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AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2019

Turno de acceso general

Nombre: OLALDE MARQUINEZ, IÑIGO
Referencia: RYC2019-027909-I
Área Temática: **Biociencias y biotecnología**
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Título:

Study of human population history with ancient DNA

Resumen de la Memoria:

My main research line has focused on the study of human population history with ancient DNA. More specifically, I use Next-Generation Sequencing techniques to recover genome-wide data from ancient humans from Europe and to make inferences about the underlying events such as migrations and admixture events. During my PhD at the Instituto de Biología Evolutiva (CSIC-UPF, Barcelona), we recovered the first complete genomes of a European hunter-gatherer (Olalde et al., Nature 2014) and a Cardial Neolithic farmer (Olalde et al., Molecular Biology and Evolution 2015), and used these data to look from a new perspective at one the oldest debates in the field of archaeology, the relation between the Mesolithic hunter-gatherers and Neolithic farmers in Europe. We discovered that Neolithic farmers did not descend from the hunter-gatherers, which indicated a large-scale migration during the Mesolithic-Neolithic transition. During my postdoc at Dr. David Reich s group (Harvard Medical School), I led two multidisciplinary projects involving more than 100 researchers. In the first one (Olalde et al., Nature 2018), we carried out a genomic study of the Bell Beaker phenomenon, a Copper Age culture that spread between 2500 and 2000 BC across western Europe and northwest Africa through both migration and cultural diffusion, according to our data. In the second one (Olalde et al., Science 2019), we focused on a smaller geographical area, the Iberian Peninsula, but sampled a much wider time-span of 8000 years to provide the most comprehensive view of human population history in this region with ancient DNA. Since October 2019, I continue my research career at the Instituto de Biología Evolutiva with a La Caixa Junior Leader Fellowship, studying the social processes underlying the big ancestry changes uncovered in my previous work and also investigating the final genetic formation of present-day populations over the last two millennia.
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Resumen del Currículum Vitae:

From 2005 to 2011, I studied a degree in Biology and Biochemistry at the Universidad de Navarra (Pamplona, Spain). During the last year of my degree, I was an Erasmus student at the University of Groningen, where I carried out a research project on insect genetics at the Centre for Ecological and Evolutionary Studies (CEES). After graduating, I received a scholarship from "La Caixa" Foundation to do a Master of Advanced Genetics at the Universidad Autónoma de Barcelona. I did my master project at the laboratory of Dr. Carles Lalueza-Fox, Instituto de Biología Evolutiva (CSIC-UPF, Barcelona), where I became in contact for the first time with ancient DNA research and learned how paleogenomics can be used to study evolution and population history. Since I had always had great interest in the prehistory of the Iberian Peninsula, I decided to stay at the laboratory of Dr. Carles Lalueza-Fox to start a PhD, applying the new DNA sequencing techniques to the study of important questions related to the peopling of the Iberian Peninsula. During my PhD, funded by a Predoctoral fellowship from the Basque Government, we recovered the first complete genomes of a European hunter-gatherer (Olalde et al., Nature 2014) and a Cardial Neolithic farmer (Olalde et al., Molecular Biology and Evolution 2015), and used these data to look from a new perspective at one the oldest debates in the field of archaeology, the relation between the Mesolithic hunter gatherers and Neolithic farmers in Europe. We discovered that Neolithic farmers did not descend from the hunter-gatherers, which indicated a large-scale migration during the Mesolithic-Neolithic transition. During my postdoc at Dr. David Reich s group (Harvard Medical School), I led two multidisciplinary projects involving more than 100 researchers. In the first one (Olalde et al., Nature 2018), winner of the 2018 Current Archaeology Award in the "Research Project of the Year" category, we carried out a genomic study of the Bell Beaker phenomenon, a Copper Age culture that spread between 2500 and 2000 BC across western Europe and northwest Africa through both migration and cultural diffusion, according to our data. In the second one (Olalde et al., Science 2019), we focused on a smaller geographical area, the Iberian Peninsula, but sampled a much wider time-span of 8000 years to provide the most comprehensive view of human population history in this region with ancient DNA. Since October 2019, I continue my research career at the Instituto de Biología Evolutiva with a La Caixa Junior Leader Fellowship, studying the social processes underlying the big ancestry changes uncovered in my previous work and also investigating the final genetic formation of present-day populations over the last two millennia.

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Nombre: MARCON , LUCIANO
Referencia: RYC2019-028176-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: lmarcon@upo.es

Título:

Systems biology approach to study embryonic self-organization

Resumen de la Memoria:

During my PhD, I exploited my multidisciplinary background to study mouse limb development by using a systems biology approach. I developed a computational model of limb morphogenesis based on experimental clonal data. The model showed that the shape of the mouse limb is the results of anisotropic growth combined with isotropic cell mixing (Marcon L et al PloS CB 2011). This work provided also a novel framework to re-asses classical limb patterning hypothesis and was highlighted in Nature Review Genetics (Muers M, Nat. Revi. Genetics 2001). By establishing a productive collaboration with the laboratory of prof. Marian Ros, I developed a theoretical approach to analyze digit patterning in Hox mutants limbs (Sheth R and Marcon L et al. Science 2012). This work showed that digits are specified by a self-organizing Turing mechanism whose periodicity can be modulated by Hox genes to form less digits (Hox mutants have up to 14 digits in one mouse limb). This important discovery represents a paradigm shift in the field and was highlighted in scientific journals (Miura T. Science Signaling 2013, Vogel G. Science 2013) and by several media. Following the growing interest on Turing systems in biology, I wrote a review on this topic (Marcon L, Sharpe Curr Opin Genet Dev. J 2012). In parallel, I trained other students to take advantage of my work on limb growth to study the patterning of three skeletal limb segments (Uzkudun M, Marcon L, Sharpe J Mol Syst Biol. 2015) and the evolution of the digits (Onimaru K, Marcon L et al Nat Commun. 2016). My work on mouse limb development culminated with the development of an integrative model of limb growth and patterning, that identified BMP, Sox9 and WNT as the main Turing molecules that pattern the digits (Raspopovic J, Marcon L et al Science 2014). This article had a great scientific impact and is considered a pioneering work in the study of tissue self-organization. During my postdoctoral studies, I followed my interest on self-organization and mouse development and I performed theoretical and experimental work as an independent EMBO long-term fellow. On the theoretical side, I developed a novel mathematical method to identify Turing networks, which shwed that self-organizing Turing patterns can be formed by systems with equally diffusing signaling molecules (Marcon L et al 2016, Diego X, Marcon L, Müller P, Sharpe J. 2017). This broke the long-standing belief in the field that Turing systems require differential-diffusivity. On the experimental side, I followed recent advances in the field of organoid biology by establishing three dimensional culture of embryonic stem cell (mESC) as a model system to study embryonic self-organization. In particular, I developed mESC spheroid cultures known as embryoid bodies as a reliable system to study the self-organization of the three germ layers and the cell movements observed during gastrulation (Marcon L and Raspopovic J, et al 2020 submitted). Recently I have started my own laboratory and the Andalusian center for Developmental Biology where I am employed within the strategic plan of a Maria the Maetzu excellence recognition. In my laboratory we combine experimental work on Embryoid Bodies and theoretical approaches to study embryonic self-organization.
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Resumen del Currículum Vitae:

My curriculum is characterized by international experiences and by various multidisciplinary scientific publications with high-impact. I started my higher education obtaining a degree in theoretical computer science at the University of Trento (Italy). Then,I attended a master in life science at the University of Edinburgh (Scotland) that was awarded with distinction. Finally, I did my PhD in Biomedicine at the Center for Genomic Regulation in Barcelona (Spain), that was graded with summa cum laude and was selected as the best doctoral thesis of the PhD program and awarded with a prize from Eppendorf. My PhD was particularly productive and resulted in the publication of four first author papers: one article in PloS Computational Biology, two articles in Science and one review in Current Opinion in Genetics & Development. In addition, I published two other articles as co-author in Molecular Systems Biology and Nature Communication.In the first article, I supervised another doctoral student, while in the second I collaborated with another post-doctoral researcher. I did my my postdoctoral research at Max Planck Institute of Tuebingen (Germany) by obtaining a EMBO long-term fellowship to support my research. During this period I published one first author paper in Elife and I performed pioneering experimental work with mouse embryonic stem cells that I have recently submitted as a part of a high-impact paper. In addition, I published two articles as co-author in Physical Review X and Nature Review Genetics. During my PhD and posdtoc,I have attended many international conferences and I presented my work with posters,selected talks and invited talks.Finally,I had the possibility attend a course focused on the art of leadership organized by EMBO. Less than two years ago, I have started my laboratory as an independent group leader at the Andalusian Center for Developmental Biology in Seville (Spain). I managed to attract a postdoctoral research with a "Juan de la Cierva Incorporacion" fellowship and I recently obtained independent funding for 126.000 and for a PhD scholarship from the research program of the Spanish ministry of science and innovation. Since 2019, I am supervising a doctoral thesis and I have supervised a bachelor internship project and I am supervising a master dissertation. I have been reviewer for PloSOne, Scientific Reports, Development, Developmental Dynamics, Physica D:Nonlinear Phenomena and WIREs Systems Biology and Medicine. Last year, I wrote a chapter of the book Evolutionary Systems Biology vol 2 as a co-corresponding author that is currently in press. Finally, I am part of the scientific advisory board of the 13th conference of the Spanish

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Society for Developmental Biology.

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Turno de acceso general

Nombre: MOMPEAN GARCIA, MIGUEL ANGEL
Referencia: RYC2019-026574-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: mmompean@iqfr.csic.es

Título:

The homo- and hetero-oligomeric foldomes of functional and pathological amyloids

Resumen de la Memoria:

Many aspects relating protein aggregation to neurodegenerative diseases are still unknown. This encumbers the development of effective treatments. Amyloids are assumed to be made of one type of protein, but my recent elucidation of the first hetero-amyloid structure, the RIPK1-RIPK3 necrosome, suggests that amyloids composed of two distinct proteins playing key roles in health and disease may be common. In fact, a viral protein (M45) can displace one partner (RIPK1) to form a distinct hetero-amyloid (M45-RIPK3) that facilitates infection. The main goal of my research is to characterize the formation, structure and energetics of representative functional and pathological hetero-amyloids. I do this using NMR spectroscopy and energy calculations, featuring novel technical innovations that I am developing. TDP-43, an essential protein involved in RNA splicing, transport and regulation, forms aggregates implicated in several neurodegenerative diseases. These illnesses include ALS, Frontotemporal Dementia and LATE a recently reported pathology that accounts for up to 20% of all dementia cases. I hypothesize that TDP-43 forms functional hetero-amyloids in condensates like the myo-granule or stress granule. I also envision that TDP-43 assembles into harmful hetero-amyloids with nuclear pore proteins and CPEB3, a functional amyloid whose aggregation is key for memory consolidation. This would disrupt nucleocytoplasmic transport and block the engraving of new memories, respectively. By comparative analysis of the richly diverse hetero-amyloid foldome of TDP-43, the defining features of innocuous versus harmful amyloids will be revealed. Taking a leaf from the viral (M45) playbook, this will enable the design of new proteins capable of reprogramming toxic amyloids to convert them into benign ones. The concept of hetero-amyloid multiples the number of possible amyloids one hundred fold. My research will provide the vision and tools need to explore this fascinating new field.

