DCEXS-UPF (Barcelona) International PhD call 2019

The Department of Experimental and Health Sciences of the Pompeu Fabra University (DCEXS-UPF) opens a call for the academic year 2019-20, for accomplished and driven students with an excellent academic record to carry out a PhD in Biomedicine.

The research and teaching excellence of the DCEXS-UPF is widely acknowledged. The DCEXS-UPF was one of six research units in Spain to be awarded the "María de Maeztu" distinction and grant in 2014. Furthermore, the DCEXS-UPF offers a unique and international research environment and cutting-edge scientific facilities, thanks to its privileged location in the Barcelona Biomedical Research Park (PRBB).

Seventeen groups led by recognized scientists performing research in biomedicine (see below for more information) are looking for candidates to sponsor their applications to competitive calls such as FI and FPU. Candidates can choose one or two groups they would like to join (please see the Selection process section).

Training and advantages

The UPF's PhD programme in Biomedicine follows the latest regulations for doctoral studies in Spain, the so-called Royal Decree (RD) 99/2011, which were introduced to comply with the guidelines and recommendations of the European Higher Education Area (EHEA) on doctoral studies. The contents of this doctoral programme have been accredited by the Catalan University Quality Assurance Agency (AQU Catalonia) with the highest qualification of progressing towards excellence.

All of the PhD programme activities are carried out in English, and every year attracts a large number of international students. These activities aim at preparing students to become independent researchers pursuing a scientific career. Successful candidates will have access to a wide range of academic activities, as well as ad hoc training in scientific skills, and access to the PRBB Intervals programme, an interdisciplinary education programme for professionals working in the PRBB.

Requirements

Candidates must have obtained a University Degree and a Master's Degree in natural or medical sciences (Biology, Medicine, Biochemistry, Biomedicine, Chemistry, Physics, etc), or in other quantitative sciences (Mathematics, Computer Science, etc) within the European Higher Education System (min. 300 ECTS), or an equivalent university degree, of at least 300 ECTS, that would allow the candidate to start a PhD thesis in their home country by September 2019; candidates who expect to be awarded such degree by September 2019 are eligible to apply.

Candidates are advised to check that they fulfil the requirements for admission to the UPF PhD in Biomedicine as those who do not fulfil these requirements will be considered ineligible.

**Note:* It is not necessary to start the admission process for the PhD programme at this stage.

Candidates will be required to present their academic record and those who obtained their degree and/ or Master's in a country other than Spain will have to include the conversion of their grades to the Spanish 0-10 scale.

Candidates must have excellent academic qualifications and good command of English. Research experience and authorship of scientific publications will be a plus.

The DCEXS promotes diversity in an inclusive environment that welcomes applicants regardless of age, disability, gender, nationality, race, or religion.

Application

To apply, please register and send the required documents through this online form.

Selection process and calendar

The call will be open until June 16th 2019 at 12h.

The pre-selection of the candidates will be based on academic qualifications and research experience. Candidates will receive feedback on pre-selection in late June. Pre-selected candidates will be interviewed in the DCEXS facilities or via Skype during July and will receive feedback before August.

Selected candidates are expected to start from March 2020.

Contact:

Dr. Regina López

phdfellowships.dcexs@upf.edu

Universitat Pompeu Fabra Barcelona
Department of Experimental and Health Sciences

EXCELENCIA MARÍA DE MAEZTU
GOBIERNO DE ESPAÑA MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD
MDM-2014-0370

Principal Investigator: Berta Alsina

Morphogenesis and Cell Signaling in Sensory Systems

http://www.upf.edu/web/alsina_lab

Research project title

Deciphering the roles of novel genes in neurosensory development

Research project summary

Cranial sensory neural stem cells through the transcriptional activation of a set of genes initiate their differentiation into sensory neurons and exit from the sensory epithelium to form the sensory ganglia in a process of EMT. Our group has a long-lasting experience in the study of the molecular and cellular mechanisms of PNS neurogenesis and morphogenesis of epithelial placodes. We have recently identified new genes specifically expressed in the head PNS by RNA-seq and we are currently investigating the migratory behaviours of neuronal precursors at single cell level. The aim of this project is to decipher the role of the identified genes on EMT, differentiation, migration or neuronal identity by the generation of specific zebrafish CRISPR mutants and transgenic reporter lines. The student will learn the main principles of tissue and organ formation, will manipulate zebrafish embryos, develop new tools of genetic engineering and gene editing by crispr and learn supraresolution imaging technologies. The student will grow scientifically in a vibrant environment at the PRBB, in close relationship with other groups investigating how organs are formed in vivo and in vitro (CRG, EMBL). The student will integrate also in a lab with teaching duties and will have the opportunity to mentor younger undergraduate or master students during the PhD.

Preferred background of candidates

We are seeking for highly motivated students with a Bachelor Degree in the field of Life Sciences and a Master Degree in Biomedical Sciences or Neuroscience. Candidates should have score over 8,5. Previous experience in Developmental Biology, Zebrafish or Neurobiology will be considered. Good communication skills and fluent Written and Spoken English is also required.

