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Hosted by Assoc. Prof Cynthia He

Defining the molecular architecture of motile cilia transition zone and its role during mammalian motile ciliogenesis

By **Mu He**

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Cilia are essential organelles for sensory and motility functions. Impaired cilia motility can result in diseases such as Primary Ciliary Dyskinesia (PCD), which leads to infertility, chronic nasal infections, and bronchiectasis in human patients. Despite their clinical relevance, the mechanisms regulating cilia motility are not fully understood. The transition zone (TZ) is a specialized domain at the ciliary base, and mutations in TZ genes are associated with various ciliopathies. In primary cilia, TZ proteins regulate signaling and membrane protein trafficking, and their molecular assembly is well characterized. However, TZ organization and its role in motile cilia remain uncharacterized. To address this, we first employed super- resolution microscopy and ultrastructure expansion microscopy (U-ExM) to define the TZ architecture, providing a benchmark for TZ assembly in motile cilia. Using the distal appendage marker CEP164 and a battery of TZ markers, we analyzed the domain organization of different TZ proteins from the basal body. In parallel, we characterized several PCD mouse models exhibiting nasal mucus obstruction and hydrocephalus. The respiratory cilia in mutant animals exhibited impaired TZ organization and lacked a central pair apparatus. Our findings suggest a conserved role for the TZ in driving cilia motility as well as maintaining structural integrity, broadening our understanding of TZ function in motile ciliopathies.

About the Speaker

Dr. Mu He is an Assistant Professor in the School of Biomedical Sciences, The University of Hong Kong. She graduated with a BS from Cornell University in 2007. She pursued her graduate research in the laboratory of Katheryn Anderson at the Memorial Sloan Kettering Cancer Center from 2008 to 2014. Her PhD thesis focused on the genetic and molecular connections between primary cilia and the mammalian Hedgehog signalling (PNAS 2009, Development 2010, JCB 2012, NCB 2014). To follow how embryonic forms acquire physiological functions, she pursued her postdoctoral training with Lily Jan at University of California, San Francisco from 2014 to 2020. In collaboration with Chan Zuckerberg Biohub, she constructed a comprehensive single cell atlas of the developing trachea of mice and humans to better understand the developmental programs and cellular composition that establish the airway mucosal barrier (PNAS 2017, eLife 2020, Nat Physics 2020, Nature 2020). As an independent group leader in HKU, Mu is leveraging the power of stem cell biology, live imaging, organoids, and single-cell technologies to reveal the unifying principles for tissue regeneration and repair. The ultimate goal is to translate basic biomedical discovery into effective therapies for patients affected by respiratory diseases, including COVID-19, asthma, COPD, and cancers.