DCEXS-UPF (Barcelona) PhD fellowships 2017

Call for applications

The Department of Experimental and Health Sciences of the Pompeu Fabra University (DCEXS-UPF) opens a call for the academic year 2017-18, 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 was one of six research units in Spain to be awarded the "María de Maeztu" distinction and grant by the Ministry of Economy, Industry and Competitiveness in its first call. 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.

11 fellowships are offered in groups led by recognized scientists performing research in biomedicine (see below for more information). Candidates can choose up to 3 groups they would like to join (see section Selection process and calendar).

Fellowships, training, and advantages

The UPF's PhD programme in Biomedicine has been verified by the ANECA (Spanish National Agency for the Evaluation, Quality, and Accreditation). In October 2011, the doctoral programme in Biomedicine was awarded the "Mention towards Excellence" (MEE2011-0323) by the Ministry of Education. Successful candidates will have access to a wide range of academic activities, as well as ad hoc training in specific scientific skills; UPF and PRBB seminars, conferences and symposia; and career development courses, not only at UPF, but also through the PRBB Intervals Programme.

Fellowships will be funded by the Spanish National Sub-Programme for Training, as well as by the DCEXS-UPF. All fellowships 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.

Requirements

Candidates must have obtained a University Degree and a Master's Degree in natural or medical sciences (Biology, Medicine, Biochemistry, Biomedicine, Chemistry, Physics, Bioengineering, etc), or in other quantitative sciences (Mathematics, Computer Science, etc) within the

European Higher Education System (minimum 300 ECTS), or an equivalent university degree that would allow the candidate to start a PhD thesis in their home country by September 2017. Candidates who expect to be awarded with such degree by September 2017 are eligible to apply. Candidates are advised to check that they would 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. If you are selected, you will be provided with a support letter from your supervisor.*

Candidates from any nationality are eligible. Candidates must have excellent academic qualifications (will be required to present their academic record) and good command of English. Previous research experience and authorship of scientific publications will be a plus.

Application

To apply, please register and send the required information and documents via web.

Please ensure that all information -including reference letters- is uploaded before the deadline, as incomplete proposals will be disregarded.

Selection process and calendar

The call will be open until the 5th of May 2017.

The pre-selection of the candidates will be based on academic qualifications and research experience. Candidates will receive feedback on pre-selection in mid-May.

Pre-selected candidates will be interviewed by the Principal Investigators in the DCEXS facilities or via Skype during June 2017 and will receive feedback by the end of June.

**Note*: pre-selected candidates will have at least one interview, but they will not necessarily be interviewed by the all the Principal Investigators they selected.

Contracts are expected to start from January 2018 (depending the publication and resolution of the National Sub-Programme for Training call).

Contact:

Dr. Regina López

phdfellowships.dcexs@upf.edu

Principal Investigator: Elena Bosch

Evolutionary Population Genetics Lab

http://biologiaevolutiva.org/ebosch/

Research project title

Deciphering genetic adaptations in humans

Research project summary

During the transition from hunter-gatherer groups to agricultural societies, humans confronted major cultural, demographical and ecological challenges. Our hypothesis is that the environmental changes associated with the Neolithic transition shaped the human genome, leaving many diverse signatures of adaptation. To elucidate novel insights into our understanding of the adaptive allelic variants and phenotypes resulting from such cultural transition we will apply several state-of-the-art evolutionary strategies to detect different modes of selection in genomic data from human populations differing in their lifestyles. Besides detecting the signatures of hard selective sweeps we will focus on detecting soft sweeps, including selection form standing variation and polygenic adaptation. Subsequently, the functional variation linked to these signatures will be experimentally validated through the relevant molecular biology techniques. Several experimental designs will be set up to interrogate potential phenotypic molecular differences between the ancestral and derived alleles of the genomic variants linked to signatures of selection. Experimental validation could include in vitro biochemical characterization of proteins, functional characterization in cell lines, use of reporter gene assays or other gene expression assays, among others. Furthermore, we also plan to compile and/or perform relevant phenotype association studies to identify the adaptive phenotypes. This research will not only bridge the gap between the genomic and functional evidence for human adaptive phenotypes but may also provide molecular mechanistic details for variation that may be related to present-day metabolic and infectious diseases.

