UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Integrative Biology, Physiopathologies »

Proposal for a Master 2 internship – 2024-2025

Title : Deciphering the multiscale regulation of imprinted genes during mouse neural commitment

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Summary :

Genomic imprinting is a key epigenetic process in which about 150 mammalian genes are expressed on only one allele, depending on their parental origin. Most of these are required for key biological processes, including brain function and behaviour.

Allele-specific expression along each imprinted domain is regulated by a key region, the imprinting control region (ICR). In addition to DNA methylation imprints that constitutively mark ICRs on their maternal or paternal alleles, other levels of regulation, including histone modification and chromatin looping, account for the complex and specific spatio-temporal expression patterns of imprinted genes. However, how ICR dynamically orchestrates allele-specific coordination between these regulatory layers along large imprinted domains and fine-tunes the allelic expression of distal genes during lineage commitment remains poorly understood.

The aim of this internship, to be followed by a PhD, is to characterise the details of the fine-tuned regulation of the imprinted domain *Peg13* during neural commitment.

It will use a multiscale integrative allelic resource being established by the host team on a brain organoid model based on hybrid mouse embryonic stem cells to explore how transcription factors, chromatin signatures and 3D conformation interact to regulate imprinted expression during neural commitment. A regulatory model will be built from the exploration of this resource and further tested using a range of molecular, cellular, cell imaging and functional in cell approaches.

By identifying novel players in the fine-tuned regulation of imprinted genes in the brain, this work will provide a relevant framework for understanding the causes of imprinting-related neurobehavioural disorders.

Methodologies (key words) : Brain organoid, ES cell differentiation, Omic related to epigenetic analyses (HiC-capture, Cut&Run..), FISH, RT-qPCR, bioinformatics,

Publications of the research group on the proposed topic (3 max.)

Rengifo Rojas C et al., (2024) "Biallelic non-productive enhancer-promoter interactions precede imprinted expression of Kcnk9 during mouse neural commitment"**.** HGG Adv.30:100271. doi: 10.1016/j.xhgg.2024.100271.

Montibus B et al. (2021). « TET3 controls the expression of the H3K27me3 demethylase Kdm6b during neural commitment." *Cell Mol Life Sci.* 78(2):757-768.

S. Maupetit-Mehouas *et al*, (2016) "Imprinting control regions (ICRs) are marked by mono-allelic bivalent chromatin when transcriptionally inactive.", *Nucleic Acids Res* 44 (2):621-635