Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, May 21, 2021 @12 p.m.

presented by:

Charlotte Townsend

(Advisor: Dr. Shaun Sanders)

"Mechanisms of Dynamic Palmitoylation of Voltage Gated Potassium Ion Channels"

Neurons are electrically excitable cells; their physiological function depends on the correct targeting of ion channels to specific subcellular locations. Within neurons, K_v1 channels are clustered in regions of excitability, such as the axon initial segment (AIS) where they play a critical role in shaping and modifying electrical impulses or action potentials. The disruption in K_v1 trafficking is associated with various channelopathies including episodic ataxia type-I and epilepsy, emphasizing the importance of K_v1 channels in neuronal function. However, the molecular mechanisms governing the precise axonal distribution of K_v1 channels remain poorly understood. The AIS is dynamic and plastic, such that there are alterations in morphology and ion channel composition in response to neuronal activity. The post translational lipid modification, palmitoylation is critical for the clustering of K_v1 channels at the AIS. Palmitoylation involves the covalent attachment of long-chain fatty acids to cysteine residues via a thioester linkage. Due to the reversible nature of palmitoylation, it is well suited to dynamically regulate protein localization in response to changes in neuronal activity. Therefore, I hypothesize that dynamic palmitoylation of K_v1 channels is required for the precise regulation of neuronal excitability. I will determine whether K_v1 channel palmitate cycling is regulated by neuronal activity, define the thioesterase(s) responsible for the depalmitoylation of K_v1 channels and identify the thioesterase binding motif on K_v1 channels. The results of this research may provide a greater understanding of the mechanisms involved in dynamic K_v1 palmitoylation and could offer novel therapeutic targets for treating various K_v1 related channelopathies.