Selected references

- Taberner L, Bañón A, Alsina B. (2018). Anatomical map of the cranial vasculature and sensory ganglia. J Anat.
- Hoijman E, Fargas L, Blader P and Alsina B (2017). Pioneer neurog1 expressing cells ingress into the otic epithelium and instruct neuronal specification. eLife.
- Alsina B and Whitfield TT (2016). Sculpting the labyrinth: morphogenesis of the developing inner ear. Seminars in Cell and Developmental Biology.
- Hoijman E, Rubbini D, Colombelli J and Alsina B (2015). Mitotic cell rounding and epithelial thinning regulate lumen growth and shape. Nat Commun
- Rubbini D, Robert-Moreno À, Hoijman E, Alsina B. (2015). Retinoic acid mediates Hair Cell regeneration by prepressing p27kip and sox2 in supporting cells. J Neurosc.
- Iturbide A, Pascual-Reguant L, Fargas L, Cebrià JP, Alsina B, García de Herreros A, Peiró S (2015). LOXL2 Oxidizes Methylated TAF10 and Controls TFIID-Dependent Genes during Neural Progenitor Differentiation. Mol Cell

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EXCELENCIA MARÍA DE MAEZTU
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MDM-2014-0370

Principal Investigator: David Andreu

Proteomics and Protein Chemistry

http://www.upf.edu/uprot/

Research project

Developing broad spectrum antivirals against Zika and other Aedes-born viral diseases.

Research project summary

Viruses infecting the brain (Zika, Dengue, Chikungunya, measles, etc.) and other CNS loci are a worldwide threat, causing thousands of severely impaired neurological victims every year. A recent case in point is the Zika virus (ZKV) outbreak in South America. Like Dengue or Chikungunya, ZKV is spread by Aedes mosquitos and causes serious CNS disorders, but its consequences outdo other viruses when it infects pregnant women, where it translocates the blood placental barrier and the developing fetal blood-brain barrier, causing microcephaly in the newborn baby. Co-infections with different Aedes-borne viral species are not unlikely, a reality largely overlooked in antiviral drug development programs. Drugs capable of targeting several viral species are sorely needed, particularly those with the ability to traverse blood-brain and blood-placenta barriers and thus hit ZKV.

The Ph.D. candidate will join an interdisciplinary consortium focused on developing such broad-spectrum, one size-fits-all antiviral drugs, an approach recently supported in La Caixa Health (HR17_00409) and EU (H2020-FETOPEN nº 828774) calls. The research project will involve design, synthesis, structural analysis and biophysical characterization of a novel class of such antiviral agents, to be tested in animal models of the above-described diseases.

Preferred background of candidates

Chemistry (medicinal, organic, peptide/protein); biotechnology & pharmacy candidates also considered.

Selected references

- Neves V, Aires-da-Silva F, Morais M, et al. (2017) ACS Chem. Biol., 12, 1257–1268.
- Freire JM, Veiga AS, Rego de Figueiredo I, et al. (2014) FEBS J., 281, 191-215.

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MDM-2014-0370

Principal Investigator: José Ayté

Oxidative Stress and Cell Cycle

https://www.upf.edu/web/osccg/

Research project

Controlling the cell cycle: elaborating an integrative map of the genetic regulators of DNA synthesis and tumor progression.

Research project summary

At the Oxidative Stress and Cell Cycle group (Universitat Pompeu Fabra) we are ultimately interested in deciphering the mechanisms that control cell cycle progression (see https://www.upf.edu/web/osccg). Inactivation of the Retinoblastoma protein (pRB) leads to unregulated cell cycle progression promoting uncontrolled cell growth, genomic instability and aneuploidy, hallmarks of tumor progression. pRB tumor suppressor activity is achieved through binding and regulating the E2F family of transcription factors. It is well known that a tumor process is very complex, accumulating numerous secondary mutations that aim to eliminate the brakes to the proliferative process. Even though many individual regulators of the pRB-E2F complex are known, an integrative view of all the regulatory events controlling the G1/S transition is required to anticipate putative interventions able to block proliferative processes.

The PhD candidate will characterize the regulation of the yeast MBF complex (functional homolog of protozoa RB/E2F). Like its mammalian counterpart, the regulated activity of this complex is essential for the G1/S transition: cells with hypoactive MBF complex are unable to complete S phase while cells with hyperactive MBF show genomic instability. The candidate will perform a triple whole-genomic screen searching for global regulators of MBF. We have developed a reporter strain in the laboratory that measures MBF activity in vivo as a YFP/RFP output, either on FACS or on an automated fluorescence microscope. These screenings will allow the creation of a complete map with all the MBF regulators and, by extrapolation, will establish the nodes that regulate globally the pRB pathway.

As a plus, the PhD candidate will have the opportunity to participate in teaching of Biology and Medicine studies.

Preferred background of candidates

Biochemistry, Microbiology, Molecular and Cell Biology and Genetics.

Selected references

Full list can be downloaded from https://www.upf.edu/web/osccg/relevant-articles

- Knezevic et al. (2018) FEBS Journal 285:3870.
- Boronat et al. (2017) PLoS Genetics 13:e1006858.
- Alves-Rodrigues et al. (2016) Cell Reports 14:885.
- Encinar del Dedo et al. (2015) PLoS Genetics 11:e1005106.
- García-Santamarina et al. (2014) Nature Protocols 9:1131.
- Calvo, I.A. et al. (2013) Cell Reports 5:1413.
- Calvo, I.A. et al. (2012) Nucleic Acids Research 40:4816.
- Gómez-Escoda et al. (2011) EMBO Reports 12:84.
- Zuin, A. et al. (2010) EMBO Journal 29:981.
- Moldón et al. (2008) Nature 455:997.

Principal Investigator: Robert Castelo

Functional Genomics

http://functionalgenomics.upf.edu

Research project title

Interaction and expression variance heterogeneity in genetics of disease

Research project summary

Finding the genetic component of molecular phenotypes, such as gene expression, has been traditionally restricted to the identification of genetic variants affecting the mean level of gene expression. These associations between genetic variants and gene expression profiles are commonly known as eQTL associations and our group has developed methodology and software to identify such eQTLs (Tur et al., 2014) adjusting for indirect effects. However, it has been recently acknowledged that genetic variants may also affect the variability of gene expression and that such associations, known as evQTLs, are important to understand the genetic control of transcriptional regulation.