I hold two BSc degrees (Chemistry and Biochemistry), an MSc (the prestigious European Master in Theoretical Chemistry and Computational Modelling), and a PhD in Biophysics. I obtained a JdC-Incorporación (ranked #1 in Biosciences). Since 2011, I have been training in NMR (theoretical, hardware, and experimental) in solution and the solid-state (including hyperpolarization schemes), as well as in Quantum Mechanical calculations and in Molecular and Spin Dynamics simulations. Since 2019, I am the principal investigator of the above project, and I am building my own group at the IQFR/CSIC thanks to the generous funding from the Junior Leader Program from La Caixa (300.000 , 3 years). This program awarded 11 grants to 484 applications received, being the most competitive in Spain in 2019 (success rate 2%). The Junior Leader Program follows the Peer Review Guide established by European Science Foundation, and as such includes a pre-selection by various experts in the field and a final face-to-face interview before a multidisciplinary commitee. At both steps, my research line, career and trajectory were ranked with the highest mark in my field by the Life Sciences panel.
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Resumen del Currículum Vitae:

EDUCATION

2015: PhD in Biophysics, Grade: Excellent Cum Laude. Autonomous University of Madrid, Spain. Thesis: Structural and computational studies of amyloids and noxious folds in biomolecules .

2015: BSc Biochemistry, University of Murcia, Murcia, Spain

2013: European Master in Theoretical Chemistry and Computational Modelling (EMTCCM), Grade: Excellent with Honours, Consortium (26 universities from 6 countries)

2010: BSc Chemistry, Major in Fundamental Chemistry, University of Murcia, Murcia, Spain.

PROFESIONAL EXPERIENCE

Principal Investigator:
2019 today: La Caixa Junior Leader Retaining Fellow at IQFR/CSIC, Madrid, Spain.

2016 today: Invited position: Associate in the Chemistry Dept. at Columbia University, New York, USA.

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2016 2018: Co-PI of a Research and Discovery (R&D) with Wageningen University and Research (WUR) and U. of Castile-La Mancha (UCLM)
Main responsibility: fabrication of NMR microcoils; design and implementation of NMR experiments.

2016 2018: Postdoctoral Researcher at UCLM. Research area: Small-volume NMR & hyperpolarization schemes.

2015 2016: Postdoctoral Researcher at the IQFR/CSIC, Madrid, Spain. Research area: NMR spectroscopy and computational studies of amyloids.

2011 2015: PhD candidate Spanish National Research Council/ Rocasolano Institute for Physical Chemistry / Dept. of Biological Physical Chemistry / Madrid / Spain
Research area: NMR spectroscopy of biomolecules

CAREER RECORD

19 scientific publications* in peer-reviewed international journals:
CELL (1), Nat Commun (1), JACS (1), EMBO Rep (1), PLoS Biol (1), J Biol Chem (1), FEBS J (1), Brain Pathol (1), J Phys Chem Lett (2), Front Mol Neurosci (1), RSC Adv (1), Arch Biochem Biophys (2), Biopolymers (1)

Corresponding Author in 5. First author in 14. 5 publications without PhD supervisor. H-index=10 (Scopus). Citations since 2014= 244 (Scopus)
2 highlighted in News and Views type article; 1 selected as journal cover (FEBS J)
1 selected as highlight paper by the Harvard Medical School
4 selected as highlight papers by the Spanish Society of Biophysics

PARTICIPATION IN RESEARCH PROJECTS

Since 2011, I have been directly participating in National, European, and North-American projects aimed at studying amyloids in diverse contexts such as memory consolidation, neurodegeneration, and cell signalling: LCF/BQ/PR19/ 11700003 (La Caixa Foundation), CTQ2017-84825-R (MINECO, SPAIN), CTQ2014E 54987-P (MINECO, SPAIN), R01 AI045937 (NIH USA), MCB 1412253 (NSF USA), EU JPND AC14/00037 (EU Joint Programme in Neurodegenerative Diseases), and SAF2013E49179-C2-2-R (MINECO, SPAIN)

MAJOR COLLABORATIONS INDEPENDENT OF ANY PHD OR POSTDOC SUPERVISOR

Prof. Ann McDermott (Columbia University, New York, NY, US)
Prof. Hao Wu (Harvard Medical School, Boston, MA, US)
Prof. Margaret Sunde (The University of Sydney, Sydney, AU)
Dr. Emanuele Buratti (ICGEB, Trieste, Italy)

JOURNAL REFEREEING

I have reviewed papers at JACS, Front. Genet, Cell Mol. Life Sci., EMBO Rep., and J. Comput Aided Model. Design

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Nombre: LEROY , FELIX
Referencia: RYC2019-028008-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: felxfel@aol.com

Título:

Top down regulation of motivated behaviors by lateral septal integration of cortico-hippocampal inputs

Resumen de la Memoria:

My research focuses on determining basic cellular- and circuit-based mechanisms by which higher-order brain areas such as the hippocampus and the neocortex relay cognitive information to the hypothalamus in order to modulate innate behaviors. I particularly focus on learned and innate social behaviors. In addition, I am investigating how neuronal plasticity rules, mostly described ex vivo so far, can support learning-related behaviors in vivo. As alterations in higher brain regions contribute to neuropsychiatric diseases associated with disordered social behavior, insights into both the normal and abnormal function of these circuits are of critical importance.

My Ph.D. studies published in eLife and other journals provided new insight and challenged existing dogma as to how spinal motor neurons are affected in amyotrophic lateral sclerosis. During my post-doctorate, I made remarkable progress in determining how the brain controls social interactions. First, I published a study in Neuron in which I employed a multidisciplinary approach, including modern anatomical tracing, slice electrophysiology, optogenetics, chemogenetics and behavioral tests, to characterize a new form of synaptic plasticity in the CA2 region of the hippocampus, and demonstrate its importance in social memory. Then, in a second study published in Nature, I discovered a novel circuit linking CA2 to a subnucleus in the hypothalamus by which CA2 promotes social aggression, providing the first defined circuit linking social memory (episodic memory) to aggression (motivated behavior).

In the future, I plan to use a wide range of advanced technical and experimental skills including in vivo calcium imaging, to understand how cognitive information originating in the hippocampus or pre-frontal cortex can regulate innate motivated behaviors (social interactions, aggression, mating, feeding) controlled by specific hypothalamic nuclei. Furthermore, my translational studies on mouse models of autism and schizophrenia can potentially lead to new strategies to compensate the deficits in social interactions occurring during these diseases. Thus, my study may suggest new approaches to treat abnormal social cognition associated with psychiatric diseases.
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Resumen del Currículum Vitae:

I am a neuroscientist conducting post-doctoral training at Columbia University. My interests are focused on determining basic cellular and circuit-based mechanisms by which neurons in the central nervous system perform specific behavioral tasks, from movement control in the spinal cord to memory storage in the hippocampus. My current goal is to understand how defined neural circuits enable higher order brain regions to regulate innate motivated behaviors. In addition, I am also investigating how neuronal plasticity rules can support learning-related behaviors in vivo.

After completing my Ph.D. at Paris Descartes University, where I worked on the spinal cord, I moved to the laboratory of Steven Siegelbaum to study memory encoding. I became interested in the CA2 hippocampal region that is necessary for social memory. After discovering a new form of plasticity in CA2 that may support social memory encoding (Leroy et al., Neuron 2017), I began examining how CA2 output could mediate other social behaviors. Based on my finding that CA2 projects to the lateral septum, an area implicated in aggression, I focused on whether CA2 might modulate social aggression. As a core motivated behavior, aggression is controlled by a hypothalamic nucleus, specifically the ventro-lateral part of the ventro-medial hypothalamic nucleus (VMHvl). I discovered that CA2 upregulates VMHvl activity, thereby enhancing aggression, through a disynaptic disinhibitory circuit in the lateral septum that is modulated by the social neuropeptide arginine vasopressin (Leroy et al. Nature 2018).

My previous experience in electrophysiology and genetic-based anatomical tracing now enables me to discover new brain circuits and probe their function using in vivo chemogenetic or optogenetic cell-type specific manipulations in an integrated approach linking neuronal circuits to behavior. Recently, I have used fiber-photometry and miniature endoscopes to directly record neuronal activity while freely-moving mice engage in motivated behaviors. How higher-brain regions regulates motivated behaviors (sociability, aggression, mating, feeding) controlled by various hypothalamic nuclei is still poorly understood. I hypothesize that integration of hippocampal and cortical inputs within the lateral septum coupled to neuromodulation regulates the tonic inhibition provided by the lateral septum onto each hypothalamic nucleus, thereby regulating each motivated behavior. Furthermore, as hippocampus, prefrontal cortex and lateral septum are implicated in several neuropsychiatric disorders associated with altered social behavior and aggression, including schizophrenia, autism and Alzheimer s disease, insights into how lateral septum integration regulates social interactions are important for understanding both basic neural mechanisms as well as how disease processes lead to altered aggression.

During the course of my scientific studies, I mentored 6 graduate and undergraduate students which are still in the academic field. I also aquired independent fundings to support my undergraduate and graduate studies as well as during my postdoc. Finally, I participate in reviewing/editing activities in 6 scientific journals and scientific agencies.

