

Target Oriented Structural Genomics on post-translational modification and protein transport at the KEK-PF

Ryuichi Kato¹, Masato Kawasaki¹ and Soichi Wakatsuki¹

¹ Structural Biology Research Center, Photon Factory, IMSS, High Energy Accelerator Research Organization (KEK), 1-1 Oho, Tsukuba, Ibaraki, 305-0801, Japan

Our Structural Biology Research Center in KEK-PF serves as one of the nine consortia of Protein 3000 (a national project of Japan), one is comprehensive program and the other is target oriented structural genomics programs. Our consortium consists of eleven universities and four research institutes including structural biologists (both X-ray and NMR), bioinformaticians, biochemists and cell biologists, pursuing structural and functional analyses in the field of post-translational modification and transport.

Cell signaling and intracellular trafficking are the means by which eukaryotic cells deliver cargo proteins to various organelles, cell membranes, and extracellular destinations. During the trafficking process, more than half eukaryotic proteins undergo post-translational processing and modification such as glycosylation. Accurate distribution and modification of the proteins are crucial for a range of cellular functions and activities. An increased understanding of the biological and biomedical function of transport and modification proteins is indispensable for progress in the treatment of human diseases.

To facilitate the current research program, the Structural Biology Research Center of KEK-PF has taken the lead by coordinating the research network. As part of the project, we have sought to maximize the efficiency of large-scale expression, purification, and crystallization of proteins by trying to eliminate bottlenecks in each process. Each structural analysis project maintains close contacts with groups responsible for functional analyses. Our initial research plan was to accomplish structural and functional analyses of more than 70 proteins in five years. To date, the number of structures determined gets over 100, and that of data collected is 50. Thus, the twice of initial target number will be achieved soon. In addition, we are currently working on about 150 additional targets. Furthermore, we have submitted 11 domestic and two international patent applications, based on our R&D and structural and functional studies of the target proteins.

KEK-PF is one of the powerful synchrotron facilities which operate high-throughput protein crystallography beamlines in Japan. To cooperate promoting the Protein 3000 Project, the Structural Biology Research Center has established an operation scheme to reserve about 30% of the beam time of our beamlines for users of the eight university consortia. We served total 213 days beam time to users from the beginning of the project. We also developed a Web-based beam time reservation system to facilitate the project.