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Regulatory Mechanisms of Primary Ciliary Resorption and Cell Cycle Progression by a Dynein Light Chain, Tctex-1

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The primary cilium is a microtubule-based sensory organelle that transduces its signals through specifically distributed receptors and ion channels on the ciliary membrane. The proximal region of the ciliary axoneme is surrounded by an invaginated membrane, called ciliary pocket. Primary cilium is formed during the G0/G1 phase in many cell types, including neural progenitor cells, and is resorbed as the cells re-enter cell cycle. Dysregulation of the ciliary dynamics is associated with hereditary disorders, such as microcephaly. Tctex-1, a cytoplasmic dynein light chain, has a dynein-independent role when it is phosphorylated at Thr94. We have shown that (T94)Tctex-1 phosphorylated by the action of insulin-like growth factor 1 accelerates branched actin organization and clathrin-dependent endocytosis at the ciliary pocket. The machinery was critical for ciliary resorption, cell cycle re-entry, and self-renewal of the neural progenitor cells in the developing neocortex. However, it remains unclear how Tctex-1 regulates the endocytosis. In the present study, we identified microtubule-associated serine/threonine kinase 4 (MAST4), a function-unknown protein, as a binding protein to Tctex-1. In retinal pigmented epithelial cells (RPE-1), a model cell line for cilia researches, we found that knockdown of MAST4 suppressed endocytosis, ciliary resorption, and cell cycle re-entry, emphasizing on the significance of phospho-(T94)Tctex-1-MAST4 pathway as a part of such biological events.