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Nombre: PEREZ GARCIA, VICENTE
Referencia: RYC2019-026956-I
Área Temática: **Biociencias y biotecnología**
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Título:

Deciphering the common molecular mechanisms of cell invasion shared between trophoblast and cancer cells

Resumen de la Memoria:

I started my research career investigating the phenotype of regulatory T (Treg) cells in patients with Rheumatoid Arthritis (RA) (Sempere-Ortells JM et al., Autoimmunity, 2009). Then, I did my PhD at the National Center for Biotechnology (Autonomous University of Madrid, Summa Cum Laude and 9 publications) focusing my attention on how phosphoinositide 3-kinase (PI3K) isoforms dimerize to regulate the phosphatase and tensin homolog (PTEN) activity (Kumar A.*, Redondo-Muñoz J.*, Perez-Garcia V.* et al., Mol. Cell Biol. 2011; *Equal contribution; Pérez-García V. et al, Mol. Cell Biol.,2014. I also visited Dr Peter Andrews lab in the Centre for Stem Cell Biology (CSCB) in Sheffield (UK), where I developed new human embryonic stem cell lines. After my PhD, I moved to the Babraham Institute in Cambridge to do my postdoc in the lab of Myriam Hemberger focusing on epigenetics, ageing and placental development (5 publications). Firstly, I successfully managed to implement the CRISPR/Cas9 genome editing system in the difficult-to-transfect trophoblast stem cells (Branco MR, Dev. Cell, 2016). This challenging task became a breakthrough in my research career allowing me to collaborate with several groups (Lopez-Tello J. et al., eLIFE, 2019; Chrysanthou S. et al., Stem Cell Reports, 2018; Perez-Garcia & Fineberg, Nature, 2018; Branco MR et al. Dev. Cell, 2016) and also to lead the establishment of international collaborations. At the same time, I supervised my first PhD student and we described how abnormal embryonic development in aged female mice is associated with severe placentation defects (Woods L *& Perez-Garcia V.* et al., Nature Commun., 2017, *Equal contribution). To date, I have been the mentor/supervisor of three PhD students and one Erasmus+ PhD student. Since finishing this project, I have been involved in the Deciphering the Mechanisms of Developmental Disorders (DMDD) consortium. This program is a systematic screen of mouse embryonic lethal genes including phenotypic analysis of structural abnormalities in mutant embryos and mutant placentas. We showed (using CRISPR-Cas9 genome editing system) that placental defects very commonly underlie embryo lethality. (Perez-Garcia V.* & Fineberg E.*, Nature, 2018; *Equal contribution; (Woods L., Perez-Garcia V.*& Hemberger M*, Front. Endrocrinol., 2018; *co-corresponding author). Succeeding my postdoctoral training, I was awarded a Grant by the University of Cambridge (Centre for Trophoblast Research, full costing = 210.000) and I have been invited the Sir Henry Dale Fellowship Interview (June 2020, full costing = 1.200.000) to investigate the similarities between trophoblast cells and cancer cells. Trophoblast cells share some key similarities with metastatic cancer cells, in particular with regard to cell invasiveness and the capacity to breach basement membranes. The fact that cell invasion does exist in health (trophoblast invasion) and disease (metastasis in cancer) points to common and conserved pathways between both processes. Due to my background in cancer signalling, epigenetics and placental development, I am putting to work the skills developed during my postdoc including CRISPR-Cas9 technology, RNA-seq and ChIP-seq (low input) to investigate the commonalities between the trophoblast invasion capacity and cancer cells using human endometrial and trophoblast organoids as a model.
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Resumen del Currículum Vitae:

Following my bachelor s degree in Biology (University of Alicante, graduated with honours), I did my PhD in cancer signalling at the National Center for Biotechnology (Autonomous University of Madrid, Ana Clara Carrera's lab, Summa Cum Laude and 9 publications). During my PhD, I described the existence of heterocomplexes composed by the main phosphoinositide 3-kinase isoforms which are formed following tyrosine kinase receptor activation. These findings are important to better understand how PI3K regulates the lipid messenger PI (3,4,5) P3 production and open new avenues to investigate cancers where PI3K pathway is mutated (Kumar A.* & Redondo-Muñoz J.* & Perez-Garcia V.* et al., Mol Cell Biol. 2011, *Equal contribution; Perez-Garcia V. et al., Mol. Cell Biol., 2014). Then, I moved to Cambridge to do my postdoc at the Babraham Institute in the lab of Myriam Hemberger (epigenetics programme). There, I had a successful postdoctoral training (5 publications in total) that resulted in two relevant first author publications in the journals Nature and Nature communications. My contribution to the field of placental development and fertility demonstrate how embryonic lethal mutations impact on placental development (Perez-Garcia V.* & Fineberg E.* et al. Nature, 2018, *Equal contribution) and how ageing affects reproductive success (Woods L.* & Perez-Garcia V.* et al., Nature commun., 2017, *Equal contribution). In addition, I was invited to write a review based on the topic of our Nature publication where I am co-corresponding author (Woods L., Perez-Garcia V.* & Hemberger M.*, Front. Endrocrinol., 2018; *Equal contribution). To date, I have been mentor/supervisor of 3 PhD students and one Erasmus+ PhD student. I have also been invited to review several manuscripts for Peer-Review Journals (Scientific Reports, Human Molecular Reproduction and Biology of Reproduction). Moreover, I pioneered the implementation of CRISPR/Cas9 genome editing system in trophoblast stem cells (the precursors of the differentiated cells of the placenta). Improving the method in this difficult-to-transfect cell line allowed me to establish national and international collaborations. My research formation has been complemented with teaching duties at several universities (Alicante, Madrid, Murcia, Medellin (Colombia) and Queens' College-Cambridge). Regarding outreach science, as an active member of the Spanish Research UK-Cambridge, I have been involved in the organization of several public engagement activities (Babraham schools' day, Cambridge Science

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Festival, twilight teacher training sessions, Art&Science, Pint of Knowledge, etc). After my postdoc, I was awarded a grant at The University of Cambridge (Centre for Trophoblast Research) to develop my independent project as a Next Generation Fellow (full costing = 210000) and I have been invited to the Sir Henry Dale Fellowship Interview (June 2020, full costing = 1.200.000). To date, I have been the mentor/supervisor of 3 PhD students and 1 Erasmus+ student. Due to my background in cancer signalling, epigenetics and placental development, I am putting to work my skills including CRISPR-Cas9 technology, RNA-seq and ChIP-seq (low input) to investigate the molecular mechanisms of cell invasion shared between the trophoblast cells and metastatic cancer cells using human endometrial and trophoblast organoids as a model.

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Nombre: WELZ , PATRICK-SIMON
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Área Temática: **Biociencias y biotecnología**
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Título:

Tissue Communication in Health and Disease

Resumen de la Memoria:

Throughout my scientific career I have been interested in studying how cells and tissues integrate extrinsic information, may it be signals from the external or the internal environment, into the regulation of their physiology. I have used my training in mouse genetics to generate and investigate new mouse models that allow deciphering how cells and tissues sense and respond to their environment.

During my PhD Thesis in the laboratory of Prof. Dr. Manolis Pasparakis I was trained in mouse genetics. I used various mouse models to investigate how innate immunity- and microbiota-related cues regulate intestinal epithelial homeostasis. My work let to the discovery of a new necrotic cell death pathway, also termed necroptosis, in the intestinal epithelium. I found that this pathway can be activated by cytokines and that increased activation of this necroptotic pathway, which also occurs in inflammatory bowel disease patients, leads to a break down of the intestinal epithelial barrier and a severe microbiota-induced inflammatory response in the intestine.

During my postdoctoral stay in the laboratory of Dr. Salvador Aznar Benitah I used my background in mouse genetics to study how the circadian clock network incorporates environmental cues for establishing a synchronized tissue physiology. To do so, I have conceived and generated a novel mouse model. This mouse model allows Cre-recombinase-dependent expression of the functional circadian clockwork exclusively in specific tissues, while lacking a functional clock in all other organs. In collaboration with the laboratory of Paolo Sassone-Corsi at the UC Irvine, we found that light can synchronize the circadian clocks of the epidermis and liver in the absence of circadian clocks in all other tissues. However, in the absence of light, communication between clocks in different tissues is required to maintain a synchronized temporal physiology in the liver and epidermis. Thus, my postdoctoral work establishes a two-branched model for the daily synchronization of tissue function: an autonomous" branch, whereby light synchronizes circadian clocks without any commitment of other clocks, and a memory branch, which is depending on communication between circadian clocks in different tissues to maintain synchronized tissue physiology in the absence of light.
Currently, we are dissecting the tissues and signalling mechanism participating in the light-dependent autonomous pathway and the light-independent memory branch. Additionally, we teamed up with a network of collaborators to study how the communication between clocks in different tissues impacts on tissue physiology. In that regard, we are using the Bmal1-stopFL mouse model for investigating the local and systemic impact of the circadian clock network in the immune system (Andres Hidalgo, CNIC, Madrid; Christoph Scheiermann, LMU/University of Geneva, Munich/Geneva), in skeletal muscle (Pura Muñoz-Cánoves, UPF) and in liver (Paolo Sassone-Corsi, UCI, Irvine; Achim Kramer, Charite, Berlin).
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Resumen del Currículum Vitae:

My scientific output throughout my career includes so far 9 published scientific papers (all in Q1), 1 review and 1 preview, which have in total been cited 875 times (WoS). I have contributed to 3 publications as the first author. One of these first author publications has been published in the journal Nature and the other two in the journal Cell . Furthermore, I am corresponding author of the review and of one of the publications in Cell.

During my postdoctoral stay in the laboratory of Dr. Salvador Aznar Benitah (03/2013 present), first at the CRG Barcelona and later at the IRB Barcelona, I have conceived and generated a novel mouse model (Bmal1-stopFL mice) that allows studying how cellular physiology can be synchronized on the tissue and organismal level through communication between circadian clocks in different tissues. This work has so far led to one first and corresponding author publication and another first author publication, both in the journal Cell in 2019. I have also been able to present a talk about my postdoctoral work at one of the most prestigious conferences for Chronobiology, the "Gordon Conference for Chronobiology" in 2019.
Furthermore, my work has led to the establishment of a network of collaborators, including the laboratories of Paolo Sassone-Corsi (USA), Achim Kramer and Christoph Scheiermann (Germany), Pura Muñoz-Cánoves and Andres Hidalgo (Spain), which are all using the Bmal1-stopFL mouse model to investigate how communication between clocks in different tissues impacts on cell and organ function, or on systemic metabolism.
My work in the laboratory of Salvador Aznar Benitah also includes the supervision of a PhD Thesis (09/2017 ongoing) and a Master student (09/2017 07/2018). I was able to obtain competitive funding during my postdoctoral work from the European Molecular Biology Organization (EMBO Long-Term Fellowship; 01/09/2013-31/08/2015) and from the spanish Ministerio de Economía y Competitividad (Juan de la Cierva Postdoctoral Incorporación; 20/04/2016-19/04/2018).

