the organisation of the components of a transport receptor complex in the secretory pathway. Knowledge of these transport processes may ultimately lead to new strategies for the treatment of other inherited and acquired diseases in which protein secretion is impaired

Keywords: Glycoprotein transport, ER quality control, Protein complex

FA1-MS9-T05

Structural basis for the membrane targeting of the exocyst complex. Masami Yamashita[a], Kazuo Kurokawa[b], Yusuke Sato[a], Atsushi Yamagata[a], Hisatoshi Mimura[a] Azusa Yoshikawa[a], Ken Sato[c], Akihiko Nakano[b,d], Shuya Fukai[a]. [a]*Synchrotron Radiation Research Organization and Institute of Molecular and Cellular Biosciences, The University of Tokyo, Japan.* [b]*RIKEN Advanced Science Institute, Japan.* [c]*Graduate School of Arts and Science, The University of Tokyo, Japan.* [d]*Graduate School of Science, The University of Tokyo, Japan*.
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Cell polarization is a critical process for differentiation and proliferation in eukaryotes. A prominent example of the polarization is budding in yeast, during which required proteins and lipids are carried in secretory vesicles and transported to the bud tip by exocytosis. The exocyst complex is a large hetero-octameric protein complex critical for cell polarization, which regulates exocytosis in yeast and mammal. The exocyst complex is composed of Sec3, Sec5, Sec6, Sec8, Sec10, Sec15, Exo70 and Exo84. The exocyst complex tethers secretory vesicles to specific regions of the plasma membrane by recognizing small GTPase and phosphoinositide $PI(4,5)P_2$ on the membrane. Although how the exocyst complex recognizes both small GTPase and $PI(4,5)P_2$ on the plasma membrane has been unknown, the GTPase and $PI(4,5)P_2$ binding region of exocyst subunit has been identified. For instance, the N-terminal region of yeast Sec3 (Sec3-N) is sufficient for the binding to the small GTPase Rho1 and $PI(4,5)P_2$. Here we have determined the crystal structure of yeast Sec3-N in complex with Rho1 at 2.6 Å. The crystal structure exhibits that Sec3-N adopts pleckstrin homology (PH) fold, despite having no detectable sequence homology with other PH domains of known structure. Furthermore, clusters of conserved basic residues constitute a positively charged cleft, which was identified as a binding site for $PI(4,5)P_2$. The structure and structure-based site-directed mutagenesis studies *in vitro* and *in vivo* show that the small GTPase and $PI(4,5)P_2$ regulate the localization of the exocyst complex at the specific site of plasma membrane in a complementary fashion[1].

[1] Yamashita M *et al*., *Nature Struct. Mol. Biol.*, 2010, 17, 180-186.

Keywords: protein X-ray crystallography, protein transport, protein structures