

Wednesday June 19, 2019- 10h30
Conference room SV 1717 - EPFL - Lausanne

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“NFYB-1 regulates mitochondrial function and longevity via lysosomal prosaposin”

Host: Prof. Johan Auwerx

Abstract:

Mitochondrial activity is critical for cellular vitality and organismal longevity, yet underlying regulatory mechanisms in metazoans remain elusive. To identify mitochondrial regulators, we performed an RNAi screen leveraging the remarkable mitochondrial changes in *C. elegans* upon recovery from adult reproductive diapause. We discovered NFYB-1, a subunit of the NF-Y transcriptional complex, as a crucial regulator of mitochondrial function. Loss of NFYB-1 leads to reduced mitochondrial gene expression, mitochondrial fragmentation, and abolition of longevity triggered by mitochondrial impairment. Moreover, NFYB-1 deletion disrupts mitochondrial UPR^{mt} factors and mitochondrial-to-cytosolic stress response (MCSR). Multi-omics analysis indicates that NFYB-1 serves as a potent repressor of several ER genes and the ER stress response, as well as lysosomal prosaposin. Downstream of NFYB-1, limiting prosaposin expression alters ceramide and cardiolipin pools, restores mitochondrial fusion, gene expression and longevity. Thus, the NFYB-1/PSAP axis coordinates lysosomal to mitochondrial communication to prolong life.

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