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

- - 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 Genetics 10(2): e1004128
- - Carnero-Montoro et al (2012). Evolutionary and functional evidence for positive selection at the human CD5 immune receptor gene. Mol Biol Evol 29(2): 811–823.

Principal Investigator: Francesc Calafell

Genomics of Individuality

http://biologiaevolutiva.org/fcalafell/

Research project title

Population genomics of the Western Mediterranean

Research project summary

The availability of very large numbers of genetic polymorphisms covering the whole genome (or, actually, of whole genomes) has allowed dissecting the traces left by population history in a genome with unprecedented levels of precision. Genomes can be *painted* by the provenance of each block or haplotype, and, thus, genetic admixture can be finely tracked. Also, homozygosity runs inform us on the extent of endogamy within a population.

In this framework, we are interested in the population history of both shores of the Western Mediterranean. We are investigating patterns of gene flow among them, or, on the contrary, physical or cultural barriers that may have isolated some of them. To that effect, we are using SNP arrays and whole genomes obtained from hundreds of individuals.

Additionally, two more issues interest us: the phylogeography of the Y chromosome, based on whole sequences of this patrilinearly-transmitted chromosome, and the application of massive parallel sequencing to forensic genetics, and, in particular, to the identification of remains in mass graves from the Spanish Civil War.

Within the framework of the group's interests and projects, the selected candidate is expected to focus on the analysis of whole genome sequences in terms of population history.

Preferred background of candidates

Candidates should have a strong background in bioinformatics, with skills in handling large datasets in a Linux environment. However, a purely technical profile is not sufficient, and a background in biology/genetics is required. An interest in history and the humanities in general is highly desirable.

Selected references

- Solé-Morata N, Bertranpetit J, Comas D, Calafell F (2015) Y-chromosome diversity in Catalan surname samples: insights into surname origin and frequency. European Journal of Human Genetics, 23:1549-1557.
- Calafell F, et al. (2016) An assessment of a massively parallel sequencing approach for the identification of individuals from mass graves of the Spanish Civil War (1936-1939). Electrophoresis, in press.

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 genomewide 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

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: Eulàlia de Nadal & Francesc Posas

Cell Signaling Research Group

Cell Signaling Research Group

https://www.upf.edu/cellsignaling/

Research project title

Understanding stress adaptation in mammals

Research project summary

The main focus of our group is to understand how cells detect and respond to environmental changes. We have focused our studies on the characterization of the stress signal transduction pathways, especially those controlled by MAP kinases of the Hog1/p38 family, also known as the stress activated MAP kinases (SAPK). We study the molecular mechanisms required to respond to changes in the extracellular environment and the adaptive responses required for cell survival. Proper adaptation to stress involves the modulation of several basic aspects of cell biology, such as the control of cell cycle progression and regulation of gene expression (Nadal-Ribelles et al., Mol Cell, 2014; Duch et al., Nature, 2013). Remarkably, many of those aspects are conserved between yeast and mammals (de Nadal et al., Nat Rev Genet, 2011).

The PhD fellow funded by this call will participate in the characterization of the molecular mechanisms required for stress-adaptation mediated by the mammalian SAPK p38. Although our knowledge of the transcriptional control by p38 has increased over the years, we plan to assess systematically the role of chromatin structure in p38-mediated gene expression and also the modulation of alternative splicing by the SAPK. On the other hand, we will study how p38 regulates cell cycle progression. We have already shown that p38 mediates a transient G1 arrest through the phosphorylation of a CDKi and the down-regulation of cyclin expression. This delay in cell cycle is activated by the phosphorylation of RB, a key negative regulator of the G1/S phase transition in mammalian cells (Gubern et al., Mol Cell, 2016).

