Poster Presentation

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Preliminary crystallographic analysis of SETMAR bound to DNA

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SETMAR, a recently identified double strand break (DSB) repair enzyme in the human genome, contains an N-terminal SET domain and a C-terminal MAR domain. This chimeric protein arose through the fusion of a mariner-family DNA transposase gene, Hsmar1, downstream of a SET histone methyltransferase gene approximately 50 million years ago [1]. Although the SETMAR transposase domain retains the ability to bind terminal inverted repeat (TIR) DNA sequence, which is the hallmark of DNA transposons, it is no longer a functional transposase [2]. Nonetheless, the transposase domain with only 19 amino acid substitutions as compared to the ancestral Hsmar1 transposase has been under a strong selective evolutionary pressure suggesting that the transposase domain is functionally important. Determining how SETMAR interacts with DNA is central to understanding the molecular basis of its evolved DNA repair activity. Toward this goal, we have focused initially on the interaction of the DNA-binding domain (DBD) of the SETMAR transposase domain with TIR DNA. The DBD of SETMAR has been overexpressed and purified. A complex formed between SETMAR DBD and its transposon TIR DNA has been crystallized by using the hanging-drop vapor diffusion method. The crystals diffract to 3.15 Å resolution and exhibit orthorhombic symmetry (C2221), with unit-cell dimensions of a=72.233 Å, b=164.385 Å, and c=67.957 Å. As there is no suitable search model available, we are currently pursuing experimental phasing approaches in order to solve this structure. We anticipate the structural analysis of DBD of SETMAR bound to transposon DNA will provide insight into the mechanism by which SETMAR recognizes both TIR and non-TIR DNA.

[1] *R. Cordaux, S. Udit, M. A. Batzer, et al, PNAS 2006, 103, 8101-8106.,* ***[2]*** *Y. Roman, M. Oshige, Y. J. Lee, et al, Biochemistry 2007, 46, 11369-11376.*

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