Life Science:


"Fuji"- Wisteria

A fine X-ray beam penetrates the crystals of biological macromolecules and exposes their structural secrets, and bright synchrotron radiation contributes to expand the range of the analysis. However, many protein crystals, particularly tiny and/or ill-diffracting crystals, remain to be analyzed. Therefore, SPring-8 structural biology beamlines are continuously being developed for such tough samples. As a result of the incorporation of accumulated developmental knowledge and leading-edge technologies, the RIKEN microbeam beamline for structural biology (BL32XU) was established in 2010 under a national research project entitled Targeted Protein Research Program, which aims at advancing research and technologies as the next phase of structural genomics research. This beamline provides the world's finest and brightest X-ray beam with a size range of 1 μm^2 - 10 μm^2 with a flux density of 10^{10} photons/sec/μm^2. This beam is considered to affect any quantitative and qualitative changes in structural studies. The operation of the beamline has already been started and is open for people who are part and not part of the project. Thus, results obtained from the beamline would be actively reported in the near future.

This year, many outstanding results have been reported, particularly in the research field of nucleic acid-protein interactions. Yamashita *et al*. determined the structure of microRNA and the exportin complex. microRNA, a family of non-coding RNAs, is a key component in gene silencing by RNA interference. This molecule is produced in nuclei and exported to the cytosol by a large protein machinery. Kurumizaka *et al*. determined the unstable structure of the histone variant H3T. Histone is the key protein for DNA packaging and dynamically regulates chromatin by modifying itself. This protein might affect chromatin reorganization during sperm production. Ito *et al*. determined the structure of the glutamine transamidosome complex containing tRNA(Gln), Glu-tRNA

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synthase and amidotransferase. The result indicates that error-free consecutive reactions are maintained by a dynamical structure of the multienzyme complex. Yanagisawa *et al*. performed structural and functional analyses of an aminoacyl-tRNA synthetase paralog, GenX, an enzyme that works with a tRNA mimicry protein, EF-P, similarly to aminoacyl-tRNA synthase and tRNA, and that shows a good example of convergent evolution.

Definitely, there are many remarkable reports in other fields, and four topics were selected. Inaba *et al*. determined the structure of human Ero1α, a flavoenzyme responsible for protein disulfide generation. The structural relationship among its four regulatory cysteines and FAD with the enzymatic function is clearly depicted. Takeda *et al*. revealed the mechanism of the regulation of the actin capping protein CP by the structures of two types of protein complex. CP functions to stop actin polymerization and affects cell motility. One of the inhibitors unexpectedly initiates the twisting motion of the heterodimeric CP structure, leading to depolymerization. Okumura *et al*. employed macromolecular crystallography and a chemical biology approach, providing a clue that the nuclear protein Pirin regulates melanoma cell migration. A small Pirin-binding compound was identified by chemical array screening and its binding structure was determined by synchrotron. This combinatory approach may be spread for investigating unknown protein functions. Nojiri *et al*. determined the crystal structure of copper-dependent nitrite reductase and the cytochrome *c* complex, which is essential to biological nitrite reduction in the global nitrogen cycle. The hydrophobic electron-transfer path is discovered at the docking interface of two proteins. Higuchi *et al*. showed the structure of oligomeric cytochrome *c* and the mechanism of its domain swapping polymerization by the combination of crystal analysis with X-ray solution scattering. Protein denaturants possibly form insoluble amyloid fibers and the mechanism of the protein polymerization is also interesting from the point of view in neurodegeneration.

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