More interestingly, evQTLs are often the result of statistical interactions between genetic loci, and therefore, their identification can be used as a fast strategy to detect interacting effects, which otherwise require the exploration of a vast combinatorial search space. Interacting genetic effects have been reported to be one of the possible mechanisms behind the phenomenon of genetic disorders of reduced penetrance, which our group has been recently investigating (Puigdevall et a., 2019). In this doctoral research project we plan to investigate the association between evQTLs, disease-causing mutations and disease-penetrance genetic modifiers, using recent methodological advances from our group (Costa and Castelo, 2016; Roverato and Castelo, 2017; Puigdevall and Castelo, 2018) and developing new ones.

Preferred background of candidates

Solid background in quantitative sciences including, but not limited to, mathematics, statistics, physics or computer science, with a strong motivation for tackling questions in biology and human disease.

Selected references

- Tur I., Roverato A. and Castelo R. Mapping eQTL networks with mixed graphical Markov models. Genetics, 198:1377-1383, 2014.
- Costa D. and Castelo. R. Umbilical cord gene expression reveals the molecular architecture of the fetal inflammatory response in extremely preterm newborns. Pediatric Research, 79:473-481, 2016.
- Roverato A. and Castelo R. The networked partial correlation and its application to the analysis of genetic interactions. Journal of the Royal Statistical Society, Series C -Applications, 6:647-665, 2017.
- Puigdevall P. and Castelo. R. GenomicScores: seamless access to genomewide position-specific scores from R and Bioconductor. Bioinformatics, 34:3206-3210, 2018.
- Puigdevall P., Piccari L., Blanco I., Barberà J.A., Geiger D., Badenas C., Milà M., Castelo R. and Madrigal I. Genetic linkage analysis of a large family identifies FIGN as a candidate modulator of reduced penetrance in heritable pulmonary arterial hypertension. Journal of Medical Genetics, 2019, in press.

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MDM-2014-0370

Principal Investigator: David Comas

Human Genome Diversity

http://www.biologiaevolutiva.org/dcomas

Research project title

Human population genomics: implications for health and disease

Research project summary

The knowledge of the evolutionary history of our species has been approached using data from diverse disciplines including molecular genetics. Our genome provides us information, not only about the molecular processes such as recombination and mutation but also provides us information about the processes that have shaped its composition, such as migrations, admixture, expansions and adaptations. The improvement of genotyping and sequencing techniques and the advancement of computational capacities have allowed us to manage large population datasets to infer human population evolutionary history.

In this context, our group is interested in the population history of humans from its origins as species to the local demography and adaptation of specific human groups. Within this landscape, we have been dealing with high throughput analysis of genome-wide data and complete genome sequences to tackle demographic and adaptation events.

The present PhD project will be focused on the analysis of large SNP data arrays and complete genome sequences to unravel the population evolutionary history (including demography and adaptation) of several human groups, from African populations to specific isolated groups such as Roma (aka Gypsies).

Preferred background of candidates

The candidates should have a background in biology/genetics and experience of techniques used in bioinformatics and genomics, with expertise in handling large datasets, scripting and use of High-Performance Computing Linux cluster.

Selected references

- Henn BM, Botigué LR, Gravel S, Wang W, Brisbin A, Byrnes JK, Fadhlaoui-Zid K, Zalloua PA, Moreno-Estrada A, Bertranpetit J, Bustamante CD, Comas D (2012) Genomic Ancestry of North Africans Supports Back-to-Africa Migrations. *PLoS Genetics* 8(1)e1002397
- Mendizabal I, Lao O, Marigorta UM, Wollstein A, Gusmão L, Ferak V, Ioana M, Jordanova A, Kaneva R, Kouvatsi A, Kučinskas V, Makukh H, Metspalu A, Netea MG, de Pablo R, Pamjav H, Radojkovic D, Rolleston SJ, Sertic J, Macek M Jr, Comas D*, Kayser M* (2012) Reconstructing population history of European Romani from genome-wide data. *Current Biology* 22:2342-2349
- Arauna LR, Mendoza-Revilla J, Mas-Sandoval A, Izaabel H, Bekada A, Benhamamouch S, Fadhlaoui-Zid K, Zalloua P, Hellenthal G, Comas D (2017) Recent historical migrations have shaped the gene pool of Arabs and Berbers in North Africa. *Molecular Biology and Evolution* 34:318-329
- Lorente-Galdos B, Lao O, Serra-Vidal G, Santpere G, Kuderna LFK, Arauna LR, Fadhlaoui-Zid K, Pimenoff VN, Soodyall H, Zalloua P, Marques-Bonet T, Comas D (2019) Whole-genome sequence analysis of a Pan African set of samples reveals archaic gene flow from an extinct basal population of modern humans into sub-Saharan populations. Genome Biology (in press)

Principal Investigator: Juana Díez

Virology Unit

https://www.upf.edu/web/virology-unit

Research project

Systems biology approaches to uncover key determinants of emerging virus infections and novel antiviral therapies

Research project summary

Our group is interested in different aspects of the biology of positive-strand RNA viruses. This large viral group includes important human pathogens such as the mosquito-transmitted Dengue virus, West Nile virus or Chikungunya virus that have dramatically expanded to new geographical areas, including Europe. They critically rely on their capacity to multiply in both humans and mosquitoes. How they efficiently adapt to the requirements of such divergent host environments, and how they modify the cellular transcription and translation landscape to favour their expansion, are unknown. Elucidating these fundamental questions is essential to understand how emerging viruses cycle between different hosts, a crucial aspect of their evolution and expansion, and will provide targets for therapeutic intervention. We will apply a highly innovative systems biology approach to study translational control of virus-host interactions in a broad in-vitro and in-vivo setting. This project is funded with an InfectERA European grant and involves collaboration with multiple laboratories in Europe.

