

DCEXS-UPF (Barcelona) International PhD call 2020

The [Department of Experimental and Health Sciences](#) of the [Pompeu Fabra University](#) (DCEXS-UPF) opens a call for the academic year 2021-22, 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, for instance, the DCEXS-UPF has been awarded the "María de Maeztu" distinction and grant in 2014 and 2018. 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 \(PRBB\)](#).

Eight PhD contracts are offered in groups led by recognized scientists performing research in biomedicine, please see below for more information on the scientific projects.

Contracts, training and advantages

Contracts will be funded by the Spanish "Researcher Training Program" as well as by the DCEXS-UPF. All positions will offer the same wage conditions, for 4 years, and fellows will be registered in the Spanish Social Security System, which provides health and occupational insurance coverage. Academic costs (except fees) are also covered.

The UPF's PhD programme in Biomedicine has been certified by the ANECA and in October 2011 it was awarded the "Mention towards Excellence". Since the academic year 2012-13, the 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 verified by the Catalan Agency for Quality Assessment and Accreditation with a qualification "Quality Label towards Excellence".

The PhD programme, all of whose activities are carried out in English, attracts every year a large number of international students. These activities aim at preparing students to become independent researchers pursuing a scientific career. Fellows 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 excellent academic qualifications and good command of English. Research experience and authorship of scientific publications will be a plus.

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 disciplines (Mathematics, Computer Science, Bioengineering, etc) within the European Higher Education System (minimum 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 2020 (candidates who expect to be awarded such degree by September 2020 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 will be considered ineligible. **Please note that it is not necessary to start the admission process for the PhD programme at this stage**; if you are selected we will help you prepare your application for admission.

All candidates will be required to present their academic record.

Reference letters will be requested for **pre-selected** candidates. Also, pre-selected candidates who obtained their degree and/ or Master's in a country other than Spain will have to present the [conversion](#) of their grades to the Spanish 0-10 scale.

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 information and documents through this [online form](#).

You will be able to choose one or two positions in order of preference.

Deadline for applications: 28th August 2020 at 17h CET.

Selection process and calendar

The pre-selection of the candidates will be based on academic qualifications and research experience. Candidates will receive feedback on pre-selection before the 10th of September.

Pre-selected candidates will be interviewed by at least one Principal Investigator in the DCEXS facilities or via videoconference during September and will receive feedback in early October.

Contracts are expected to start from June 2021 (depending on the publication and resolution of the "Researcher Training Program" call).

Contact:

Dr Regina López

phdfellowships.dcexs@upf.edu

Principal Investigator: Berta Alsina

Morphogenesis and Cell Signaling in Sensory Systems

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

Research project

Functional characterization of inner ear regulatory elements in vivo by the crispr1 and crisprA system

Research project summary

Over one million regulatory elements have been identified across the human genome in the last decade, however, it remains to be assessed their functionality for most of them. Recent works have used the crispr1 or crisprA methodology, that modifies gene expression by targeting a modified version of the Cas9 to regulatory elements, to identify and functionally characterize the regulatory elements in vitro and in vivo (Gasperini et al. 2019; Matharu et al., 2019).

The inner ear is one of the most sophisticated sensory organs of our head. Thanks to specialized mechanotransducing cells (the hair cells) and sensory neurons, auditory and balance information is captured and transmitted to the brain. Over 5% of the world's population – or 466 million people – has disabling hearing loss (432 million adults and 34 million children) (ref). Congenital sensorineural deafness is due to mutations in genes involved in hair cell or sensory neuron development, either in the coding region or regulatory elements. Recent Genome Wide Association Studies (GWAS) have identified novel variants linked to deafness, some of them in regulatory elements. Moreover, in our laboratory, we are currently performing ATAC-seq and RNA-seq studies of hair cells and sensory neurons to identify putative regulatory elements regulating these two cell types.

