MASTER 2 BMC
PARCOURS GENOPATH
ANNÉE 2021-2022

Titre du sujet de stage : Uncovering Hox-splicing networks in *Drosophila* development

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

Institut de Génomique Fonctionnelle de Lyon (IGFL)

ENS Lyon – UMR CNRS 5242

32, 34, avenue Tony Garnier,

69007 Lyon

Directeur : Francois Leulier

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

Group *Ontogenesis and Molecular interactions*

Institut de Génomique Fonctionnelle de Lyon (IGFL)

ENS Lyon – UMR CNRS 5242

32, 34, avenue Tony Garnier,

69007 Lyon

Directeur d'équipe : Samir Merabet

Nom, tel, adresse e-mail de l'encadrant de stage :

Supervisor : Julie Carnesecchi

julie.carnesecchi@ens-lyon.fr

Sujet de stage :

Transcription Factors (TFs) are the key players of cell fate decision in all living organisms. They do so by recognising DNA-binding sites and regulating target genes in a precise spatial and temporal manner. Although most TFs act at the DNA layer, few TFs can bind RNA and modulate splicing thereby increasing mRNAs and proteins diversity. Yet, how the RNA-function of TFs impact on cell fate decision is enigmatic. Solving this problem will provide unique entry points to **understand the mechanisms orchestrating cell and tissue diversity in animals** and their aberrant regulation in diseases.

Research focus:

Splicing relies on the sequential assembly and disassembly of the spliceosome to be active. This remarkable structure contains core RNA-protein modules (snRNP) and is guided by many accessory proteins to drive fine-tuned splicing events in precise cell or tissue context. Our goal is to investigate the intricate interactions between TFs and splicing factors, and how they contribute to cell fate decision.

To do so, we specifically **decipher how TF-splicing networks coordinate tissue development in the *Drosophila* embryo.** We previously uncovered an interplay between the Hox TF Ultrabithorax (Ubx) and splicing factors, which is essential for muscle development. The nature and the molecular function of these interactions are unknown. The goal of the Master internship will be to **elucidate the molecular interaction between Ubx and splicing factors** and **its impact on muscle development**.

Technologies utilisées : To study RNA-protein, protein-protein interactions, a variety of methods will be used, from *in vitro* (EMSA, co-immunoprecipitation, GST-pull down) to *in vivo* (live imaging, super resolution microscopy, split-system), relying the powerful *Drosophila* genetic toolbox.

Mots clés : Gene regulation, Hox, RNA, splicing, protein interaction, imaging, *Drosophila*, muscle, cell fate

Publications d'intérêt :

Carnesecchi, J.*, Boumpas, PP., van Nierop y Sanchez, P., Domsch, K., Pinto, H.D., Pinto, B.P, and Lohmann, I. (2021). The Hox transcription factor Ultrabithorax binds RNA and regulates co-transcriptional splicing through an interplay with RNA polymerase II. *BioRxiv pre-print. *corresp.*

Carnesecchi, J., Sigismondo, G., Domsch, K., Baader, C.E.P., Rafiee, M.-R., Krijgsveld, J., and Lohmann, I. (2020). Multi-level and lineage-specific interactomes of the Hox transcription factor Ubx contribute to its functional specificity. *Nat Commun 11, 1388.*