Funded PhD project in the team Studying the Dynamics of Proteomes, Grenoble, France

Title of the project:

Studying novel histone acylations in the regulation of gene expression

Project summary:

In the nucleus of eukaryotes, DNA wraps around octamers of **histone proteins** to form a structure called chromatin. Dynamic **post-translational modifications** (PTMs) of histones are essential to regulate gene expression. In the present project, we aim to study the role of various **novel acylations of histone H3**, to improve our understanding of their functions in the **regulation of gene expression**. We will explore these questions in the context of **mouse spermatogenesis**, a biological model perfectly adapted to the exploration of the functional role of new histone marks.

Roles of the PhD student:

The PhD student will work during his research project with **large-scale proteomics technologies**, on **integrative bioinformatics analysis of multi-omics data** (proteomics, epigenomics and transcriptomics) as well as on the **experimental validation** of his discoveries with different **biochemical methods**.

In details, the PhD student will perform the preparation of histone samples for their proteomic analysis, interpret these data to highlight variably modified lysine residues in the course of mouse spermatogenesis. He/she will also perform different experiments of biochemistry: confirm proteomics results by Western Blots; affinity-purify crosslinked protein/DNA complexes using antibodies raised against selected histone modifications, to identify both the proteins preferentially binding onto them (by proteomics) and the genomic regions bound by these histone molecules (by ChIP-seq). The student will also be implicated in the integration of the ChIP-seq data with available RNA-seq data to assess the impact on gene expression of histone lysine modifications. This training is compatible with a future career in either the academic or the private sector.

Desired skills:

This PhD project lies at the interface between analytical chemistry, biology and bioinformatics to handle large-scale omics datasets. The candidate should have at least a theoretical training in some analytical techniques to characterize biomolecules, and a strong interest to learn proteomics. He/she should ideally have had classes and/or practical experience in biochemistry. The candidate should also be interested in bioinformatics analysis and biological interpretation of large-scale multi-omics datasets (R language). This PhD project will be performed under the guidance of Delphine Pflieger, who is an expert in the proteomic analysis of histones, and in tight collaboration with Julie Cocquet (Institut Cochin, Paris), expert in mouse spermatogenesis, and Christophe Battail (CEA Grenoble), expert in bioinformatics of genomics data.

How to apply:

Please send a CV, a motivation letter and at least one letter of recommendation to Delphine Pflieger, at delphine.pflieger@cea.fr.

Location:

You will work in the EDyP team (Studying the Dynamics of Proteomes), whose main specialty lies in the use of mass-spectrometry-based proteomics to characterize complex protein samples. The lab is equipped with latest generation MS instruments and has developed software tools to help identify and quantify proteins and their post-translational modifications.

Website:

http://www.edyp.fr/web/2019/10/22/integrative-omics/

Keywords:

Histone lysine acylations, selective protein assemblies, quantitative proteomics, functional genomics, spermatogenesis, multi-omics data integration.

Relevant publications of the group:

El Kennani S, Adrait S, […], Pflieger D*, Govin J*.
MS_HistoneDB, a manually curated resource for proteomic analysis of human and mouse histones.
Epigenetics & Chromatin, 2017, Jan 10;10:2. doi: 10.1186/s13072-016-0109-x.

El Kennani S*, Crespo M, Govin J, Pflieger D*.
Proteomic analysis of histone variants and their PTMs: strategies and pitfalls.
Proteomes. **2018** Jun 21;6(3). pii: E29. doi: 10.3390/proteomes6030029

Crespo M, […], Battail C*, Cocquet J*, Pflieger D*.
Multi-omic analysis of gametogenesis reveals a novel signature at the promoters and distal enhancers of active genes.
Nucleic Acids Res., 2020. doi:10.1093/nar/gkaa163

Hseiky A, Crespo M, Kieffer-Jaquinod S, Fenaille F, Pflieger D*.
Small Mass but Strong Information: Diagnostic Ions Provide Crucial Clues to Correctly Identify Histone Lysine Modifications.
Proteomes. 2021 Apr 23;9(2):18. doi: 10.3390/proteomes9020018.