



LIFE SCIENCES SEMINAR SERIES 2024 – 2025

# Mechanisms of axon dysfunction in lysosome-transport disorders

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**11:00 am – 12:00 noon**



**LT, Choh-Ming Li Basic Medical Sciences Building (BMS)**

## Abstract

In neurons, specific mRNAs are packaged within RNA granules for transport along the axon, allowing for localized translation away from the soma. Recent research has shown that some RNA granules hitchhike on axonal lysosome-related vesicles. To analyze the importance of this pathway, we disrupted the entry of these vesicles into the axon by knocking out the lysosome-kinesin adaptor BORG in human iPSC-derived neurons. RNA-Seq of axons isolated from wild-type and BORG-deficient neurons identified a significant subset of mRNAs, particularly those encoding ribosomal and mitochondrial proteins, that rely on lysosome-related vesicles for their axonal transport. Proteomic analyses confirmed a depletion of mitochondrial proteins in BORG-deficient axons. This depletion leads to mitochondrial abnormalities, eventually causing axonal degeneration. Furthermore, our analyses revealed a mechanistic link between BORG deficiency and common neurodegenerative disorders. These findings underscore the critical importance of mRNA transport via lysosome-related vesicles in maintaining axonal homeostasis and highlight the severe consequences of failure in this transport mechanism, ultimately leading to axonal degeneration.

**ALL ARE WELCOME**