Poster Presentation

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Crystal structure of Msm Eis bound with paromomycin

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The Rv2416c gene of Mycobacterium tuberculosis (Mtb) encodes the enhanced intracellular survival (Eis) protein that enhances intracellular survival of the pathogen in host macrophages during infection. The Eis protein is secreted by Mtb into the cytoplasm of the phagocyte during intracellular infection and modulates the host immune response. It was shown to confer resistance to aminoglycosides by acetylation. Interestingly, nonpathogenic Mycobacterium smegmatis (Msm) contains a homologous eis gene (MSMEG_3513) that encodes a homolog of Mtb Eis. We discovered that Mtb Eis is an Nε-acetyltransferase, acetylating Lys55 of DUSP16/MKP-7, a JNK-specific phosphatase, whereas Msm Eis is an Nα-acetyltransferase (Kim et al., 2012). We also reported that Msm Eis acetylated the aminoglycosides as quickly as, or more rapidly than, Mtb Eis (Kim et al., 2012). Here we present the crystal structure of Msm Eis in the paromomycin-bound form. This structure provides a detailed structural view of the interactions between paromomycin and Msm Eis. Glu137 and Gly401 of Msm Eis are key residues that interact with paromomycin. Our work may facilitate a structure-guided discovery of Mtb Eis inhibitors as a novel anti-TB drug.

[1] *K.H. Kim, et al. Proc. Natl. Acad. Sci. USA, 2012, 109, 7729-7734*

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