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Throughout my PhD Thesis (04/2008 04/2012) and a short postdoctoral stay (04/2012 03/2013) in the laboratory of Prof. Dr. Manolis Pasparakis at the Institute for Genetics, University of Cologne (Germany), I have been trained in mouse genetics. I applied that knowledge to study how innate immunity-dependent and microbiota-related cues regulate intestinal epithelial homeostasis. This work resulted in a first author publication in the scientific journal Nature , as well as in several contributions to other studies published in scientific journals of Q1. The Graduate School for Biological Sciences of the University of Cologne awarded my publication in Nature with the best publication prize 2011 . My PhD Thesis has been graded with summa cum laude (best possible grade). For my PhD period I obtained a fellowship covering my salary from the International Graduate School in Genetics and Functional Genomics at the University of Cologne.

I have studied Biology at Bielefeld University (Germany), and I have gained further international research experience during my external Diploma Thesis (comparable to a Master Thesis) at Aarhus University (Denmark) (05/2006 06/2007).

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Turno de acceso general

Nombre: BRUMOS FUENTES, JAVIER
Referencia: RYC2019-026537-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: jbrumos@ncsu.edu

Título:

Phytohormones, gene expression regulation, and development.

Resumen de la Memoria:

Plants exhibit an extraordinary phenotypic plasticity that allows them to thrive in their ever-changing environment despite their sessile nature. Plants achieve this plasticity by integrating all external cues with their own internal growth-and-development programs. Improving our understanding on how this integration process works is critical for agriculture to meet the increasing demand for food, raw materials, and energy, in the face of climate change. Plant hormones play a central role in the signal integration process modifying the organism s internal programs to best respond to the surrounding conditions.

My research bridges basic plant molecular biology with applied approaches in crop science. My program focuses on the study of hormonal and gene regulatory networks involved in the plant s response to the environment, aiming to enable the rational improvement of new, more resilient crop varieties with the help of innovative techniques such as synthetic biology and gene editing approaches.

Throughout my entire career, I have focused on understanding the connections between genetics, environmental changes, and phenotypic plasticity. I graduated in Agriculture Engineering from the Polytechnic University of Valencia. During this time, I had the opportunity to work in Dr. Ari Pappinen s laboratory at the University of Helsinki where I learned different molecular and in vitro plant propagation techniques. My PhD focused on the characterization of abiotic stress responses in citrus in the group of Dr. Manuel Talón at the Valencian Institute for Agricultural Research, IVIA (Valencia). After finishing my PhD, awarded the Premio extraordinario biotecnologia 2011 of the Polytechnic University of Valencia, I moved to the lab of Dr. Jose Alonso at North Carolina State University where my research has concentrated on the plant hormones auxin and ethylene and the basic mechanisms that control the signal integration process and the plants response to their surroundings. Currently, I am a PI of a National Institute of Food and Agriculture grant of USDA studying translational regulation during tomato fruit ripening. This funding enables the application of my experience in basic plant molecular biology to deliver solutions that modern agriculture is demanding.

The Ramon y Cajal contract is an ideal opportunity to reinforce and continue my Plant Science research program and to allow me to contribute to innovation in the Spanish Plant Biotechnology area applied to food production and agriculture.

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Resumen del Currículum Vitae:

My scientific career has been developed in three different and excellent research groups. I started working in Dr. Ari Pappinen s group at the University of Helsinki when I was an undergraduate student. During this training period, I learned basic molecular and plant tissue culture techniques, published a research article and most importantly I grew a deep love for plant biology.
I completed my PhD in Dr. Manuel Talon s group at the Instituto Valenciano de Investigaciones Agrarias (IVIA) taking a multidisciplinary approach using functional-genomics, molecular biology, and plant physiology to study abiotic stresses in citrus. The results of my PhD work were published in twelve research articles and a book. I was awarded Extraordinary Doctoral Thesis Award from the Universidad Politecnica de Valencia. I presented my work at international conferences and got involved in mentoring students which turned out to be one of my passions.
I was awarded with a Post-doctoral fellowship from the Spanish Department of Education to join the laboratory of Dr. Jose Alonso at North Carolina State University where I have worked on two main topics. On the first one, I have been studying how plants produce auxin, where this auxin is made, how the biosynthesis is regulated, and what the physiological significance of such regulation is. On the second one, my interests concentrated on deciphering the effect of ethylene on the regulation of gene expression. Utilizing Ribo-seq, we have been able to show that ethylene can modulate the translation of a specific group of genes independently of their transcription. During this time, I have published nine articles, I have presented my work at different forums as ASPB in 2016 and ICAR in 2018 as invited speaker. I have also been deeply involved in mentoring (more than 30 students) and teaching at the undergraduate and graduate level. I have organized more than 50 outreach events as the manager of the laboratory outreach program, I have developed and coordinated our latest initiative "Plants4Kids.org videos". I have had the opportunity to contribute to the plant biology community reviewing scientific articles for Nature Communications, Developmental Cell, The Plant Journal, BMC Plant Biology, Frontiers of Plant Science, Genes, The International Journal of Molecular Sciences, and Plant Direct among others. I have been fortunate to be involved in the organization of the Plant Molecular Biology Consortium seminars at the NC Biotechnology center. I am a workshop-session organizer for the upcoming ICAR 2020 in Seattle, US.
I have been developing my own research lines revolving around the regulation of gene expression with special interests on how auxin

production is regulated and how ethylene modulates the translation of specific transcripts. For the latter, I have been awarded a National Institute of Food and Agriculture (NIFA) grant from the US Department of Agriculture (USDA) to lead the study of "The Regulation of Translation in Tomato Fruit Ripening". My research program focuses on basic research that will provide a refined picture of the molecular mechanisms regulating plant development according to external cues and to generate biotechnological-breeding tools for the rational production of more resilient crops as well as improved agricultural practices.

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Turno de acceso general

Nombre: MARIOTTI , MARCO
Referencia: RYC2019-027746-I
Área Temática: **Biociencias y biotecnología**
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Título:

Comparative genomics of selenocysteine, the 21st amino acid, and other forms of stop codon readthrough

Resumen de la Memoria:

Selenium is a trace element essential for human health. It is required to make selenocysteine (Sec), the 21st amino acid found in selenoproteins (oxidoreductases mainly involved in redox homeostasis). Translation deviates from the genetic code for selenoproteins: the UGA codon, normally a stop, is recoded to insert Sec instead. Due to recoding, selenoprotein annotation in genomes is challenging and involved extensive manual curation. Through my work, I contributed to scale up selenium research in the era of genomics. I built selenoprotein bioinformatics tools that became gold standards, and I characterized the distribution and evolution of selenium utilization throughout the tree of life. I annotated selenoproteomes in diverse organisms, discovered selenocysteine in new lineages, and studied in detail genes central to selenium biology (SPS, SelenoP). I also investigated additional cases of recoding, both to describe biodiversity and to elucidate elements relevant for human biology and biotech applications.
In the next years, I will build upon up my earlier work to characterize the diversity of selenium utilization across eukaryotes and prokaryotes, and leverage its diverse distribution to understand the evolutionary rationale of selenocysteine usage. Meanwhile, I will expand my research to investigate mechanisms of stop codon readthrough (SCR) other than selenocysteine. Through evolutionary detection of protein conservation, I will predict SCR at large in lineages of insects and other metazoa, and thus outline its functions, evolution and putative sequence stimulators. I will employ genetic reporters to assay and identify genuine SCR stimulators, define their sequence determinants, and characterize regulatory and developmental functions of SCR. In this context, I will prioritize the analysis of one specific gene in honey bee, as my preliminary results indicate a non-canonical form of SCR. Lastly, I will explore the translational potential of SCR genetics, in a novel form of gene therapy aimed to rescue pathogenic nonsense mutations.

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Resumen del Currículum Vitae:

My scientific path crosses the intersection of computational, evolutionary, and molecular genomics. Although diverse in scope, my projects share a common comparative genomics perspective. I consider genetic biodiversity, at disposal in form of rapidly increasing nucleotide sequences, as the central asset of present-day biology. My research leverages molecular data from diverse lineages, which I interrogate through the lens of evolution to understand biological functions and mechanisms.
I use bioinformatics as main method of discovery. I typically work on large-scale omics data, including nucleotide and protein sequences derived from genome assemblies, as well as transcriptomics and proteomics. During my Ph.D., I learned about genome sequencing and assembly, RNAseq analyses, RNA structure, and gene finding with Roderic Guigó. As postdoc, I received training in large scale phylogenetics and gene evolution with Toni Gabaldón. I also worked on protein translation and its exceptions with John F. Atkins and Pavel V. Baranov, learning to design and perform wet-lab experiments. Today I work in the lab of Vadim N. Gladyshev, world-renowned expert of redox biology and aging, where I was recently promoted to Instructor (junior faculty at Harvard Medical School).
I dedicated the majority of my research so far to the biology of selenium. This trace element plays diverse essential roles for human health as part of selenocysteine (Sec), the 21st amino acid found in selenoproteins. Notably, translation deviates from the genetic code for selenoproteins: the UGA codon, normally a stop, is recoded for Sec insertion. Due to recoding, annotation of selenoproteins in genomes is challenging and typically involved meticulous case-by-case curation. Through my career, I built bioinformatics tools that became gold standards of selenium genomics, and I characterized the distribution, evolution and function of selenoprotein genes.
Today, I am well established in this field, as testified by a conspicuous list of publications, two awards at the most prestigious selenium conference, invitations to teach workshop participants, frequent requests for peer-review work, and four invited contributions to book chapters. I now look forward to establish my own research group in Europe, and I consider the Ayuda Ramon y Cajal as a fitting opportunity.
My research plan builds upon my earlier work on Sec, and also expands to additional forms of recoding. In particular, I investigate the phenomenon of stop codon readthrough, where Sec constitutes one example among many cases. My plan is motivated by the recent discovery that readthrough occurs in thousands of genes (particularly in insects), and yet its mechanisms and functions are mostly unknown. To delve into this unexplored diversity, I formulated a strategy that combines bioinformatics and experiments to discover and characterize stop codon readthrough at unprecedented scale. Besides elucidating this important process for animal biology, I aim to explore its potential for translational applications in biomedicine and biotech.
My career has been characterized by ability and motivation to independently lead research studies, to establish successful collaborations, and to attract funding at each stage. At this point in my scientific path, I have built a prestigious reputation and formed a wide network of international collaborators. I believe that these elements will ensure my successful transition to independen

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Turno de acceso general

Nombre: OROSA PUENTE, BEATRIZ
Referencia: RYC2019-027309-I
Área Temática: **Biociencias y biotecnología**
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Título:

Improving plant immunity using post-translational modifications

Resumen de la Memoria:

I am fascinated by the ability of plants to perceive, anticipate and swiftly respond to environmental changes and pathogens. My PhD (University of Barcelona, Spain) was on the complex defence response of Arabidopsis plants to fungal pathogens. During my PhD and afterwards, I had the opportunity to work on human autoimmunity at the Institute of Health Research (Santiago de Compostela, Spain), publishing four first author manuscripts, two in top ranking journals in Rheumatology. This provided me with a holistic view of cell biology, and insights into evolutionary similar and distinct features of eukaryotic immunity between plants and animals.

