Funded post-doctorate in 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. Acetylation of histone lysines has been discovered more than 50 years ago; this PTM is now well known to be associated with increased chromatin accessibility and active gene transcription. Importantly, abnormal regulation of this histone mark can lead to developmental defects and cancers. Lysine acetylation is classically described to mark active transcription both when localized at gene promoter regions, or when present at distant genomic regions, called distal enhancers, that regulate gene expression via long-range interactions made by chromatin looping. However, the presence of this mark alone appears insufficient to define active promoters and enhancers. Over the past decade, a wealth of other lysine acylations resembling acetylation but varying in length and hydrophobicity have been described, whose functions largely await characterization. In the present project, we aim to study the role of various novel acylations of histone H3 at promoters and distal enhancers, to improve our understanding of their functions in the regulation of gene expression and to compare them to acetylation-dependent mechanisms. We will explore these questions in the context of mouse spermatogenesis, in which several new lysine acylations were discovered.

Your tasks:
- Preparation of histone samples for their exploratory and targeted proteomic analyses; interpretation of these data to quantify lysine acylations in successive male germ cell stages.
- Affinity-purification of crosslinked protein/DNA complexes using antibodies raised against selected histone modifications, to identify both the genomic regions bound by these histone molecules (by ChIP-seq) and the proteins preferentially binding onto them (by proteomics).
- Opportunity to spend several months in the laboratory of Till Bartke (Helmholtz Zentrum München, Munich, Germany) to learn and apply the technique of nucleosome pulldown.
- Be involved in the integration of the ChIP-seq data with available RNA-seq data to assess the impact on gene expression of selected histone lysine modifications.
- The hired post-doctorate will be responsible for carrying out and orienting the project, while benefitting from regular interaction with the PIs collaborating on this project.

Desired skills:

This post-doctoral project lies at the interface between biochemistry, analytical chemistry and bioinformatics to handle large-scale omics datasets. The candidate should have a solid experience in biochemistry to prepare and characterize protein complexes (immuno-purification, Western Blots, etc) and/or in proteomics (preferentially in the field of quantitative analysis of protein modifications). The candidate should also be interested in learning how to make biological sense from large-scale omics datasets (e.g. RNA-seq data) using scripts written in R language. He/she is expected to master speaking and writing in English, to be able to write articles, and to be endowed with team spirit. We are looking for a highly motivated and qualified individual holding, or shortly expecting to be awarded, a PhD degree in **biochemistry or analytical chemistry.** The candidate will have proven research skills in biochemistry and proteomics attested by a track record of research achievement and publications in internationally recognized peer-reviewed journals.

Only applications from junior candidates (i.e. with < 2 years of postdoctoral experience) with the above-described profile will be considered.

Keywords:
Histone lysine acylations, selective protein assemblies, quantitative proteomics, functional genomics

Contact person:
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Host laboratory:
Team "Studying the Dynamics of Proteomes" (EDyP): http://www.edyp.fr/web/research-activity/
EDyP team is located on the CEA center of Grenoble. Research in biology is supported by a large technological expertise (omics technologies, structural biology, imaging, pharmacology and preclinical expertise) developed through several facilities and national infrastructures. Grenoble is an international center of excellence for research and development. The city hosts research organizations such as EMBL, CNRS, Inserm, INRIA, INRAE and CEA and benefits from an outstanding location at the foot of the French Alps.

Collaborators:
Julie Cocquet, Institut Cochin, Paris, France (expertise in the study of genetic/epigenetic regulation during mouse spermatogenesis).
Christophe Battail, CEA Grenoble, France (expertise in the bioinformatics handling of genomics data).
Till Bartke, Helmholtz Zentrum München, Munich, Germany

Other information:
Duration: 2.5 years.
Salary: about 2600 Euros brutto.
Start date: maximum end of 2022.
Please send a CV, a motivation letter and two letters of recommendation to D. Pflieger (delphine.pflieger@cea.fr).

Relevant publications:

El Kennani S, Adrait S, Shaytan A, Khochbin S, Bruley C, Panchenko AR, Landsman D, **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** May 7;48(8):4115-4138. . 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