Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, March 8, 2024 @ 12:45 p.m.

presented by:

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(Advisor: Dr. Angela Scott)

"Astrocyte-Mediated Signalling Dysregulation in Fragile X Syndrome: Intersection of Oxidative Stress and Immune Activation in the Cortex"

Fragile X Syndrome (FXS) is a neurodevelopmental disorder (NDD) that is the leading genetic cause for inherited intellectual disability and autism spectrum disorders. It affects 1 in 7000 males compared to 1 in 11 000 females, who show symptoms such as cognitive, social, and learning impairments. While the underlying genetic cause is known, the subsequent cellular and molecular mechanisms of the disorder remain unclear. Recent work has identified significant changes to the evolutionarily conserved purinergic signalling system within the FXS brain. Specifically, activation of the purinergic receptor P2X7 seems to contribute to the aberrant neuro-inflammatory response and elevated oxidative stress reported in astrocytes, a primary glial cell population in the brain. Activation of P2X7 potentially leads to elevated activity of NADPH oxidase 2, an enzyme that produces reactive oxygen species, and STAT3, a transcription factor that promotes pro-inflammatory factor production. By utilizing a transgenic mouse model (Fmr1 KO mouse model), we aim to examine the role of P2X7 in FXS pathophysiology related to oxidative stress and neuroinflammation. This research will give us important information about the molecular mechanisms that contribute to FXS and potentially other comorbid NDDs, such as autism. Given the growing and widespread prevalence of NDDs, this work could have global implications for individuals at risk.

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