of the N and C termini of the domain were found to participate in the domain architecture by forming an extended portion of the first helix alpha-1, and a novel looping motif that traverses straight along the domain surface, respectively. The motifs combine to increase the domain surface of WRN HRDC, which is larger than that of Sgs1 and E. coli. In WRN HRDC, neither of the proposed DNA-binding surfaces in Sgs1 or E. coli is conserved, and the domain was shown to lack DNA-binding ability *in vitro*. Moreover, the domain was shown to be thermostable and resistant to protease digestion, implying independent domain evolution in WRN. Coupled with the unique long linker region in WRN, the WRN HRDC may be adapted to play a distinct function in WRN that involves protein-protein interactions.

Keywords: protein crystallography, DNA repair enzymes, disease

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Macromolecular crystallography at the Penn State X-ray core facility

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The newly established core facility at the Huck Institutes of Life Sciences, Pennsylvania State University, is equipped with state-of-the-art crystallization equipment and X-ray instrumentation and offers crystallography services within and out of Penn State. Visit http://www.huck.psu.edu/facilities/xray-crystallography-up/ for more information. We are facilitating a number of exciting projects from various research groups at Penn State including proteins from the phage T4 DNA replisome, plant cell wall protein, expansin, RNA polymerase from Archaea, RNA dependent RNA polymerase, bacterial enhancer binding proteins, chromatin enzymes and transcription factors. We welcome collaborations from out of Penn State as well. A description of the facility research and the services offered will be presented at the meeting.

Keywords: protein crystallography, protein-DNA complexes, enzyme structure function

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Crystal structure of the Mus81-Eme1 complex

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The Mus81-Eme1 complex is a structure-specific endonuclease that efficiently cleaves the nicked Holliday junction, 3'-flap, and replication fork structures, and plays an important role in rescuing stalled replication forks and resolving the meiotic recombination intermediates in eukaryotes. We determined the crystal structure of the Mus81-Eme1 complex. Unlike previous prediction, both Mus81 and Eme1 consist of a central nuclease domain, two repeats of the helix-hairpin-helix (HhH) motif at their C-terminal region, and a linker helix that restrains the movements of each domain. We show that a flexible intra-domain linker that formed with 36 residues in the nuclease domain of Eme1 is essential for the recognition of DNA. A central groove that is sufficient to bind single-stranded DNA is formed between the nuclease domain of Mus81 and the HhH2 domains of Mus81-Eme1, and the top wall of this central groove functions as a bump for the passage of the 3'-flap or leading strand and directs it to the active site cleft in Mus81. Our structure, in conjunction with FRET and biochemical analysis, explains the basis for substrate preference, specific cleavage at several bases from the 5' end of the downstream, and provides a model for the protein-substrate DNA interaction.

Keywords: Mus81-Eme1, Holliday junction, endonuclease

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Structural studies on the promoter recognition of transcription factor HNF-6

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Hepatocyte nuclear factor-6 (HNF-6), a liver-enriched transcription factor, controls the development of various tissues, such as the pancreas and liver, and regulates the expression of several hepatic genes. This protein belongs to the ONECUT class of homeodomain proteins composed of a single cut domain and a characteristic homeodomain. This transcription factor has two distinct modes of DNA binding and transcriptional activation that use different coactivators depending on the target gene. The homeodomain of HNF-6 is involved in binding to the transthyretin (TTR) promoter, whereas it is not required for binding to the HNF-3β promoter and involved in transcriptional activation. The cut domain is involved in both DNA binding and transcriptional activation at both promoters. At first, we have analyzed the crystal structure of the DNA-binding domain of HNF-6 protein complexed with the TTR promoter DNA[1]. In the complex structure, the two domains, together with the linker region, wrap around DNA and make contact with each other. The structure revealed the DNA recognition mechanism of this protein and the structural basis for the dual mode of action of this protein. Secondly, to examine the two distinct modes of HNF-6 more in detail, we have crystallized the DNA-binding domain of HNF-6 complexed with the HNF-3β promoter.
[1] Structure. 2007 Jan;15(1):75-83.

Keywords: X-ray crystallography of biological macromolecules, DNA-binding proteins, DNA-protein interactions

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Redesign a non-specific endonuclease

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Recognition between proteins and DNA has been studied extensively