東京大学大学院理学系研究科 生物化学専攻/GCOE セミナー

演者: Dr. Tomoko Obara Dept. of Cell Biology University of Oklahoma Health Science Center Oklahoma City, OK 73104, USA 演題: The Basal body protein Wtip regulates cilia mediated processes by modulating non-canonical Wnt signaling 目時: 平成 22 年 12 月 25 日(土) 11: 00~12:00 場所: 東京大学理学部 3 号館 4 階 416 号室

Cilia are antennae-like organelle characterized by the presence of nine peripheral doublets of microtubules. They originate from the basal body, which is located just below the cell surface and is analogous to the centrioles. In the past few years the importance of cilia has been realized by the observation that many gene products mutated in human diseases are localized in the cilia and/or basal bodies/centrosomes. These so called ciliopathies share some common and unexpected clinical phenotypes such as polycystic kidney disease, nephronophthisis, Senior-Loken syndrome type5, orofaciodifital syndrome type I and Bardet-Biedl syndrome which made refocused to our understanding of various human diseases. Unfortunately, many of the underlying cellular signaling events still remain unclear.

Wilm Tumor suppressor gene (Wt1) interacting protein (Wtip) maps to human chromosome 19, a region linked to familial focal segmental glomerulosclerosis (FSGS). It contains three LIM and a PDZ binding domain. However, the precise *in vivo* function of the Wtip is still unknown. To elucidate the function of Wtip, we studied its function during the zebrafish embryonic development.

Unexpectedly, zebrafish Wtip protein was found to localize in the basal bodies/centrosomes. Using MO-mediated knockdown, *wtip* morphants revealed kidney cyst formation accompanied by cloaca obstruction, hydrocephalus, body axis curvature and heart edema, which are similar to our previous studies in the *pkd2* morphants. We further characterized the phenotype in the pronephros and found out that Wtip is required to maintain planar cell polarity (PCP), cilia length, numbers and cilia proteins trafficking defects for Polycysin-2 and Ift88. In addition to the kidney defects, we also discovered that loss of *wtip* results left-right asymmetry and conversion extension cell movement defects such as widened rhombomeres, somites and a shortened body axis due to KV defects such as cilia length, number, KV's cell shape accompanied by a defect in centrosome migration to the apical cell surface. Moreover, we explored whether these phenotypes caused by loss of *wtip* are due to PCP signaling, by analyzing potential association to the core PCP and basal body protein Vangl2 which is essential to maintain actin organization. Based on these data we propose that Wtip may provide a new player in ciliopathies modulating non-canonical Wnt signaling.

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