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

Title of Project：Regulation of Cell Dynamism by phosphoinositides

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Research Area：Cell Biology
Keyword：plasma membrane, inositolphospholipids, membrane shaping, cell dynamics

【Purpose and Background of the Research】

Plasma membranes generate a variety of ignals for cell growth, differentiation and movement in response to extracelluar stimuli, such as hormones and growth factors. Basically, signals are generated by the interaction between cytosolic proteins and plasma membranes, mainly composing of lipid bilayers. Among components of membrane lipids, phosphoinositides are known to play important roles in generation of second messengers, such as IP3 and diacylglycerol.

We have shown that phosphoinositides in plasma membrane regulate cell movement and cell shaping through their specific binding proteins.

However, it is still unclear how phosphoinositides play a role in cell movement, membrane trafficking and cell adhesion. In this project, we would like to clarify a signal generating mechanism through phosphoinositides in cell dynamism.

【Research Methods】

We already screened rat brain extracts and culture cell lysates to look for phosphoinositide-binding proteins and found 400 hundreds of proteins. Among them, we chose three promising binding proteins, such as PSTPIP1/2, PIR121/Sra1 and SH3YL1. These proteins play important roles in phagocytosis, macropinocytosis and cell adhesion, respectively.

We will clarify how these phosphoinositide binding proteins form signaling complex at plasma membrane and generate signals through specific membrane structures.

【Expected Research Achievements and Scientific Significance】

In this project, we looked for new phosphoinositide-binding proteins and found 400 hundreds of proteins. Among them we chose three promising proteins, which are known as causative proteins of some disease.
Through examining the function of these proteins, we would like to clarify how phosphoinositide-binding proteins shape membranes and act as interface proteins which associate a variety of signaling proteins with membranes , resulting in regulation of dynamic cell motility. Finally, we would like to develop new concept of anti-cancer and anti-inflammatory drugs.

【Publications Relevant to the Project】

Takenawa T. and Suetsugu S. Cordinated regulation of membrane and cytoskeleton by WASP/WAVE family proteins and their binding partoners. Nature Rev. Mol. Cell Biol. 8, 37-48 (2007)
Itoh T., Hasegawa, J., Tsujita, K., Kanaho, Y., and Takenawa, T. The tyrosine kinase Fer is a downstream target of the PLD-PA pathway that regulates cell migration. Sci Signal. 2, ra52. (2009)

【Term of Project】 FY2011-2015

【Budget Allocation】 154,900 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.med.kobe-u.ac.jp/lipid/