Preferred background of candidates

We are seeking a talented and highly motivated PhD student with a master on Biomedicine, Biology or similar finished on September 2017 the latest.

Candidates should have previous Molecular and Cell Biology research experience and a strong commitment to scientific research. Candidates must have a good knowledge of English and have an interactive personality.

Selected references

- Gubern A, Joaquin M, Marquès M, Maseres P, Garcia-Garcia J, Amat R, González-Nuñez D, Oliva B, Real FX, de Nadal E*, Posas F*. The N-terminal phosphorylation of RB by p38 bypasses its inactivation by CDKs and prevents proliferation in cancer cells. Mol Cell. 64(1):25-36 (2016).
- Nadal-Ribelles M&, Solé C&, Xu Z, Steinmetz LM, de Nadal E*, Posas F*. Control of Cdc28 CDK1 by a stress-induced lncRNA. Mol Cell. 53:549-61 (2014)
- Duch A, Felipe-Abrio I, Barroso S, Yaakov G, García-Rubio M, Aguilera A, de Nadal E, Posas F. Coordinated control of replication and transcription by a SAPK protects genomic integrity. Nature 493:116-9 (2013)
- de Nadal E, Ammerer G, Posas F. Controlling gene expression in response to stress. Nat Rev Genet. 12:833-45 (2011)

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: Juana Díez

Virology Unit

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

Research project title

Global definition of emerging virus – host interaction networks

Research project summary

RNA viruses are a major threat to human health. They also provide a fascinating window into cell biology since they interact intimately with the infected cell. Aims of the project are to decipher how emerging mosquito-borne viruses such as Dengue virus, Zika virus or Chikungunya virus efficiently translate their genomes in both mosquito and human translation machineries and how they modify the host gene expression program to their benefit.

Preferred background of candidates

Biology, Biochemistry, Cellular Biology, or Virology

Selected references

https://www.ncbi.nlm.nih.gov/pubmed/?term=diez+juana

Principal Investigator: Jordi García Ojalvo

Dynamical Systems Biology lab

http://dsb.upf.edu

Research project title

Dynamics of autoimmunity

Research project summary

The goal of this PhD project is to develop and implement an integrative computational model of the immune system that accounts for the cellular response associated with autoimmune diseases, in particular multiple sclerosis. The model will be constrained by experimental data coming from a variety of laboratories around Spain, within the context of the Spanish Network of Multiple Sclerosis (REEM, http://www.reem.es/en_index/). A top-down data analysis approach will also be implemented, using machine learning methods, with the ultimate goal of stratifying patients according to their disease progression and response to therapies.

Preferred background of candidates

The ideal candidate should have a quantitative background in an area such as systems biology, biomedical engineering, physics, mathematics or computer science. Candidates trained in biology or biomedicine, but with an interest in quantitative approaches to biological processes, will also be considered.

Selected references

- L. Espinar, M. Dies, T. Cagatay, G. M. Süel, and J. Garcia-Ojalvo, "Circuit-level input integration in bacterial gene regulation," Proceedings of the National Academy of Sciences of the United States of America, vol. 110, no. 17, pp. 7091–6, Apr. 2013.
- I. Pertsovskaya, E. Abad, N. Domedel-Puig, J. Garcia-Ojalvo, and P. Villoslada, "Transient oscillatory dynamics of interferon beta signaling in macrophages," BMC Systems Biology, vol. 7, no. 1, p. 59, Jul. 2013.
- J. Liu et al., "Metabolic co-dependence gives rise to collective oscillations within biofilms," Nature, vol. 523, no. 7562, pp. 550–554, Jul. 2015.
- A. Prindle, J. Liu, M. Asally, S. Ly, J. Garcia-Ojalvo, and G. M. Süel, "Ion channels enable electrical communication in bacterial communities," Nature, vol. 527, no. 7576, pp. 59–63, Oct. 2015.
- S. Valverde, S. Ohse, M. Turalska, B. J. West, and J. Garcia-Ojalvo, "Structural determinants of criticality in biological networks," Frontiers in Physiology, vol. 6, p. 127, May 2015.
- B. Sancristobal, B. Rebollo, P. Boada, M. V. Sanchez-Vives, and J. Garcia-Ojalvo, "Collective stochastic coherence in recurrent neuronal networks," Nat Phys, vol. 12, no. 9, pp. 881–887, Sep. 2016.