The overarching goal of the project is to characterize functionally hair cell and inner ear sensory neuron gene regulatory elements by using the crispr1 and crisprA system in vivo.

Our laboratory has a long expertise in inner ear development using the zebrafish as a model organism. We have several transgenic reporter lines that label specifically hair cells or sensory neurons, in which transcriptomic analysis can be done. For this project, several databases of deafness genes and regulatory variants will be analysed and mapped into ENCODE and laboratory information of regulatory elements. With this information, we use the dCAS-KRAB system to inhibit them and assess the effects on gene regulation by RNA-seq and cell function. The functional characterization of these elements will allow developing therapies to rescue deafness in vivo.

Preferred background of candidates

We are seeking a highly motivated student with interest in Cellular and Developmental Biology, live imaging and crispr technologies. Good skills in English spoken and written are required. Experience in animal (zebrafish or mouse) handling will be considered.

Selected references

- 1- Gasperini M et al. A Genome-wide Framework for Mapping Gene Regulation via Cellular Genetic Screens [published correction appears in Cell. 2019 176(6):1516
- 2- Matharu Net al. CRISPR-mediated activation of a promoter or enhancer rescues obesity caused by haploinsufficiency. Science. 2019;363(6424):eaau0629.

Click [HERE](#) for our laboratory publications

Principal Investigator: Elena Bosch

Evolutionary Population Genetics

<http://biologiaevolutiva.org/ebosch/>

Research project

Human adaptation: from the genomic signal to the adaptive phenotype

Research project summary

The primary goal of this research proposal is to understand how adaptive selection has shaped the genetic and phenotypic variation in present-day human populations using genomic data. For that, we propose first to: (i) compile genome-wide data across several populations to analyze the footprints of positive (adaptive) selection by considering different modes of selection (hard and soft sweeps and polygenic selection) and second (ii) try to understand the biology behind the detected selection signals by using in silico functional predictions, molecular biology techniques and different association approaches to locate and experimentally validate any putative adaptive functional (coding and non-coding) variant, determine their corresponding adaptive phenotypes and try to identify the environmental selective pressures at play. The search of positive selection will be done at genome-wide level, in general, as well as for predefined groups of genes (pathways and/or biological networks). Moreover, we plan to analyze several populations under particular environmental pressures or for which we will have phenotypic data including several Pygmy populations from across southeast Asia and Andean highlanders from Peru.

Preferred background of candidates

We welcome candidates with backgrounds in either theoretical, computational or experimental fields such as bioinformatics, statistics, anthropology, evolutionary genetics, functional genetics, theoretical and experimental population genetics.

Selected references

- Urnikyte et al. (2019). Patterns of genetic structure and adaptive positive selection in the Lithuanian population from high-density SNP data. *Sci Rep.* 9(1):9163.
- Rodríguez et al. (2017). Antagonistic pleiotropy and mutation accumulation influence human senescence and disease. *Nat Ecol Evol* 1, Article number: 0055.
- Engelken et al. (2016). Signatures of evolutionary adaptation in quantitative trait loci influencing trace element homeostasis in liver. *Mol Biol Evol* 33(3): 738-754.
- Engelken et al. (2014). Extreme Population Differences in the Human Zinc Transporter ZIP4 (SLC39A4) are Explained by Positive Selection in Sub-Saharan Africa. *PLOS Genet* 10(2): e1004128

Principal Investigator: David Comas

Human Genome Diversity

<http://www.biologiaevolutiva.org/dcomas/>

Research project

Genome wide approach to demography and adaptation in human populations

Research project summary

Despite the pivotal effect of genetic adaptation, the distribution of the human genomic variation is highly influenced by the demographic history, especially regarding low-frequency coding variants. The analysis of human groups that have experienced special demographic events characterized by founder effects and extensive genetic drift after bottlenecks during their population history (also known as population isolates), has allowed the discovery of genetic variants associated to Mendelian disorders and even complex traits. Human populations that have undergone episodes of population bottlenecks and isolation, normally linked with consanguinity practices, typically show elevated levels of background parental relatedness and of autozygosity, which increases risk of Mendelian disorders and complex diseases, where many recessive variants with moderate effects genome-wide are causative of this increased risk. On the contrary, migration events might have diluted the effects of isolation, although genome traces of past population history are easy to detect in the genomes of present day populations.

