Centrioles, Centrosomes, and Cilia in Health and Disease

Tang K. Tang （唐堂）

Institute of Biomedical Sciences, Academia Sinica

The centrosome is composed of a pair of centrioles (mother and daughter) surrounded by pericentriolar material (PCM). The main function of centrosome is to organize dynamic arrays of microtubules (MTs) and serve as a MT-organizing center (MTOC), which controls a series of cellular processes including cell polarity, division, and cell migration. The cilium is a microtubule-based structure, that protrudes from the basal body (mother centriole) and could sense extracellular signals and regulate cell homeostasis and development. During the past 20 years, my laboratory has reported several key proteins, including CPAP (Nat Cell Biol 2009, Cell Rep 2016, J Cell Sci 2020, Front Cell Dev Biol 2022), STIL (EMBO J 2011, J Biomed Sci 2022), CEP135 (EMBO J 2013), CEP120 (J Cell Biol 2013, Sci Rep 2019, Genes & Dev 2021), RTTN (Nat Commun 2017), and Myosin-Va (Nat Cell Biol 2019) that participate in centriole duplication, mitosis, and cilia formation. Primary microcephaly (MCPH) is a neurodevelopmental disorder characterized by small brain size with mild to severe intellectual disability. Centrosome abnormalities have been proposed to contribute to aneuploidy, cancer, and primary microcephaly, but their underlining mechanisms remain incomplete understood. We have produced microcephaly *CPAP* conditional knockout mice, human iPSC-derived brain organoids carrying *CPAP* mutant protein, and cells overexpressing centriolar protein STIL to study their physiological roles in brain development and their pathological linkage with primary microcephaly and tumorigenesis. The results from these promising experimental models will be discussed.