Principal Investigator: Elena Hidalgo

Oxidative Stress and Cell Cycle

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 currently centered in studying 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 cell survival to stress and on aging.

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 carbonylated proteins.

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 appreciated.

Selected references

- Zuin et al. 2010. Life-span extension by calorie restriction relies on the Sty1 MAP kinase stress pathway. EMBO J. 29:981-991.
- Sansó et al. 2011. Gcn5 facilitates Pol II progression, rather than recruitment to nucleosome-depleted stress promoters, in Schizosaccharomyces pombe. Nucleic Acids Res. 39:6369-6379.
- Fernández-Vázquez et al. 2013. Modification of tRNALysUUU by Elongator is essential for efficient translation of stress mRNAs. PLoS Genet. 9:e1003647.
- Calvo et al. 2013. Dissection of a redox relay: H2O2-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.
- Shah et al. 2016. A transcript-specific eIF3 complex mediates global translational control of energy metabolism. Cell Reports 16:1-12.

Principal Investigator: Miguel López-Botet

Inhibitory and activating receptors of the innate immune system

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

Research project title:

Molecular basis of the adaptive NK cell response to human cytomegalovirus: role of viral factors (M. López-Botet, coordinator). Programa Estatal I+D Retos, Ministry of Economy and Competitiveness (SAF2016-80363-C2-1-R; 2017-2019).

Research project summary

The team has a long-standing experience in research on the biology of human Natural Killer (NK) cells, which contribute to the innate immune response against infections and tumors. The role of NK cells in the response to human cytomegalovirus (HCMV) is currently being studied. HCMV infection may cause severe congenital neurological disorders in newborns, and constitutes a common complication for immunocompromised individuals.
We originally reported that HCMV promotes in some individuals a steady state expansion of a subset of NK cells whose hallmark is expression of the CD94/NKG2C receptor. The molecular and cellular mechanisms underlying the individual variability of this adaptive NK cell response pattern, and its implications in defense to other pathogens and tumors remain open issues. We hypothesize that the differentiation and expansion of adaptive NKG2C+ NK cells are driven by cognate interaction(s) of the CD94/NKG2C receptor with viral ligand(s) expressed by infected cells, being hampered by viral immune evasion strategies. The following objectives will be addressed: a) Characterization of specific ligand(s) for the CD94/NKG2C receptor in HCMV-infected cells. b) Identification of HCMV immune evasion mechanisms influencing the development and effector functions of NKG2C+ adaptive NK cells.

Preferred background of candidates

Immunology, Molecular Biology, Virology,

Selected references

- Gumá M et al. (2004). Imprint of human cytomegalovirus infection on the NK cell receptor repertoire. Blood. 104: 3664-3671.
- Gumá M et al. (2006) Expansion of CD94/NKG2C+ NK cells in response to human cytomegalovirus-infected fibroblasts. Blood. 107:3624-3631
- Magri G et al. (2011) NKp46 and DNAM-1 NK cell receptors drive the response to human cytomegalovirus infected myeloid dendritic cells overcoming viral immune evasion strategies. Blood 117:848-56.
- Muntasell A et al. (2013) NKG2C zygosity influences CD94/NKG2C receptor function and the NK-cell compartment redistribution in response to human cytomegalovirus. Eur J Immunol. 43:3268-78.
- López-Botet M et al. (2014) The CD94/NKG2C+ NK-cell subset on the edge of innate and adaptive immunity to human cytomegalovirus infection. Semin Immunol. 26:145-51.
- Costa-Garcia M et al. (2015) Antibody-mediated response of NKG2Cbright NK cells against human cytomegalovirus J Immunol. 194:2715-24.
- Muntasell A et al. (2016) Relationship of NKG2C Copy Number with the Distribution of Distinct Cytomegalovirus-Induced Adaptive NK Cell Subsets. J Immunol. 196:3818-27.

