[MS5-P07] On the Structural Features of Acetylation of Enhanced Intracellular Survival (Eis) from Mycobacterium tuberculosis by MKP-7: Docking Study using HADDOCK. Hye-Jin Yoon,[1] Kyoung Hoon Kim,[1] Jin Kuk Yang,[2] Hyunsik Kim,[3] Soonmin Jang,[3] and Se Won Suh[1,4]

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The intracellular pathogen Mycobacterium tuberculosis (Mtb) causes tuberculosis. The Enhanced intracellular survival (Eis) protein, secreted by Mtb, enhances survival of Mycobacterium smegmatis in macrophages. We reported that Mtb Eis initiates the inhibition of JNK-dependent autophagy, phagosome maturation, and reactive oxygen species generation by acetylating dual-specificity protein phosphatase 16 (DUSP16)/ mitogen-activated protein kinase phosphatase-7 (MKP-7). Mtb Eis is an efficient Nε-acetyltransferase, rapidly acetylating Lys55 of DUSP16/MKP-7, a JNK-specific phosphatase. However, the detailed action of Mtb Eis as an Nε-acetyltransferase is poorly understood due to a lack of structural information on the complex between Mtb Eis and DUSP16/ MKP-7. In this study, we have attempted to search the possible complex structure of Mtb Eis with the kinase interaction motif or docking domain of DUSP16/MKP-7 using a molecular docking approach. Previous experimental evidence indicates that Mtb Eis exists as a hexamer in solution. However, our docking results seem to indicate that the hexameric Eis is not suitable for an interaction with DUSP16/MKP-7 and may have to dissociate into dimers or monomers for an optimal interaction. Further experiments are necessary to test the hypothesis.

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