Preferred background of candidates

The candidate should be fluent in English, highly motivated and passionate about science. Previous experience in Cell biology and/or Molecular Biology and/or Virology will be highly appreciated.

Selected references

- Xrn1 promotes transcription, translation and decay of mRNAs coding membrane proteins. Nature Communications. In press

- A novel translational control mechanism involving RNA structures within coding sequences. Genome Research 27(1): 95-106. 2017.

- Soraphen A: A broad-spectrum antiviral natural product with potent anti-hepatitis C virus activity. Journal of Hepatology. Oct;63(4):813-21. 2015

Principal Investigator: José Manuel Fernández-Fernández

Laboratory Of Molecular Physiology

https://www.upf.edu/web/lmp/entry/-/-/15483/adscripcion/jose-manuel-fernandez

Research project

Hypoglycosylation of $Ca_V2.1$ and Piezo channels: new pathological mechanisms and therapeutic targets for neurological disorders in phosphomannomutase 2 deficiency

Research project summary

Phosphomannomutase Deficiency (PMM2-CDG, OMIM 601785), caused by deficiency in PMM2 enzymatic activity due to genetic mutations, is the most frequent congenital disorder of N-linked glycosylation (CDG). PMM2-CDG symptoms include severe neurological alterations. Progressive atrophy of the cerebellum is usually found in all PMM2-CDG patients, leading to the ataxia cerebellar syndrome, movement coordination disorders, abnormal eye movements, dysarthria and intellectual disability. Also, the stroke-like episode (SLE) is one of the unpredictable and serious neurological complications occurring in PMM2-CDG. Mechanisms underlying both SLE and cerebellar syndrome in PMM2-CDG are unknown and there are no guidelines for their prevention, detection and treatment. SLEs also complicate paroxysmal neurological diseases such as familial hemiplegic migraine (FHM), mostly caused by mutations in *CACNA1A* (encoding the neuronal pore-forming $Ca_V2.1$ channel α_{1A} subunit). We have recently reported an interesting similarity between clinical, neuroimaging and neurophysiological traits of PMM2-CDG patients and patients with CACNA1A mutations, including SLEs, ataxia, eye movement alterations and cerebellar atrophy. Accordingly, we found increased $Ca_V2.1$ activity (as occurs for FHM/ataxia CACNA1A mutations) due to deficient N-glycosylation, which may contribute to the development of both SLE and cerebellar syndrome in PMM2-CDG patients. Besides, we identified mild cranial trauma as a potential SLE trigger in PMM2-CDG patients. Mechanosensitive ion channels, including the Piezo family channel, have been suggested to underlie the transduction of different mechanical forces into a variety of neurological responses in the brain: i.e. neuronal excitability and neurotransmission; and YAP-related brain cell specification, neuropathic pain, and altered cerebellar development. Furthermore, our preliminary data show alteration of Piezo1 function due to N-hypoglycosylation.

Our working hypothesis is that hypoglycosylation of both $Ca_V2.1$ and Piezo channels contribute to neurological symptoms in PMM2-CDG patients, by favoring excitatory synaptic transmission in response to mechanical stimulation (as occurs after head trauma). The overall objective of this proposal will be to study how hypoglycosylation affect the function of neuronal $Ca_V2.1$ and Piezo channels, and its relevance in SLEs and cerebral syndrome in PMM2-CDG, by using heterologous expression systems, cultured neurons (obtained from both wild-type and PMM2-CDG knock-in mice), and iPSC-derived neurons from fibroblasts of patients with PMM2-CDG and healthy volunteers.

Preferred background of candidates

Bachelor degree in Biological or Biomedical Sciences, or in Physics. Background in cell cultures, western blot analysis, molecular biology and electrophysiological techniques will be advantageous.

Selected references

- Int J Mol Sci. 2018 Feb 22;19(2). pii: E619. doi: 10.3390/ijms19020619.
- Proc Natl Acad Sci U S A. 2018 Feb 20;115(8):1925-1930. doi: 10.1073/pnas.1718177115.

Principal Investigator: Oriol Gallego

Live-cell structural biology

www.gallegolab.org

Research Project:

Advanced light microscopy to time-resolve the mechanism of exocytosis

Research project summary:

The project aims to decipher the mechanism of exocytosis, a long-standing question in cell biology that is crucial to understand how cells control their surface composition and cell growth. Exocytosis is an essential cellular process conserved in all eukaryotes that is directly involved in cell growth, establishment of cell polarity, morphogenesis and neurobiology. Not surprisingly, a long list of diseases arises when the exocytic machinery is perturbed, such as cancer, metastasis, Polycystic kidney disease and the Joubert-Syndrome.

Understanding the molecular mechanisms that drive life (and those that lead to death) requires structural characterization of the protein machinery sustaining the biology of the cell. Ideally, experimental evidences should be obtained at atomic resolution, in real-time and in a totally physiological context. However, historically, structural biology has been largely centered around in vitro approaches, which provide high-resolution measurements but with poor physiological relevance.

Our group, in the frontier between cell biology and structural biology, develops new methods of fluorescence microscopy that allow the study of macromolecular complexes directly in living cells beyond the limits of current approaches. We have developed a new live-cell structural biology method based on cell engineering and advanced fluorescence microscopy. Our approach allows visualizing the architecture of complex molecular assemblies directly in living cells and thus we are capable of solving questions in cell biology that were not accessible by other techniques (Picco et al, 2017, Cell).

