



## Small molecule stabilization of protein interactions to promote axon regeneration

### SEMINAR & VISITING SPEAKER SERIES

#### DATE

Wednesday, November 13, 2019  
12:00 PM (Noon)

#### LOCATION

BMSB, Theatre C, Bannatyne  
Campus

#### SPEAKER

Alyson Fournier, PhD

Professor  
Faculty of Medicine  
McGill University

#### BIO

Dr. Alyson Fournier (PhD) is a Professor in the Faculty of Medicine at McGill University in Montreal, Canada. She completed her Ph.D. in Neuroscience at McGill University (1998) and conducted her postdoctoral training at Yale University with Dr. Strittmatter working on neurodevelopment and regeneration. Since 2003 Dr. Fournier has led a research lab at the Montreal Neurological Institute studying molecular mechanisms regulating axon degeneration and regeneration. Dr. Fournier's group studies neuronal signalling in response to acute nerve cell injury and inflammation for the conception and validation of new therapeutic targets to promote neuroprotection and repair.

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Damaged central nervous system (CNS) neurons have a poor ability to spontaneously regenerate, causing persistent functional deficits after injury. Therapies that stimulate axon growth are needed to repair CNS damage. 14-3-3 adaptors are hub proteins that are attractive targets to manipulate cell signaling. We have identified a positive role for 14-3-3s in axon growth and have shown that fusicoccin-A (FC-A), a small-molecule stabilizer of 14-3-3 protein-protein interactions, stimulates axon growth in vitro and regeneration in vivo. Further screening of FC-A derivatives has revealed potent axon growth-promoting compounds. Through mass spectrometry, we find that FC-A and a potent derivative, stabilize interactions between 14-3-3 proteins and multiple components of the Rap1 pathway to facilitate axon growth. Thus, FC-A and its derivatives exhibit remarkable polypharmacology facilitating axon regeneration. These findings show that 14-3-3 adaptor protein complexes are druggable targets and identify a new class of small molecules that may be further optimized for the repair of CNS damage.

#### OBJECTIVES

1. Define 14-3-3- adaptor proteins and small molecules targeting these proteins
2. Describe the influence of small molecules targeting 14-3-3 proteins on axon regeneration in a pre-clinical optic nerve injury model
3. Discuss the mechanism used by these small molecules to promote axon regeneration