Overview of Taiwan-Japan joint symposium (2SDP) on structural biology using X-ray crystallography and cryo-EM at the 2019 BSJ meeting

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Cryo-electron microscopy (cryo-EM) is rapidly becoming a leading player in structural biology, while X-ray crystallography still prevails as a powerful traditional tool for studying 3D structures of proteins (Fig. 1). The Taiwan-Japan joint symposium on structural biology using X-ray crystallography and cryo-EM, chaired by myself and Prof. Ken Yokoyama from Kyoto Sangyo University, was held as a session in the BSJ meeting in Miyazaki Japan in the afternoon of 25th September 2019. In this symposium, six researchers from Taiwan and Japan presented cutting-edge results using the two methods as described below.

The first speaker was Prof. Masahide Kikkawa from the University of Tokyo, who talked about cryo-EM analysis of cilia and microtubule-based motor proteins. Prof. Kikkawa and his group knocked-out efca1 in zebrafish, encoding calaxin, and found that the mutant zebrafish have situs inversus due to the irregular ciliary beating of Kupffer’s vesicle cilia (Sasaki et al. 2019), and also analyzed a complex between dynein microtubule binding domain and microtubule using high-resolution cryo-EM. From these findings, he proposed a bound-unbound switching mechanism of the motor protein.

The next speaker was Dr. Shang-Te Danny Hsu from Academia Sinica, who talked about cryo-EM analysis of a feline coronavirus spike protein. Feline infectious peritonitis virus (FIPV) is an alphacoronavirus that causes nearly 100% mortality rate without effective treatments. Dr. Hsu and his colleagues have solved a 3.3 Å cryo-EM structure of an FIPV spike protein, responsible for host recognition and viral entry (Yang et al. 2020). In his talk, he presented an insight inspired by the EM structure for a better molecular understanding of the pathogenesis of FIP.

The third speaker was Dr. Kuen-Phon Wu from Academia Sinica, who talked about cryo-EM studies of bacterial glutamine synthetase. Bacterial glutamine synthetase (GS) is a dodecameric enzyme which responds in cellular glutamine biosynthesis as well as nitrogen fixation. Dr. Wu and his colleagues have determined the structures of GS in the catalytic cascade by cryo-EM at 2.6 Å resolution. He presented the new structures and a possible mechanism of recruiting magnesium, consuming ATP, and converting glutamine from glutamate.

The fourth speaker was Prof. Jun-ichi Kishikawa from Kyoto Sangyo University, who talked about single-particle analysis of membrane-embedded domain V₀ of V-ATPase. V-ATPases are composed of hydrophilic V₁ and membrane-embedded V₀ (Fig. 1). The atomic structures of the V₁ part and a rotational mechanism inspired by the structures have already been elucidated under the condition of the V₀ structure missing (Arai et al. 2013). The group of Profs. Kishikawa and Yokoyama have solved the cryo-EM structures of a whole V-ATPase complex from Thermus thermophilus at low to middle resolution (Nakanishi et al. 2018). Recently, they have succeeded in solving the cryo-EM structure of the V₀ part at a higher resolution. In his talk, he presented a new structure of V₀ and proposed that the V₀ part adopts an autoinhibited form when V₁ dissociates from V₀.

The fifth speaker was prof. Kazuhiro Abe from Nagoya University, who talked about the transport mechanism of the gastric proton pump, H⁺,K⁺-ATPase, which is responsible for acidifying the gastric juice up to pH 1 and thus an important drug target for treating gastric acid-related diseases. Prof. Abe and his colleagues have solved the crystal structures of the H⁺,K⁺-ATPase in two different conformations (Abe et al. 2018). In his talk, he presented these cryo-EM structures and discussed the reasons why the pump is able to fulfill the
requirements for the generation of a million-fold proton gradient across the membrane.

The last speaker was Prof. Hui-Chih Hung from National Chung-Hsing University, who talked about p53 function regulated by PAD4 through protein citrullination. Peptidylarginine deiminase 4 (PAD4)-catalyzed citrullination has been shown to play an emerging role as a potential cancer therapeutic target (Liu et al. 2017). Prof. Hung and her group have elucidated that p53 protein can be citrullinated by PAD4 in vitro and in the cell. Structural and functional analysis demonstrated that citrullination has detrimental effects on p53 tetramerization and thus impairs their DNA-binding ability. In her talk, she presented direct evidence of the PAD4-p53 interaction and proposed a potential mechanism of how PAD4 involves in p53 target gene regulation by citrullinating p53.

Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by the author.

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