Spring 2025

Biochemistry and Molecular Biology Brown Bag Series

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Graduate Student

"Investigating the Role of PERK in Type 2 Diabetes Associated Cognitive Impairment"

Tuesday, February 11, 2025

11:00 AM

Location 125 Oelman Hall

Lab: Keiichiro Susuki, Ph.D.

Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

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https://science-math.wright.edu/biochemistry-and-molecular-biology

Abstract

Type 2 diabetes is highly associated with cognitive impairment. We seek to elucidate the underlying mechanisms by focusing on the neuron's axon initial segment (AIS). This specialized region at the beginning of the axon produces action potentials. Even subtle shortening of the AIS length has been shown to decrease neuronal excitability. AIS length is shorter in type 2 diabetic mice with cognitive impairment, although the mechanism remains unknown. Endoplasmic reticulum (ER) stress and subsequent unfolded protein response (UPR) have been implicated in the pathophysiology of diabetic brain complications. Of the three UPR pathways, PERK has been most strongly linked to neurodegenerative conditions with cognitive impairment. To test the hypothesis that the PERK pathway mediates AIS shortening, we treated mouse cortical neuron cultures for up to 24 hours with tunicamycin, a known ER stress inducer. We recorded neuronal network activity by multi-electrode arrays, and measured AIS structural changes by immunofluorescence. Here we show that ER stress induction decreases neuronal network activity and shortens the AIS length. Additionally, co-treatment with PERK-specific inhibitor GSK2606414 prevents this ER stress-induced AIS shortening. Our results identify PERK as a potential target for treatment of type 2 diabetes associated cognitive impairment.