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

Parcours : **Biologie et Développement Cellulaires 'BDC'**
http://www.master2bdc.fr/
Fiche de Projet de Stage de M2, 2024-2025

Unité INSERM ou CNRS ou Université : Institut Curie, CNRS UMR 3215 / INSERM U934 **Intitulé Equipe :** Stem cells and tissue homeostasis **ED d'appartenance :** ED515 - Complexité du Vivant **Responsable de l'Équipe :** Allison Bardin	**Responsable du Stage :** Allison Bardin & Louis Gervais **Contacts** Adresse : Institut Curie 26 rue d'Ulm 75005 Paris - France Email : allison.bardin@curie.fr & louis.gervais@curie.fr Tel : 01 56 24 65 62 - 01 56 24 65 80

Titre du projet : The role of heterochromatin in the control of adult intestinal stem cells in Drosophila

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)

Adult stem cells (ASCs) ensure the renewal and repair of organs throughout life by producing specialized tissue cells. Chromatin organization, by modulating gene expression, participates in the establishment of transcriptional programs dictating the choice between stem cell renewal and differentiation. Many studies have highlighted the importance of epigenetic regulation of stem cells, especially during development. However, our **understanding of chromatin organization and its role in ASCs**, in the context of tissue homeostasis, remains partial due to the lack of good *in vivo* study models.

The *Drosophila* intestine is an excellent example of an adult tissue in constant renewal thanks to its intestinal stem cells, comparable to those of the skin, lungs or intestine in mammals. Using this model, we seek to better understand how control of chromatin organization influences the regulation of gene expression in ASCs, thus contributing to tissue homeostasis.

In previous work, we have shown that **HPla protein-associated heterochromatin** is spatially reorganized during differentiation. The project presented here is organized around this plasticity of heterochromatin and has two main objectives (1) Deepen our **understanding of the role and organization of heterochromatin in the intestinal lineage** and (2) Study **how stem cells integrate environmental signals at the level of heterochromatin to adjust their activity.** This will involve :

• A characterization of the organization of heterochromatin organization in each cell type of the intestinal lineage by immunostaining for heterochromatin marks and genome-wide mapping of these marks.
• An analysis of the intestinal lineage in mutant or RNA interference contexts for heterochromatin regulators.
• An investigation of the influence of the environment on heterochromatin in the intestine.

The student will use genetic tools available in *Drosophila*. He/she will perform immunostaining followed by microscopy and image processing. The use of CUT&Run will allow the student to approach high-throughput sequencing and acquire notions of data analysis.

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

1. Josserand M., Rubanova N…, Gervais L*., Bardin A.J.* (2023). Chromatin state transitions in the Drosophila intestinal lineage reveal principles of cell type specification. Dev. Cell. Dec 18;58(24):3048-3063.e6. 10.1016/j.devcel.2023.11.005. * Co-corresponding authors.

2. Gervais L*…, Bardin A.J*. (2019). Stem Cell Proliferation Is Kept in Check by the Chromatin Regulators Kismet/CHD7/CHD8 and Trr/MLL3/4. Dev. Cell 49, 556-573.e6. * Co-corresponding authors.

3. Andriatsilavo M., Stefanutti M …, Gervais L., Gillet-Markowska A., Al Zouabi L., Schweisguth F., Bardin A.J. (2018). Spen limits intestinal stem cell self-renewal. PLoS Genet. 2018 Nov 19;14(11):e1007773. doi: 10.1371/journal.pgen.1007773.

4. Gervais, L., and Bardin, A.J. (2017). Tissue homeostasis and aging: new insight from the fly intestine. Curr. Opin. Cell Biol. 48, 97–105.