Master internship offer

Title : Sperm chromatin organization and paternal chromosome integrity in the zygote

LBMC – Laboratory of Biology and Modeling of the Cell - ENS de Lyon

Host team : Epigenetics and Zygote Formation du Zygote

http://www.ens-lyon.fr/LBMC/equipes/epigenetique-et-formation-du-zygote

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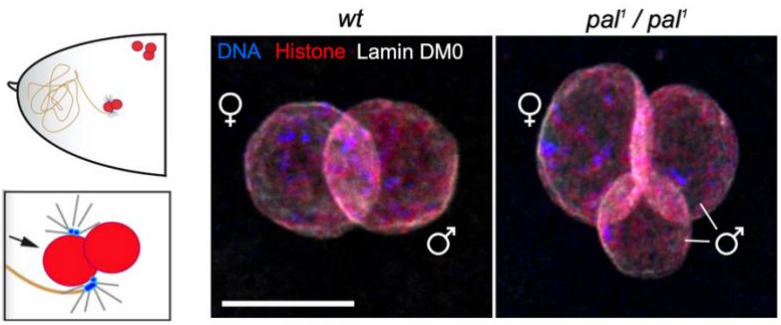
Project description

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 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.

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

Key words : *Drosophila melanogaster*, chromatin, histones, protamines, zygote, spermiogenesis spermatozoa.

Publications :

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*)

Orsi G, Tortora MMC, Horard B, Baas D, Kleman JP, Bucevičius J, Lukinavičius G, Jost D, Loppin B (2023) “Biophysical ordering transitions underlie genome 3D re-organization during cricket spermiogenesis.” *Nature Comm.* 14 :4187.

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.

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.