# MASTER 2 BMC
# PARCOURS GENOPATH
# ANNEE 2024-2025

## Titre :

**Rôle de l'organisation de la chromatine dans la régulation de l'expression des gènes**

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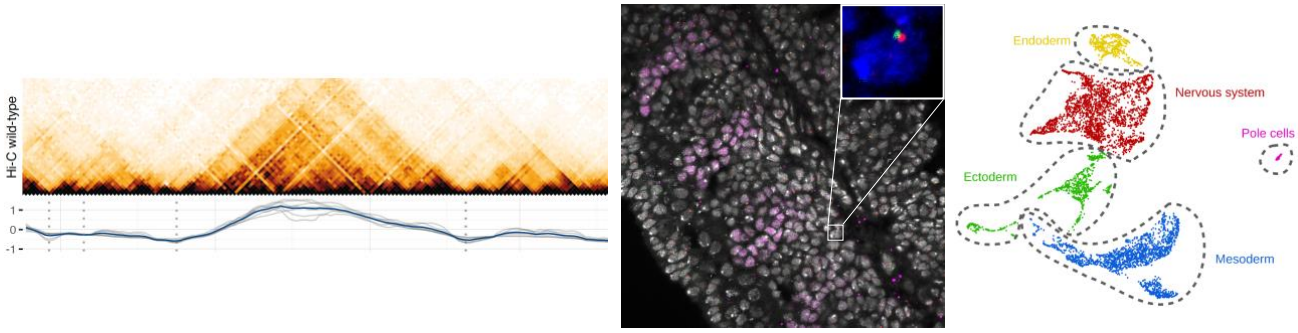
**Sujet de stage :**
Our team investigates how gene expression is precisely regulated both in time and space during embryogenesis, allowing the development of a complex organism from a single pluripotent cell. The main drivers of this regulation are short regulatory elements called enhancers, which can dictate the spatial and temporal expression of a gene, even when located at large genomic distances from the promoter of that gene. Our goal is to understand how gene expression is regulated by enhancers, how this regulation is affected by the 3-dimentional organization of the genome in the nucleus, and how spatio-temporal expression patterns vary during embryonic development. For this purpose, we two different model organisms, the *Drosophila melanogaster* embryo and the *Oikoplora dioica* zooplankton, and combine a large array of genetics, genomics (including single-cell OMICs), imaging (including spatial transcriptomics) and computational approaches.
Different projects can be envisioned depending on the students' interests. The projects can be either purely experimental, purely computational or a combination of both. Potential projects include but not limited to:

- Characterize the effect of mutations in enhancers using quantitative immunostaining, Flow cytometry, and single-molecule FISH
- Explore the role of insulator elements in setting up long-range enhancer-promoter interactions

- Study the role of RNA modifications in chromatin organization using Hi-C
- Explore the spatio-temporal activity of enhancers using single-cell RNA-seq and spatial transcriptomics
- Characterize the 3D chromatin organization landscape of the highly scrambled genome of the zooplankton Oikopleura dioica




**Modèle et techniques utilisées :**

Nous utilisons 2 espèces modèle différentes :
- l'embryon de Drosophile
- le zooplancton Oikopleura dioica

En fonction des projets, nous utilisons une large variété de techniques allant de la génétique, la génomique (next-generation sequencing y compris en cellule unique), l'imagerie (y compris des méthodes de pointe en transcriptomique spatiale). De nombreux projets peuvent combiner des expériences « à la paillasse » et de la bio-informatique.

**Publications d'intérêt :**

Balasubramanian D*, Borges Pinto P*, Grasso A*, Vincent S, Tarayre H, Lajoignie D, Ghavi-Helm Y. Enhancer-promoter interactions can form independently of genomic distance and be functional across TAD boundaries. **NAR**. 2023. doi:10.1093/nar/gkad1183

Ghavi-Helm Y, Jankowski A, Meiers S, Viales RR, Korbel J, Furlong EEM. Highly rearranged chromosomes reveal uncoupling between genome topology and gene expression. ***Nature Genetics***. 2019. doi:10.1038/s41588-019-0462-3.

Ghavi-Helm Y, Klein FA, Pakozdi T, Ciglar L, Noordermeer D, Huber W, Furlong EE. Enhancer loops appear stable during development and are associated with paused polymerase. ***Nature***. 2014. doi: 10.1038/nature18962.

Moretti C, Stévant I, Ghavi-Helm Y. 3D genome organisation in Drosophila. ***Brief Funct Genomics***. 2020 Mar 23;19(2):92-100. doi: 10.1093/bfgp/elz029. (Review)