PHD FELLOWSHIP ON GENE THERAPY

INPhINIT is a new doctoral fellowship programme devoted to attracting international Early-Stage Researchers **promoted by the "la Caixa" Foundation** with the aim of supporting the best scientific talent and fostering innovative and high-quality research in Spain by recruiting outstanding international students and offering them an attractive and competitive salary and environment for conducting research of excellence. More information about the program here.

We are recruiting an outstanding **PhD candidate of any nationality** to be recruited by the INPhINIT program to enjoy a 3-year employment contract at the Functional and Translational Neurogenetics Unit at the Institute for Health Science Research Germans Trias i Pujol (IGTP) located in Badalona (Barcelona), Spain. More information about the Neurogenetics Unit here.

The candidate would work on the project: **AAV-mediated gene therapy for Friedreich Ataxia**.

The candidate must have a strong motivation for scientific research and solid background in molecular biology, biochemistry, and/or cell biology with a particular interest in **neuroscience**. Undergraduate or post-graduate laboratory experience on molecular or cellular biology is strongly recommended. Two letters of recommendation from graduate mentors would be requested during the selection process. Solid knowledge with certificate of English language is required (see bases).

The successful candidate would establish a personal career development plan including transnational, intersectoral and interdisciplinary mobility opportunities, and attend a full range of complementary training courses and workshops.

Deadline for submitting applications:

1. **INCOMING**: for Candidates who must **not** have resided or have carried out their main activity (work, studies, etc.) in Spain for more than 12 months in the 3 years immediately prior to the call deadline. **Deadline: 6th February 2019.** More information here

2. **RETAINING**: Candidates must have resided or have carried out their main activity (work, studies, etc.) in Spain for more than 12 months in the 3 years immediately prior to the call deadline. **Deadline: 27th February 2019.** More information here.

Please send your CV, motivation letter, and 2 references before January 15th to neurogenetica@igtp.cat.

Research project:

Friedreich's ataxia (FRDA) is a rare inherited progressive, neurodegenerative disease with a typical onset in the adolescence or childhood. The clinical signs consist of progressive sensory and cerebellar ataxia, speech disorder, cardiomyopathy, diabetes, and loss of reflexes. FRDA is the most common form of inherited ataxia, with an estimated prevalence is of 4.3 cases per 100,000 inhabitants. There is no cure or effective treatment for FRDA. The disease is caused by a DNA mutation consisting of an unstable expanded GAA triplet in homozygosis within the frataxin gene, resulting in a decrease of mitochondrial protein frataxin. The age of onset is often correlated with the number of GAA repeats. Frataxin deficiency results in deficit of mitochondrial function, increased free-radical production, and mitochondrial accumulation of iron, damaging principally cerebellar, spinal cord, heart and liver functions.

A new generation human recombinant vector based on adeno-associated virus expressing human frataxin protein have been generated. The vector is optimized for neuronal transduction of dorsal root ganglions in the spinal cord and neurons in the deep cerebellar nuclei, the two target nerve structures primarily affected in FRDA. The construct includes unique DNA regulatory elements and modifications that enable optimal and cell-specific *in vivo* expression of human frataxin in transduced cells. The project aims to obtain an in vivo proof-of-concept in a disease mouse model demonstrating that recombinant frataxin protein efficiently transduces and localizes to cellular mitochondria in target cells and tissues of both the central nervous system (CNS) and periphery, which mainly include dorsal root ganglia neurons in the spinal cord as well as cerebellar, cardiac and pancreas cells. Sensorial electrophysiological evoked potentials of periphery nerves and motor coordination of treated FRDA mice will evaluate efficacy of the product in preventing onset of the clinical signs.

Research Group description:

The **Neurogenetics Research Unit** was founded by Dr. Antoni Matilla in 2009. It is located in the Can Ruti Campus and is integrated within the Department of Neurosciences of the Hospital Germans Trias i Pujol (HUGTiP). It also provides genetics diagnoses to the Neurology and Pediatrics Services from the University Hospital Germans Trias i Pujol (HUGTiP) and external Hospitals from all over Spain.

Scientific research in the Unit investigates the genetic and molecular mechanisms underlying neurodegenerative processes. The ultimate goal of the research is to identify genes, their products and molecular pathways involved in order to effectively provide genetic diagnosis and selective therapeutic approaches to patients. The Unit uses multidisciplinary strategies to identify genes, proteins and other gene products involved in the function and dysfunction of the nervous system by using next-generation RNA and DNA sequencing, functional assays, biochemical, proteomics, and molecular neurosignalling studies.

An important objective of the Unit is to identify and implement treatments for various neurodegenerative diseases. To achieve this, in 2015 the functional biology and experimental therapies laboratory (FBET) was established by Dr. Antoni Matilla and Dr. Ivelisse Sánchez-Díaz. The laboratory uses gene therapy technology based on adenoassociated virus vectors (AAV), screenings of drug compounds and genetic libraries, and in vitro and in vivo preclinical testing of new therapeutic candidates.

Furthermore, we develop large-scale genomics technologies and bioinformatics tools to identify genetic causes underlying neurological diseases.

The **Germans Trias i Pujol Research Institute (IGTP)** is a public research centre located in Badalona a few kilometers away from Barcelona, in the Autonomous region of Catalonia in Northern Spain dedicated to increasing scientific knowledge and transferring it to improve the care and lives of patients. IGTP is accredited as Research Centre of Excellence by both the Spanish Ministry and the Catalan Government and is included in the top 10 Health Research Institutions in Spain. More information about the Institute here.

In June 2018 the IGTP incorporated the new **Comparative Medicine and Bioimage Centre (CMCiB),** a state-of-the-art centre dedicated to biomedical research and training. This new research infrastructure aims to become a reference centre for comparative medicine, surgery, bioimaging and computational models in Europe, while at the same time developing alternative in vivo research methods. More information about the CMCiB here.