Principal Investigator: Andreas Meyerhans

Virology Unit

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

Research project title

Mechanisms of HIV latency control

Research project summary

It is now evident that the commonly used antiretroviral drugs will not be able to eliminate HIV from an infected individual. For attempting to achieve an HIV cure, it is essential to better understand (i) immune control mechanisms of the chronic infection state and their regulation, (ii) the reservoir of latently infected cells, and (iii) mechanisms of latency reversal. We recently started to collaborate with clinicians, immunologists and geneticists in Barcelona to address these issues. The specific aim of the PhD project is to understand HIV latency control in different T cell subsets and to define the controlling elements.

Preferred background of candidates

We are looking for a highly motivated PhD student who can integrate himself smoothly into the project team and can follow an independent research question. The candidate should have an excellent background in human biology and be keen to address challenging problems in infection biology. Knowledge of molecular virology, flow cytometry, and next generation sequencing technology will be of help but are not an essential prerequisite.

Selected references

- Peligero C, et.al., PD-L1 Blockade Differentially Impacts Regulatory T Cells from HIV-Infected Individuals Depending on Plasma Viremia. PLoS Pathog. 11(12):e1005270 (2015).

- Tsunetsugu-Yokota Y, et.al., Homeostatically maintained resting naive CD4+ T cells resist latent HIV reactivation. Frontiers in Micobiology 7:1944 (2016).

- Chen HC et.al., Position effects influence HIV latency reversal. Nature Structural & Molecular Biology 24(1):47-54 (2017).

Principal Investigator: Ricard Solé

ICREA-Complex Systems Lab

http://complex.upf.edu

Research project title

Mathematical and computational approaches to the analysis, characterisation and engineering of synthetic ecosystems.

Research project summary

Within one of our main research fields, namely Bioengineering the Biosphere (http://complex.upf.edu/research/bioengineering-the-biosphere) we have proposed the idea that future adaptation approaches to climate change and its consequences will require using synthetic biology methods to effectively redesign some endangered habitats to avoid their collapse. Several general scenarios have been presented as potential approaches to this goal. They all involve the design and engineering of novel ecological interactions and a preliminary phase (to be developed in this project) is the development of a multi scale theory of Terraformation connecting all key components from genetic engineering to community ecology. This will also be part of another major research domain within the Complex Systems Lab (http://complex.upf.edu/research/major-synthetic-transitions) involving the study of major evolutionary transitions using a new approach, namely the design, modelling and synthesis of alternative living structures and communities.

Preferred background of candidates

The candidate is expected to be familiar with both mathematical models in biology, bioengineering, genetic engineering and synthetic biology as well as a wide range of biological concepts associated to ecology and evolutionary biology. Advanced programming skills are also required.

Selected references

- R Sole (2016) Synthetic transitions: towards a new synthesis. Phil. Trans. Royal Soc. B 371 (1701), 20150438

- R Sole, DR Amor, S Duran-Nebreda, N Conde, M Carbonell and R Montañez (2016). Synthetic collective intelligence. Biosystems 148, 47-61

- R Sole (2015) Bioengineering the biosphere? Ecological Complexity 22, 40-49

- R Sole, R. Montañez and S. Duran-Nebreda (2015) Synthetic circuit designs for earth terraformation. Biology Direct 10:37

Principal Investigator: Olga Valverde

Neurobiology of Behaviour

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

Research project title

Environmental factors contributing to the cocaine relapse in mice. Protective effects of cannabidiol.

