

Control of Axon Degeneration by the Neuronal Cell Body

January 28

Tuesday, 12:30 pm

Weekly Colloquium

Billings Building
Rosedale Conference Room



Speaker: David J. Simon, Ph.D.
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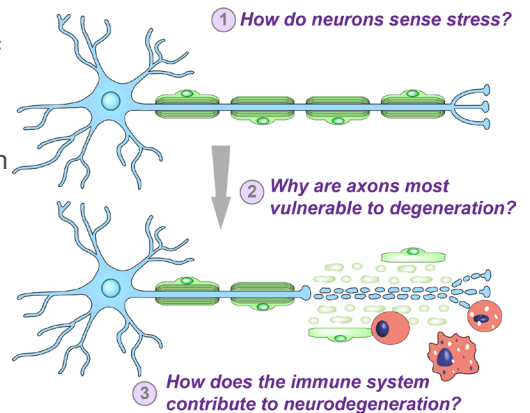
Host: Dianna E. Willis, Ph.D.

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Abstract

How do some neurons survive a lifetime while others succumb to neurodegeneration? We take a 'bottom-up' approach to this question by first understanding the molecules and pathways that control neuronal survival, and then working upstream to ask how cellular stresses including misfolded proteins, physical injury, and loss of neurotrophic support disrupt these pathways to promote degeneration. A particular focus has been on survival of the axon, the long cable-like structures that connect neurons and degenerate earliest in many neurodegenerative diseases. We found that axon degeneration is controlled by bi-directional signaling to and from the cell body, leading us to now ask how the cell body controls the localized death of the axon. We further seek to identify proteins that sense the kind of cellular stresses that are not, in themselves, damaging and determine how these proteins signal within a neuron to promote degeneration. Finally, we are interested how neuronal survival is affected by nearby inflammation, in particular in identifying endogenous protective mechanisms that allow the neuron to withstand chronic low-level inflammation without degenerating. Our ultimate goal is understanding how a neuron reacts to its environment and how environmental stimuli affect the balance between survival and death. In support of these questions we employ a range of molecular, genetic, biochemical, and imaging techniques.



1. Wang G*, Simon DJ*, Wu Z, Heller E, O'Rourke MK, Hertz NT, Molina H, Zhong G, Tessier-Lavigne M, Zhuang, X. Structural plasticity of actin-spectrin membrane skeleton and functional role of actin and spectrin in axon degeneration. *eLife*. 2019; 8:e38730.
2. Simon DJ*, Pitts J*, Hertz NT, Yang J, Yamagishi Y, Olsen O, Tessier Mark M, Molina H, Tessier-Lavigne M. Axon degeneration gated by retrograde activation of somatic pro-apoptotic signaling. *Cell*. 2016; 164(5):1031-45.
3. Simon DJ, Weimer RM, McLaughlin T, Kallop D, Stanger K, Yang J, O'Leary DDM, Hannoush RN, Tessier-Lavigne M. A caspase cascade regulating developmental axon degeneration. *J. Neurosci*. 2012; 32(49):17540-53.