The present project aims to determine the effects of past history (demography and adaptation) in present day populations by a genome wide approach (using a compendium of complete sequences, exomes, and genome wide markers), and its effects in health and disease.

Preferred background of candidates

We are seeking for an open-minded highly motivated candidate with a background in Evolutionary Genetics, Computation Genomics, Molecular Anthropology, Population Genomics. Good skills in English spoken and written, and IT knowledge are required.

Selected references

- Biagini SA, Solé-Morata N, Matisoo-Smith L, Zalloua P, Comas D, Calafell F (2019) People from Ibiza: an unexpected isolate in the Western Mediterranean. *European Journal of Human Genetics* 27:941-951
- Lorente-Galdos B, Lao O, Serra-Vidal G, Santpere G, Kuderna LFK, Arauna LR, Fadhlouli-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* 20:77
- Font-Porterías, Arauna LR, Poveda A, Bianco E, Rebato E, Prata MJ, Calafell F, Comas D (2019) European Roma groups show complex West Eurasian admixture footprints and a common South Asian genetic origin. *PLoS Genetics* 15(9): e1008417
- Serra-Vidal G, Lucas-Sanchez M, Fadhlouli-Zid K, Bekada A, Zalloua P, Comas D (2019) Heterogeneity in Palaeolithic population continuity and Neolithic expansion in North Africa. *Current Biology* 29:3953-3959

Principal Investigator: Oriol Gallego

Live-cell Structural Biology

www.gallegolab.org

Research project

Advanced microscopy of supra-assemblies regulating cell growth

Research project summary

We look for an enthusiastic PhD student that is willing to develop a new microscopy technique that allows us to understand how cells regulate the expansion of their membranes and how they can adapt this process to grow under different environments. Membrane expansion is essential to control cell growth, the cell surface composition, cell polarity, morphogenesis, cell differentiation and neurobiology. This is a process controlled by large and dynamic protein machines formed by multiple protein complexes that assemble transiently and that act in a coordinated manner. Despite the work of many laboratories, the dynamism and complexity of this process did not allow resolving the mechanism behind the action of such large protein machinery. To be successful, we will use *Saccharomyces cerevisiae* as a model organism and we will develop new methods that combine light microscopy and electron microscopy. Thus, we will be able to time-resolve the cell machinery with unprecedented resolution. The development of this technology will be done together with other members of the lab and in collaboration with groups in Switzerland and Australia.

Ours is interdisciplinary research in the frontier of cell biology, biophysics, computational modelling and structural biology. We develop methods of fluorescence microscopy that allow the structural analysis of molecular assemblies in vivo. We then integrate the structural and biophysical measurements in computational models, which allows us to solve questions in cell biology that were not accessible by other techniques (Picco et al, 2017, Cell; Irastorza-Azcarate et al, 2019, Structure). We are well equipped, with have our own microscope for live-cell imaging and single-molecule localization microscopy.

Preferred background of candidates

- Background in Biophysics, Optical physics, Biomedical Sciences, Biology, Biochemistry, or similar.
- A minimum of 1-year expertise in a research lab is required.
- Expertise in fluorescence microscopy, programming or membrane trafficking is a plus.
- Excellent written and oral communication skills in English.

Selected references

- Picco, A., ... Gallego, O., (2017) "The in vivo architecture of the exocyst provides structural basis for exocytosis." Cell 168, 400-412.e18.
- Irastorza-Azcarate, I., ... Gallego, O., (2019) "Live-cell structural biology to solve biological mechanisms: the case of the exocyst" Structure 27, 886-892.

