

Biographical sketch

Nansen Neuroscience Lecture 2023 “Roles of the lactate shuttle: focus on brain physiology and pathologies”

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The Nansen Neuroscience Lecture 2023 is given by Pierre Magistretti on his discovery of the pivotal role played by glial cells, specifically astrocytes, in the realm of neuroenergetics. Magistretti's revolutionary work has unveiled a previously uncharted domain in neuroscience, challenging the conventional perception of glial cells merely as adhesive agents (“glia” means “glue”). With patience, persistence, and insatiable curiosity, his contributions mark a series of seminal findings that have reshaped our understanding of brain energy metabolism.

One of the hallmark contributions of Magistretti's work is elucidation of the mechanisms that link brain energy metabolism with neuronal activity, a fundamental physiological function of glial cells (Pellerin & Magistretti, PNAS, 1994; Magistretti et al., Science, 1999). The impact of his work is manifold. Firstly, it underpins the coupling between neuronal activity and energy supply, precisely when and where it is needed. Furthermore, it has direct implications for the understanding of signals detected by functional brain imaging techniques, particularly positron emission tomography (PET) used for assessing glucose utilization (Pellerin & Magistretti, PNAS, 1994; Cholet et al., JCBFM, 2003; Magistretti & Pellerin, Phil. Trans. Roy. Soc., 1999).

A key observation by Magistretti is the role of astrocytes in glucose uptake during neuronal activation, and in releasing lactate – a metabolic byproduct – even in the presence of enough oxygen to oxidise it (a phenomenon known as the Warburg effect). Importantly, lactate emerges not only as an energy substrate but also as a critical signaling molecule that governs the expression of various genes implicated in synaptic plasticity. Over the past decade, Magistretti's work has uncovered the paradigm-shifting role of astrocyte-produced lactate in neuronal plasticity, diverse forms of memory, and neuroprotection (Suzuki et al., Cell, 2011; Boury-Jamot et al., Mol. Psy., 2016; Jourdain et al., Sci. Rep., 2016 and 2018).

These insights have kindled novel prospects for therapeutic interventions targeting cognitive deficits and neuropsychiatric disorders. Notably, Magistretti's lab has demonstrated that administration of lactate has antidepressant effects, comparable to those of traditional antidepressants, across animal models of depression (Carrard et al., Mol. Psy, 2016), including the role of neurogenesis in the antidepressant action (Carrard et al., Mol. Psy., 2021). These effects are orchestrated by the induction of genes involved in plasticity and neurogenesis, attesting to the signalling role of lactate.

The Nansen Neuroscience Lecture 2023 celebrates Pierre Magistretti's extraordinary journey of discoveries offering insights into the brain's intricate mechanisms and the multifaceted roles of glial cells in synaptic plasticity and neuroprotection.