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Editorial

Crystallographic Studies of Enzymes

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Abstract: Enzymes are biological catalysts, which work to accelerate chemical reactions at the molecular level in living organisms. They are major players in the control of biological processes such as replication, transcription, protein synthesis, metabolism, and signaling. Like inorganic catalysts, enzymes function by decreasing the activation energy of chemical reactions, thereby enhancing the rate of the reactions. Enzymes are widely used for chemical, food, pharmaceutical, medicinal, analytical, clinical, forensic, and environmental applications. Therefore, studies on their structure, mechanism, and function, using a wide range of experimental and computational methods, are necessary to understand better enzymes in biological processes. For this special issue, “Crystallographic Studies of Enzymes”, we have collected research papers on enzymes with structural aspects and functional aspects; here we briefly discuss the contents of such research papers as follows, with the aim of suggesting new directions of investigation in the fields of enzyme research, protein engineering, and drug development.

Topoisomerase IV is an enzyme crucial in chromosomal DNA segregation and cell division, composed of two ParC and two ParE ATPase subunits. Crystallographic studies of the ParE ATPase domain from Xanthomonas oryzae [1] were conducted by a group led by Yong-Seok Heo at Konkuk University. The group has also determined the structure of the ATPase domain in complex with novobiocin, a complex that allows more potent inhibitors toward topoisomerase IV.

Sangho Lee group at Sungkyunkwan University focused on ketol-acid reductoisomerase (IlvC) from Streptococcus pneumoniae [2]. This enzyme is one of the key players in the branched-chain amino acids (BCAAs) biosynthesis, necessary for the survival and virulence of bacterial pathogens. Using crystallographic analysis, small-angle X-ray scattering, and site-directed mutagenesis, they clarified that D83 in the NADP(H) binding site and E195 in the Mg²⁺ binding site are the most critical amino acids in the catalysis.

Jungwoo Choe and his coworkers at the University of Seoul determined crystal structures of flavin-dependent monooxygenases from Alicyclobacillus acidocaldarius in apo- and FAD-bound state [3]. Interestingly, they proposed that this protein is highly related to DszC (sulfoxidase), DnmZ, and Kijd3 (nitrososynthases).

Biochemical characterization and crystal structure determination of a monodehydroascorbate reductase (MDHAR) from Deschampsia antarctica [4] were done by Han-Woo Kim with his Korea Polar Research Institute co-workers. They demonstrated that this enzyme is responsible for cold-tolerance and ROS-induced abiotic stress.

Another article related to yeast proteins was published by a group led by Hyun Ho Park at Chung-Ang University. They addressed structural information on the active site mutant form (R326A) of Osm1, a soluble fumarate reductase [5]. Fumarate reductase is an essential component in maintaining the redox balance in cells, catalyzing the reduction of fumarate to succinate.

Crystallographic studies of fatty acid amide hydrolase (FAAH) from Candida albicans [6] were conducted by a group at Kyungpook National University including Jeong Ho Chang. The research...
group showed that the transmembrane domain and the hydrophobic cap of rat FAAH were completely absent in the fungal FAAH. Their study provided invaluable insights for the development of potent inhibitors towards pathogenic microorganisms. This group also determined the crystal structures of an NADPH-dependent methylglyoxal reductase in apo- and NADPH-complexed form [7]. As a key enzyme in the methylglyoxal detoxification pathway, it can reduce directly the level of cytotoxic methylglyoxal.

Ki Hyun Nam at Korea University determined the crystal structure of proteinase K from *Parengyodontium album* in complex with triglycine (Gly-Gly-Gly) [8]. He also proposed that triglycine could be applied to identify the substrate recognition sites in peptide binding enzymes.

Byung Woo Han’s group at Seoul Nation University reported the crystal structure of FolC from *Helicobacter pylori* [9]. Considering the fact that FolC plays crucial roles in the folate metabolism by attaching L-Glu to dihydropteroate and folate, bacterial FolC could be an attractive universal target against pathogenic bacteria.

Lin-woo Kang-directed research group at KonKuk University determined the crystal structure of GroEL from *Xanthomonas oryzae* [10]. Bacterial GroEL/GroES complex regulates the protein folding pathway and protects nascent proteins against misfolding and unwanted aggregation. Thus, this GroEL structure will help understand the function and mechanism of the GroEL/GroES complex.

Ae-Ran Kwon and coworkers at Daegu Hanny University and Seoul National University reported the crystal structure of MccB from *Staphylococcus aureus* in its apo- and pyridoxal 5'-phosphate (PLP)-bound forms [11]. This enzyme is involved in the bioconversion of methionine into cysteine. The article addresses the molecular clues into how homologous enzymes with PLP catalyze different metabolic reactions.

In the review article by Oh et al. [12], 136 crystal structures (424 PDB codes) of bacterial carboxylic ester hydrolases (CEHs), which are known to catalyze the hydrolysis of carboxylic esters into alcohols and acids, from 52 genera and metagenomes were classified based on catalytic machinery and structure and their structural and functional implication were discussed. Therefore, it is expected that this review paper could provide comprehensive understanding of the bacterial CEHs in structural and functional aspects.

In conclusion, this special issue presents advances in recent crystallographic studies of enzymes, and could serve as a convenient starting point for encouraging future studies.

Conflicts of Interest: The authors declare no competing financial interests.

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