This structure and the result of inhibition by ADP will be available for design of new drugs which inhibit ADPRTs such as S. enterica SpvB, which is required for human macrophage infection.

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Keywords : ADPRT, iota toxin, complex structure

MS36.P16

Acta Cryst. (2011) A**67,** C475

Structural basis for the helicobacter pylori-carcinogenic TNF⟨-inducing protein

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Stomach cancer is strongly associated with infection by Helicobacter pylori. In 2005, we identified a new H. pylori gene encoding a TNF-⟨ inducing protein (Tip⟨) that acts as a carcinogenic factor. Tip⟨ is secreted from H. pylori as a homodimer whose subunits are linked by disulfide bonds. Using blast search, there is no similar sequence with Tip⟨, thus it is unique carcinogenic factor protein. We also characterized a Tip⟨ deletion mutant (del-Tip⟨) that lacks the N-terminal six amino acid residues (LQACTC), including two cysteines (C5 and C7) that form disulfide bonds, but nonetheless shows a weak ability to induce TNF-a expression.

Here we report the crystal structure of del-Tip⟨ at 2.47Å resolution. As expected, the structure of del-Tip⟨ is novel; It has a novel elongated structure containing a 40 Å-long a helix, and forms a heart-shaped homodimer via non-covalent bonds. Moreover, their circular dichroism spectra strongly suggest that the structures of the del-Tip⟨ and Tip⟨ homodimers are very similar. We conclude that the TNF-⟨ inducing activity is correlated with the dimer formation. It means that strong dimer via covalent bond shows the strong activity for Tip⟨ and weak activity for del-Tip⟨ with weak interaction. Tip⟨'s unique mode of dimer formation provides important insight into protein-protein interactions and into the mechanism underlying the carcinogenicity of H. pylori infection.

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Keywords: TNF-⟨ inducing protein, helicobacter pylori, carcinogenic factor

MS36.P17

Acta Cryst. (2011) A**67,** C475

A Model of action for peripheral Membrane-Associated GT-B Glycosyltransferases

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Peripheral membrane-associated GT-B glycosyltransferases (GTs) are a ubiquitous family of enzymes that play essential roles in a variety of important biological processes in all living organisms. They transfer a sugar moiety from nucleotide- or lipid-phospho-sugar donors to a wide range of membrane-associated acceptors. Here we focus in PimA, an essential enzyme involved in the biosynthesis of phosphatidyl-myo-inositol mannosides (PIMs), which are key glycolipids of the mycobacterial cell envelope[1]. PimA is a paradigm of this family of GTs, which the molecular mechanism of substrate/membrane recognition and catalysis is still unknown. We have solved the crystal structure of PimA from *M. smegmatis* in complex with its donor substrate GDP-Man[2]. The notion of a membrane-associated protein via electrostatic interactions is consistent with the finding of an amphipathic α-helix in the N-terminal domain of PimA. Based on structural, biophysics and biochemical studies, we proposed a model of interfacial catalysis in which PimA recognizes the fully acylated acceptor substrate, phosphatidyl-myo-inositol (PI), with its polar head within the catalytic cleft and the fatty acid moieties only partially sequestered from the bulk solvent. In addition, we provided strong evidence showing that PimA undergoes significant conformational changes upon substrate binding[3]. Altogether, our experimental data support a model wherein the flexibility and conformational transitions confer adaptability of PimA to the substrates, which seems to be of importance during catalysis. The proposed mechanism has fundamental implications for the comprehension of the peripheral membrane-associated GTs at the molecular level.

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Keywords: membrane glycosyltransferase, tuberculosis, catalysis

MS36.P18

Acta Cryst. (2011) A**67,** C475-C476

Structural studies on FlhBc from *Salmonella typhimurium* and *Aquifex aeolicus*

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Many bacteria swim in liquid environment by means of flagella. The bacterial flagellum is a huge complex structure made from more than 30 different proteins. All flagellar axial proteins are transported across cytoplasmic membrane by the flagellum-specific secretion apparatus, which shares similarity to the type III secretion system of the bacterial needle utilized by some bacteria in pathogenesis. The protein transport is highly regulated. Membrane protein FlhB has been found to play an active role in this regulation. The protein consists of two domains: a hydrophobic N-terminal part, which is predicted to have four transmembrane helices, and a C-terminal cytoplasmic