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

Title of Project : Roles of Cell Adhesion and Signaling in Cell Morphogenesis

Yoshimi Takai
(Kobe University, Graduate School of Medicine, Professor)

Research Area : Biological science

Keyword : Cell signal transduction

【Purpose and Background of the Research】

Cell morphogenesis in multicellular organisms is regulated by external circumstances and a variety of stimulants including growth factors and chemokines. Cell shape determination and alternation are essential for existence and survival of multicellular organisms. The irreversible disruption of cell morphology would lead to severe impairment of tissue functions, which might cause life-threatening disorders. In this context, the understanding of the molecular mechanisms of cell morphogenesis is quite important both biologically and medically. We, therefore, clarify these molecular mechanisms in terms of cell adhesion and signaling, particularly focusing on nectins, which we first identified as a new type of cell adhesion molecule (CAM).

【Research Methods】

To achieve our research objectives, we plan to carry out the following works.

(1) Determination of the localization of adherens junctions (AJs) and tight junctions (TJs) and the cell height in epithelial cells

After the establishment of cell-cell junctions in epithelial cells, the cell surface is separated into two regions: the apical and basolateral regions. TJs, which divide these regions, always localize at the apical side of AJs. However, it is unclear how the localization of AJs and TJs is determined. To explore this, we attempt to completely reconstruct AJs and TJs in fibroblasts that do not possess AJs nor TJs.

(2) Cell morphogenesis during epithelial-mesenchymal transition (EMT) and mesenchymal-epithelial transition (MET)

At the beginning of EMT, the formation of the leading edge is observed at the end of the epithelial cell colony, and induces cell movement. We investigate the involvement of signaling molecules, such as small G proteins, and CAMs, such as nectins and nectin-like molecules, in cell movement. This investigation would provide a clue to reveal the mechanisms of EMT. We also examine the mechanisms of MET using the experimental methods as described in (1).

(3) Mechanisms of the synapse formation and remodeling and the axon specification in neurons

During the synapse formation, puncta adherentia junctions are formed by the function of the nectin-afadin system. In addition, CAST and S-SCAM, which we previously identified, localize at the active zone and the post synaptic density, respectively, and play a pivotal role in the synapse formation and remodeling. We extend these results by examining the mechanisms of cell morphogenesis in neurons.

【Expected Research Achievements and Scientific Significance】

In addition to previous research achievements from other labs, we can propose novel molecular mechanisms and scientific significance of cell morphogenesis in various types of cells by systematically analyzing the crosstalk among cell-cell adhesion, cell-matrix adhesion, and their signaling pathways. It is of note that our research plan is based on the new CAM nectins. The findings obtained from this study would provide a new paradigm in biological science and a new therapeutic approach for many diseases.

【Publications Relevant to the Project】

- Takai, Y., Miyoshi, J., Ikeda W., and Ogita H. Nectins and nectin-like molecules: roles in contact inhibition of cell movement and proliferation. ***Nat. Rev. Mol. Cell Biol.***, 9; 603-615. (2008)
- Takai, Y., Ikeda, W., Ogita, H., and Rikitake, Y. The Immunoglobulin-like cell adhesion molecule nectin and its associated protein afadin. ***Annu. Rev. Cell Dev. Biol.***, 24; 309-342. (2008)

【Term of Project】 FY2009-2013

【Budget Allocation】 160,000 Thousand Yen

【 Homepage Address and Other Contact Information】

http://www.med.kobe-u.ac.jp/mcb/index.html