My interest in plant homeostasis in the presence of external stressors led me to a postdoctoral position with Ari Sadanandom (Durham University), where I specialised in post-translational modifications (PTM), studying SUMOylation and ubiquitination in response to stress. I published seven peer-reviewed manuscripts, including three as first author in high impact journals (Science, Nature Communications and PLoS Genetics). We described how PTMs play a key role in perceiving and responding to environmental stress (pathogens and drought); understanding these mechanisms gives us the opportunity to modulate the amplitude and intensity of plant responses, boosting plant coping mechanisms and decreasing agricultural losses by biotic and abiotic stresses. My increasing interest in the complexity of PTMs led me to Steven Spoel s group (University of Edinburgh) to study the fundamental mechanisms underlying the ubiquitin-mediated regulation of plant immunity. I am committed to addressing the global challenges of world hunger and climate change, and I believe our expanding knowledge of PTMs is a previously untapped resource that can be exploited to enhance plant resistance against diseases with long-lasting benefits to our society and our planet. My multidisciplinary background and my passion for translational research allow me to approach fundamental questions from a different perspective, and has provided me with a broad skillset that matches the challenging of being a group leader.

During my career, I have had an important role designing, coordinating and developing collaborative projects with respected scientists in the plant field (i.e. Prof Malcolm Bennett, University of Nottingham; Prof Paul Birch, James Hutton Institute; or Prof Ferenc Nagy, Biological Research Centre, Hungary). I have also supervised MSc and PhD students, many of whom I continue to mentor by providing scientific and career advice well after my formal supervision has ended; it is a pleasure to inspire and train the next generation of scientists.

I am at the optimal stage in my career to establish an independent research group to develop my vision to enhance plant resistance to pathogens. I have the experience, the curiosity, the motivation and commitment to be a world-leading scientist and a valuable addition to Spanish bioscience. This fellowship is the stepping stone I need to start my own research group leading to impactful research outputs, and will be fundamental for my growth and recognition as a scientist, and to maintain and forge networks with previous and future collaborators and nurture collaborative links across the Spain and Europe.

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Resumen del Currículum Vitae:

Versatility and multidisciplinarity are the two main key points of my curriculum. I have worked in different research areas (plant-pathogen interactions, human autoimmunity and post-translational protein modifications) and professional environments (Universities of Barcelona, Santiago de Compostela, Durham and Edinburgh), which has provided me with a broad skill set and a flexible mind set to approach questions from different angles.

After a challenging PhD studying plant-pathogen interactions in the University of Barcelona, I worked in the Institute of Health Research IDIS (University of Santiago de Compostela) on human autoimmune diseases, where I published my first peer-reviewed manuscripts, two in top tier Rheumatology journals (Annals of the Rheumatic Diseases and Arthritis & Rheumatology). We described the role of lysophosphatidic acid (LPA) receptors as promising new targets for therapeutic treatments, which led to the development of a patent. However, I wanted to continue my research in plant molecular biology, which led me to a postdoctoral position with Ari Sadanandom at Durham University (UK). I specialised in post-translational modifications (PTM), studying SUMOylation and ubiquitination in response to stress. We described how PTMs play a key role in perceiving and responding to environmental stressors such as pathogens and drought, and published our findings in the highest impact journals. My increasing interest in the complexity of PTMs led me to Steven Spoel s group at the University of Edinburgh (UK). Here, I am working in the fundamental mechanisms underlying the regulation of plant immunity by PTMs.

During my career, I have participated in 13 peer-reviewed publications, all of them without my PhD supervisor, and I am the first author in eight of them, published in high impact journals such as Science, Nature Communications or PLoS Genetics. I have established a network of international collaborators, and I am well known in the international field of plant posttranslational modifications; for instance, I am a member of the Organising Committee of the next International Conference on Plant Proteostasis 2020 (Madrid).

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One of my passions is science communication and training. I have supervised both MSc and PhD students, many of whom I continue to mentor after my formal supervision has ended. In Durham University I was involved in teaching Research Masterclasses (Dept of Biosciences) between 2013 and 2018; I planned and delivered short practical classes for 2nd year biology students based around crop improvement. This commitment to communicate science extends beyond academic boundaries; I was one of the founding members of InvestigArte , a scientific-artistic divulgation contest that between 2012 and 2014 tried to use art as a vehicle to divulgate the ongoing science to the public.

After 2 postdoctoral positions, 6 years abroad, 4 different Universities and countless hours leading innovative research, I am ready to establish my research group and consolidate my position as a world leading scientist, developing an ambitious research plan to understand how post-translation modifications regulate plant responses and applying this knowledge to enhance disease resistance in plants. I have the experience, the curiosity, the motivation and commitment to be a world-leading scientist and a valuable addition to Spanish bioscience.

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CONVOCATORIA 2019

Turno de acceso general

Nombre: COLIZZI , FRANCESCO
Referencia: RYC2019-026768-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: cecio.colizzi@gmail.com

Título:

Advanced molecular simulations for fragment-based lead discovery

Resumen de la Memoria:

The leitmotiv of my research has been the disentanglement, by means of computational methods, of the relationships linking structure, dynamics, and function of different molecular systems ranging from small organic molecules, pharmaceutical ligand-target complexes, to large nucleic-acid processing machineries. My scientific trajectory has led me over the years to move across different geographical and thematic areas; from Italy to Switzerland, United States, Canada, and ultimately to Spain; from molecular modeling to drug discovery, computational chemistry, computational biophysics, and ultimately back to drug discovery. Such mobility has dramatically enhanced my capability to integrate knowledge from different fields and lead the successful development of interdisciplinary projects.

During my Ph.D. in computational medicinal chemistry at the University of Bologna, I pioneered the use of pulling molecular dynamics (MD) simulations to discern active from inactive binders and to assist the design of novel enzyme inhibitors with antimalarial activity [JACS 2010]. The innovative nature of this strategy has been highlighted in Nature News & Views. As a graduate student, I also visited the University of California San Francisco (UCSF) where I contributed to the first automatic workflow for parsing and docking the entire Protein Data Bank [DockBlaster Project].

As a postdoctoral researcher in computational biophysics of RNA at the International School for Advanced Studies (SISSA), I disclosed unexpected features of nucleic acid dynamics [JACS 2012] that modulate the function of gene-expression machines [PNAS 2019], and I have been awarded funding for an independent drug discovery project aimed at identifying modulators of an antibacterial RNA target [Methods Mol. Biol. 2014]. In collaboration with molecular biologists and synthetic chemists, I led a structure-based screening campaign and two out of the six compounds eventually tested for activity showed a low-micromolar dissociation constant. One of these two compounds was included into a patent application.

After a 2-year long sabbatical period (with no affiliation) in Quebec, Canada, I returned to academia to join the Orozco Lab at the Institute for Research in Biomedicine (IRB Barcelona) where, supported by a Marie Sklodowska-Curie Individual Fellowship, I am developing MD simulations approaches for the quantitative characterization of molecular interactions [Angew. Chem. 2019] and for fragment-based ligand discovery in tight contact with biochemists and X-ray crystallographers. Moreover, actions are being taken to further develop and commercialize the devised technologies (secreto industrial process started). I constantly aim at acquiring state-of-the-art computational methods from various disciplines and at extending their applicability to the drug discovery and biological worlds, in a collaborative framework [Nat. Methods 2019].

Overall, my scientific path demonstrates an extraordinary degree of scientific adaptability & maturity to evolve independent research and thinking, ability to secure funding, produce research outcomes at the highest level and possess leadership and management skills. I aim to hold a Ramon y Cajal fellowship at any host Institution where I could develop independent research in advanced molecular simulations for drug discovery against difficult targets.

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Resumen del Currículum Vitae:

I graduated in Chemistry and Pharmaceutical Technologies at the University of Bologna (UniBo) with a 1-year Master-thesis internship in molecular modelling at the Swiss Federal Institute of Technology Zurich, Switzerland. Supported by an Italian Ministerial Fellowship (33K euros), I obtained my Ph.D. from UniBo defending a thesis in computational medicinal chemistry. As a graduate student, I also received a Marco Polo scholarship (6K euros) to visit the Shoichet Lab at UCSF where I enabled docking from a PDB code alone for large-scale automated docking screens (https://blaster.docking.org/).

As a postdoc in computational biophysics of RNA at SISSA, I disclosed new paradigms in the folding of nucleic acids (JACS 2012 and PNAS 2019), and I have been awarded a Young SISSA Scientist grant (17K euros) for an independent antibacterial drug discovery project (two low-micromolar inhibitors found; patent filled) developed in collaboration with RNA microbiologists at the Université de Sherbrooke, Canada.

After a 2-year long career break to re-join my spouse in Quebec, Canada, I relaunched my academic career by joining the Orozco Lab at IRB Barcelona, where I am in charge of supervising all the drug-related projects of the group as well I have become the go-to person for free-energy calculations. I got granted a Marie Sklodowska-Curie Individual Fellowship (158K euros) and a Beatriu de Pinos fellowship (92K euros; declined) and I am leading a network of external collaborations in chemoinformatics, biochemistry and X-ray crystallography towards the development of the protected DynaFrag technology (Trade Secret process started) to overcome current bottlenecks in fragment-based lead discovery.

Overall, I have secured more than 200K euros of funding by European and National grants to develop my research. I delivered more than 10 seminars as invited speaker at International Conference or Institutions. I have 15 articles published, with more than 700 citations, in JCR

peer-reviewed journals (e.g.: JACS, Angewandte Chemie, PNAS and Nature Methods), including 2 book chapters; 7 publications as first author (6 first in first decile, D1), of which 6 also as corresponding author. My total number of publications in D1 is 10. I got 1 article (JACS 2010) highlighted in Nature News & Views (Nature 2010, 466, 42-3), 2 articles (JACS 2010 and PNAS 2019) have been recommended by Faculty of 1000 and I got 1 article (Angew. Chem. 2019) highlighted as paper of the month by the Sociedad de Biofísica Española, it also made the cover of Biofísica Magazine, Jan-April 2019).