This project will benefit from new live-cell imaging assisted by intracellular nanotools to push the resolutive power of fluorescence microscopy and to time-resolve the mechanism of exocytosis. The student will be part of a newly emerging research lab devoted to study supra-molecular machineries that control exocytosis. We are building a team of scientist with different expertise where the student will be trained in a wide panel of disciplines and where he/she is expected to contribute and collaborate. In this multidisciplinary project, the student, will integrate complementary techniques (Cross-linking Mass spectrometry, DNA engineering, etc) to resolve the higher-order mechanism that controls exocytosis in the model organism Saccharomyces cerevisiae. During the progression of the project the student will acquire a strong expertise in DNA editing tools, advanced light microscopy and image analysis. Depending on the student's skills and interest, the project could also involve in silico integration of acquired data to model 3D structures of large protein complexes controlling cell growth.

Preferred background of candidates

Biophysics, Optical physics, Biomedical Sciences, Biology, Biochemistry, or similar. Expertise in yeast genetics, membrane biophysics, fluorescence microscopy or image analysis is a plus.

Selected references

Picco, A., Irastorza-Azcarate, I., Specht, T., Böke, D., Pazos, I., Rivier-Cordey, A-S., Devos, D.P., Kaksonen, M., Gallego, O., (2017) "The in vivo architecture of the exocyst provides structural basis for exocytosis." Cell 168, 400-412.e18.

Irastorza-Azcarate, I., Castaño-Díez, D., Devos, D.P., Gallego, O., (2019) "Live-cell structural biology to solve biological mechanisms: the case of the exocyst" Structure (In press).

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MDM-2014-0370

Principal Investigator: Jordi García-Ojalvo

Dynamical Systems Biology

https://www.upf.edu/web/dsb

Research project title

Dynamics of bacterial ecosystems at the single-cell level

Research project summary

Bacteria are among the most successful life forms on Earth, and constitute one of the main determinants of the health of many multicellular organisms, as well as of the environment itself. In humans, for instance, the bacterial microbiome underlies our ability to process nutrients, regulate our immune system, produce essential molecules such as vitamins, and fight pathogenic bacteria. However, in spite of its importance for our health, little is known of how the bacterial ecosystems that live in our bodies regulate themselves and respond to external factors such as nutrient availability and antibiotic use.

This project aims at advancing our understanding of the bacterial microbiome from the viewpoint of its dynamics at the single-cell level. The selected PhD candidate will use time-lapse fluorescence microscopy in combination with microfluidics to monitor the response of bacterial gene networks to a variety of time-dependent external factors, mimicking those existing in our bodies, in order to identify general principles that explain how different species in bacterial ecosystems (including bacterial biofilms) interact with each other in dynamical environments. The experimental observations will be interpreted with the help of mathematical models of the underlying phenomena, which will provide predictions to be verified with further experiments. Modeling and data analysis will be performed by either other members of the lab or by the PhD candidate her/himself, depending on her/his background and interests in this respect. This PhD project is financed by an FPI grant from the Spanish State Research Agency (AEI).

Preferred background of candidates

Biology (especially microbiology). Candidates with other backgrounds (such as physics, biomedical and chemical engineering, and biotechnology) with a strong interest in systems biology will also be considered.

Selected references

Liu et al, *Nature* 523: 550–554 (2015).
Liu et al, *Science* 356: 638–42 (2017).
Martinez-Corral et al, *PNAS* 115: E8333–40 (2018).
Park et al, *Cell Systems* 6: 216-229.e15 (2018).
Martinez-Corral et al, *Philosophical Trans. of the Royal Society B* 374: 20180382 (2019).
Lee et al, *Cell* 177: 352-360.e13 (2019).

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MDM-2014-0370

Principal Investigator: Elena Hidalgo

Oxidative Stress and Cell Cycle Research Group

www.upf.edu/osccg

Research project title

Activation of signaling cascades and alteration of the cellular proteostasis network by oxidative stress – Influence on aging

Research project summary

Our work is centered in the study of how reactive oxygen species such as H_2O_2 modify proteins, both regarding signaling (reversible cysteine oxidation) and toxicity (protein carbonylation), using fission yeast as a model system:

a. *Cellular responses to oxidative stress.* We study the sensing and transcriptional outputs of signal transduction cascades, and their influence on stress survival and on aging. We have designed fluorescence tools (genetically-encoded protein sensors) to measure in vivo intracellular H_2O_2 fluctuations, and will use them to explore the role of peroxide waves in cell cycle control and signalling.

b. *Protein oxidation, protein misfolding and proteostasis network.* Part of the toxicity associated to oxidative stress and to aging is protein oxidation. We study the networks controlling the synthesis and degradation of misfolded proteins, and will study the role of different chaperones in their fate.

Preferred background of candidates

The main requirement for application is to have completed graduate studies such as Biology, Biotechnology, Chemistry or Biochemistry, and a master (M.S.). Previous research experience in yeast genetics and molecular biology will be highly appreciated.

Selected references

Fernández-Vázquez et al. 2013. Modification of $tRNA^{Lys}_{UUU}$ by Elongator is essential for efficient translation of stress mRNAs. **PLoS Genet**. 9:e1003647.

Calvo et al. 2013. Dissection of a redox relay: H_2O_2-dependent activation of the transcription factor Pap1 through the peroxidatic Tpx1-thioredoxin cycle. **Cell Reports** 5:1413-1424.

García-Santamarina et al. 2014. Monitoring *in vivo* reversible cysteine oxidation in proteins using ICAT and mass spectrometry. **Nature Prot**. 9:1131-1145.

García et al. 2014. Binding of the transcription factor Atf1 to promoters serves as a barrier to phase nucleosome arrays and avoid cryptic transcription. **Nucleic Acids Res**. 42:10351-10359.

Encinar del Dedo et al. 2015. A cascade of iron-containing proteins governs the genetic iron starvation response to promote iron uptake and inhibit iron storage in fission yeast. **PLoS Genet**. 11:e1005106.

