Internship Proposal

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Project Title:
Regulation of neuronal trafficking by adaptor proteins that recruit motors to cargo

Level:

Master Student

Project Summary:

We are interested in how motor proteins transport organelles and vesicles along the microtubule cytoskeleton in neurons, a process that is perturbed in virtually all neurodegenerative diseases. To uncover conserved molecular mechanisms of transport and how transport is impacted by mutations associated with disease, we use the transparent animal Caenorhabditis elegans. In this powerful model system, the effect of engineered mutations on neuronal trafficking can be examined in vivo using live fluorescence microscopy. In this project we are examining proteins that function as adaptors between motors and their cargo. By determining where and when opposing motors become active on cargo, adaptors act as key regulators of bi-directional transport.

Work to be developed by the student:

Mutations in adaptor proteins generated by genome editing will be combined with fluorescent reporters for different types of organelle and vesicle cargo, and cargo motility in neurons will examined by live fluorescence imaging in intact animals on a spinning disk confocal microscope. Students have the opportunity to learn molecular cloning techniques, CRISPR/Cas9-mediated genome editing, genetics, live fluorescence microscopy, and image analysis.

References:

Celestino R, Gama JB, Castro-Rodrigues AF, Barbosa DJ, Rocha H, d'Amico EA, Musacchio A, Carvalho AX, Morais-Cabral JH, Gassmann R. JIP3 interacts with dynein and kinesin-1 to regulate bidirectional organelle transport. J. Cell Biol. (2022) 221(8). doi:10.1083/jcb.202110057.

Celestino R, Henen MA, Gama JB, Carvalho C, McCabe M, Barbosa DJ, Born A, Nichols

PJ, Carvalho AX, Gassmann R, Vögeli B. A transient helix in the disordered region of dynein light intermediate chain links the motor to structurally diverse adaptors for cargo transport. PLoS Biol. (2019) e3000100. doi:10.1371/journal.pbio.3000100.

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