At UniBo, I was teaching assistant for four semesters of the course Advanced Methodologies in Medicinal Chemistry (4 ECTS); I was also guest lecturer in Structure-based drug design at SISSA. I supervised undergraduates doing Master-thesis internship at both UniBo and IRB Barcelona, advised two graduate students, and mentored visiting students and postdocs. Moreover, I combine the intense focus on research with a consistent record of rewarding outreach activities (e.g. European Researchers Night, Pint of Science). I tutored about 15 secondary junior-high students in four years (Batx2Lab programme). In 2019, I conceived, organized, and managed SURf (Sulphur Uranium Rutherfordium) , a 2-day divulgative event that combined chemistry talks with surf classes for teenagers.

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Turno de acceso general

Nombre: MARIETTE , MYLENE
Referencia: RYC2019-028066-I
Área Temática: **Biociencias y biotecnología**
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Título:

Acoustic developmental programming and heat adaptation

Resumen de la Memoria:

Whilst my research career has covered a large range of topics, my current focus is on acoustic developmental programming and thermal regulation in birds. Recently, I discovered that zebra finch parents produce a peculiar vocalisation when incubating in the heat and that experimental exposure of embryos to this call adaptively altered their subsequent development in a temperature-dependent manner (Mariette & Buchanan 2016, Science). I then found that these heat-calls are also produced in other contexts than incubation, including outside the nest, and that they are a reliable signal of heat-stress, that is repeatable within individual and dependent on body-size (Mariette et al 2018, Sci. Rep). These findings are remarkable because they demonstrate that sound alone is capable of channelling development, and they reveal the only known strategy to date for transgenerational adaptation to heat in endotherms. My research therefore potentially revolutionise our understanding of developmental plasticity and species adaptive potential in changing environments, and hence has fundamental implications in evolutionary biology and conservation. Together with my students and collaborators, I am now investigating the i) epigenetic, neurological, physiological and behavioural mechanisms allowing a reprogramming of development by acoustic signals, ii) embryonic sensitivity to sounds and vibrations, iii) production of heat-calls across birds species and environments, iv) thermal adaptation to temperature extremes; and so in the broader context of v) animal ecology and evolution. Prior to this, I had demonstrated for the first time the importance of coordination in parental care in short-lived avian species and the role of acoustic communication between breeding partners in this process. Throughout my career, I have also been working on social networks, habitat selection, foraging strategies and mate choice, which I intend to pursue. Overall, I have worked on a large diversity of projects, with many collaborators, at multiple universities in Europe and Australia, in three different languages (I am fluent in English, French and Spanish). This rich experience has given me a very strong theoretical and empirical background in behaviour, ecology and evolution and has allowed me to develop a high-impact independent research line, of international renown. I use a diversity of state-of-the-art methodologies ranging from real-time qPCR, cellular respiration quantification and endocrine assays to experimental playbacks and individual remote sensing in the wild. A lot of my work has focused on the zebra finch, a classic model species in genetics, neurobiology, behaviour and physiology, that is extensively studied worldwide, but that I also study in the wild, as a keystone species of the Australian arid-zone to gain insight into species adaptation to unpredictable and extreme environments. By bringing a better understanding of species adaptation to their environment, my work has strong relevance for species conservation, including for predicting the impact of climate change. To make my impact meaningful to society, I also endeavour to bring my findings to the public through diverse media outputs.
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Resumen del Currículum Vitae:

I am a Behavioural Ecologist fascinated by the evolution of life history strategies, cooperation and acoustic communication, and their implications for species persistence under global change. After various projects in Europe, Canada, Mexico and New Zealand throughout my undergraduate, I conducted my PhD in Australia, followed by a research fellow position in France, before going back to Australia in 2013. Since my PhD, I have been employed full time on prestigious competitive research fellowships, and I have been extremely successful securing funding throughout my career, as a sole investigator (>672,000AU$= 415,000 euros) and in collaborative teams (>1.2M AU$= 750,000 euros). My research is innovative, high impact, comprehensive, and has consistently challenged the accepted view. I was very fortunate to do my PhD in the wild on the zebra finch, a classic model species in genetics, neurobiology and physiology. After revealing behavioural coordination as an adaptive strategy for parental care and the role of acoustic communication in this process, I recently discovered that parents program the development of their offspring for high temperatures, via prenatal acoustic communication. To foster excellence in research, my strategy is to publish high quality papers of significant impact in my field. I have published my findings in leading interdisciplinary journals such as Science (Mariette & Buchanan 2016), Nature Communication, Proc. Roy. Soc, and Sci Rep, as well as in some of the highest ranking journals in Ecology & Evolution (Nature Ecol Evol, Ecology, Am Nat, Horm Behav, J Evol Biol). My excellent H-index of 16, and impressive number of citations (788 citations on Web of Science; H index=18, i10-index=24, 1071 citations on Google Scholar) for my career stage (8.5 years post PhD) in Ecology & Evolution also attest of my high impact in the field. I have constructed an innovative and relevant research area as an independent researcher, whilst building an extensive and highly productive collaborative network across Europe, Australia and North America (71 co-authors on my publications). I have put a special emphasis on supervising and supporting students; I am currently the primary supervisor for 3 PhD students, and I have previously co-supervised the theses of 2 PhD, 4 masters, 1 honours, and 4 undergraduate students, who all successfully contributed to published work. Throughout my career, I have also actively engaged in building a supportive and stimulating research environment by organising discussion groups, conferences and websites, and providing support and feedback to colleagues, students and supervisors. I also play a considerable role as a reviewer and associate editor, by providing constructive comments on many papers for over 20 international journals. I have endeavoured to communicate my

results to the public through press releases, interviews and writing popular sciences pieces (including for children), as well as to highlight the conservation value of my work and the importance of Nature for Society.

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CONVOCATORIA 2019

Turno de acceso general

Nombre: ORTEGA PORTERO, ESTHER
Referencia: RYC2019-028540-I
Área Temática: **Biociencias y biotecnología**
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Título:

Structural studies of replication-transcription conflicts in eukaryotes

Resumen de la Memoria:

My research career has been dedicated to the structural and functional characterization of proteins and macromolecular complexes involved in essential cellular processes. During my scientific career - which comprises 13 years of work in 5 different research institutes - I applied complementary structural techniques including X-ray crystallography, small X-ray angle scattering (SAXS) and Electron Microscopy, that in conjunction with other biophysical techniques, have allowed me to address fundamental and important questions in different scientific areas: cellular adhesion, DNA transcription, epigenetics and DNA replication. My main research goal is to produce advances in the knowledge of these complex biological processes and address important questions from a molecular and structural point of view

During my PhD at the CIC-IBMCC (University of Salamanca) my main research interest was the structural characterization of a conserved domain of the plakin protein family and study its implications to the elastic properties of this protein family which are present in tissues that experience mechanical stress. In my postdoctoral training at EMBL Grenoble, I was granted with a competitive postdoctoral fellowship from the EMBL Interdisciplinary Postdoc Programme , to focus my research in the structural and functional characterization of a chromatin modifying enzyme (p300) which is involved in gene regulation by chromatin acetylation.

Results obtained during the trajectory of my scientific career lead to the publication of eight peer-review scientific articles, three of them during my postdoctoral research in high-impact scientific journals: one as first author in Nature, (2018), first co-author in Nature Chemical Biology (2016) and co-author in Nature Structural Molecular Biology, (2013). All my publications accumulate about 340 citations in total (a h index 7).

During the progress of my research projects, I have gained autonomy and independence to establish new research lines in my host research group, designing long-term experimental plans and goals, do troubleshooting in a productive manner and work efficiently. I have reinforced my maturity as researcher in project management: by the supervisión and mentoring of four undergraduate and master students and through the interaction with several Facilities and external collaborations.

The acquisition of a multidisciplinary training, solid skills in structural biology, management skills and broad experience in the chromatin field are solid premises to develop ambitious research projects that allow me to consolidate my independent research career.

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Resumen del Currículum Vitae:

My research career has been focused in the structural and functional characterization of proteins and macromolecular complexes involved in essential cellular processes. During my PhD thesis, I applied several structural techniques (X-ray crystallography, SAXS and EM by negative staining) in order to elucidate the structure and the function of a conserved domain within of the plakin protein family, that is essential for the maintenance of the integrity of tissues that experience mechanical stress. In my first postdoctoral stay at EMBL Grenoble, my scientific goals have been focused on the structural and functional characterization of p300, a DNA transcriptional co-activator that has histone-acetyltransferase activity and plays an important role in transcription regulation by chromatin acetylation, by combining structural techniques and biophysical approaches. During these 6 years, I have deciphered the molecular mechanisms of p300 activation by transcription factors activation by dimerization, we have deciphered and understood the molecular basis of the regulation of its enzymatic activity and we have shed light in the connection between cell metabolism processes and the gene regulation by p300. Currently, my scientific goals are focused on deciphering the molecular mechanisms of the redeposition of parental histones (that bearing epigenetic marks) during DNA replication in eukaryotes by the application of cryo-EM techniques at the Francis Crick Institute.

In order to achieve these goals, I have developed excellent skills in molecular biology, biochemical techniques and protein biophysical characterization in conjunction with structural techniques. I have acquired a solid knowledge and background in different scientific areas, but mainly focused in the chromatin and the gene regulation field.

The development of my scientific career has reached a high research productivity, which is reflected in the publication of 8 peer-review scientific articles, most of them in high-impact scientific journals. Among them, three articles in the first decile (D1) and 6 in total in the first quartile (Q1). I am first author of two articles published in JBC Journal, (2011 & 2016) during my PhD - and other 3 during my first

postdoct: one as first author in Nature (2018), first co-author in Nature Chemical Biology, 2016) and co-author in Nature Structural Molecular Biology, (2013). All these publications accumulate about 339 citations in total, a h index=7 and 28.3 average citations/per year.

The development of these projects have enforced my scientific maturity as researcher by addressing fundamental and relevant questions of biological processes, obtaining a multi-disciplinary background, developing project management skills, stablishing successful collaborations, mentoring students and obtaining competitive fellowships to work in prestigious European Research Institutes under the supervision of young leader scientists working in the molecular mechanisms of DNA transcription and replication in eukaryotes.

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AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2019

Turno de acceso general

Nombre: SANCHEZ GURMACHES, JUAN
Referencia: RYC2019-026773-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: juansangu@gmail.com

Título:

Molecular regulation of adipocyte development and functions

Resumen de la Memoria:

Maintaining tissue homeostasis usually requires 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 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.

