Thursday April 3, 2014
10.30 am

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“Mitofusin 2 in POMC Neurons Connects ER Stress with Leptin Resistance and Energy Imbalance”

Hosts: Kristina Schoonjans and Johan Auwerx

Conference Room: AI 1153 (*)
EPFL - Lausanne

Abstract
Mitofusin 2 (MFN2) plays critical roles in both mitochondrial fusion and the establishment of mitochondria-endoplasmic reticulum (ER) interactions. Hypothalamic ER stress has emerged as a causative factor for the development of leptin resistance, but the underlying mechanisms are largely unknown. Here, we show that mitochondria-ER contacts in anorexigenic pro-opiomelanocortin (POMC) neurons in the hypothalamus are decreased in diet-induced obesity. POMC-specific ablation of Mfn2 resulted in loss of mitochondria-ER contacts, defective POMC processing, ER stress-induced leptin resistance, hyperphagia, reduced energy expenditure, and obesity. Pharmacological relieve of hypothalamic ER stress reversed these metabolic alterations. Our data establish MFN2 in POMC neurons as an essential regulator of systemic energy balance by fine-tuning the mitochondrial-ER axis homeostasis and function. This previously unrecognized role for MFN2 argues for a crucial involvement in mediating ER stress-induced leptin resistance.

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