Lausanne Integrative Metabolism and Nutrition Alliance (LIMNA) SEMINAR

Wednesday April 9, 2014
2.00 pm

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www.neurometabolic-lab.org www.peroxisomedb.org

“Sirtuin1 prevents axonal degeneration in adrenoleukodystrophy”

Hosts: Kristina Schoonjans and Johan Auwerx

Conference Room: Al 1153 (*)
EPFL - Lausanne

Abstract
Oxidative stress and mitochondria dysfunction are noxious factors, intertwined in the ethiological core of most common neurodegenerative conditions. In the peroxisomal disease adrenoleukodystrophy, caused by loss of function of the peroxisomal transporter of very long-chain fatty acids Abcd1, we have identified an early oxidative stress leading to late onset axonal degeneration and disability. In this study, we demonstrate that excess of the VLCFA C26:0 generates mitochondrial ROS, resulting in mitochondrial DNA and protein oxidation. This is concomitant with mitochondrial depletion in spinal cords attributable to an impairment of SIRT1/PGC-1a pathway. Treating X-ALD mice with resveratrol, a SIRT1 activator, or overexpressing SIRT1 by transgenesis, normalises mitochondria numbers and respiration, preserves energetic homeostasis including NADH and ATP levels and most importantly, halts axonal degeneration and related motor disability. These results link mitochondria malfunction to axonal damage, and underscore the Sirt1/PGC-a axis as a pivotal therapeutic target for neurodegenerative disease.

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(*) IMPORTANT NOTICE: All external participants have to pass through SV Reception/Welcome Desk to be able to access to Al 1153. Contact person to call at arrival at SV Reception Desk: Johan Auwerx 30951 / Administrative Assistant: 39522.