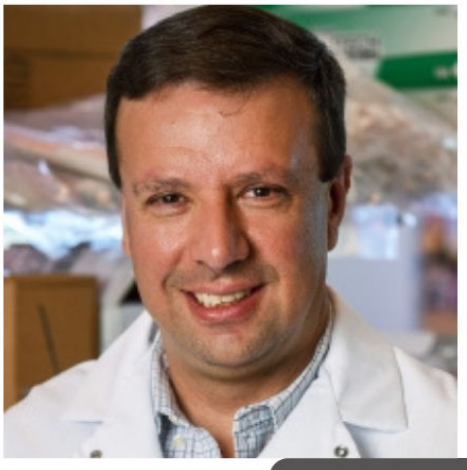
Johns Hopkins University

Department of Biology Seminar Series

Thursdays, 4:00pm

For more information go to: *https://bio.jhu.edu/events*

Mudd Room 100 - November 16th, 2023



Jason Meyer

Department of Medical & Molecular Genetics

Indiana University School of Medicine

Host: Bob Johnston

"Retinal ganglion cells and glial interactions in a human pluripotent stem cell model of neurodegeneration and neuroinflammation""

In optic neuropathies including glaucoma, the connection between the eye and the brain is damaged, leading to the degeneration of retinal ganglion cells (RGCs) and eventual vision loss or blindness. A need exists to better understand the maturation of human RGCs as well as their degeneration, with the goal of developing new therapeutics for diseases like glaucoma. Human pluripotent stem cells (hPSCs) provide an advantageous model for the study of RGC development and disease as they can be differentiated in large, reproducible quantities to serve as an in vitro platform to study cellular development and aspects of disease pathology. Efforts within my lab have broadly focused on the development and maturation of RGCs from hPSCs, occurring in a temporal fashion to yield morphological and functional characteristics similar to their in vivo counterpart. To apply these results to the study of optic neuropathies, we have used CRISPR/Cas9 gene editing to insert glaucoma-associated gene variants such as the OPTN(E50K) glaucomatous mutation into hPSCs to model RGC degeneration. RGCs harboring this mutation exhibited numerous degenerative phenotypes including neurite retraction and autophagy dysfunction. Additionally, as many cell types within the retina contribute to the health and maturation of RGCs, we have developed a co-culture system of hPSC-derived RGCs and glia to better understand the interaction between these cell types. When grown in co-culture, hPSC-derived RGCs demonstrated significantly enhanced and accelerated morphological and functional maturation, indicating an important relationship between these cells in a healthy state. Glia also play a role in neurodegenerative phenotypes in other diseases of the CNS, with these deficits profoundly effecting the health of surrounding neurons and as such, glia induced to a disease state demonstrated intrinsic deficits and yet also exhibited significant effects upon the degeneration of RGCs. Taken together, results of these studies demonstrate the utilization of hPSCs to model RGC maturation and degeneration relevant to glaucoma, and could provide a new therapeutic target for pharmacological screenings and cell replacement therapies to reverse blindness in optic neuropathies.