## Crystal Structure of SUMO1-conjugated Thymine DNA Glycosylase

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SUMO (Small ubiquitin-like modifier) is post-translationally attached to many proteins and regulates the function or localization of modified proteins. Thymine DNA glycosylase (TDG), which plays an integral role in base excision repair of G-U or G-T mismatch DNA, is shown to be modified by SUMO-1 or SUMO-2/3. SUMO modification of TDG promotes the TDG dissociation from its product DNA containing an abasic site. However, the molecular mechanism of the SUMOylation-induced DNA release of TDG has not been revealed yet. Here we determined the crystal structure of SUMO-1 modified TDG central region (SUMO1-TDG). The structure revealed that TDG and SUMO-1 interact with each other through both covalent and non-covalent interactions, and these interactions likely induce the structural rearrangement of the C-terminal region of TDG. This induced structural change includes the alpha-helix formation, which protrudes from the body of the protein and seems to make a steric crash with DNA bound to TDG. Thus, this steric clash seemingly enhances the release of the product DNA from TDG. Results from biochemical assays using a series of TDG mutants support this structure and function model for molecular mechanism of SUMOylation-dependent TDG dissociation from DNA.

Keywords: SUMO, DNA repair, protein modification