1st zygotic mitosis

MASTER 2 BMC PARCOURS GENOPATH ANNÉE 2024-2025

Titre du sujet de stage :
Paternal chromatin poisoning in Wolbachia-induced cytoplasmic incompatibility

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Sujet de stage :

Our group focuses on chromatin and epigenetic changes related to sexual reproduction, particularly on the structural changes undergone by paternal chromatin during the formation of haploid gametes and after fertilization during zygote formation. Cytoplasmic incompatibility, a conditional sterility syndrome observed in many arthropods, illustrates improper integration of paternal chromosome during the formation of the zygote. This syndrome is caused by *Wolbachia*, widespread endosymbiotic bacteria (which lives inside the host cells). These bacteria are known to manipulate their host's reproduction to favor their vertical transmission through eggs, using a variety of sophisticated mechanisms. In Cytoplasmic Incompatibility (CI), *Wolbachia* present in the male germline alters sperm so they can only create viable offspring when fertilizing an egg already infected by the same Wolbachia strain. In contrast, uninfected eggs are killed during the first mitotic division. This mechanism effectively selects infected eggs and allows *Wolbachia* to invade insect populations. This principle is, in fact, the basis of the global program to control mosquitoes that transmit the dengue virus (informative video here: https://www.worldmosquitoprogram.org/).

CI was discovered several decades ago, but the underlying molecular mechanisms involving two molecular effectors were only elucidated recently (1). Our recent research on transgenic Drosophila

expressing effectors from *Culex pipiens* mosquitoes (*Pip*) reveals that the effector CidB functions as a toxin, accumulating in the nuclei of spermatozoa. During fertilization, in eggs that are not infected by Wolbachia, CidB interferes with the replication of paternal chromosomes, resulting in embryo death (2;3). In contrast, eggs infected with Wolbachia are protected by the expression of the second effector, CidA, which acts as an antidote.

We have begun investigating another pair of effectors, CifA and CifB, found in the *Wolbachia* strain infecting *Drosophila melanogaster* (*wMel*). This research aims to investigate how the host influences the biology of the effectors, and the mechanism through which CI is rescued, either by CifA expression or by *Wolbachia* itself.

The internship program will focus on either:

- decrypting the mechanisms of paternal DNA replication poisoning by the *wPip* CidB toxin
- characterizing the *in vivo* distribution and function of CifA/B effectors.

Technologies utilisées :
Drosophila genetics (crosses, phenotypic analysis, fertility test, ...), inducible transgenes (UAS- Gal4 system), cytology/microscopy (dissections, embryo collections, immunofluorescence, confocal microscopy ...), molecular biology and biochemistry.

Mots clés : *Wobachia*, Cytoplasmic Incompatibility, toxin-antitoxin, chromatin, sperm chromatin, DNA replication, mitosis, zygote, drosophila.

Publications d'intérêt:

1- Beckmann, J. F., Bonneau, M., Chen, H., Hochstrasser, M., Poinsot, D., Merçot, H., Weill, M., Sicard, M., & Charlat, S. (2019). The Toxin-Antidote Model of Cytoplasmic Incompatibility: Genetics and Evolutionary Implications. *Trends in Genetics: TIG*, *35*(3), 175–185.

2 – Terretaz, K., Horard, B., Weill, M., Loppin, B., Landmann, F. (2023) Functionnal analysis of Waolbachia Cid effectors unravels cooperative interactions to target host chromatin during replication. PLOS Pathogen, 19 (3)

3- Horard, B., Terretaz, K., Gosselin-Grenet, A.-S., Sobry, H., Sicard, M., Landmann, F., and Loppin, B. (2022). Paternal transmission of the Wolbachia CidB toxin underlies cytoplasmic incompatibility. *Current Biology*, 32(6):1319-1331.

4- Hochstrasser M. (2022). Cytoplasmic incompatibility: A Wolbachia toxin-antidote mechanism comes into view. *Current Biology : CB*, *32*(6), R287–R289.