Principal Investigator: Ana Janic

Cancer Biology

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

Research project

Deconstructing p53-activated DNA repair mechanisms for tumor suppression

Research project summary

Mechanisms critical for tumor suppression downstream of p53 remain largely unexplored, despite their great interest for cancer biology. Recent studies, including ours, have challenged the significance of classical p53 downstream functions (of apoptotic cell death, cell cycle arrest, and cell senescence) in tumor suppression. Strikingly, however, we discovered that p53-mediated tumor suppression in the hematopoietic compartment requires DNA damage repair. In this project we aim to identify: i) how p53 controls a DNA repair-coordinated program to protect tumorigenesis; ii) how tissue specificity controls which p53-regulated DNA repair effectors are crucial for tumor suppression; iii) how we could use p53-dependent DNA repair signaling therapeutically to kill tumor cells. We aim to tackle these broad questions using CRISPR-Cas9-based strategies in genetically engineered mouse models and cancer cell lines. In sum, the success of this project in identifying unknown molecular regulatory nodes between DNA repair and p53 will increase our understanding of the molecular interactions regulating p53 loss-mediated cancer development and progression.

Preferred background of candidates

Candidates must have excellent academic qualifications. Previous research experience, authorship of scientific publications, experience in IT knowledge, especially Python and/or R Programming languages, will be a plus. Candidates are required to master the English language.

Selected references

1. Janic *et al.*, DNA repair processes are critical mediators of p53-dependent tumor suppression. *Nature Medicine*, 2018.
2. 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
3. Valente *et al.*, Janic* and Strasser*. p53 efficiently suppresses tumour development in the complete absence of its cell cycle inhibitory and pro-apoptotic effectors p21, Puma and Noxa. *Cell Reports*, 2013. *joint last authors

Principal Investigator: Tomas Marques-Bonet

Comparative Genomics

<http://biologiaevolutiva.org/tmarques/>

<https://www.ibe.upf-csic.es/marques>

Research project

Population genetics of primates

Research project summary

Genomic diversity is at the core of many evolutionary inferences. The finer study of primates, our closest relatives, is relevant for several reasons. They are the only living organisms with whom we share a higher proportion of genetic material as we have a shared evolutionary history over time. Thus, studying the genetics of the primates is a necessary endeavour to define the similarities among primates, the uniqueness of humans, and to strengthen the foundations of primate management and conservation. The latter of which should be an international effort, as these species should be considered a treasure of humanity. Determining the genomic variants of endangered species is crucial then for future management of both captive and wild-born primates. However, much of the current knowledge of genetic variation in primates has been determined by studies based on partial genomic information. These studies have proven to be partially useful for the study of natural populations, but there have been certain limitations given the nature of the markers (mtDNA or microsatellites). We have generated high-quality full genome information for a large panel of primates all over the world. The reconciliation of taxonomic and genetic data needs to be made the highest priority, especially with regards to conservation biology. Millions of humans have now been genotyped and, scientifically, there does not impede procuring a similar barcode catalogue of variation from some of the most endangered primates in the world – a catalogue that will lay the groundwork for future research in conservation genetics in order to preserve the natural populations of our closest relatives.

Preferred background of candidates

Computational genomics. Evolutionary genomics. Statistical population genomics.

Selected references

- Prado et al. Nature 2013
- DeManuel et al. Science 2016
- Kulhwilm et al. Nat Ecol Evol. 2019
- Walker et al. Nature 2019
- Singing et al. Science 2020

Principal Investigator: Francisco J. Muñoz

Molecular Physiology

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

Research project

Identification of the role of new calcium regulators in the production of amyloid beta-peptide and amyloid neurotoxic effects.

