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Symposium

Mechanisms of cell proliferation through primary cilium

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Primary cilium is a nonmotile sensory organelle that possesses selective membrane receptors. The cilium is dynamically regulated in a cell cycle-dependent manner; it is displayed at the G₀/G₁ phase of many cell types, including neural progenitor cells, and resorbed prior to the S phase. The ciliary dynamics has pivotal roles in development of many tissues/organs. However, the molecular mechanism how the cilium controls cell proliferation remains largely unknown. We found that IGF-1 was one of the growth factors that promoted proliferation of neural progenitors. Tctex-1, a light chain of cytoplasmic dynein that plays a key role in ciliary resorption, can be free from dynein complex when it is phosphorylated at Thr 94. We also found that phospho-Tctex-1 was enriched at the ciliary base in the cells. Molecular approaches analyzed in an immortalized retinal pigment epithelial cell line revealed the physical and functional interaction of phospho-Tctex-1 with the regulators of actin dynamics such as annexin A2, Arp2/3 complex and Cdc42, which promoted branched actin polymerization and dynamin- and clathrin-dependent endocytosis at peri-ciliary region. Our study demonstrated that these mechanisms collectively regulate ciliary resorption and proliferation of neural progenitors.