LIFE SCIENCE :

"Kiri" - Paulownia

Structural biology propels exhaustive explorations of the structural and functional details of biological macromolecules. For this purpose, the development and upgrade of SPring-8 structural biology beamlines are moving forward and continuing. As a result, the number of structures determined is increasing yearly. Moreover, in this year, we are able to produce many fruitful results in broad biological fields as follows.

The structure of human proteins can be used as basis for drug development. Leukotriene C_4 synthase is embedded in the nuclear membrane and related to allergic reactions. Ago *et al*. determined the structures of its trimeric integrated membrane protein. Its active site located between adjacent subunits and two arginine residues performs an acid-base catalysis. Endotoxin is a material released by the lysis of pathogenic bacteria and causes an immune response. The structure of the complex of the MD-2 protein and its antiendotoxic lipid was determined by Satow *et al*. Their results suggested a principal role of MD-2 in the endotoxin shock mechanism. Reelin is a signaling protein that interacts with lipoprotein receptors and regulates correct cell positioning during brain development. The structures of the repeated portions in reelin were determined by Nogi *et al*. They investigated new insights into a long rod of the entire structure and the candidates of the receptor-binding interface.

STRUCTURAL BIOLOGY

The association and dissociation of any protein unit are clues for investigating biological phenomena. Structural biology provides the observation direct or indirect of these phenomena. Akiyama *et al*. revealed the oscillatory mechanism of the circadian clock using KaiABC proteins by SAXS analysis. The phosphorylation-dependent structural change of KaiC promotes the oscillatory association and dissociation of KaiA and KaiB to KaiC. Fukunaga *et al*. revealed structurally the cysteinyl-tRNA synthesis by SepRS and SepCysS in an archaeal bacterium. This reaction starts uniquely with a noncanonical *O*-phoshoserine, and the formation of the protein complex is essential to prevent mistranslation. This unique secure strategy is also interesting from the viewpoint of evolutional process of the genetic code. Higuchi *et al*. determined the structure of the DIX domain, a component of the Wnt signaling pathway that is a major cancer pathway. Its structure showed an ubiquitin-like fold and seemed to be polymerized with a long helical chain. This dynamic property might be important for regulating the association to partner proteins. Miki *et al*. determined the three structures required in synthesis of complex metal center, $NiFe(CO)(CN)_2$, of [NiFe] hydrogenase. From three independent structures, it is suggested that the HypCD complex captured its Fe atom and forms a ternary complex with thiocyanated HypE to obtain CN ligands. To complete the metal center, thiol redox signaling similar to the ferredoxin:thioredoxin reductase-like cascade is adopted.

Basic biological phenomena were also able to be solved using crystal structures. Imada *et al*. showeded the structure of FliI, a component of the bacterial export apparatus for secreting flagellar axial proteins. Since this component is highly similar to the F_1 portion of F_0F_1 ATP synthase, both machines might have evolved from a common ancestral system. The entry of macromolecules into the cell nucleus is strictly regulated by importin proteins. Transportin is a transport receptor of the system and binds signal sequences of substrate proteins. The structures of substrate-free and -bound forms of transportin were determined by Sato *et al*. Binding/release of substrates might be regulated by the interaction with the signal sequences and RanGTP to the two arches of the superhelical S-like structure of transportin. Magnesium homeostasis is essential for regulating many enzymatic processes including the utilization of ATP. Nureki *et al*. revealed the structure of a magnesium transporter and suggested its selective membrane transport mechanism. A high concentration of magnesium ion mediates the interaction between cytosolic and transmembrane domains, which would close the ion-conducting pore. Endocytosis is a dynamic cellular process for the uptake of materials from the outside of the cell. Shimada *et al*. revealed the structure of the EFC domain that assists in the tubulation of the cell membrane. The diameter of curvature of its spiral/ring structure is consistent with the size of the tubular membrane. This shows that the EFC domain plays a leading role in the invagination step of endocytosis.

Finally, we report over 2000 citations of an article on the structure of bovine rhodopsin determined with a SPring-8 beamline in 2000.

Masaki Yamamoto and Yoshitsugu Shiro