Boronat et al. 2017. Lack of a peroxiredoxin suppresses the lethality of cells devoid of electron donors by channelling electrons to oxidized ribonucleotide reductase. **PLoS Genet.** 13:e1006858.

Domenech et al. 2018. Using in vivo oxidation status of one- and two-component redox relays to determine H2O2 levels linked to signaling and toxicity. BMC Biol. 16:61.

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MDM-2014-0370

Principal Investigator: Ana Janic

Cancer Biology

https://www.upf.edu/web/cancer-biology

Research project

Unrevealing mechanism for p53-mediated tumour suppression

Research project summary

Cancer is a disease that affects one of three of us at some point in our lives. The tumour suppressor gene p53 is mutated in ~50% of human cancers. Given the obstacles to developing strategies for targeting wild-type or mutant, further understanding of basic p53 biology is required for successful clinical translation. Recent studies have challenged the previously understood model of how the p53 gene is involved in tumour suppression. This research project focuses on understanding the complexity of the p53 network in tumour suppression in different contexts. It will utilize *in vivo* and *in vitro* approaches to investigate p53-dependent mechanisms in solid tumours as well as blood cancers.

The Janic laboratory has a strong focus on understanding how tumour suppressors work in the context of the whole organism. We have made seminal contributions into the identification of the critical pathways for p53-mediated tumour suppression (1-3)

Preferred background of candidates

The PhD role will involve the use of a wide variety of experimental techniques, including mouse models of cancer, tissue/tumour pathology, CRISPR-Cas9 gene-editing technology, next-generation sequencing, molecular biology, cell culture and flow cytometry. Previous research experience will be highly appreciated, good communication and networking skills, experience in use of the programs to analyse genomic and/or expression data is desirable.

Selected references

- Janic *et al.,* DNA repair processes are critical mediators of p53-dependent tumor suppression. *Nature Medicine*, 2018.
- Valente *et al.,* Strasser* and Janic*. Combined loss of PUMA and p21 accelerates c-MYC-driven lymphoma development considerably less than loss of one allele of p53. *Oncogene*, 2016. *joint last authors
- Valente *et al.,* Janic* and Strasser*. p53 efficiently suppresses tumour development in the complete absence of its cell cycle inhibitory and pro-apoptotic effecters p21, Puma and Noxa. *Cell Reports*, 2013. *joint last authors

Principal Investigator: Cristina López-Rodríguez and Jose Aramburu

NFAT proteins and immune cells

https://www.upf.edu/web/biomed/entry/-/-/23934/adscripcion/CRISTINA-LOPEZ-RODRIGUEZ
https://www.upf.edu/web/biomed/entry/-/-/15818/adscripcion/JOSE-ARAMBURU

Research project

Control of immune response programming in homeostasis and disease

Research project summary

A major interest of our group is to identify new mechanisms that control the capacity of immune cells to assemble complex gene expression programs that confer them effectiveness and adaptability against multiple threats to the organism. We study several processes, such as the communication between immune cells in the rejection of transplants, defense against pathogens such as viruses, and antitumor immunotherapy.

The selected person will develop the Doctoral Thesis acquiring experience in innovative techniques of analysis of cellular differentiation and reprogramming, gene expression and chromatin modifications, as well as in mechanisms of regulation of immune responses and mouse models of human pathologies.

Preferred background of candidates

Candidates must have a Degree (or Bachelor's degree) in Biochemistry, Biotechnology, Biomedical Engineering, Biology, or similar. Candidates in their Master Degree are encouraged to apply. Average scores: Approximately 2.5 or above (scale 1-4), or 8.4 or above (scale 1-10) for the Bachelor Degree. Language: fluency in English, written and spoken.

It will be a plus to have a clear motivation for a career in biomedical research, as well as the ability to confront and solve scientific problems. Prior experience (master thesis level or end-of-degree work project) in immunology, gene expression analysis techniques (such as RT-qPCR and ChIP), or work with mouse models will also be considered positively. It will also be appreciated to have one or two contact persons (telephone and e-mail address) who can provide references.

Selected references

- Buxadé et al., 2012 J Exp Med
- Ortells et al., 2012 Nucleic Acids Res
- Berga-Bolaños et al., 2013 Proc Natl Acad Sci USA
- Aramburu et al., 2014 Science Signaling
- Tellechea et al., 2018 J Immunol
- Buxadé et al., 2018 J Exp Med
- Aramburu and López-Rodríguez, 2019 Frontiers Immunol

Universitat Pompeu Fabra Barcelona
Department of Experimental and Health Sciences

EXCELENCIA MARÍA DE MAEZTU
GOBIERNO DE ESPAÑA MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD
MDM-2014-0370

Principal Investigator: Tomàs Marquès

Comparative Genomics

http://biologiaevolutiva.org/tmarques

Research project

Patterns of geographic dispersion in great apes

Research project summary

The current knowledge of genetic variation in apes studies have proven to be useful for the study of natural populations, but there have been certain limitations given the nature of the samples. In any case, the application of these methods to the genetics of the preservation of apes is limited by the lack of good quality DNA. In the recent years, we have shown that it is possible to study full genome information from apes (Prado-Martinez et al. Nature 2013, Xue et al. Science 2015; deManuel et al. Science 2016; Nater et al. Current Biology 2017). However, all this work is based on DNA derived from high quality samples. We are now reaching a plateau in terms of access to these sequences and novel approaches are needed. The objective of this project is, therefore, to study the geographic variability in genetic patterns of apes using non invasive samples from different locations to ascertain the natural genetic diversity of this species. This should allow us to detect stratified variants by geographic location, patterns of global dispersion, gene flow and selection and that, at the same time, allows us to apply them to the field of conservation in order to georeference in the future unknown samples.

