

Poster Presentation

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Toxins from TA system of Helicobacter pylori and insight into mRNase activity

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The toxin-antitoxin (TA) systems widely spread among bacteria and archaea are important for antibiotic resistance and virulence. The bacterial kingdom uses TA systems to adjust the global level of gene expression and translation through RNA degradation. The HP0892-HP0893 and HP0894-HP0895 toxin-antitoxin systems are the only two known TA systems belonging to *Helicobacter pylori*. In both of these TA systems, the antitoxin binds and inhibits the toxin and regulates the transcription of the TA operon. However, the precise molecular basis for interaction with substrate or antitoxin and the mechanism of mRNA cleavage remains unclear. Therefore, here an attempt was made to shed some light on the mechanism behind the TA system of HP0892-HP0893 and HP0894-HP0895. Here, we present the crystal structures of apo- and copper-bound HP0894 at 1.28 Å and 1.89 Å, respectively, and the crystal structure of the zinc-bound HP0892 toxin at 1.8 Å resolution. Reorientation of residues involving the mRNase active site was shown. Through the combined approach of structural analysis along with isothermal calorimetry studies and structural homology search, the amino acids involved in mRNase active site were monitored. In the mRNase active site of HP0894 toxin, His84 acts as a catalytic residue and reorients itself acting as a general acid in an acid-base catalysis reaction, while His47 and His60 stabilize the transition state. Glu58 acts as a general base, and substrate reorientation is caused by Phe88. In the mRNase active site of HP0892 toxin, the most catalytically important residue, His86, reorients itself to exhibit RNase activity while Glu58 acts as a general base. His47 and His60 are considered to be involved in enzymatic activity. Glu58 and Asp64 are involved in substrate binding and specific sequence recognition. The mutational constructs were used for isothermal calorimetric studies to analyze the effect of catalytic residues.

Keywords: Toxin-antitoxin system, *Helicobacter pylori*, metal