Crystal Structure of SUMO2-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. TDG (Thymine DNA glycosylase), which plays an important 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 SUMO modification over the TDG dissociation from DNA has not been revealed yet. Simultaneously, the functional difference between SUMO-1 and SUMO-2/3 modification is also unclear if it exists. Here we solved the crystal structure of TDG central region in conjugated to SUMO-2 (SUMO2-TDG). Within the structure we've determined, TDG and SUMO-2 are interacted intermolecularly through both covalent and non-covalent interactions as seen in the crystal structure of SUMO1-TDG (as will be presented by Shirakawa et al.). From the mutational analyses, we could not find the difference in SUMO / TDG interactions between SUMO-1 and SUMO-2/3. These observations strongly suggest the equivalence of functional consequence of the modification among SUMO isoforms. The effect of mutations over the DNA binding activity of SUMO2-TDG is under examination.

Keywords: SUMO, ubiquitin, DNA repair