MASTER 2 Fundamental and Clinical Neurosciences

Internship proposal 2026-2027

(internship from January to June 2027)

Host laboratory:
Centre de Recherche en Neurosciences de Lyon
Inserm U1028, CNRS UMR5292, Université Lyon 1
Centre Hospitalier Le Vinatier – Bât. 462 NeuroCampus
95, Boulevard Pinel - 69500 Bron

Host team
Equipe GENDEV – Génétique des anomalies du neurodéveloppement
https://www.crnl.fr/fr/equipe/gendev

Internship supervisors : DELOUS Marion, Team leader, marion.delous@inserm.fr

Project title : Deciphering the physiopathological mechanisms of microcephalic syndromes linked to defective minor splicing

Project summary :
Splicing of pre-messenger RNAs is a crucial step in gene expression. For the majority of species, it is ensured by two distinct machineries, the major and minor spliceosomes. In 2011, the GENDEV team showed that mutations in U4atac, a specific component of the **minor spliceosome** that removes minor introns in ~750 genes in the human genome, are responsible for the **microcephalic** dwarfism syndrome, called Taybi-Linder (TALS). To understand the pathophysiological mechanisms underlying this syndrome, the team has developed different zebrafish models (CRISPR/Cas9 induced "indel" or "humanised" mutants). During his/her internship, the student will characterize the phenotype of **the zebrafish mutant lines**, by analysing the global morphology and the **behaviour** of the larvae – in response to different stimuli. At the cellular level, the student will study the **brain morphology and activity** by performing confocal imaging.

3-5 recent publications :
- Guguin J, *et al.* A TALS-like associated *RTTN* mutation impedes neural rosette formation in human cortical organoids. medRxiv doi: https://doi.org/10.1101/2024.04.03.24303866 (**2024**)
- Khatri D, *et al*. Deficiency of U4atac snRNA results in ciliary defects. *PNAS* 120(9):e2102569120 (**2023**)
- Benoit-Pilven C, *et al*. Clinical interpretation of variants identified in *RNU4ATAC*, a non-coding spliceosomal gene. *PLoS One*, 15(7):e0235655 (**2020**)
- Cologne A, *et al*. New insights into minor splicing - A transcriptomic analysis of cells derived from TALS patients. *RNA* 25(9):1130-1149 (**2019**)