



## Numbing intraneuronal Tau levels to prevent neurodegeneration in tauopathies

### SEMINAR & VISITING SPEAKER SERIES WORLD WIDE NEURO PLATFORM

#### DATE

Monday, May 31, 2021  
12:00 PM (noon) CST

#### WORLD WIDE NEURO LINK

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#### MEETING ID & PASSCODE

None required

#### SPEAKER

Michel Cayouette, PhD

Director, Cellular Neurobiology Research Unit, Montreal Clinical Research Institute (IRCM)  
Professor, Université de Montréal, Department of Medicine

#### BIO

Dr. Cayouette is Director of the Cellular Neurobiology Research Unit at the Montreal Clinical Research Institute (IRCM) since 2004. He is also a Full Research Professor in the Department of Medicine at Université de Montréal, and Adjunct Professor in the Department of Anatomy and Cell Biology at McGill University. His research focuses primarily on the cellular and molecular mechanisms regulating neural development and regeneration. Specifically, his lab uncovered a transcriptional cascade regulating how progenitor cells change over time to give rise to specific cell types appropriate for a given developmental stage in the mouse retina. They also discovered key regulators of asymmetric cell divisions in neural progenitors that contribute to the production of cell diversity in the nervous system. In 2017, Dr. Cayouette received the prestigious Research Scholar Emeritus award from the Fonds de recherche du Québec – Santé (FRQS) and he holds the IRCM Foundation Gaétane and Roland Pillenière Chair in Retina Biology. He is Director of the FRQS Vision Health Research Network, a provincial initiative dedicated to promote research capacity and international visibility for more than 100 vision scientists in Quebec by funding collaborative projects and various infrastructures. He is also Chair of the Scientific Advisory Board of Fighting Blindness Canada and sits on their Board of Directors since 2014. He is member of the CIHR College of Reviewers and the Faculty of 1000 Prime, and sits on the

Editorial Boards of various journals such as Stem Cells (Wiley), Frontiers in Neuroscience and the Journal of Experimental Neuroscience (SAGE Publishing). His research program is funded by a Canadian Institutes of Health Research (CIHR) Foundation grant, the FRQS, Fighting Blindness Canada, and the Krembil Research Foundation.

#### RESEARCH

Intraneuronal accumulation of the microtubule associated protein Tau is largely recognized as an important toxic factor linked to neuronal cell death in Alzheimer's disease and tauopathies. While there has been progress uncovering mechanisms leading to the formation of toxic Tau tangles, less is known about how intraneuronal Tau levels are regulated in health and disease. Here, I will discuss our recent work showing that the intracellular trafficking adaptor protein Numb is critical to control intraneuronal Tau levels. Inactivation of Numb in retinal ganglion cells increases monomeric and oligomeric Tau levels and leads to axonal blebbing in optic nerves, followed by significant neuronal cell loss in old mice. Interestingly, overexpression of the long isoform of Numb (Numb-72) decreases intracellular Tau levels by promoting exocytosis of monomeric Tau. In TauP301S and triple transgenic AD mouse models, expression of Numb-72 in RGCs reduces the number of axonal blebs and prevents neurodegeneration. Finally, inactivation of Numb in TauP301S mice accelerates neurodegeneration in both the retina and spinal cord and leads to precocious paralysis. Taken together, these results uncover Numb as an essential regulator of Tau homeostasis in neurons and as a potential therapeutic agent for AD and tauopathies.

#### OBJECTIVES

Learn something new about Tau trafficking!

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