MS5-P51 Crystal structure of *M. tuberculosis*' toxin in complex with its neutralizing antitoxin

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As most of bacteria and archaea, *Mycobacterium tuberculosis* (the causative agent for tuberculosis in human) possesses toxin-antitoxin systems on its chromosome. Studies tracking the systems' role in bacterial and archaeal physiology found evidences support that the system is related to dormant formation. Given the fact that dormancy is the key tactic *Mycobacterium tuberculosis* adopts to evade host's immune response and to obtain tolerance against antibiotics, toxin-antitoxin systems are believed to be an attractive target for new antibiotics development. Here, we present crystal structure of MazE(Antitoxin)-MazF(Toxin) pair from *Mycobacterium tuberculosis* determined at 2.3Å. It shows two C-terminal α-helices of MazE lie on the crevice at the center of MazF dimer and this $MazE_1$-$MazF_2$ heterotrimer dimerizes to form $MazE_2$-$MazF_4$ heterohexamer.

Keywords: M. tuberculosis, Toxin-antitoxin system, MazEF

MS5-P52 Elucidating the role of Esterase-6 from *Drosophila melanogaster* in the olfactory response

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Carboxylesterases are abundant in the genomes of insects and have been investigated for their diverse roles in insecticide resistance, lipid metabolism and reproduction. They can be subdivided into eight subfamilies which include α-esterases, β-esterases, juvenile hormone esterases, acetylcholinesterases and four other proteins with an esterase like fold. There is little known at a structural level about the β-esterases despite the key role they have in the reproductive success of *Drosophila melanogaster*. Low expression hampers studies into insect carboxylesterases including the β-esterase, esterase-6. In this work esterase-6 was successfully heterologously expressed in *Escherichia coli* and crystals were obtained following lysine methylation. The structure of esterase-6 shows a unique entry to the active site compared to other carboxylesterases, which is a result of a loop insertion. In comparison to the closest homologs, the change of entry to the active site results in a smaller binding site. Enzyme kinetics, docking experiments and molecular dynamics showed that short chains esters are preferred substrates for the enzyme and the proposed substrate for 30 years, 11-cis- vaccenyl acetate is not the substrate for esterase-6. The successful recombinant expression of esterase-6 opens up a route for expression of other carboxylesterases and the first structure of a β-esterase has been solved giving a possible target for insecticides, an indication of the substrate specificity of β-esterases, and elucidating the mode of action of an enzyme that has been a mystery for over 30 years.