Conférence

CRCHUM

Université de Montréal

AXE NEUROSCIENCES

Philip C. Wong, Ph.D.

Professor
Departments of Pathology and Neuroscience
Johns Hopkins Medicine

An AAV gene therapy for ALS guided by a functional fluid biomarker

Recent human studies strongly support the view that the loss of splicing repression by an RNA binding protein, termed TDP-43, underlies the pathogenesis of amyotrophic lateral sclerosis (ALS), a neurodegenerative disorder currently without any disease modifying therapy. To address this unmet need, we validated a blood-brain-barrier crossing AAV (AAV-PHP.eB) gene therapy to complement the loss of TDP-43 splicing repression by delivering intravenously a splicing repressor (termed CTR) to adult central neurons. Using a mouse model to model early phase of motor neuron disease (ChAT-Cre;Tardbpf/f mice), we show that such a mechanism-based therapy when delivered during early symptomatic stage of disease attenuates motor neuron disease. Using an autoregulatory element from the 3'UTR of TDP-43, we show that CTR is maintained at low levels leading to no overt phenotype. Together, these results validate an effective treatment strategy even when delivered after symptom onset and thus for ALS provide an unprecedented opportunity towards clinical testing of this mechanism-based gene therapy.

Le vendredi 14 mars 12 h à 13 h

Amphithéâtre CRCHUM - Pavillon R - R05.212
900 rue Saint-Denis
Montréal (QC) H2X 0A9

Lien Zoom :
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L'AUDACE DE CHERCHER PLUS LOIN

Séminaire organisé par Nicole Leclerc
Information : nicole.leclerc@umontreal.ca