Preferred background of candidates

Candidates should have a very strong theoretical background in population genetics and preferably in the use and analysis of next-generation sequence methods (Illumina).

Selected references

Marc de Manuel et al. “Chimpanzee genomic diversity reveals ancient admixture with bonobos” Science 2016 354 (6311), 477-481

Javier Prado-Martinez*, Peter H. Sudmant*, et al. (2013). “Great ape genetic diversity and population history.” Nature 2013 Jul 25;499(7459):471-5. doi: 10.1038/nature12228. Epub 2013 Jul 3.

J Hernandez-Rodriguez et al. “The impact of endogenous content, replicates and pooling on genome capture from fecal samples” Molecular Ecology Resources, 2018 10:46AM EST | DOI: 10.1111/1755-0998.12728

Sojung Han et al. “Genetic variation in Pan species is shaped by demographic history and harbors lineage-specific functions” Genome Biology and Evolution 2019, evz047, https://doi.org/10.1093/gbe/evz047 07 March 2019

Martin Kuhlwilm*, Marc de Manuel*, Alexander Nater*, Maja P. Greminger*, Michael Krützen, Tomas Marques-Bonet “Evolution and demography of the great apes.” Current Opinion in Genetics & Development 2016.

Universitat Pompeu Fabra Barcelona
Department of Experimental and Health Sciences

EXCELENCIA MARÍA DE MAEZTU
GOBIERNO DE ESPAÑA MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD
MDM-2014-0370

Principal Investigator: Pura Muñoz

Cell Biology

http://www.upf.edu/cellbiology/

Research project

Study of the mechanisms underlying the decline of stem cell regenerative potential with aging.

Research project summary

At present, the major interest of our group is to understand muscle stem cell regulation and functions during skeletal muscle regeneration and aging. Our group has provided insights for muscle stem cell regenerative decline during aging (Sousa-Victor P. et al. Nature 2014). Geriatric muscle stem cells switch quiescence into senescence, due to de-repression of p16INK4a. Furthermore, we demonstrated that p16INK4a silencing in geriatric muscle stem cells restores quiescence and muscle regenerative functions. Recently, we also unveiled that the process of autophagy is essential to maintain stemness in aging (Garcia-Prat et al, Nature 2016). These findings may provide a basis for stem cell rejuvenation in sarcopenic muscles.
We aim to continue unveiling the mechanisms underlying the decline of stem cell regenerative potential with aging, and in particular the failure in proteostasis and entry into senescence of aging stem cells, as well as potential mechanisms to reverse these aging-associated defects.

Preferred background of candidates

We are looking for highly motivated candidates with a B.S. in Life Sciences (minimum score 8,5) and Master in Biomedical Sciences (minimum score 8,5). The most likely successful candidates will have excellent previous experience in cellular and molecular biology. Previous stages in other laboratories will be highly valued.

Selected references

Related publications of the group include:

- Proteostatic and Metabolic Control of Stemness. García-Prat L, Sousa-Victor P, Muñoz-Cánoves P. **Cell Stem Cell** 20:593-608, 2017
- Solanas G, Peixoto FO, Perdiguero E, Jardí M, Ruiz-Bonilla V, Datta D, Symeonidi A, Castellanos A, Welz PS, Caballero JM, Sassone-Corsi P, Muñoz-Cánoves P*, Benitah SA*. Aged Stem Cells Reprogram Their Daily Rhythmic Functions to Adapt to Stress. **Cell** 170:678-692, 2017
- Autophagy maintains stemness by preventing senescence. García-Prat L, Martínez-Vicente M, Perdiguero E, Ortet L, Rodríguez-Ubreva J, Rebollo E, Ruiz-Bonilla V, Gutarra S, Ballestar E, Serrano AL, Sandri M, Muñoz-Cánoves P. **Nature** 529:37-42, 2016
- Geriatric muscle stem cells switch reversible quiescence into senescence. Sousa-Victor P, Gutarra S, García-Prat L, Rodriguez-Ubreva J, Ortet L, Ruiz-Bonilla V, Jardí M, Ballestar E, González S, Serrano AL, Perdiguero E, Muñoz-Cánoves P. **Nature** 506:316-21, 2014

Principal Investigator: Francisco J. Muñoz

Aging Brain and Neurodegeneration

https://www.upf.edu/web/lmp/aging-and-neurodegeneration

Research project

Study on the role of oxidative stress in the onset of Alzheimer's disease: activation of the amyloidogenic pathway in the cholinergic basal forebrain.

Research project summary

The hypothesis of this research project is that the cholinergic circuitry is more sensitive to oxidative stress. This hypothesis includes the following consequences that will be addressed as objectives to demonstrate: i) Cholinergic neurons have reduced cell viability due to oxidative damage and loss of calcium homeostasis which will make them more susceptible to apoptosis; ii) Oxidative stress activates kinases (JNK and p38 MAPK) that results in increased transcription of BACE1. Oxidative stress also induces BACE1 translation from the kinases that phosphorylate eIF-2alpha factor (PERK and PKR). Therefore BACE1 expression in these neurons is greater than in the rest of the brain and the production of Aß is permanently higher than in other neurons; iii) Increased Aß aggregation will result in oligomers and fibers both locally and in their post-synaptic terminals, which also induces the aggregation of the Aß released by other neurons, a situation that will be especially harmful in the entorhinal cortex and hippocampus; iv) The degeneration of cholinergic neurons produces an increase of their metabolites in CSF that may be markers of the initiation and progression of AD; v) Finally the main interest of this project is to elucidate the mechanisms that induce the neurodegeneration of NBM to identify specific therapeutic targets against AD.