Research project summary

Substantance use disorder is a chronic and relapsing psychiatric disorders (DSM5) characterize for the high consumption of a drug in spite of the negative consequences that this consumption produces in the health of the individuals. Drug consumption is maintained to avoid the negative consequences of abstinence. The development of drug addiction is under the influence of genetic and environmental factors. Our goal is to investigate the behavioral and biochemical features of the craving and the relapse to cocaine consumption using the self-administration paradigm in C57BL6/JC mice. We will stress the phases of extinction and relapse by a priming of cocaine or by the exposure to a stressful stimulus due their relevance for the relapse to cocaine abuse. We will evaluate two different environmental factors related to cocaine relapse: i) the binge alcohol consumption during the adolescence, and ii) the chronic stress induced by the maternal separation. We will investigate the protective effects of a chronic tretament with cannabidiol on the capability of cocaine to induce relapse to the consumption. We will analise the behavioral parameters of extinction and relapse in all these different experimental conditions. In the case of animal exposed to maternal separation the differential sex effects on craving will be also analysed. Moreover, biochemical and molecular studies will be carried out in different brain areas relatated to addictive disorders, including prefrontal cortex, dorsal striatum, amygdala and hippocampus. We will investigate glutamatergic signaling by evaluating the levels of AMPA and NMDA receptors in these areas due to their implication in the development of aberrant plasticity related to addiction. Finally, we will measure the endocannabinoid and dynorphin levels in the above mentioned brain areas as biomarkers of the rewarding system state. Our proposal pretends to advance in the knowledge of the mechanisms underliying the craving and the relapse phenomena related to cocaine consumption and to explore the utility of cannabidiol as a new possible therapeutic tool for the management of craving and the relapse in cocaine addiction.

Preferred background of candidates

Biologist, pharmaceutics, biochemists, biomedicine scientists.

Selected references

- Esteve-Arenys A, Gracia-Rubio I, Cantacorps L, Pozo OJ, Marcos J, Rodríguez-Árias M, Miñarro J, Valverde O. Binge ethanol drinking during adolescence modifies cocaine responses in mice. J Psychopharmacol. 2017 Jan;31(1):86-95.
- Gracia-Rubio I, Valverde O, Martinez-Laorden E, Moscoso-Castro M, Milanés MV, Laorden ML. Maternal Separation Impairs Cocaine-Induced Behavioural Sensitization in Adolescent Mice. PLoS One. 2016 Dec 9;11(12):e0167483. doi: 10.1371/journal.pone.0167483.
- Blanco-Gandía MC, Cantacorps L, Aracil-Fernández A, Montagud-Romero S, Aguilar MA, Manzanares J, Valverde O, Miñarro J, Rodríguez-Arias M. Effects of bingeing on fat during adolescence on the reinforcing effects of cocaine in adult male mice. Neuropharmacology. 2017 Feb;113(Pt A):31-44.
- Johansson EM, García-Gutiérrez MS, Moscoso-Castro M, Manzanares J, Valverde O. Reduced Contextual Discrimination following Alcohol Consumption or MDMA Administration in Mice. PLoS One. 2015 Nov 13;10(11):e0142978.
- Gracia-Rubio I, Moscoso-Castro M, Pozo OJ, Marcos J, Nadal R, Valverde O. Maternal separation induces neuroinflammation and long-lasting emotional alterations in mice. Prog Neuropsychopharmacol Biol Psychiatry. 2016 Feb 4;65:104-17.
- Mateos-García A, Manzanedo C, Rodríguez-Arias M, Aguilar MA, Reig-Sanchis E, Navarro-Francés CI, Valverde O, Miñarro J, Arenas MC. Sex differences in the long-lasting consequences of adolescent ethanol exposure for the rewarding effects of cocaine in mice. Psychopharmacology (Berl). 2015 Aug;232(16):2995-3007.