MASTER 2 BMC
PARCOURS GENOPATH
ANNÉE 2018-19

Titre du stage

Epigenetics of cancer and stem cells:
a CRISPR screening approach to study DNA methylation

Nom, adresse de l'Unité d'accueil / Nom du responsable de l'unité :

Epigenetics and Cell Fate Unit/ UMR7216 CNRS/Univ. Paris 7

Dir: Jonathan Weitzman

Nom, adresse de l'Equipe d'accueil / Nom du responsable d'équipe :

Dynamics and Interpretation of DNA methylation - Team Defossez

Nom, tel, adresse e-mail de l'encadrant de stage :

Pierre-Antoine Defossez, 01 57 27 89 16, pierre-antoine.defossez@univ-paris-diderot.fr
Université Paris 7, case 7042, 75205 Paris CEDEX 13

Sujet de stage :

DNA methylation is essential in mammals. It controls: chromatin assembly; the expression of imprinted genes; the expression of tissue-specific genes; and the repression of transposable elements. Abnormalities of DNA methylation are linked to human diseases, such as ICF syndrome, Prader-Willi and Angelman syndromes, and many cancers. Our team works on the mechanisms of DNA methylation establishment, maintenance, and functional interpretation. We are looking for an M2 candidate, either for just a one-year internship, or to continue by a PhD. We have had 100% success at getting PhD fellowships for our students so far (7 out of 7).

We offer a choice of two projects:

1-Mechanisms of DNA methylation in mouse ES cells
The project aims at identifying factors that are necessary for DNA methylation in mammals. It uses as a model system mouse ES cells, and a genome-wide CRISPR screening approach. Previous experience with ES cells, and basic bioinformatic skills are a plus, but are not strictly required.

2-Mechanisms of abnormal gene repression in cancer cells

This project aims at understanding what causes the abnormal epigenetic repression of genes in cancer cells, and to determine how this process can be acted on therapeutically. For this project as well, we are developing a CRISPR screen. Experience with tissue culture, molecular biology, and bioinformatics, are a plus, but are not strictly required.

The M2 student will be closely supervised by an experienced scientist. We use cutting-edge techniques including epigenomics, proteomics, CRISPR, and live-cell imaging. We are confident we offer an excellent chance to learn a lot, working on an exciting project in a stimulating environment.

Technologies utilisées :
Cell culture, molecular biology, genomics, CRISPR, genetic screens.

Mots clés :
Epigenetics, mammals, DNA methylation

Publications d'intérêt :

Loss of the methyl-CpG binding protein ZBTB4 alters the mitotic checkpoint and promotes tumorigenesis
Roussel-Gervais A., Naciri I., Kirsh O., Kasprzyk O., Velasco G., Grillo G., Dubus P., Francastel C., and Defossez P.A.
Cancer Res. 2017 Jan 1;77(1):62-73.

Methylation of DNA Ligase 1 by G9a/GLP Recruits UHRF1 to Replicating DNA and Regulates DNA Methylation.
Ferry L, Fournier A, Tsusaka T...Shinkai Y, and Defossez PA.
Mol Cell. 2017 Aug 17;67(4):550-565.

Stabilization of the methyl-CpG binding protein ZBTB38 by the deubiquitinase USP9X limits the occurrence and toxicity of oxidative stress in humancells
Miotto B, Marchal C, Adelmant G, Guinot N, Xie P, Marto JA, Zhang L, and Defossez P.A.
Nucleic Acids Research, 2018 Feb 27. doi: 10.1093/nar/gky149