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 2023-2024

Unité INSERM ou CNRS ou Université : Sorbonne-université -Institut de Biologie Paris Seine - Laboratoire de Biologie du développement – UMR7622 **Intitulé Equipe :** Cycle et Détermination Cellulaires **ED d'appartenance :** CDV -ED 515 **Responsable de l'Equipe :** Michel Gho	**Responsable du Stage :** Agnes Audibert **Adresse** : SU – IBPS -UMR7622 9 quai Saint Bernard 75005 Paris **Email** : agnes.audibert@sorbonne-universite.fr **Tel** : 0144272249

Titre du projet : Characterization of spatio-temporal organization of constitutive heterochromatin in developmental cellular contexts to advance understanding of diseases genesis.

Satellites DNA is the major component of constitutive heterochromatin (C-het) of the eukaryotic genome and recent discoveries highlight their fundamental role in cell determination and disease[1,2]. Satellite DNAs are non-coding, repetitive DNA abundant in centromeric, pericentromeric and telomeric regions. They are characterized by the histone mark H3K9me2/3, which is recognized by the HP1 protein[3]. Under physiological conditions, some satellites DNA are transcribed at low level, as they are temporally and spatially regulated[4]. However, in different pathological conditions such as in cancers of the pancreas, lung, kidney and prostate, a significant increase in satellite DNA transcripts is observed[5]. In addition, HP1 is deeply associated with tumorigenesis via modulating diverse molecular mechanisms such as cell cycle, and the regulation of oncogenes or tumor suppressors[6]. Thus, satellite DNA is not as stable and inert as originally thought. Furthermore, c-het has been described as organized into subdomains that change during cell cycle progression and the establishment of cell identity[1,7].
The aim of this project is to analyze the spatio-temporal dynamics of satellites sequence and the effects of their perturbations on development, using the *Drosophila* mechanosensory organs (bristles). Using original tools "TALE-light"[8] to follow directly heterochromatic sequences *in vivo*, we show that c-het accessibility changes during cell cycle progression. Thus, we propose to analyze the involvement of different satellite DNA sequences during development. The M2 student will continue *in vivo* experiments to follow satellites dynamics during bristle cell lineage commitment using TALE-light[8]. He/She will investigate their role in coordinating cell proliferation and cell identity establishment under conditions where particular satellites sequences organization or transcription will be disrupted by overexpression of specific TALE-light or by modifying histone marks on satellites by epigenome editing. Moreover, to investigate the transcriptional control of satellite $(AAGAG)_n$, the student will analyze the formation of the bristles in context of GAF loss or gain of function since this transcription factor is required to silence this satellite during embryo development[9].
This project will help understand how some satellite sequences contribute to generate cellular diversity and will provide insights into the mechanisms underlying identity changes in tumorigenesis.

1.McCarthy, R. L. *et al. Trends Biochem. Sci.* **48**, 513–526 (2023).
2.Carone, D. M. *et al*. *Semin. Cancer Biol.* **23**, 99–108 (2013).
3.Janssen, A., *et al*. *Ann. Rev. of Cell and Dev. Biol.* **34**, 265–288 (2018).
4.Sermek, A., *et al*. *Int. J. Mol. Sci.* **22**, 1–16 (2021).
5.Ting, D. T. *et al. Science* **331**, 593–596 (2011).
6.Jeon, Y. H. *et al. Cancers (Basel).* **14**, 1–15 (2022).
7.Swenson, J. M., *et al*. *Elife* 1–37 (2016).
8.Yuan, K., *et al*. *Cur. Biol.* **24**, R144–R145 (2014).
9.Gaskill, M. M. *et al*. *Dev. Cell* **58**, 1610-1624.e8 (2023).

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

- Cortical Cyclin A controls spindle orientation during asymmetric cell divisions in Drosophila. (2022) Darnat P, Burg A, Sallé J, Lacoste J, Louvet-Vallée S, Gho M, Audibert A. Nat Commun. 2022 May 17;13(1):2723. doi: 10.1038/s41467-022-30182-1.

- A neural progenitor mitotic wave is required for asynchronous axon outgrowth and morphology. Lacoste J, Soula H, Burg A, Audibert A, Darnat P, Gho M, Louvet-Vallée S. Elife. 2022 Mar 7;11:e75746. doi: 10.7554/eLife.75746.

- Simon F, Ramat A, Louvet-Vallée S, Lacoste J, Burg A, Audibert A*, Gho M*. (2019) Shaping of Drosophila Neural Cell Lineages Through Coordination of Cell Proliferation and Cell Fate by the BTB-ZF Transcription Factor Tramtrack-69. Genetics. Jul; 212(3):773-788. * These authors contributed equally to this work

- Ramat A, Audibert A, Louvet-Vallée S, Simon F, Fichelson P, Gho M. (2016). Escargot and Scratch regulate neural commitment by antagonizing Notch activity in Drosophila sensory organs. Development. 143(16):3024-34.

- Ayeni JO*, Audibert A*, Fichelson P, Srayko M, Gho M, Campbell SD. (2016) G2 phase arrest prevents bristle progenitor self-renewal and synchronizes cell division with cell fate differentiation. Development. 143(7):1160-9. These authors contributed equally to this work