Research project summary

Alzheimer's Disease (AD) is a major public health problem for which nowadays there is no accurate early diagnosis or effective treatments. Since the characterization of amyloid-beta-peptide (A β) deposition in senile plaques and the subsequent formation of intraneuronal neurofibrillary tangles are the two defining pathological hallmarks of AD, a fair amount of research has been directed towards the identification of the molecular mechanism controlling A β production, aggregation and toxicity. AD is considered a multifactorial complex disease that is influenced by environmental factors and multiple genetic variants, probably each of them with small effect. Accordingly, progress towards defining the genetic basis and molecular mechanisms of susceptibility to AD has been slow. Interestingly, we have found in widescreen in yeasts that several genes involved in intracellular calcium homeostasis would be working actively in the pathophysiology of AD. THE MAIN GOAL OF THIS PhD RESEARCH PROJECT is to identify new target genes and molecular mechanisms affecting A β production and A β -induced neurotoxicity as follows:

Objective 1. Identification of new target genes directly affecting A β neurotoxicity by silencing/overexpressing the mammalian orthologs.

Objective 2. Characterization of novel calcium-mediated molecular mechanisms affecting A β neurotoxicity

Objective 3. Effect of calcium signalling in A β production

Preferred background of candidates

Degree in Experimental Sciences. Background in Cell cultures, Western Blot analysis and Molecular Biology techniques. Experience in basic research in Alzheimer's disease or other neurodegenerative processes will be advantageous.

Selected references

1. Picón-Pagès P, et al. Human Albumin Impairs Amyloid β -peptide Fibrillation Through its C-terminus: From docking Modeling to Protection Against Neurotoxicity in Alzheimer's disease. *Comput Struct Biotechnol J*. 17:963-971. 2019.
2. Valls-Comamala V, et al. The antigen-binding fragment of human gamma immunoglobulin prevents amyloid β -peptide folding into β -sheet to form oligomers. *Oncotarget*. 8:41154-41165. 2017.
3. Guivernau B, et al. Amyloid- β peptide nitrotyrosination stabilizes oligomers and enhances NMDAR-mediated toxicity. *J Neurosci*. 36:11693-11703. 2016.
4. Ramos-Fernández E, et al. Glutamatergic stimulation induces GluN2B translation by the nitric oxide-Heme-Regulated eIF2 α kinase in cortical neurons. *Oncotarget*. 7:58876-58892. 2016.
5. Bosch-Morató M, et al. Increased amyloid β -peptide uptake in skeletal muscle is induced by hyposialylation and may account for apoptosis in GNE myopathy. *Oncotarget*. 7:13354-71. 2016.
6. Ill-Raga G, et al. Physiological Control of Nitric Oxide in Neuronal BACE1 Translation by Heme-Regulated eIF2 α Kinase HRI Induces Synaptogenesis. *Antioxid Redox Signal*. 22: 1295-1307, 2015.
7. Ill-Raga G, et al. Fibrinogen nitrotyrosination after ischemic stroke impairs thrombolysis and promotes neuronal death. *Biochim Biophys Acta Mol Basis Dis*, 1852:421-8, 2015

Principal Investigator: Olga Valverde, MD PhD

Neurobiology of Behaviour

<https://www.upf.edu/web/gredec>

Research project

Cannabidiol effects on the different phases of cocaine addictive process. Influence of circadian rhythms on these effects.

