**Crystal Structure of hMTH1 in Complex with its Reaction Product, 8-oxo-dGMP**

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8-Oxoguanine (8-oxoG) generated in the chromosomal DNA, RNA and free nucleotides by reactive oxygen species has high mutagenic potency due to its mispairing with adenine. *E.coli* MutT, which hydrolyzes 8-oxo-dGTP to 8-oxo-dGMP, prevents the misincorporation of 8-oxoG into DNA and the subsequent A:T to C:G transversion mutations. The mammalian counterpart of MutT, MutT homolog-1 (MTH1) can hydrolyze 8-oxo-dGTP less efficiently than MutT and a variety of oxidized purine nucleoside triphosphates. It is interesting to elucidate the structural basis for the difference in substrate-specificity between MutT and MTH1.

In this work, we have determined the crystal structure of hMTH1 (human MTH1) complexed with a product, 8-oxo-dGMP. The binding mode of 8-oxo-dGMP in the substrate-binding pocket of hMTH1 is quite different from one found in MutT-8-oxo-dGMP complex. It reveals the difference in preference of 8-oxo-dGTP to a normal nucleotide dGTP between hMTH1 and MutT. The structure of hMTH1-8-oxo-dGMP complex provides implications for the recognition mechanism of the most effective substrate, 2-OH-dATP by hMTH1.

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