P-3 11:20 ~ 12:00 Plenary Talk III

Structural Basis of Two DNA Interacting Proteins: DNA Repair Enzyme, Photolyase and Replication Initiator Protein, RepE

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Photolyase (DNA photoreactivating enzyme) has activities of DNA damage recognition and binding, photon absorption, energy transfer from chromophore to DNA, resulting in photoreversal of UV-induced pyrimidine dimer to monomer. We have determined crystal structures of two photolyases from a cyanobacteruim, *Anacyctis nidulans*[1], and a thermophilic bacterium, *Thermus thermophilus*[2]. It was found that the structures of apoproteins have a similar folding but that there are different binding modes of light-harvesting chromophores[1]. A thymine molecule was found at the hole of a putative substrate-binding site of the thermophilic enzyme[2]. On the basis of these three-dimensional structures, the recognition of damaged DNA and the role of the light-harvesting and catalytic chromophores will be discussed.

DNA replication is provoked by the binding of initiator proteins to the region of DNA replication origin. A replication initiator protein of mini-F plasmid in *Escherichia coli*, RepE, exhibits two major functions. A RepE monomer functions as a replication initiator, but a RepE dimer functions as an autogenous repressor. We have determined the crystal structure of RepE complexed with iteron DNA[2]. The structure showed a new type of DNA-binding modes. The RepE protein is composed of two distinct N- and C-terminal domains, which are structurally similar to each other and related by a non-crystallographic dyad, although no such similarity has been expected from its amino acid sequence. The helix-turn-helix motifs of both domains bind to the major groove of DNA with different binding affinities. The recognition helix of the C-terminal domain makes multiple specific contacts with the DNA bases, while that of the N-terminal domain has nonspecific interactions with the DNA backbones. It is suggested that the C-terminal domain plays the leading role in DNA binding, while the N-terminal domain has the additional role in dimerization. This functional difference of both domains is essential for the differential binding to the origin and the operator.

1) T. Tamada, *et al.*, Nature Struct. Biol., 4, 887-891 (1997).
2) H. Komori, *et al.*, submitted for publication.
3) H. Komori, *et al.*, EMBO J., 18, 4597-4607 (1999).