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The role of primary cilium in cell growth and differentiation

Masaki Inagaki, Daishi Yamakawa, Kousuke Kasahara

Dept. Physiol., Mie Univ. Grad. Sch. Med

Primary cilia are microtubule-based sensory organelles that organize numerous key signaling during development and tissue homeostasis. Defects in primary cilia formation and dysregulated ciliary functions result in multiple genetic diseases, such as obesity, polycystic kidney and tumorigenesis. We have previously shown that a centriolar protein trichoplein functions as a negative regulator of ciliogenesis by activating Aurora A kinase. In proliferating cells, trichoplein is stabilized by USP8 deubiquitinase that is phosphorylated and activated by EGFR kinase. When cells are exposed to cell cycle arrest signals, such as serum starvation, the EGFR-USP8 pathway is down-regulated, and thereby $CRL3^{KCTD17}$ ubiquitin E3 ligase induces trichoplein degradation and ciliogenesis. Recently, we found that trichoplein knockout mice were obesity-resistant, and high-fat diet consumption had little effects on body weight. The mice have long cilia in various tissues and restrict both the high-fat diet- and the injury-mediated adipogenic differentiation. Moreover, trichoplein knockdown suppresses adipogenic differentiation of murine mesenchymal-like C3H10T1/2 cells through the long cilia-mediated inhibition of insulin signal. In this session, I would like to talk about the roles of primary cilia in cell growth and differentiation.