Johns Hopkins University

Department of Biology Seminar Series

Thursdays, 4:00pm

For more information go to: *https://bio.jhu.edu/events*

Zoom link: *https://zoom.us/j/97925356454?pwd=bjNuTlY1dU9BcXcvRFdleis2TVNadz09*

Mudd Room 100 - September 29nd, 2022

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Host: Andrew Gordus

Compartmentalized Cell Elimination: Death in Three Acts

Programmed cell death (PCD) is a critically important event for normal development and homeostasis. Morphologically complex cells are characterized by their elaborate architecture comprising long processes, such as axons and dendrites in neurons. While complex cells are very common, their programmed elimination is poorly studied.

We discovered a novel, "tripartite" killing program that eliminates the morphologically complex tail-spike epithelial cell (TSC) during *C. elegans* embryonic development. This intricate program, called Compartmentalized Cell Elimination (CCE), is also seen in the sex-specific CEM neurons, suggesting CCE is a broad and universally-used elimination program. CCE is characterized by the differential and highly ordered dismantling of three cell regions-the cell soma, soma-proximal process and soma-distal process. Of particular note, the single process/dendrite of these cells displays two very different elimination morphologies, each strikingly reminiscent of forms pruning in neurites, namely fragmentation and retraction. Pruning is an important form of region-specific elimination that helps refine and sculpt the nervous system during development. Our CCE system offers a unique *in vivo* setting to decipher the molecular mechanism of pruning, which is poorly understood. We have performed unbiased forward genetic screens and have retrieved several CCE-defective mutants. With this genetic tool-kit at hand we are well-poised to define CCE at a molecular level and by extension PCD and neurite pruning.

My talk will primarily focus on three aspects of CCE and the programmed elimination of complex cells: initiation, execution and clearance. I will be discussing the role of mitochondrial transport in the initiation of CCE and the role of a caspase in regulating this transport. I will next discuss how the stability of the endoplasmic reticulum (ER) plays a role in CCE execution by promoting the ordered dismantling of microtubules and involvement of conserved molecular players related to neurodegeneration. Finally, I will discuss the selective autophagy and antioxidant resistance machineries promote corpse clearance during CCE under stress conditions presenting a novel pathway promoting lysosomal transport.