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10.30am

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“Mitochondrial biogenesis in the rodent CNS – an in vivo study”

Hosts: Kristina Schoonjans and Johan Auwerx

Conference Room: AI 1153
EPFL - Lausanne

Abstract
Replication of mitochondrial DNA is an essential component of growth of the mitochondrial network or biogenesis. We optimized a technique, which tags replicating mitochondrial DNA using a thymidine analogue, bromodeoxyuridine (BrdU) to investigate the changes in this biogenesis signal in rodent models of neuroinflammation. Upon scanning of the CNS using the BrdU method, we found that there are certain hotspots of mtDNA replication in neuronal populations, which implicates a stark difference in the rate of mitochondrial turnover. It turns out that these cells correspond to regions of the brain, which are known to be vulnerable in certain diseases with a mitochondrial component to pathology.

A time series investigation of a ‘pulse and chase’ protocol also suggested that while mitochondria are distributed all through motor neurons, the DNA replication signal only appears in the cell body initially and then slowly distributes to the extremities of the axons. Furthermore, the signal we observe responds to changes in energy demand, as tested by unilateral electrical stimulation of the sciatic nerve. This suggests an increase in mitochondrial biogenesis in corresponding motor neuron cell bodies as well as dorsal root ganglion cells. With the generation of new drugs, which target the mitochondrial life cycle, this work provides critical information, which can aid the targeting of mitochondrial dynamics as a therapeutic target in neurological disease.