Department of Molecular and Cellular Biology

Graduate Seminar MCB*7500

Friday, June 9, 2023 @12:45 p.m.

presented by:

Evan Perehiniak

(Advisor: Dr. Marc Coppolino)

"Phosphorylation as a regulatory mechanism in SNARE-mediated trafficking during ECM degradation"

Cell interactions with the extracellular matrix (ECM) are important for many cellular processes, including cell adhesion and migration. Cell-ECM interactions are controlled through the coordinated activities of an array of proteins, including focal adhesion proteins, actin-regulating proteins and proteins which regulate membrane and ECM remodeling. The localization of these proteins at sites of cell-ECM interaction is crucial for cell adhesion and migration as this allows for localized biochemical signaling, reorganization of the actin cytoskeleton, and ECM remodeling. The transport of cellular components is dependent on intracellular vesicle trafficking pathways, mediated by soluble N-ethylmaleimide-sensitive factor (NSF) attachment protein receptors (SNAREs). SNAREs mediate the trafficking of molecules by facilitating membrane fusion, which is important for many biological processes. In these capacities, SNARE function is biochemically regulated, for example through post-translational modifications such as phosphorylation. While much evidence suggests that SNAREs have central roles in cell-ECM interactions, the mechanisms through which SNAREs are regulated in this context are not understood, and phosphorylation of SNAREs represents a potentially important regulatory mechanism involved in SNARE-mediated trafficking. Previous work in the Coppolino lab has defined a role for the SNARE complex containing Stx4, SNAP23, and VAMP7 during matrix metalloproteinase-based ECM degradation. This SNARE complex appears to be regulated by phosphorylation as decreased Stx4 phosphorylation correlated with increased SNARE complex formation and ECM degradation. We propose to investigate the phosphorylation of SNAREs, including Stx4, SNAP23, and VAMP7, using site-directed mutagenesis and to examine how this phosphorylation influences SNARE complex formation during cell-ECM interactions.