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

Biological Sciences (Biology)

Title of Project : Elucidation of the mechanism of the control of protein trafficking at mitochondrial membranes

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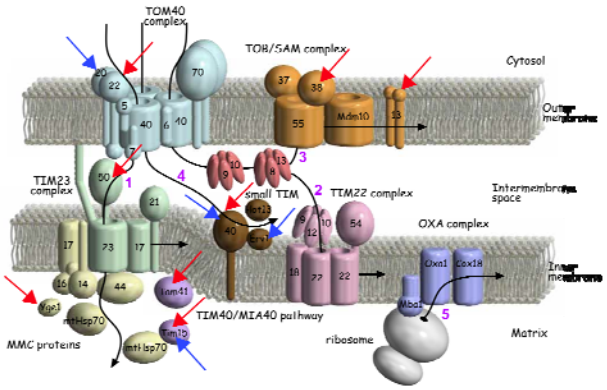
Research Area : Biology, Biological science, Structural biochemistry

Keyword : Protein, Organelles

【Purpose and Background of the Research】

Mitochondrial functions in yeast cells rely on the elaborate system that controls the trafficking of over 1000 different mitochondrial proteins. Our view on the mitochondrial protein traffic has been changing significantly due to recent findings of the mitochondrial internal structures, relationship between lipid compositions and mitochondrial protein traffic, redox control of the intermembrane space, mitochondrial-ER connections etc. In the present project, we are aiming at revealing the entire picture of the mitochondrial protein traffic control system, highlighting the emerging concept of mitochondrial internal structures, connection with other organelles, new roles of membrane lipid compositions and redox state within mitochondria etc. By doing so, we anticipate that a new paradigm of the relationship between intracellular structures and cellular functions will be unveiled.



【Research Methods】

(1) Search for components of the mitochondrial-ER tethering complex, (2) search for components of the contact site between the outer and inner mitochondrial membranes, (3) elucidation of the roles of Tim21-Qcr6 interactions in protein sorting between the inner boundary membrane and cristae membrane, (4) search for new outer membrane factors mediating assembly of TA (tail-anchor) proteins into the outer membrane by identifying the crosslinking partners for Tom22, (5) elucidation of the functional network of components involved in protein and lipid biogenesis by characterizing the functions of Art5, a multi-copy suppressor for the maintenance factor Tam41, (6) revealing the structural basis of the functions of redox translocators including Tim40/Mia40 in the intermembrane space, and (7) determination of the structures of the translocator components including membrane-embedded ones.

【Expected Research Achievements and Scientific Significance】

Our goal is to understand the mechanism of the control of mitochondrial protein trafficking by revealing the entire network and interplay of the translocators and related soluble factors as well as shedding light on the roles of mitochondrial internal membrane structures, redox control and tethering with other organelles such as the ER. This will pave the way to complete understanding of the principle of biogenesis of mitochondrial structures, and hopefully to the new technology of 'organelle engineering' that will allow us to alter and design new organellar functions.

【Publications Relevant to the Project】

S. Kawano, K. Yamano, T. Endo et al. (2009) Structural basis of yeast Tim40 as an oxidative translocator in the mitochondrial intermembrane space. *Proc. Natl. Acad. Sci. USA 106*,14403-14407.

Y. Tamura, Y. Harada, T. Endo et al. (2009) Tim23-Tim50 pair coordinates functions of translocators and motor proteins in mitochondrial protein import. *J. Cell Biol. 184*, 129-141 (2009)

【Term of Project】 FY2010-2014

【Budget Allocation】 162, 000 Thousand Yen

【 Homepage Address and Other Contact Information】

http://biochem.chem.nagoya-u.ac.jp/