Life Science
Structural Biology

Proteins are produced according to genetic information coded in the genome and are key molecules in biological systems. In order to understand the nature of biological systems, it is essential to understand the relationship between the structure and function of biological macromolecules, e.g., proteins and nucleic acids. Protein crystallography (PX) and small-angle X-ray scattering (SAXS) are powerful experimental techniques that enable the determination of three-dimensional protein structures and actively performed at SPring-8.

After the completion of the Human Genome Project, structural genomics research projects have been progressing worldwide. At SPring-8, the Protein 3000 project, a Japanese structural genomics project, has been progressing rapidly owing to high-throughput PX beamlines and has been working to elucidate the structure and function of proteins found in various biological systems. The number of determined protein structures using SPring-8 beamlines grows larger every year, and 366 structures were added to the Protein Data Bank (PDB) in 2006. The summary of the Protein 3000 project was described in the last two articles. Furthermore, the number of crucial structural analysis and more detailed structure-function studies are increasing. Herein, selections of remarkable structures determined at SPring-8 are described.

The first three articles are related to the structures of membrane proteins. The drug complex of the AcrB structure revealed a rotating mechanism of drug export from bacterial cells. The Dsb enzyme complex, important in disulfide bond oxidation, showed the utilization of quinine and the DsbA-DsbB transfer of the oxidative state. The membrane binding protease FtsH showed a substrate-translocation mechanism involving open-close motions of subunits driven by ATPase activity.

In studies of nucleotide-protein interaction, many fruitful results were reported. The complex structure of DEAD-box RNA helicase clearly showed the relationship between ATPase activity and the RNA unwinding mechanism. It was found that tRNA modification with pseudouridine is essential for the formation of the H/ACA box ribonucleoprotein particle.

The structure of peptidylarginine deminase 4 revealed that the modification of the N-terminal peptide of histone involves no sequence specific recognition. The firefly luciferase structure revealed the mechanism underlying the yellow-green light of firefly emission and facilitated the engineering of emission wavelength by structure based protein design. The structure of geranylgeranyl pyrophosphate synthase clarified the key residue involved in substrate chain elongation. γ-Glutamyltranspeptidase structures were used to show the reaction mechanism of the enzyme by observing them at a slow reaction speed in crystalline state.

SAXS revealed the dynamical conformational change of multisubunit and/or multidomain orientations. The large molecular complex of an extracellular signaling two-component regulatory system and a fatty acid β-oxidation multienzyme complex were elucidated along with their structural flexibilities in combination using PX results. SAXS measurement of the initially collapsed conformation showing the largest protein size supports the scaling law under various protein conditions. A noncrystalline diffraction study of amiloid fibrils suggested the scales of its aggregated β-structure.

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