My postdoctoral research delineated a whole new conceptual framework in adipose tissue development that now is used and accepted by the field. Some key model-changing accomplishments are that I (1) showed that both brown and white adipocyte precursors and mature adipocytes are heterogeneous in its developmental origin, among and within fat depots; (2) found evidence of lineage dynamics and plasticity including sex-linked, and diet-induced lineage distribution; (3) defined that subcutaneous and visceral white adipocytes originate from distinct lineages. Based on these results, I hypothesized that the lineage heterogeneity I observed could explain the functional diversity of adipose tissue and fat pattering in healthy and obese-lipodystrophic humans. As a proof of principle, I generated a variety of loss of function mouse models of several critical nodes of the PI3K/Akt pathway using Cre-Lox technology in specific subsets of adipocyte precursors using the developmental information I gathered. I found that differences in the activation of the PI3K/Akt signaling pathway between adipocyte lineages determine adipose tissue distribution, fat pad size, and adipocyte metabolism.

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.

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 last year. Since July 2017, I have raised over $2 millions in funding to cover the first years of my independent research. I have available laboratory and office space for up to 10 people. I successfully obtained competitive extramural funding and published peer reviewed papers as corresponding author. Additionally, I play a strong role in the academic and administrative activities of CCHMC.

In the next years, I will create a lab in Spain in which 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. 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:

I started studying adipose tissue during my graduate work at the lab of Dr Navarro at the Department of Physiology at the University of Barcelona. This work resulted in five first author publications and fourteen additional publications. I also obtained a competitive 4-year full scholarship to support me during this time.

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. This ongoing work resulted in multiple key publications for the field in journals like Cell Metabolism, Molecular Cell, Cell Reports, Nature Communications, Trends in Cell Biology, Stem Cell Reports. For my postdoctoral studies. I obtained two postdoctoral fellowships (Generalitat de Catalunya and American Heart Association).

Now, 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 last year. Since July 2017, I have raised over $2 millions in funding to cover the first years of my independent research. I have available laboratory and office space for up to 10 people. I successfully obtained competitive extramural funding and published peer reviewed papers as corresponding author. Additionally, I play a strong role in the academic and administrative activities of CCHMC.

Other scholarly activities include: Paper peer reviewer (i.e. 10 papers in 2019 in journals like Cell Stem Cell (3), Molecular Metabolism (2)), Grant reviewer (i.e. American Heart Association. 2019 Career Development Award; 2019 Marie Skłodowska-Curie Actions Individual Fellowships (European Research Council, European Commission)), Thesis committee member (i.e. four for 2019), Invited talks and reviews.

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Total of 36 publications (7 corresponding authors; 12 first author). Total citations (Scopus) 1212, h-index 22.

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Turno de acceso general

Nombre: PARDO VAZQUEZ, JOSE LUIS
Referencia: RYC2019-026380-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: jose.pardo.vazquez@gmail.com

Título:

Toma de decisiones: fenomenología conductual y bases neurales

Resumen de la Memoria:

La mayor parte de mi carrera ha estado dedicada a la comprensión de la fenomenología conductual y las bases neurales de la toma de decisiones. Para ello he utilizado diferentes modelos animales, métodos electrofisiológicos y aproximaciones estadísticas.
Durante el doctorado y primer postdoc, hice contribuciones originales y relevantes para la comprensión de los correlatos cerebrales de las decisiones perceptivas, analizando la actividad de neuronas individuales de la coreteza premotora ventral (PMv) de primates no-humanos. Encontramos que PMv, un área tradicionalmente relacionada con la preparación motora, también participa en las discriminaciones visuales y representa toda la información necesaria para evaluar las consecuencias de las decisiones previas. Esto nos llevó a sugerir que PMv podría estar implicada en los ajustes conductuales basados en la experiencia previa, una propuesta que he confirmado experimentalmente. También durante mi primer postdoc, lideré una línea de investigación dirigida a comprender cómo se representan, en el cerebro, las consecuencias de nuestras decisiones. Demostramos que es posible decodificar, utilizando un modelo simple de clasificación, el resultado de las decisiones perceptivas a partir de la actividad electroencefalográfica registrada en participantes humanos.
Mi segundo postdoc me dio la oportunidad de aprender nuevos métodos para registrar y analizar el comportamiento y la actividad cerebral. Diseñé y llevé a cabo una serie de experimentos conductuales de localización del sonido en ratas y humanos, con el objetivo de comprender el mecanismo responsable de una de las leyes psicofísicas más antiguas y mejor establecidas: la ley de Weber (LW). Combinando una descripción conductual detallada con la aplicación de modelos computacionales, propusimos una nueva regularidad psicofísica, que denominamos equivalencia entre tiempo e intensidad en la discriminación (TIED). La TIED aporta la primera explicación mecanicista de la LW y, al incluir el tiempo de reacción, va más allá de esta ley y permite hacer nuevas predicciones, algunas de las cuales hemos verificado empíricamente. Además, en una serie de experimentos electrofisiológicos en ratas anestesiadas, caracterizamos la respuesta de poblaciones neuronales a sonidos lateralizados, en función del estado de activación cortical. Encontramos que la estructura de las representaciones neuronales depende del nivel de activación: en estados inactivos la mayoría de las neuronas prefieren sonidos contralaterales de alta intensidad mientras que, en registros más activos, la respuesta neuronal fue prácticamente simétrica para estas dos dimensiones. Los cambios en la geometría de la actividad poblacional se traducen en cambios en la sensibilidad a la lateralización del sonido, que aumenta con la activación cortical hasta alcanzar valores muy similares a los que encontramos a nivel comportamental
Actualmente estoy utilizando técnicas no-invasiavas de estimulación cerebral para estudiar el papel de diferentes áreas corticales en procesos cognitivos superiores, como la memoria de trabajo y la toma de decisiones.
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Resumen del Currículum Vitae:

Finalicé la Licenciatura en Psicología (Univ. de Santiago de Compostela; USC) en 2002 e inicié los cursos de doctorado de Psicología Experimental en la misma universidad, obteniendo el Diploma de Estudios Avanzados (DEA) en 2004. Completé mi formación en estudio de las bases cerebrales del comportamiento con el Máster de Neurociencia y Biología de la Conducta de la Univ. Pablo de Olavide (Sevilla).
Mi carrera científica comenzó en 1999, estudiando la relación temporal óptima entre los estímulos en el condicionamiento clásico en ratas (Esmoris et al., 2003). En 2002 cambié de modelo animal para estudiar la capacidad de la memoria de trabajo (MT) en humanos y su relación con el rendimiento en tareas verbales y no-verbales (Pardo-Vazquez y Fernández-Rey, 2008, 2012). En 2004 me fue concedida una Beca de Formación de Personal Investigador, para explorar el papel de la corteza premotora ventral (PMv) en la MT y la toma de decisiones, analizando neuronas individuales en primates no-humanos. Nuestro trabajo contribuyó a redefinir la función de PMv, asociándola a procesos cognitivos superiores (Pardo-Vazquez et al., 2008, 2009; Acuña y Pardo-Vazquez, 2011). Obtuve el título de doctor en 2008, recibiendo el Premio Extraordinario de Doctorado de la Facultad de Medicina de la USC. Durante mi primer postdoc lideré una investigación en la que estudiamos las bases neurales de la monitorización del rendimiento en humanos, revelando la existencia de representaciones ensayo a ensayo de las consecuencias de nuestras decisiones en la actividad electroencefalográfica (Pardo-Vazquez et al., 2014; Padron et al., 2016). Para mi segundo postdoc me trasladé a Lisboa (Champalimaud Foundation), con un Long-Term Fellowship del Human Frontier Science Program. En esta etapa adquirí las habilidades y conocimientos necesarios para registrar y analizar la actividad de poblaciones de neuronas y para relacionar esta actividad con la estimulación sensorial (Kobak et al., 2019). Además, lideré junto con el Dr. Renart una serie de experimentos conductuales que nos permitieron dar la primera explicación matemática de la Ley de Weber y proponer una nueva regularidad psicofísica, la equivalencia tiempo-intensidad en las discriminaciones (TIED; Pardo-Vazquez et al., 2019). La TIED es una herramienta prometedora para aumentar nuestro conocimiento de la relación entre la experiencia subjetiva y el mundo físico. Durante los últimos años participé en una colaboración multidisciplinar para caracterizar el papel del termorreceptor TRPM8 en la regulación de la temperatura y la ingesta de comida (Reimundez et al., 2018). Además, dirigí una línea de investigación en la que confirmé el papel de PMv en las adaptaciones conductuales basadas en la experiencia previa (Pardo-Vazquez and Acuña, 2018).

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Turno de acceso general

He dado clases de diferentes materias en la licenciatura de Medicina y en los grados de Óptica y Farmacia en la USC, y he supervisado Trabajos de Fin de Grado en la USC y la Univ. de Vigo. Además, publiqué varios capítulos de un manual de psicología experimental (Fernandez-Rey et al., 2005) y participé también como editor en la segunda edición de este manual (Fernandez-Rey et al., 2010). También di clases en el International Neuroscience Doctoral Programme en la Champalimaud Foundation. Finalmente, he supervisado una Tesis de Doctorado en la USC y una Trabajo de Fin de Máster en la Univ. da Coruña.

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AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2019

Turno de acceso general

Nombre: ORTEGA CANO, JUAN ALBERTO
Referencia: RYC2019-026980-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: jalbertortega@gmail.com

Título:

Development of Human in vitro Models for the Study of Neurological Disorders

Resumen de la Memoria:

During my pre- and post-doctoral research career I have addressed 3 major topics:

1. Study the role of different morphogenes in the cerebral cortex development. I have studied the function of multiple cytokines in the rodent and human cerebral cortex development, and how perinatal insults trigger alterations in their expression levels. Abnormal levels of these cytokines in critical periods of the cortical development, lead to important alterations in the generation and maturation of different neural cell types, what causes severe morphological and functional cortical anomalies associated to different neurodevelopmental disorders, such as schizophrenia, autism or epilepsy.

2. Study the development and degeneration of the human central nervous system (CNS) utilizing novel human in vitro models. I have developed outstanding in vitro human models based on human neural progenitors isolated from aborted fetuses, human embryonic and induced pluripotent stem cells (iPSC), that can be reprogrammed into different neural cell types affected in distinct neurological diseases. These approaches granted unrestricted access to the CNS of patients and have allowed for the study of development and disease in the human context, under each patient unique genetic constellation.

3. Design novel biofunctionalized materials to:
a. Develop more translational in vitro systems. I have designed biomaterials that better mimic the physicochemical cues present in the extracellular matrix (ECM) of the CNS, and reproduced necessary physiological microenvironments for a proper neuronal development and maturation.
b. Improve functional regeneration after traumatic injury in the CNS. I have implemented biofunctionalized materials that can simultaneously deliver neural stem cells and neuroprotective signals to improve neural replacement, and functional recovery after a spinal cord injury.