Preferred background of candidates

B.S in life sciences; knowledge of Cell culture, molecular biology of proteins and mRNA, spectrometry and spectrofluorometry, flow cytometry and immunofluorescence.

Selected references

- Picón-Pagès P, Garcia-Buendia J, Muñoz FJ. Functions and dysfunctions of nitric oxide in brain. Biochim Biophys Acta Mol Basis Dis S0925-4439(18)30452-6. 2018.
- Guivernau B, Bonet J, Valls-Comamala V, Bosch-Morató M, Godoy JA, Inestrosa NC, Perálvarez-Marín A, Fernández-Busquets X, Andreu D, Oliva B, Muñoz FJ. Amyloid-β peptide nitrotyrosination stabilizes oligomers and enhances NMDAR-mediated toxicity. J Neurosci. 36:11693-11703. 2016.
- Ramos-Fernández E, Tajes M, Ill-Raga G, Vargas L, Busquets-García A, Bosch-Morató M, Guivernau B, Valls-Comamala V, Gomis M, Grau C, Fandos C, Rosen MD, Rabinowitz MH, Inestrosa N, Maldonado R, Altafaj X, Ozaita A, Alvarez A, Vicente R, Valverde MA, Muñoz FJ. Glutamatergic stimulation induces GluN2B translation by the nitric oxide-Heme-Regulated eIF2α kinase in cortical neurons. Oncotarget. 7:58876-58892. 2016.

Principal Investigator: Andrés Ozaita

Neurophar

https://www.upf.edu/ca/web/neurophar

Research project title

Mechanistic insights on the modulation of cognitive functions by cannabinoid receptors in health and disease

Research project summary

Intellectual abilities gradually deteriorate through life, and they are also altered in intellectual disability disorders. The endocannabinoid system, present in the brain and heavily located in synaptic contacts, is a relevant player in the modulation of cognitive performance.

In this project we will evaluate the structural and molecular impact on brain cannabinergic synapses after pharmacological treatments improving cognitive performance. For this purpose we will use well-established mouse models of intellectual disability disorders together with 3D-imaging and multi-omics approaches.

The results expected will allow identifying the neurobiological mechanisms contributing to enhanced cognitive abilities of pharmacological treatments in health and disease conditions with potential clinical purposes.

Preferred background of candidates

Biomedical sciences, Bioinformatics, Bioengineering

Selected references

Navarro-Romero et al. Cannabinoid type-1 receptor blockade restores neurological phenotypes in two models for Down syndrome. Neurobiol Dis. 125:92-106 (2019).

Salgado-Mendialdúa et al. Δ9-tetrahydrocannabinol modulates the proteasome system in the brain. Biochem Pharmacol. 157:159-168 (2018).

Busquets-Garcia et al. Hippocampal Protein Kinase C Signaling Mediates the Short-Term Memory Impairment Induced by Delta9-Tetrahydrocannabinol. Neuropsychopharmacology. 43:1021-1031 (2018).

Ozaita A, Aso E. The cannabis paradox: when age matters. Nat Med. 23:661-662 (2017).

Busquets-Garcia et al. Peripheral and central CB1 cannabinoid receptors control stress-induced impairment of memory consolidation. Proc Natl Acad Sci U S A. 113:9904-9 (2016).

Principal Investigator: Cristina Pujades

Development of the Vertebrate Central Nervous System

https://www.upf.edu/web/devbiol/cns

Research project

Tissue compartmentalization and cell fate decisions during embryonic development

Research project summary

We are interested in understanding how tissue compartmentalization and cell fate decisions take place in the Central Nervous System during embryonic development. We use the developing brain of the vertebrates - the hindbrain - as model to study how cell diversity in generated during neural development. The project will focus in understanding how brain morphogenesis and cell fate acquisition are intertwined during the establishment of different cell lineages. Imaging tools (3D+time imaging), and genome-editing technology will be combined using zebrafish embryos.

Preferred background of candidates

We are seeking for highly motivated and enthusiastic candidates with Graduate studies related to Biomedicine. They will integrate the International PhD Program in Biomedicine of the Department of Experimental and Health Sciences (UPF), which has been awarded with the Quality Mention by ANECA (National Agency for Quality and Assessment, Spain).

Candidates are required to be proficiency in English.

The candidates will benefit from working in a dynamic group, at a university department that received the Maria de Maetzu Award for its scientific excellence. We are located within the PRBB in Barcelona, a vibrant research park harboring several research institutions and cutting-edge core facilities.

Selected references

- Letelier, J, Terriente, J, Belzunce, I, Voltes, A, Undurraga, C, Polvillo, R, Devos, L, Tena, J, Maeso, I, Retaux, S, Gomez-Skarmeta, JL, Martinez-Morales, JR, Pujades, C. The evolutionary emergence of the rac3b/rfng/sgca regulatory cluster refined mechanisms for hindbrain boundaries formation; PNAS 2018
- Dyballa, S, Savy, T, Germann, P, Mikula, K, Remesikova, M, Spir, R, Zecca, A, Peyrieras, N, Pujades, C. Distribution of neurosensory progenitor pools during inner ear morphogenesis unveiled by cell lineage reconstruction; eLife 2017
- Terriente, J, Pujades, C. Cell segregation in the hindbrain: do boundaries matter? Cell Mol Life Sci 2015
- Zecca, A, Dyballa, S, Voltes, A, Bradley, R, Pujades, C. The order and place of neuronal differentiation establish the topography of sensory projections and the entry points within the hindbrain; J Neuroscience 2015
- Calzolari, S, Terriente, J, Pujades, C. Cell segregation in the vertebrate hindbrain relies on actomyosin cables located at the interhombomeric boundaries; EMBO J 2014