Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, Oct. 19, 2018 in SSC 1511 @ 12:00 p.m.

presented by:

Ryan Hallam

(Advisor: S. Ryan)

"Cardiolipin-containing large unilamellar vesicles: Investigation of the subcellular localization, impact on organelle dynamics, and refolding of α-synuclein fibrils in rat primary neurons"

Parkinson's Disease (PD), the most common neurodegenerative movement disorder, is characterized predominantly by the selective degeneration of A9 midbrain dopaminergic neurons in the substantia nigra. The loss of these cells in the initial onset of PD is typically preceded by the aggregation of the protein α-synuclein, caused by misfolding of α-synuclein into toxic oligomers either sporadically or with an increased propensity due to mutation of key residues. These toxic α-synuclein oligomers wreak widespread havoc on subcellular machinery, resulting most notably in impaired intracellular degradation and mitochondrial dysfunction. Recently, it has been shown that cardiolipin (CL), a mitochondrial membrane phospholipid known to serve as an indicator of mitochondrial damage upon externalization to the outer mitochondrial membrane, is capable of pulling α-synuclein monomers away from oligomeric fibrils in a cell-free system, facilitating the adoption of an alpha-helical conformation and effectively providing a buffer for synuclein aggregation. However, it remains to be determined whether CL is capable of slowing or reversing the accumulation of synuclein aggregates in a cellular context. I propose to use large unilamellar vesicles (LUVs), spherical liposomes which can be artificially made to mimic the phospholipid composition of membranes and to include CL, to introduce exogenous CL to rat primary cortical neurons. The purpose of this project is to determine the subcellular localization of CL-LUVs, as well as to investigate the downstream cellular effects with respect to organelle dynamics and cell viability. This project will potentially provide valuable clues towards a developing a therapy to reverse α-synuclein aggregation *in vivo*.