【Grant-in-Aid for Scientific Research(S)】
Biological Sciences (Biology)

Title of Project： Non-centrosomal microtubule-dependent organization of the cells

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Research Area： Cell Biology
Keyword： Cell structure, cytoskeleton and movement, microtubule, cell polarity, cell adhesion

【Purpose and Background of the Research】

Microtubules play important roles in cellular morphogenesis and dynamics. At the interphase of cell cycle, cells have two kinds of microtubules, one nucleated from the centrosome and the other generated from non-centrosomal sites (Fig. 1). Major microtubules in epithelial cells and neurons are actually non-centrosomal. Although the mechanisms for the generation of centrosomal microtubules have extensively been studied, those for non-centrosomal microtubule are poorly understood. We recently identified a novel protein that binds the minus end of microtubules, which has been named Nezha (also called CAMSAP3), and showed that this protein nucleates microtubules at non-centrosomal sites. In this program, we will investigate the role of Nezha/CAMSAP3 and its related proteins in microtubule network formation as well as in various cell behavior, using epithelial and neural tissues.

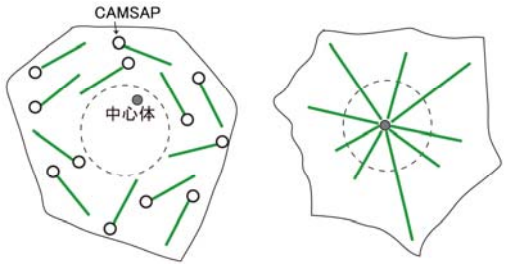

Fig. 1. Centrosome- and CAMSAP-derived microtubules. Their proportion varies between cell types.

【Research Methods】

We will use mouse intestinal epithelia and also cell lines derived from these tissues to investigate the role of CAMSAPs. We will observe the effects of CAMSAP gene knockout or knockdown on epithelial architecture. We will adopt similar methods for analysis of the role of CAMSAPs in neuronal migration and neural tissue formation. To investigate the role of CAMSAPs in cell adhesion, we will focus on a minus-end directed motor, KIFC3, as we previously found that KIFC3 moves to cell junctions in a CAMAP3-dependent manner. We will identify cargos transported by KIFC3, and analyze their functions. We will also perform molecular analysis to understand the mechanisms by which CAMSAPS regulate microtubule polymerization.

【Expected Research Achievements and Scientific Significance】

The roles of microtubules in cell formation and function seems more complicated than currently thought. We will establish a clearer image about the microtubule functions in animal cells through the comparative studies of centrosomal and non-centrosomal microtubules. These studies will uncover novel roles of microtubules in epithelial and neural morphogenesis, providing an answer to the question of how the two populations of microtubules are differentially used by a cell.

【Publications Relevant to the Project】

・Meng, W., Mushika, Y., Ichii, T., and Takeichi, M. (2008) Anchorage of microtubule minus-ends to adherens junctions regulates epithelial cell-cell contacts. Cell *135*, 948-959.
・Tanaka, N., Meng, W., Nagae, S., and Takeichi, M. (2012) Nezha/CAMSAP3 and CAMSAP2 cooperate in epithelial-specific organization of non-centrosomal microtubules. Proc. Natl. Acad. Sci. USA. *109*, 20029-20034.

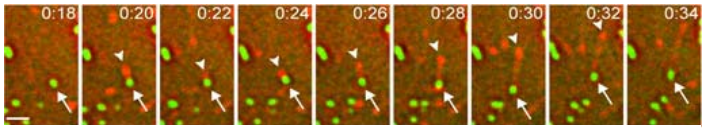

Fig. 2. Time-lapse images showing that EB1, a microtubule-plus end-binding protein, emerges and moves away from a CAMSAP3 cluster.

【Term of Project】

FY2013-2017

【Budget Allocation】

166,000 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.cdb.riken.go.jp/ctp/