Séminaire de recherche

CRCHUM

Université de Montréal

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Séminaire projet doctorat (NSC7020)

Uncovering Pathogenic Mechanisms and Drug Candidates Across the FIG4 Disease Spectrum

Charcot-Marie-Tooth disease type 4J (CMT4J) is a severe inherited neuropathy caused by recessive mutations in the phosphoinositide phosphatase *FIG4*, a gene also implicated in a broader spectrum of neurodegenerative and neurodevelopmental disorders, including Yunis-Varon syndrome and Amyotrophic Lateral Sclerosis. Disease mechanisms are often interpreted through a dosage-dependent loss-of-function model; however, this framework does not fully explain the clinical and phenotypic heterogeneity associated with different *FIG4* mutations.

To dissect mutation-specific pathogenic mechanisms in vivo, we generated *C. elegans* models carrying patient-associated mutations. Direct comparison of a truncating loss-of-function allele and a disease-relevant missense mutation revealed strikingly distinct molecular and organismal outcomes.

Building on these insights, we performed a phenotypic drug repurposing screen that identified compounds capable of ameliorating disease-relevant phenotypes. Together, these findings highlight mutation-specific mechanisms operating across the *FIG4* disease spectrum and uncover potential therapeutic avenues for CMT4J and related *FIG4*-associated disorders.

Le mardi 24 février 2026
9h à 10h

A.02.9209AB
CHUM

L'AUDACE DE CHERCHER PLUS LOIN

Séminaire organisé par Nathalie Arbour

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