Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, March 12, 2021 @12 p.m.

presented by:

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"Regulation of dynactin by palmitoylation during fast axonal transport"

The transport and distribution of organelles and proteins within different cellular compartments is essential for cellular function and relies on a microtubule-motor protein-based system. Neurons are complex, asymmetric, large cells with output projections called axons that are up to a meter in humans. Thus, efficient and precise transport is especially crucial within the nervous system. The fast movement of protein or organelle cargo along axons is known as fast axonal transport (FAT) and relies on motor proteins dynein and kinesin. Dynein moves organelles and secreted molecules, including neurotransmitters, away to the synapse from the cell body, which requires the dynactin complex. DCTN1 ($p150^{Glued}$ or Dynactin 1) is a subunit of dynactin that increases dynein processivity by serving as an extra site of contact with microtubules. The regulation of dynein in FAT is poorly understood. DCTN1 has been identified in multiple palmitoyl-proteomic studies as a palmitoylated protein. Palmitoylation involves the covalent attachment of long-chain fatty acids, typically the 16-carbon palmitate, to cysteine residues via a thioester bond and often tethers proteins to lipid membranes and regulates their function. Thus, I hypothesize that palmitoylation mediates the attachment of DCTN1 to FAT vesicles. I will determine which enzymes regulate DCTN1 palmitoylation, which cysteines are modified, and if its palmitoylation is required to tether it to FAT vesicles. The results of this study will provide a greater understanding of the regulation of FAT in neurons, as well as provide new insights into neuronal function with implications for synaptic function, and neurodegeneration.