Department of Molecular and Cellular Biology

Graduate Seminar MCB*7500

Friday, October 13, 2023 @12:45 p.m.

presented by:

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"Regulation of voltage gated potassium ion channels by palmitoylation in episodic ataxia"

Episodic ataxia type 1 (EA1) is a rare autosomal dominant neurological condition characterized by brief episodes of ataxia with constant, discrete myokymia. Mutations in the *KCNA1* gene that codes for the voltage-gated potassium channel Kv1.1 cause EA1. Neurons are electrically excitable cells that transmit information to downstream neurons via long output projections known as axons. Signals are sent down axons via electrical impulses or action potentials and neuronal excitability is the propensity of the neuron to fire action potentials. Kv1.1 channels play a crucial role in regulating action potential firing in neurons, thus regulating neuronal excitability. These channels are abundant in the axon initial segment (AIS), a region that is critical for the initiation of action potential firing. The mechanism underlying the trafficking of Kv1.1 channels to the AIS is not fully understood yet. Previous research has shown that the post-translational lipid modification palmitoylation is required for the correct targeting of $K_v1.1$ channels to the AIS. My research focuses on a subset of *KCNA1* mutations associated with episodic ataxia type 1 that lead to amino acid changes around the $K_v1.1$ palmitoylation site that likely affect palmitoylation and have not been studied in neurons. I will determine if these disease-associated variants are palmitoylated, traffic to the AIS, and affect neuronal excitability. I will then assess the associated ataxia phenotype *in vivo*. This research will expand our understanding of the etiology of EA1 and may provide evidence of aberrant palmitoylation in EA1.