

9th International Conference on

STRUCTURAL BIOLOGY

September 18-20, 2017 Zurich, Switzerland

Structural insights into the histidine trimethylation activity of EgtD from *Mycobacterium smegmatis*

Jae-hee Jeong

Pohang Accelerator Laboratory, Korea

EgtD is an S-adenosyl-L-methionine (SAM)-dependent histidine N-methyltransferase that catalyzes the formation of hercynine from histidine in the ergothioneine biosynthetic process of *Mycobacterium smegmatis*. Ergothioneine is a secreted antioxidant that protects mycobacterium from oxidative stress. Here, we present three crystal structures of EgtD in the apo form, the histidine-bound form, and the S-adenosyl-L-homocysteine (SAH)/histidine-bound form. The study revealed that EgtD consists of two distinct domains: a typical methyltransferase domain and a unique substrate binding domain. The histidine binding pocket of the substrate binding domain primarily recognizes the imidazole ring and carboxylate group of histidine rather than the amino group, explaining the high selectivity for histidine and/or (mono-, di-) methylated histidine as substrates. In addition, SAM binding to the MTase domain induced a conformational change in EgtD to facilitate the methyl transfer reaction. The structural analysis provides insights into the putative catalytic mechanism of EgtD in a processive trimethylation reaction.

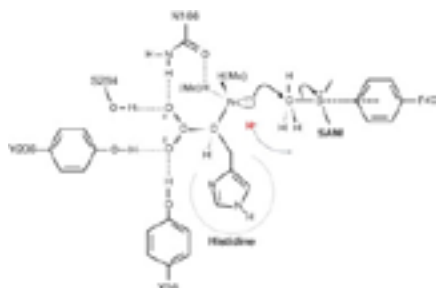


Figure1: Scheme of the proposed speculative catalytic mechanism of EgtD: The α -amino nitrogen of histidine is aligned for a direct in-line S_N2 nucleophilic attack by forming hydrogen bonding interactions with the depicted residues. The positively charged sulfonium ion of SAM will be stabilized by the charge-p interaction with Phe47. The lone pair of electrons from the nitrogen will be obtained after a proton loss to solvent, which is indicated as a red letter and a dashed arrow during the processive methylation reactions.

Biography

Jae-hee Jeong is a Researcher in Structural Biology lab of Pohang Accelerator Laboratory. She has accumulated expertise in protein-protein interaction and macromolecule X-ray crystallography after years of experience in research.

specials@postech.ac.kr

Notes: