

Department of Molecular and Cellular Biology
Graduate Seminar MCB*6500

Friday, March 15, 2024 @ 12:00 p.m.

presented by:

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(Advisor: Dr. Shaun Sanders)

"The regulation of p150Glued by S-acylation and its effect on fast axonal transport machinery in neurons "

Neurons are large, asymmetric cells with long output projections called axons extending up to a meter long in the human spinal cord. Efficient, long-distance transport of essential molecular cargo between the soma and the synapse is critical for neuronal function, with trafficking deficits resulting in various neurodegenerative diseases and neuropathies. Dynein motors are responsible for fast, continuous retrograde transport of vesicles, proteins, and organelles along axonal microtubules. Dynactin is a dynein activator complex critical for dynein processivity as the binding of multiple dynein-dynactin motors to cargo converts dynein into a unidirectional, highly processive motor. The intricate regulation of dynein interaction with its activators controls retrograde trafficking but the mechanisms that govern this process are not well understood. An important mechanism regulating intracellular protein trafficking in neurons is the covalent addition of fatty acids to cysteine residues, known as S-acylation (or palmitoylation). p150Glued (p150 hereto in) is the largest dynactin subunit that mediates dynein-dynactin microtubule binding and processive motility. The Sanders Lab recently showed that p150 is palmitoylated at cysteines 617 and 1255 in neuronal tissues. The function of p150 palmitoylation is unknown, but due to the importance of p150 in dynein-mediated fast axonal transport, my research aims to determine if p150 palmitoylation regulates fast axonal trafficking and elucidate the mechanisms governing this regulation. I hypothesize that palmitoylation of p150 inhibits the formation of the dynein-dynactin complex and, in turn, reduces dynein-mediated transport. This research will elucidate the function of p150 palmitoylation and the role of palmitoylation in regulating axonal transport.