



Monday February 4 , 2019– 10h30

Conference room AI 1153 (*)- EPFL - Lausanne

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"Novel mouse models to study mitochondrial proteostasis in

the nervous system"

Host: Prof. Johan Auwerx

Abstract:

Disturbances in the morphology and function of mitochondria cause neurological diseases, which can affect the central and peripheral nervous system. The *i*-AAA protease YME1L ensures mitochondrial proteostasis and regulates mitochondrial dynamics by processing of the dynaminlike GTPase OPA1. Mutations in *YME1L* cause a multi-systemic mitochondriopathy associated with neurological dysfunction and mitochondrial fragmentation but pathogenic mechanisms remained enigmatic. Here, we report on striking cell-type specific defects in mice lacking YME1L in the nervous system. YME1L-deficient mice manifest ocular dysfunction with microphthalmia and cataracts and at later stages of life develop deficiencies in locomotor activity due to specific degeneration of spinal cord axons. We demonstrate that YME1L ensures efficient mitochondrial transport in neurons and maintains mitochondrial proteostasis and dynamics *in vivo*. Additional deletion of *Oma1* restores tubular mitochondria but deteriorates axonal degeneration in the absence of YME1L, demonstrating that impaired mitochondrial proteostasis rather than mitochondrial fragmentation cause trafficking defects and the observed neurological dysfunction.

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