

MASTER 2 BMC PARCOURS GENOPATH ANNÉE 2021-2022

Titre du sujet de stage :

Exploring the role of the SIN3/HDAC complex in mitochondrial dynamics

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Epigenetic regulation of cell identity and environmental stress responses/PALLADINO Francesca

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Sujet de stage :

Epigenetic mechanisms are emerging as pivotal regulators of mitochondrial function. The SIN3/HDAC transcriptional coregulator complex is widely conserved in all species and governs the expression of a large repertoire of gene targets through distinct enzymes and DNA-binding partners. We are using the nematode *C. elegans* to investigate the complexity of SIN3/HDAC functions in the regulation of fertility and longevity. Recent genome wide transcriptomics analysis from the lab has revealed that loss of *sin-3* strongly perturbs expression of the mitochondrial genome and, to a lesser extent, nuclear-encoded mitochondrial genes. This suggests that SIN3 may play a central role in mediating interactions between mitochondria and nuclear compartments, which could be relevant in the reduction of fertility and lifespan observed in *sin-3* mutants. In preliminary experiment, we have in fact observed that mitochondrial morphology is affected in muscle cells of *sin-3* mutant animals. The M2 student will 1) characterize tissue-specific mitochondrial defects in *sin-3* mutants using available reporters in live and fixed samples. Animals carrying mutations in additional subunits of the SIN-3 complex identified by the lab will also be analyzed; 2) use auxin induced degradation (AID) to identify the tissues in which SIN-3 is required to preserve mitochondrial function, and maintain normal lifespan and fecundity; 3) perform transcriptomic analysis on mutants lacking different components of the SIN-3/HDAC complex to identify commonly regulated genes whose expression may contribute to our phenotypes of interest.

Technologies utilisées :

genetic analysis, microscopy, RNA extraction, RNA-seq, bioinformatics analysis of RNA-seq data
analyse génétique, microscopie, séquençage d'ARN, analyse bioinformatique

Mots clés :

chromatin, epigenetics, elegans, mitochondrial stress, longevity, germline, transcriptomics,
bioinformatics

Publications d'intérêt :

Beurton F, et al. [Physical and functional interaction between SET1/COMPASS complex component CFP-1 and a Sin3S HDAC complex in C. elegans.](#)

Nucleic Acids Res. 2019 47(21):11164-11180.

PMID: 31602465

Fabrizio P, Garvis S, Palladino F.

[Histone Methylation and Memory of Environmental Stress.](#)

Cells. 2019 8(4):339.

PMID: 30974922