Master Biologie Moléculaire et Cellulaire 'BMC',
Université de Paris - *UFR Sciences du Vivant*

Parcours : **Biologie et Développement Cellulaires 'BDC'**
http://www.master2bdc.fr/
Fiche de Projet de Stage M2, Année 2021-2022

UMR7216 CNRS/Université Paris 7 **Intitulé Equipe (comme identifiée par l'AERES):** **Domaines Fonctionnels des Génomes Eucaryotes** **ED d'appartenance : HOB** **Responsable de l'Equipe :** **Pierre-Antoine Defossez**	**Contacts** Adresse : CNRS UMR7216, Université Paris 7 Bâtiment Lamarck, case 7042 75205 Paris CEDEX13 Email : pierre-antoine.defossez@u-paris.fr Tel : 01 57 27 89 16 **Responsable du Stage: Pierre-Antoine Defossez**

Titre du projet : Epigenetics of cancer and stem cells

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 to continue on to a PhD, and offer a choice of 2 research projects.

Project 1- Dynamics of DNA methylation in stem cells

The broad question of this project is: "How is DNA remethylation coupled to DNA replication and to DNA repair?" Two proteins are known to be essential for DNA remethylation. The first is the maintenance DNA methyltransferase, DNMT1. The other is UHRF1, which interacts with DNMT1 and recruits it to DNA. A key question is: how is UHRF1 itself directed to the hemimethylated regions? We have discovered a very original for this recruitment, involving a histone mimic in a replication protein. This project follows up and expands this observation, using mouse ES cells, and complementary approaches of genomics, CRISPR mutagenesis, and live imaging.

Project 2- Epigenetic regulation of transcription in cancer

The broad question of this project is: "What drives the misexpression of epigenetically regulated genes in cancer? Can these mechanisms serve as targets for therapy?"

We have carried out large scale siRNA and gain-of-function genetic screens in normal screens to uncover signaling pathways linked to gene misexpression in cancer, and discovered a new and important cascade linking epigenetic actors to signaling. We propose additional genetic screens to further delineate the links between cellular signaling and epigenetics in breast cancer. This project involves the culture of primary human cells, viral vectors, CRISPR approaches, genomics, molecular and cellular biology.

The M2 student will be closely supervised by an experienced scientist and a technician. 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. We have had excellent success at the Ecole Doctorale, with 100% success rate (10/10 students obtained a PhD fellowship, 2 were ranked 1st).

Publications de l'équipe relatives au projet de stage (max 5)

Roussel-Gervais … and Defossez PA, Cancer Res 2017, PMID: 27815388
Ferry … and Defossez PA, Molecular Cell 2017, PMID: 28803780
Miotto … and Defossez PA, Nucleic Acids Research 2018, PMID: 29490077
Kori … Defossez PA* and Arita K*, Structure 2019, PMID: 30639225

Naciri … and Defossez PA, Nucleic Acids Research 2019, PMID: 30753595