

## MASTER 2 BMC PARCOURS GENOPATH ANNÉE 2023-2024

**Titre du sujet de stage :**

**Sperm chromatin organization and paternal chromosome integrity in the zygote**

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

LBMC – ENS de Lyon / Didier Auboeuf

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

Epigénétique et Formation du Zygote dirigée par Benjamin Loppin

<https://www.ens-lyon.fr/LBMC/equipes/epigenetique-et-formation-du-zygote>

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**Sujet de stage :**

**Background:**

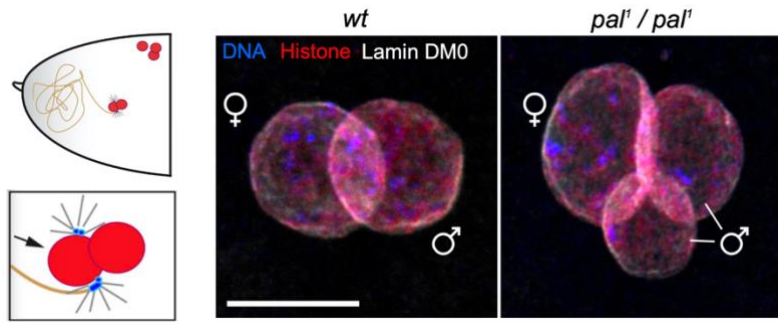
Our group study sperm chromatin organization, function and evolution using genetics and imaging in model insects. Many animals, including mammals and insects, package sperm DNA with specialized, non-histone proteins called protamines. During the differentiation of haploid spermatids into mature spermatozoa, the histone-to-protamine transition contribute to sperm chromatin compaction, a complex process associated with the shutdown of basic nuclear activities. At fertilization, protamines are rapidly eliminated and replaced with maternally-provided histones to reconstitute a nucleosomal organization of paternal chromosomes.

We use two main model insects: the fruitfly *Drosophila melanogaster* and the cricket *Gryllus bimaculatus* and develop a variety of projects. You can contact us for details about this and other possible internship projects.

**Project: Investigating the mechanism and function of the histone-to-protamine transition in *Drosophila***

In *Drosophila*, histones are almost completely replaced with protamines during spermiogenesis but the functional significance of this ultraspecialized chromatin organization is poorly understood. We have recently discovered, through the functional analysis of a rare paternal effect mutant

named *paternal loss (pal)*, that the elimination of histones in sperm is critical to protect paternal chromosomes in the egg at fertilization (Dubruille *et al.*, in revision). *pal* encodes a transition protein required for the eviction of histone H3 and H4 in spermatids. In *pal* mutant males, histones H2A and H2B are eliminated, but H3 and H4



H2B are aberrantly retained, without affecting sperm function. At fertilization, the presence of H3 and H4 in *pal* sperm leads to the misrecognition of paternal chromosomes as maternal chromosomes by the egg cytoplasm and the fragmentation of the male pronucleus.

The internship student will study the mechanism of histone H3/H4 eviction by Pal and will also characterize sperm chromatin in a new paternal effect mutant with a similar phenotype.

#### Technologies utilisées :

*Drosophila* genetics (crosses, phenotypic analyses, CRISPR/Cas9, ...), cytology/microscopy (dissections, embryo collections, immunofluorescence, confocal microscopy ...), molecular biology (DNA, western blot), epigenomics (Cut&Run)

**Mots clés :** *Drosophila melanogaster*, chromatin, histones, protamines, zygote, spermiogenesis spermatozoa.

#### Publications du laboratoire (5 max):

Dubruille R, Herbette M, Revel M, Horard B, Chang CH, Loppin B. Histone removal in sperm protects paternal chromosomes from premature division at fertilization. (in revision for *Science*)

Horard B, Terretaz K, Gosselin-Grenet AS, Sobry H, Sicard M, Landmann F, Loppin B. (2022) Paternal transmission of the Wolbachia CidB toxin underlies cytoplasmic incompatibility. *Curr Biol.* 32(6):1319-1331.e5.

Herbette M, Wei X, Chang CH, Larracuenta AM, Loppin B, Dubruille R. (2021) Distinct spermiogenic phenotypes underlie sperm elimination in the Segregation Distorter meiotic drive system. *PLoS Genet.* 17(7):e1009662

Tirmarche S, Kimura S, Dubruille R, Horard B, Loppin B (2016) Unlocking sperm chromatin at fertilization requires a dedicated egg thioredoxin in *Drosophila*. *Nature Comm.* 7:13539.

Loppin B, Dubruille R, Horard B (2015) The intimate genetics of *Drosophila* fertilization. *Open Biol.* 5(8). pii: 150076.