"la Caixa" Foundation

DOCTORAL INPhINIT FELLOWSHIPS PROGRAMME – INCOMING

PhD POSITIONS OFFER FORM

Position

Project Title/ Job Position title: *Single-cell gene regulatory network alterations upon aging and in neurodegeneration in Alzheimer's Disease*

- **Area of Knowledge: LIFE SCIENCES**

1. **Group of disciplines: (choose one option**)
   Human Biology, Microbiology, Molecular Biology, Genetics, Cellular Biology, Genomics and Proteomics, Biochemistry

2. **Research project/ Research Group description (max. 2.000 characters)**
   Our understanding of Alzheimer's Disease (AD) pathogenesis is currently limited by the impossibility of obtaining live neurons from patients and the inability to model the main risk factor of the disease: aging. Now, it may be possible to overcome these challenges by taking advantage of direct cellular differentiation methods, which allow generating neurons and glial cells in vitro from patients somatic cells bypassing the cellular reprogramming step. These cells not only have the genetic background of the patients but also retain aging-associated epigenetic changes. That is, they have morphological traits and transcriptomic profiles similar to that of aged cells in vivo.
   Here, we will take advantage of this novel system to: (i) investigate how aging modifies cell-type specific regulatory programs in neural and glial cells and gain mechanistic insights on AD pathogenesis; and (ii) study the relative contribution of autonomous and non-autonomous signaling to neurodegeneration and its alterations upon aging. We will achieve these goals by combining several ground-breaking approaches ranging from in vitro differentiation methods and CRISPR/Cas9 technology to high-throughput single-cell transcriptomics and computational modelling, which are all established in the lab and to which I have significantly contributed during my career. These studies will provide a new holistic view about the early functional alterations in AD patients that predate neurodegeneration, with a focus on cell-type specific gene and RNA regulatory networks.

3. **Job position description (max. 2.000 characters)**
   We are seeking a motivated and skilled PhD student with background in Computational Biology, Bioinformatics, Biology or similar with strong statistics and programming skills.

Hybrid students interested in developing the computational and experimental approaches are also welcomed.

The Plass Group offers a highly dynamic, international, and intellectually stimulating working environment with cutting-edge techniques such as single-cell transcriptomics, human pluripotent stem cells and genome editing. The PhD candidate will also have the opportunity to perform internships in external laboratories.

The selected candidate will be responsible for implementing and developing computational pipelines for the study of Cell-Cell communication and Gene Regulatory Networks at the single-cell level. The final aim will be to define regulators that are responsible for GRN alterations during aging and/or in AD in a cell type specific manner and assess the relative contribution of transcriptional and post-transcriptional regulators to GRN control. This work will have a strong biomedical impact and significantly contribute to deepen our understanding of why aging is the main risk factor for AD development and to pinpoint the relative contribution of different cell types to disease onset and progression. Additionally, the candidate will be involved in the design of experimental validations to confirm the finding of the analyses.

Hybrid applicants will also learn iPSC cell culture and genetic manipulation tools such as CRISPR/Cas9, single-cell omics technologies and molecular biology techniques.

Group Leader

1. Title: Dr.
2. Full name: Mireya Plass
3. Email: mplass@idibell.cat
4. Research project/ Research Group website (Url): https://p-cmrc.cat/research/plass-group/
5. Website description: Lab website at P-CMR[C] site

Additional website (optional, max. 5 websites)

1. Url: https://idibell.cat/recerca/area-medicina-regenerativa/programa-de-medicina-regenerativa/regulacio-genica-de-la-identitat-cellular/
2. Website description: Lab website at IDIBELL site