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“Building the Oligodendrocyte: Mechanisms of Acentrosomal Microtubule Nucleation and mRNA Transport”

Oligodendrocytes are extraordinary cells that make dozens of myelin sheaths that wrap around neuronal axons. I have spent my postdoc studying the cell biology of oligodendrocyte and myelin development, including how microtubules are organized and how an essential mRNA cargo is trafficked. Oligodendrocytes contain 2 classes of microtubules - radial microtubules inside processes that extend toward axons and lamellar microtubules that wrap around myelin sheaths. Golgi outposts are satellite organelles that nucleate microtubules at distances far from the centrosome in the cell body. In a screen for microtubule associated proteins, I identified TPPP as a marker for Golgi outposts in oligodendrocytes. TPPP is sufficient to nucleate microtubules in cell-free assays. In the absence of TPPP, oligodendrocytes have shorter myelin sheaths both in vitro and in vivo and mice have motor coordination defects (Fu, et al., Cell, 2019). In addition, in order to form myelin sheaths, oligodendrocytes rely heavily on transport and local translation of Mbp (myelin basic protein) mRNA, which is the most abundant mRNA in oligodendrocytes. I generated a mouse model lacking the 3’UTR region of Mbp mRNA that presents with tremors and demonstrates mRNA transport is necessary for myelination in vivo (unpublished). In addition, I performed a mass spectrometry screen for proteins associated with Mbp mRNA that identified an actin-based myosin motor and the retrograde microtubule motor dynein (Herbert, Fu, et al., PNAS, 2017). Ongoing experiments focus on the function of this myosin, which is mutated in children and adolescents with myopathy that can present with hypomyelination and white matter lesions. By performing non-biased screens, I have uncovered important mechanistic insights on the unique cell biology of oligodendrocytes and interesting functional links to white matter diseases.

Genome Auditorium
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