Internship Proposal

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Proposal At: 2026-02-13

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Project Title:
Molecular mechanisms of organelle transport along the microtubule network

Level:

Master Student

Project Summary:

Organelle transport driven by the microtubule-based motor proteins dynein and kinesin is essential for the organization and function of eukaryotic cells. By moving cargo such as mitochondria, endosomes, lysosomes, and vesicles along microtubule tracks, these motors ensure the correct spatial distribution of organelles and enable efficient intracellular communication. Kinesins generally mediate transport toward the microtubule plus end, supporting delivery of cargo to the cell periphery, while dynein transports organelles toward the minus end, contributing to trafficking toward the cell center and the perinuclear region. Disruption of this bidirectional transport system can lead to severe cellular dysfunction and has been linked to neurodegenerative diseases and developmental disorders.

This project will examine the mechanisms underlying motor recruitment to cargo and the coordination of dynein- and kinesin-driven motility by adaptor proteins. The aim is to uncover molecular principles that govern efficient bidirectional transport and its regulation in different cellular contexts.

Work to be developed by the student:

The student will study adaptor proteins that simultaneously bind to dynein and kinesin, with a particular focus on the molecular mechanisms that determine motor selection and coordinate bidirectional transport. A central goal of the project will be to identify how adaptor–motor interactions are regulated and how specific binding interfaces contribute to the recruitment, activation, and functional balance of these opposing motors on the same cargo. To address these questions, the student will apply a combination of biochemical and biophysical approaches, including isothermal titration calorimetry (ITC) and microscale thermophoresis (MST), to quantitatively characterize motor–adaptor binding interactions. In

parallel, targeted mutagenesis will be used to generate separation-of-binding mutants that selectively disrupt dynein or kinesin binding. These mutants will then be characterized in tissue culture cells to assess how altered adaptor–motor interactions impact cargo transport dynamics, thereby providing mechanistic insight into the regulation of microtubule-based organelle transport.

References:

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2. Carvalho et al. (2025). Mol. Biol. Cell. 36:ar19. doi:10.1091/mbc.e24-08-0364.
3. Singh et al. (2024). Science. 383:eadk8544–eadk8544. doi:10.1126/science.adk8544.
4. Celestino et al. (2022). J. Cell Biol. 221:e202110057. doi:10.1083/jcb.202110057.
5. Celestino et al. (2019). Plos Biol. 17:e3000100. doi:10.1371/journal.pbio.3000100.
6. Gama et al. (2017). J. Cell Biol. 5:jcb.201610108. doi:10.1083/jcb.201610108.

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