MASTER 2 BMC
PARCOURS GENOPATH
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Titre du sujet de stage :
Identification of cell-type specific targets of the SIN3 corgulator

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Sujet de stage :
Mitochondrial function relies on coordinated transcription and translation of both mitochondrial and nuclear genomes to assemble respiratory chain complexes. Across species, the highly conserved SIN3/HDAC coregulator influences mitochondrial functions, but how the loss of SIN3 impacts mitochondrial homeostasis and metabolism in the context of a whole organism remains largely unknown. Exploring this link is important because *SIN3* loss of function results in intellectual disability (ID)/autism syndromes, and SIN3 plays an important role in tumor biology. We have shown that loss of SIN-3 in *C. elegans* results in transcriptional deregulation of the mitochondrial genome and nuclear-encoded mitochondrial genes, potentially leading to mito-nuclear imbalance and mitochondrial stress. Transmission electron microscopy (TEM) and *in vivo* imaging revealed extensive fragmentation of mitochondria in all tissues examined. Consistent with defective mitochondrial function, we found oxygen consumption to be altered in *sin-3* mutant animals, while metabolomic analysis identified a signature of mitochondria stress, and deregulation of methionine and polyamine metabolic pathways. Altogether our results identify SIN3 as a key regulator of mitochondrial dynamics and metabolic flux in an organismal context, with important implications for human pathologies (manuscript submitted).

Technologies utilisées :

Mots clés :

Publications d'intérêt :