

Track « Integrative Biology, Physiopathologies »

Proposal for a Master 2 internship – 2024-2025

Title : Analysis of the impact of TET epigenetic enzyme in gene expression regulation: an epitranscriptomic view.

Laboratory : iGReD – Institut de Génétique Reproduction et Développement ; UMR6293
CNRS-UCA / UMR1103 Inserm-UCA

Laboratory director : Dr K. Jagla

Address : 28 place Henri Dunant, 63000 Clermont-Ferrand

Internship tutor : Dr Lucas Waltzer

Tel : 04 73 17 83 27

e-mail: lucas.waltzer@uca.fr

Summary :

Enzymes of the Ten Eleven Translocation (TET) family play a crucial role in the regulation of gene expression and are involved in different cancers in human, notably in the hematopoietic and nervous systems. These enzymes are well known for their function in the oxidation and demethylation of 5-methylCytosines (5mC) on DNA, a widespread epigenetic mark in mammalian genomes. Yet, these proteins also have non-canonical functions beyond 5mC DNA oxidation. In particular, it was proposed that they also act as epitranscriptomic regulators by targeting m5C on RNA, thereby regulating gene expression at the post-transcriptional level. Notably, many tRNA are methylated on m5C and this modification controls their maturation and the formation of tRNA fragments with diverse biological functions. However, the impact of TET on tRNA processing and biology remains largely unknown.

Interestingly, the drosophila genome codes for a TET enzyme but is devoid of 5mC DNA. Thus, this insect provides an excellent model organism to study the non-canonical mode of actions of TET. Thanks to the genetic tools that we developed and using a combination of transcriptomic and ChIP-seq approaches, we recently showed that TET plays an important role in the regulation of transcription in the drosophila larval brain and that this function is largely independent of its enzymatic activity. Yet we also found that TET exhibits catalytic-dependent functions, and our data suggest that these effects are post-transcriptional. As a follow-up of these results, this internship will aim to characterize further the catalytic-dependent functions of TET. The main objective of the internship will be to establish the impact of TET on tRNA expression and maturation its relationship with other epitranscriptomic enzymes.

Methodologies (key words) : transcriptomics, bioinformatics, confocal imaging, drosophila genetics

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

Gilbert *et al.*, Drosophila TET acts with PRC1 to activate gene expression independently of its catalytic activity. Science Advances (2024), in press.

Boulet *et al.*, Adenine methylation is very scarce in the Drosophila genome and not erased by the ten-eleven translocation dioxygenase. Elife (2023), doi: 10.7554/eLife.91655.