

Monday, June 3rd, 2019 – 15h00
 Department of Physiology, Bugnon 7, 1005 Lausanne
 Seminar room, 6th floor

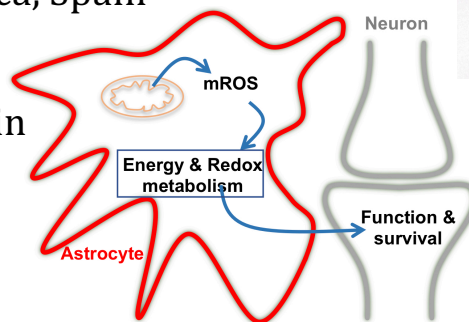
Regulation of brain metabolism and behavior by astrocytic mitochondrial ROS

Prof. Juan P. Bolaños

Neuroenergetic and Metabolism Group
 Institute of Functional Biology and Genomics
 University of Salamanca, Spain



Host : Prof. Luc Pellerin



To satisfy its high energetic demand, the brain depends on the metabolic cooperation of various cell types. For example, astrocytic-derived lactate sustains memory consolidation by serving both as an oxidizable energetic substrate for neurons and as a signaling molecule. Astrocytes and neurons also differ in the regulation of glycolytic enzymes and in the organization of their mitochondrial respiratory chain. Unlike neurons, astrocytes rely on glycolysis for energy generation and, as a consequence, have a loosely assembled mitochondrial respiratory chain that is associated with a higher generation of mitochondrial reactive oxygen species (ROS). However, whether this abundant natural source of mitochondrial ROS in astrocytes fulfils a specific physiological role is unknown. In this seminar, I would like to present data strongly suggesting that astrocytic mitochondrial ROS are physiological regulators of brain metabolism and neuronal function. We generated mice that inducibly express mitochondrial-tagged catalase in astrocytes and show this reduces mitochondrial ROS production in these cells during adulthood. Transcriptomic, metabolomic, biochemical, immunohistochemical and behavioral analysis of these mice revealed alterations in brain redox, carbohydrate, lipid and amino acid metabolic pathways that are associated with altered neuronal function and mouse behavior. We find that astrocytic mitochondrial ROS regulate glucose utilization via the pentose-phosphate pathway and glutathione metabolism, which modulates the redox status and, potentially, survival of neurons. Our data provide further molecular insight into the metabolic cooperation between astrocytes and neurons and demonstrate that mitochondrial ROS are important regulators of organismal physiology in vivo.

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Herrero-Mendez, A. et al. & Bolaños JP. The bioenergetic and antioxidant status of neurons is controlled by continuous degradation of a key glycolytic enzyme by APC/C-Cdh1. *Nat Cell Biol* 11, 747-752 (2009).

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