In the future I aim to address two important topics associated with neurodevelopmental as well as traumatic and neurodegenerative disorders:
1. Studying mechanisms that lead to high cellular complexity in the human fetal telencephalon. Specifically I will focus on better understand the role of morphogenes such as WNTs in the human CNS development. Although little is known about the role of WNTs in the subpallium, the deletion of Wnt signaling in mice severely impairs the expansion and differentiation of ventral progenitors into interneurons. This can importantly affect the human forebrain development and function, and can contribute to pathogenesis in several psychiatric disorders.
2. Improving stem cell derived neuron systems for the study and treatment of neurological disease and injury. Stem cell-based models are still fraught with important technical limitations primarily related to neuronal maturation and heterogeneity. I propose an ambitious study that aims to develop new and more efficient stem cell-based in vitro and in vivo platforms for the study and therapy of human neuronal models of injury and disease. I plan to tackle this complicated topic from different angles in collaboration with a multidisciplinary team of experts in bioengineering, proteomics, transcriptomics and electrophysiology.

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Resumen del Currículum Vitae:

I deciphered mechanisms that governs the human central nervous system development.
I have carried out multiple projects that have helped to better understand multiple developmental mechanisms of different neural cell populations along the CNS:
(1) Ziller M.J.*, Ortega J.A*, et al. Dissecting the Functional Consequences of de Novo DNA Methylation Dynamics in Human Motor Neuron Differentiation and Physiology. Cell Stem Cell. 2018. (*Equally contributing authors).
(2) Ortega J.A., et al. Oxygen levels regulate the development of human cortical radial glia cells. Cereb Cortex. 2016.
(3) Ortega J.A., Alcántara S. BDNF/MAPK/ERK-Induced BMP7 expression in the developing cerebral cortex induces premature radial glia differentiation and impairs neuronal migration. Cereb Cortex. 2010.

I studied the unique human brain cellular complexity to better understand human-specific neurological disorders.

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Turno de acceso general

As a postdoctoral researcher in Zecevic lab (University of Connecticut, US), I published 2 reviews and contributed with 2 book chapters that emphasize the importance of human in vitro systems to understand the human cortical development:
(4) Ortega J.A., et al. The subventricular zone: a key player in human neocortical development. The Neuroscientist, 2017. Review.
(5) Ayoub A.E., Dominguez M.H, Benoit J., Ortega J.A., et al. Coordination of Neuron Production in Mouse and Human Cerebral Cortex by the Homolog of Drosophila Mastermind Protein. Brain, Behavior and Evolution. 2019. Review.
(6) Radonjic N., Ortega J.A., et al. 2016. At The Top of the Interneuronal Pyramid Calretinin Expressing Cortical Interneurons. Frontiers Research Topic E-book. ISBN 978-2-88919-708-8. Frontiers Media SA
(7) Ortega, J.A., et al. 2014.The ventricular-subventricular zone: a source of oligodendrocytes in the adult brain. Frontiers Research Topic E-book. ISBN: 978-2-88919-268-7. Frontiers Media SA

Development of new and more efficient human in vitro models to study neurological diseases.
During my predoctoral training in Soledad Alcantara lab (Universidad de Barcelona, Spain) I was involved in developing new in vitro technologies to study neurodevelopmental mechanisms:
(8) Mattotti, M., Alvarez, Z., Ortega, J.A., et al. Inducing functional radial glia-like progenitors from cortical astrocyte cultures using micropatterned PMMA. Biomaterials. 2011.

Later, during my postdoctoral training in Kiskinis lab (Northwestern University, US), I utilized stem cell technologies that allow to decipher pathophysiological mechanisms and to design novel therapeutic strategies for neurological diseases such as Amyotrophic Lateral Sclerosis:
(9) Ortega J.A., et al Nucleocytoplasmic Proteomic Analysis Uncovers eRF1 and Nonsense Mediated Decay as Modifiers of ALS C9orf72 Toxicity. Accepted in January 2020, Neuron.

During this period in Kiskinis lab and in collaboration with Samuel Stupp lab (Northwestern University, US), I have also designed novel dynamic supramolecular matrices that enhance functional maturation of human iPSCs-derived neurons and regeneration after spinal cord injury:
(10) Utility U.S. Patent application: Dynamics within supramolecular matrices enhance functional maturation of human iPSCs-derived neurons and regeneration. Z. Alvarez Pinto, J.A. Ortega, K. Sato, E. Kiskinis, S.I. Stupp. (Serial Number 62/796,425. 2019. Northwestern University).

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AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2019

Turno de acceso general

Nombre: SUNYER BORRELL, RAIMON
Referencia: RYC2019-026721-I
Área Temática: **Biociencias y biotecnología**
Correo Electrónico: raimonsun@gmail.com

Título:

Mechanobiology of directed cell migration driven by physical signals

Resumen de la Memoria:

My research line focusses on interrogating how individual cells and tissues sense and respond to mechanical cues and how this relates to cell and tissue migration. In recent years we put forth a new experimental and theoretical framework to better understand the molecular mechanisms by which single cells and tissues are able to migrate following Extracellular Matrix (ECM) cues such as stiffness or ligand density.

In a first postdoc at National Institutes of Health (NIH, Bethesda, USA), I developed the experimental tools to fabricate biocompatible matrices with a unique control of spatially varying mechanical properties (PLOS ONE, 2012, IF: 3.5, 91 CITATIONS*). In a second postdoc at X. Trepat laboratory at IBEC (Barcelona), I applied those tools to study how variations of stiffness affect cell functions. We discovered a new cell migration mechanism we called Collective Durotaxis by which cell clusters follow gradients of stiffness more efficiently than single cells (SCIENCE, 2016, IF: 37.2, 131 CITATIONS*; LAB ON CHIP, 2016, IF: 5.6, 28 CITATIONS*; NATURE MATERIALS, 2013, IF: 36.4, 129 CITATIONS*). Since that discovery collective durotaxis is emerging as an important migratory mechanism with strong implications in morphogenesis, tumor metastasis, fibrosis and wound healing.

The research I conducted has resulted in 20 publications and accumulated more than 1010 citations* with and h-index of 15* (5 first author and 2 corresponding author publications). We also obtained funding to transfer technology I developed to market (ERC-PoC, 148,963). My goal for the next few years is to establish an independent research line. As a proof of my capacity to lead scientific projects, I recently co-supervised a study that unveils new mechanisms in the formation and maintenance of tissue boundaries (NATURE MATERIALS, 2017 IF: 39.373, 21 CITATIONS*). Besides this study, I am currently the principal investigator of the DYNAGEL project (Jovenes Investigadores MICIU 2018, 189,970), coordinating the implementation of some parts of the MICIU Generación de Conocimiento mGradient (375,100), which I helped to conceive and co-wrote with Prof. X.Trepat and coordinating the CADHForce project (CIBER-BBN), which I conceived and wrote. Finally, I am co-directing the PhD thesis of two students.

Becoming a Ramón y Cajal fellow will allow me to apply to new funding programs and continue developing hybrid cross-disciplinary approaches to shed light on significant biological processes that potentially impact the lives of everyone.

*Source: SCOPUS

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Resumen del Currículum Vitae:

1. Contributions:
20 Scientific publications | h-index of 15 | Total of 1010 citations (Scopus)
First author publications: 5 one in Science (2016) and another one in Lab on a Chip (2015)
Corresponding author publications: 5 one in Nature Materials (2017)
9 predoctoral publications and 11 postdoctoral publications
Average citations/year during the postdoctoral period (2009-2019): 88.5 (Scopus)
Transfer of technology I developed to market (ERC-PoC, MICROGRADIENTPAGE, 148,963)

2) Participation in International activities:
Postdoc at the National Institutes of Health (NIH, Bethesda MD, USA) (3 years, 2010-2013)
Predoctoral International: JJ Fredberg lab (3 months, Harvard University, Boston) and Louis Néel laboratoire (3 months, CNRS, Grenoble, France)
International stays during my Postdoc: Arancha del Campo Lab (2 weeks, Max Plank Institute, Mainz)
Obtained funding for internships and postdoctoral research (BE travel award (Generalitat de Catalunya), Beatriu de Pinós Fellowship, NIH Postdoctoral Award)
Participation in several ERC projects: ERC-CoG TensionControl (1.98M), ERC-PoC MICROGRADIENTPAGE (0.15M), ERC-StG

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Turno de acceso general

GENESFORCEMOTION (1.75M)
Participation in several NIH intramural projects for example 1ZIAHD008765-09 ($0.44M) and 1ZIANS003122-01 ($1.22M)
Participation in 24 international conferences (talks and posters). For example: American Association of Cell Biology (ASCB) Meeting (2014, 2015, 2016) and 6th International Symposium Interface Biology of Implants (2019)
International collaborations: V. Weaver (Berkeley University), D. Leckband (Illinois University), J. Atencia (Maryland University, University of Maryland), Y. Zhang (Boston University) and JJ. Fredberg (Harvard University)
Recognized researcher being invited to give talks at Conferences and Research Institutions 4 times

3) Other curriculum merits:
Outreach activities: Writing popular Science articles in Investigación y Ciencia and the Magazine of the Spanish Society of Biophysics
Reviewer for the journals: Nature Communications, Langmuir, Review of Scientific Instruments
INNoVATE tech-transfer program: 1-year training on transferring technology developed in research to market (Carey Business School, Johns Hopkins University, 2012)
Teaching to undergraduate students in Medical School (University of Barcelona, 2003-2005, 20018-2019, 2019-2020)
Accreditation of Research and Lecturer (Acreditación profesor agregado y Lector) AQU (Agència per la Qualitat Universitària a Catalunya)
Reviewer for the Agencia Estatal de Investigación (AEI)

4) Leadership and research independence:
Principal Investigator of DYNAGEL Project (Retos Investigación 2018, Proyectos tipo JIN, MICIU, 189,970 , 2019-2022)
Coordinator of the project: Cell mechanosensing through cadherin complexes (CIBER-BBN, 2018-2020)
I helped to conceive, co-wrote and implement the funded ERC-PoC MICROGRADIENTPAGE (148,963)
Co-director of the study Long-lived force patterns and deformation waves at repulsive epithelial boundaries published in Nature Materials (2017) (co-corresponding author)
Direction of a master thesis (Carlos Ureña, Maximum qualification obtained)
Currently co-directing the thesis of 2 PhD students