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

Biological Sciences (Biology)

Title of Project： The roles of membrane lipids for intracellular signaling platform

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Research Project Number：17H06164　　Researcher Number：40167987
Research Area：　biological sciences
Keyword：　lipid biology

【Purpose and Background of the Research】

The cytoplasm of eukaryotic cell is elaborately subdivided into discrete, specialized, membrane-bound structures called intracellular organelles. Each organelle has been shown to have characteristic lipids such as phosphoinositides. However, the roles of these membrane lipids of organelles have remained poorly understood.

Our previous studies revealed that phosphatidylserine, a relatively minor constituent of biological membranes, was concentrated on the cytosolic leaflet of recycling endosomes and was required for the membrane traffic through recycling endosomes (PNAS 2011, EMBO 2015). These studies also revealed that the pleckstrin homology (PH) domain of evectin-2 bound specifically to phosphatidylserine.

In this project, we will identify the proteins proximal to specific phospholipids using several lipid-binding domains such as the PH domain of evectin-2 and comprehensively understand the biological functions of organelle membranes as a device for effective and accurate cellular signaling.

【Research Methods】

We have recently developed methods to identify proteins proximal to phosphatidylserine in cytoplasmic leaflet of recycling endosomes. In this project, we will apply these methods to other phospholipids present in other organelles.

【Expected Research Achievements and Scientific Significance】

Identification of proteins proximal to organelle phospholipid will address important but so far unresolved questions in membrane biology: “How and why does each organelle have characteristic phospholipids?” Our studies will also discover new drug targets in the inflammatory diseases and cancer.

【Publications Relevant to the Project】

- M Uchida, Y., Hasegawa, J., Chinnapen, D., Inoue, T., Okazaki, S., Kato, R., Wakatsuki, S., Misaki, R., Koike, M., Uchiyama, Y., Iemura, S., Natsume, T., Kuwahara, R., Nakagawa, T., Nishikawa, K., Mukai, K., Miyoshi, E., Taniguchi, N., Sheff, D., Lencer, W. I., Taguchi, T., and Arai, H. (2011). Intracellular phosphatidylserine is essential for retrograde membrane traffic through endosomes. **Proc Natl Acad Sci U S A** 108, 15846-15851.
- Lee, S., Uchida, Y., Wang, J., Matsudaira, T., Nakagawa, T., Kishimoto, T., Mukai, K., Inaba, T., Kobayashi, T., Molday, R. S., Taguchi, T., and Arai, H. (2015). Transport through recycling endosomes requires EHD1 recruitment by a phosphatidylserine translocase. **EMBO J** 34, 669-688.
- Mukai, K., Konno, H., Akiba, T., Uemura, T., Waguri, S., Kobayashi, T., Barber, G. N., Arai, H., and Taguchi, T. (2016). Activation of STING requires palmitoylation at the Golgi. **Nat Commun** 7, 11932.

【Term of Project】

FY2017-2021

【Budget Allocation】

156,700 Thousand Yen

【Homepage Address and Other Contact Information】

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