**Poster Presentation**

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## *Kinetic Crystallography on MutT and its homolog*

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Oxidized deoxynucleotides cause replicational errors because of their misincorporations into DNA. The MutT and related proteins prevent transversion mutations by hydrolyzing mutagenic oxidized nucleotides such as 8-oxo-dGTP and 2-oxo-dATP, and there is a difference in substrate specificities between them. E. coli MutT hydrolyzes 8-oxo-dGTP to 8-oxo-dGMP with extremely high substrate specificity. On the other hand, its human homolog has broad substrate specificity for oxidized nucleotides and hydrolyzes 8-oxo-dGTP as well as 2-oxo-dATP. In order to understand mechanisms of their substrate specificities, we solved the crystal structures of MutT and its homolog complexed with their substrates and revealed structural basis of the high substrate specificity of E. coli MutT for 8-oxoguanine nucleotide and the broad substrate specificity of its human honolog for oxidized nucleotides. In this paper, we report the hydrolysis mechanisms of both enzymes revealed by kinetic protein crystallography. Both hydrolysis reactions were initiated by soaking the enzyme-substrate complex crystals in divalent metal solution. After incubation under various conditions, the reactions were terminated by freezing the crystals at 100K. X-ray diffraction data were collected at Spring-8 and Photon Factory. In the MutT crystals, the structures of sequential catalytic intermediates showed the activation mechanism of the nucleophilic water molecule synchronized with the coordination of metal ions. Now by using the crystals of its human homolog, the trial of the catching the intermediate state of catalysis is in progress.

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