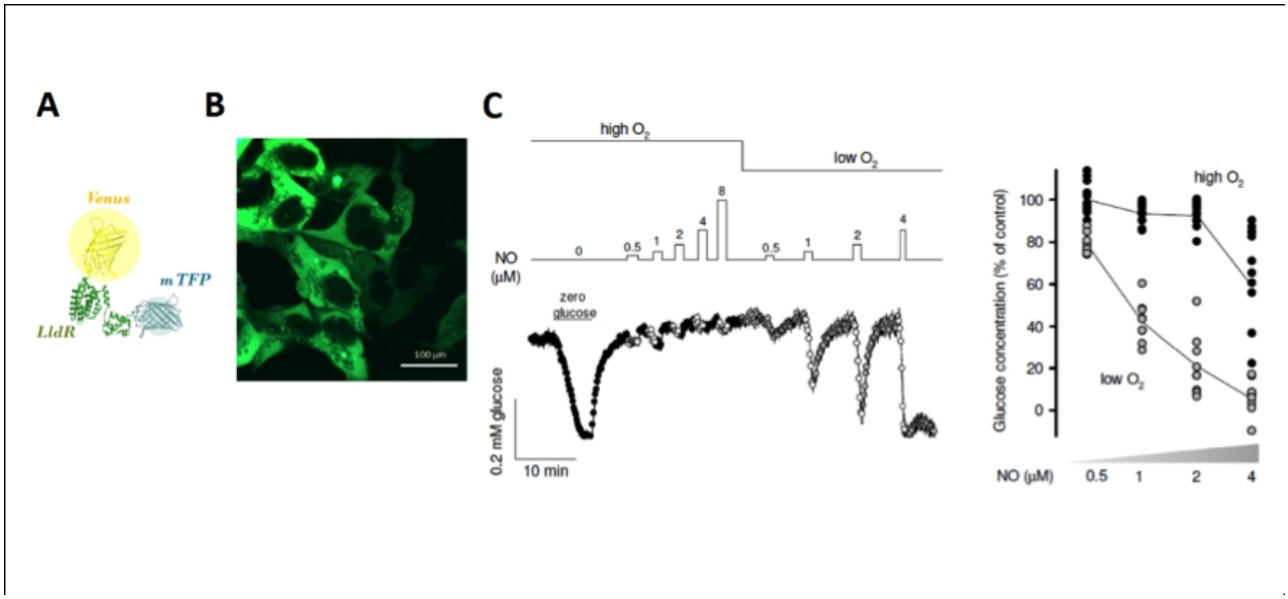
NEW EVIDENCE OF THE ROLE OF NITRIC OXIDE IN THE MODULATION OF ENERGETIC METABOLISM IN THE BRAIN

Researchers of the CECs Biology Lab contributed new evidence that Nitric Oxide can modulate the energetic metabolism of astrocytes, cells in charge of basic aspects for the maintenance and neural function in the brain. The publication was one of the most noted by the JOURNAL OF BIOLOGICAL CHEMISTRY's editorial committee.



A) Schematic representation of Laconic (LACtate Optical Nano-Indicator from CECs) used this

study. B) Mammalian cells expressing Laconic in the cytosol. C) Modulation of the intracellular concentration of glucose by nitric oxide, an effect enhanced by low oxygen concentration. Signal detected with a fluorescent nanosensor for glucose expressed in astrocytes. Article's original image.

Astrocytes are crucial cells in the brain that are intimately coupled with neural metabolism and nitric oxide (NO), an intercellular messenger involved in multiple body functions and whose prolonged exposure, irreversibly inhibits some of these processes. However, the speed and potency of the NO metabolic effects in physiological concentrations have been incompletely characterized until now.

The team lead by Felipe Barros , set out to investigate the metabolic effects of NO in astrocytes via the utilization of the spatio-temporal high resolution provided by genetically coded optical sensors, developed at the Center for Scientific Studies (CECs), with the purpose of examining if the NO is capable of modulating the energetic metabolism of astrocytes with the speed, reversibility and expected potency for a physiological signal.

Regarding this, Alejandro San Martín , first author of the article, states that "This work began during my doctoral thesis at the CECs supervised by Felipe Barros, which eventually lead to obtaining my Ph.D. in Cellular and Molecular Biology at the Austral University of Chile (UACh). It began with routine experiments, in which we used a mitochondrial toxin called azida to stimulate glucose consumption in astrocytes. Azida blocks an enzyme called Cytochrome c oxidase (CcOX), its effects over the glycolysis were so quick, potent and reversible that we asked ourselves if something similar could be observed with a CcOX endogenous blocker, just like nitric oxide. I was in a good place to test this hypothesis having already developed genetically coded nanosensors for pyruvate and lactate, metabolic intermediaries whose measurement allows for the evaluation of glycolytic and oxidative metabolism with a single cell spatial resolution and temporal resolution of seconds".

Using tools designed at CECs to evaluate cellular metabolism with a high spatial and temporal resolution, the researchers observed that nitric oxide is capable of modulating quickly and reversibly the astrocytes' metabolism. Critically, the effects were detected for concentrations that can be reached through the liberation from the endothelium under physiological conditions. These discoveries can help relaunch nitric oxidase as a mediator in neurometabolic coupling, a group of processes that ensure the appropriate supply of energy for information processing in the brain.

[1] Nanomolar nitric oxide concentrations quickly and reversibly modulate astrocytic energy metabolism. J Biol Chem. 2017 Jun 2; 292(22): 9432–9438. Published online 2017 Mar 24. doi: 10.1074/jbc.M117.777243

[2] Astrocytes take the stage in a tale of signaling-metabolism coupling. J Biol Chem. 2017 Jun 2; 292(22): 9439–9440. doi: 10.1074/jbc.H117.777243