Individual Research Project

ESR 10

THE PROJECT

Epigenetic mechanisms of depression induced by chronic stress or chronic pain in male and female mice: a systematic bioinformatic investigation across sexes and models
(project in collaboration with ESR #11)

Objectives

1/ To conduct the bioinformatic processing of next-generation sequencing data related to gene expression (generated using RNA-Sequencing) and DNA methylation (Enzymatic Methylation Sequencing, EMseq), in 2 mouse models of depression based either on chronic stress or chronic pain, in male and female mice.

2/ To characterize DNA methylation and gene expression changes associated with chronic stress- and chronic pain-induced depressive-like behaviours, in male and female mice.

3/ To conduct systems biology and integrative analyses (GO enrichments, network analyses using eg WGCNA, etc) to identify "hub" genes in each mouse model and sex.

Methodology

This research project is conceived as a joint work conducted in collaboration with ESR 11. The present ESR 10 will be responsible for the bioinformatic processing and integration of the large dataset that will be generated, while ESR11 will be responsible for conducting behavioural and molecular biology experiments.

Accordingly, the ESR 10 will be responsible for the processing of RNA-Sequencing and EM-Seq data. This will first include primary analyses of sequencing data: quality controls, trimming, alignment, gene expression counting, and methylation calling. Second, we will leverage systems biology and integrative analyses to identify molecular mechanisms of depression, in each model and sex. At the differential analysis level, we will perform group comparisons to identify changes in DNA methylation or gene expression that reveal biological pathways most altered as a function of chronic stress or pain. At the systems biology level, we will construct co-expression gene networks (using eg WGCNA). We will seek to reveal co-expression modules that significantly correlate with depression, and that are enriched in depression-related changes in gene expression or DNA methylation. Finally, we will take advantage of these integrative analyses to prioritize "hub" genes that are centrally located among most affected modules, and that will be prioritized for functional *in vivo* studies (conducted primarily by ESR 11).

Expected Results

We will determine the molecular and epigenetic signature of ACC in female and male mice and generate a list of "hub" target genes. In addition, we will compare for the first time the impact of sex differences in the epigenetic regulation of gene expression in mouse models of depression.

Supervisors and host organisations

Main supervisors and recruiting organisation:
Pierre-Eric Lutz,
CNRS, Institute of Cellular & Integrative Neurosciences (INCI UPR 3212), University of Strasbourg, Strasbourg, France

Co-supervisor:
Benoit Labonté,
Cervo Institute, Laval University, Québec City, Canada

Co-supervisor (company):
Jean-Luc Néron, Doric Lenses, Québec City, Canada

Planned mobility track and secondments:

CNRS, France: 18 months

Laval University, Canada: 15 months

Doric Lenses, Canada: 3 months

Enrolment in Doctoral degrees:

Laval University & University of Strasbourg diplomas.

THE POSITION

Duration

36 months

Salary

3 783.39 €/ per month (gross)

Allowance

Mobility allowance 600/per month (gross), family allowance if applicable 500/per month (gross)

THE CANDIDATE PROFILE

Academic prerequisite

We are looking for an enthusiastic, knowledge-driven student with a Master degree in Bioinformatics or related fields.

Knowledge on specific topics

Candidates should have a strong background in bioinformatics and programming. A good knowledge in biology is also expected.

Technical skills

Prior experience in bioinformatics is mandatory, as well as experience in the use of R or Python programming languages. Experience in the use of calcul centers and workload managers (eg Slurm), virtual environments (Conda, venv, etc) and workflow management systems (eg Snakemake) is a plus.

Exclusion criteria

Nationality is not a criterion: Researchers can be of **any nationality**. Rather, it is the location of the ESR's residence or main activity during the 3 years prior to their recruitment that shall be considered. Indeed, the candidate **must not have resided** or carried out their main activity (work, studies, etc.) **in France** (the country of the recruiting beneficiary) for more than 12 months in the 3 years immediately before the recruitment date (October 1st, 2021). Compulsory national service, short stays such as holidays, and time spent as part of a procedure for obtaining refugee status under the Geneva Convention are not taken into account.

The candidate shall, at the time of recruitment, be in the **first four years** (full-time equivalent research experience) of their research careers and **have not been awarded a doctoral degree**.

Apply for this position at https://happy-form.u-strasbg.fr/
before August 1st, 2021