

Models of Congenital Malformation and Disease

Faculty Search Seminar



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Building the oligodendrocyte: Mechanisms of acentrosomal microtubule nucleation and mRNA transport

Mutations in tubulin can lead to leukodystrophy in children, which is a white matter disorder affecting myelin development. 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 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, 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region of *Mbp* mRNA that presents with tremors and demonstrates mRNA transport is necessary for myelination *in vivo* (unpublished).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. Together, these approaches demonstrate that non-biased screens in oligodendrocytes can yield important functional and mechanistic insights on proteins involved in white matter diseases.

Thursday | February 6th | 2020 | 3 pm

PGCRL Auditorium

Hosts: Drs. Brian Ciruna & John Brumell

Dr. Meng-Meng Fu is being interviewed for a Scientist position at the Research Institute