribution of post-transcriptional gene regulation to cellular phenotypic diversity. During my career, I have been involved in several multidisciplinary projects in the context of international networks and collaborations. As a result, most of my publications combine both computational and experimental approaches to study gene regulation.
I studied Biology (UPF, Barcelona) moved by the interest to understand how genes shape organisms. After several student internships in experimental labs, I worked exclusively on computational biology for my bachelor thesis and my PhD (CRG/UPF, Barcelona), focused on understanding the regulation and functional impact of alternative splicing. With the work that I did during my PhD, I published 8 papers, 3 of them as first author.
I have carried out all my postdoctoral research outside Spain. first at the University of Copenhagen in Denmark (2011-2015) and since 2016 at the MDC in Berlin. At the Krogh lab in Copenhagen, I obtained a research grant from the Carlsberg Foundation (2014-2016; ~335.000) to investigate the role of RNA binding proteins on defining the fate of RNAs. During this period I published 7 papers (2 as first author and 1 as co-corresponding author) and 2 book chapters.
In January 2016 I moved to the laboratory of Professor Nikolaus Rajewsky at the MDC in Berlin. Here, I focused on studying gene regulation and cell differentiation using single-cell transcriptomics. We have reconstructed for the first time the cellular lineage tree of a whole adult animal and characterize its major cellular differentiation pathways (Plass et al. Science 2018). This study, together with other papers on the same topic, has been highlighted as the scientific discovery of the year by the Science Magazine.
Currently, I am developing a new computational method to quantify individual isoforms in single. This new tool will allow understanding the importance of post-transcriptional regulation in gene regulation and cell differentiation. I have obtained external funding (BP 2017) to further develop this method at the CRG in Barcelona and study the role of post-transcriptional gene regulation during neuronal differentiation.