

Saints Pères Neuroscience Seminar Series

Friday, March 22th, 2019 at 11:30

Amphi Polonovski (2nd Floor)

Centre Universitaire des Saints-Pères

45 rue des Saints-Pères, 75006 Paris

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Role of non-neuronal cells in the death of neuronal cells in ALS and neurodegeneration

Cell-to-cell communications are critical determinants of pathophysiological phenotypes, but methodologies for their systematic elucidation are lacking. During this lecture, an integrative, systems biology approach that combines proteomics and regulatory network analysis to elucidate ligand-mediated interactions between distinct cellular compartments, will be discussed. It will be shown how such an approach could help unraveling the non-cell autonomous basis of neurodegeneration by using an experimental model of amyotrophic lateral sclerosis (ALS), in which astrocytes expressing mutant superoxide dismutase-1 (mutSOD1) kill wild-type motor neurons (MNs). Integrative analysis identified the interaction between astrocyte-released N-terminal fragments of amyloid precursor protein (APP) and death receptor-6 (DR6) on MNs as the top predicted ligand-receptor pair. The inferred pathogenic role of APP and/or DR6 was confirmed in vitro in both human sporadic and mouse familial ALS models, and in transgenic mutSOD1 mice with DR6 knockdown in MNs. Importantly, the proposed methodology is not restricted to this biological context and could be generalized to a variety of other non-cell-autonomous communication mechanisms.

Those interested in meeting with the speaker please contact

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