Research project summary

The psychostimulant cocaine is the second most commonly used illicit drug after cannabis derivatives. Cocaine is a potent psychostimulant that acts on the nervous system increasing alertness, attention, feelings of well-being and energy. Its mechanism of action, that facilitates the availability of monoamines, makes it a drug with a high addictive potential. Thus, it produces high levels of craving and relapse to consumption despite does not produce physical dependence. Nowadays, it is accepted that the neuroadaptive changes developed through the action of drugs of abuse are not reversible. In the particular case of cocaine, there is currently no effective treatment for cocaine abuse and to avoid the frequent relapses after withdrawal. At this point, we and other researchers have demonstrated that repeated treatment with cannabidiol attenuates cocaine intake in an operant model of intravenous self-administration in mice. This protective effect of cannabidiol is due to the facilitation of hippocampal neurogenesis through a mechanism involving the CB1 cannabinoid receptors. However, cannabidiol has a very complex mechanism of action, and it is crucial to know the effects of cannabidiol on the different phases of cocaine addictive process. Interestingly, circadian rhythms disturbances are linked to the development and progression of neuropsychiatric illness, including substance use disorders and perturbances of the circadian system may contribute to the vulnerability for substance use and cocaine use. In the present project, we propose to experimentally explore the beneficial effects of cannabidiol in different phases of the cocaine seeking behaviour in C57BL/6 male and female mice. We will examine different phenomena including the punishment associated to cocaine intake to evaluate the compulsiveness of the response, the abstinence, craving and reinstatement after stress- and cue-induced reinstatement. Also, we will evaluate the procedure of behavioural economic demand, an accurate paradigm to evaluate the therapeutic potential of a given compound on cocaine seeking. After behavioural evaluation, brain areas related to the control of reward and motivation will be dissected to examine the underlying neurobiological mechanisms associated to the beneficial effect of cannabidiol, including the expression and signalling of CB1 cannabinoid receptors and D1 and D2 dopamine receptors, plasticity changes through the evaluation of the expression of GluA1 and GluA2 subunits of AMPA glutamate receptors, neurotrophic factors as BDNF, and neurogenesis in the dentate gyrus. Among the brain areas: mPFC, OFC, vSTR, AMY and HIP will be analysed. Thus, immunohistochemical, western blot and ELISA analysis will be carried out depending of the particular factor. Moreover, as we have mentioned, we will evaluate the role of BMAL1 transcriptional factor in the pharmacological effects induced by cocaine, and in particular the rewarding and reinforcing effects of this psychostimulant, using BMAL1 knockout mice and the corresponding WT littermates. Furthermore, the effect of cannabidiol will be also examined on the observed responses in animals with impaired circadian clock. The molecular substrate of such effects will be investigated. Finally, sex aspects will be fully considered in our proposal and for that we will carry out the most relevant experiments in male and female mice to compare behavioural and molecular differential responses in both sexes.

Preferred background of candidates

Biomedicine (Biology, Biochemistry, Biomedicine, Pharmacy), Biotechnology or Psychology.

Selected references

- Castro-Zavala A, Martín-Sánchez A, Luján MÁ, Valverde O. Maternal separation increases cocaine intake through a mechanism involving plasticity in glutamate signalling. *Addict Biol.* 2020 Apr 24:e12911. doi: 10.1111/adb.12911.
- Castro-Zavala A, Martín-Sánchez A, Valverde O. Sex differences in the vulnerability to cocaine's addictive effects after early-life stress in mice. *Eur Neuropsychopharmacol.* 2020 Mar;32:12-24. doi: 10.1016/j.euroneuro.2019.12.112.
- Cantacorps L, Montagud-Romero S, Luján MÁ, Valverde O. Prenatal and postnatal alcohol exposure increases vulnerability to cocaine addiction in adult mice. *Br J Pharmacol.* 2020 Mar;177(5):1090-1105. doi: 10.1111/bph.14901.
- Luján MÁ, Cantacorps L, Valverde O. The pharmacological reduction of hippocampal neurogenesis attenuates the protective effects of cannabidiol on cocaine voluntary intake. *Addict Biol.* 2020 Jul;25(4):e12778. doi: 10.1111/adb.12778.
- Luján MÁ, Castro-Zavala A, Alegre-Zurano L, Valverde O. Repeated Cannabidiol treatment reduces cocaine intake and modulates neural proliferation and CB1R expression in the mouse hippocampus. *Neuropharmacology.* 2018 Dec;143:163-175. doi: 10.1016/j.neuropharm.2018.09.043.