Conférence

CRCHUM

Université de Montréal

AXE NEUROSCIENCES

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From synaptic maintenance to therapy: neuromuscular junctions as a therapeutic target and source of biomarkers in ALS

Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disorder in which the early destruction of neuromuscular junctions (NMJs) triggers muscle weakness and paralysis through denervation and retraction of motor terminals from striated muscles. Glial cells at the NMJ regulate its synaptic function, stability and repair. NMJ denervation in ALS is a dynamic process of repeated denervation–reinnervation cycles, accompanied by profound synaptic and glial malfunctions. Hence, the NMJ is an important site of dynamic changes during ALS development and progression that requires additional studies to broaden our knowledge of the disease. I will present two lines of investigation that underscore the NMJ as a valuable source of therapeutic targets and biomarkers in ALS. First, I will present data demonstrating that glial endocannabinoid CB1 receptors (CB1R) are critical regulators of NMJ plasticity and repair, where glial-specific CB1R deletion accelerates denervation, delays reinnervation, and alters PSC responses. These changes closely mirror those observed in ALS, where a marked reduction of CB1R and alterations of endocannabinoid-related regulatory enzymes were found. Then, building on the mechanistic insights of denervation/reinnervation, I will discuss target discovery strategies towards biomarker identification, highlighting NMJ-related proteins as potential indicators of disease vulnerability and progression of the disease. Finally, I will outline the perspective of my future research program that aims at restoring the altered endocannabinoid signalling at the NMJ in ALS as a strategy to enhance synaptic function, preserve motor performance, and develop novel NMJ-based biomarkers.

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L'AUDACE DE CHERCHER PLUS LOIN

Séminaire organisé par Valérie Mongrain

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