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Keywords: enoyl-ACP_reductase, dimer, tetramer

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Crystal Structure of *Actinobacillus pleuropneumoniae* HMW1C glycosyltransferase

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The *Haemophilus influenzae* HMW1 adhesin is an N-linked glycoprotein that mediates adherence to respiratory epithelium, an essential early step in the pathogenesis of *H. influenzae* disease. HMW1 is glycosylated by HMW1C, a novel glycosyltransferase in the GT41 family that creates N-glycosidic linkages with glucose and galactose at asparagine residues and di-glucose linkages at sites of glucose modification. Here we report the crystal structure of *Actinobacillus pleuropneumoniae* HMW1C (ApHMW1C), a functional homolog of HMW1C. The structure of ApHMW1C contains an N-terminal all α-domain (AAD) fold and a C-terminal GT-B fold with two Rossmann-like domains and lacks the tetratricopeptide repeat fold characteristic of the GT41 family. The GT-B fold harbors the binding site for UDP-hexose, and the interface of the AAD fold and the GT-B fold forms a unique groove with potential to accommodate the acceptor protein. Structure-based functional analyses demonstrated that the HMW1C protein shares the same structure as ApHMW1C and provided insights into the mechanism of HMW1C glycosylation of HMW1.

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Keywords: HMW1C, glycosyltransferase, two-partner secretion

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Structural characterization of the fructose 1,6-bisphosphatase (II) from *M. tuberculosis*

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In spite of the availability of effective chemotherapy and Bacille-Calmette-Guerin (BCG) vaccine, tuberculosis remains a widespread fatal infection world-wide. Many factors such as, human immunodeficiency virus (HIV) co-infection, drug resistance, lack of patient compliance with chemotherapy, delay in diagnosis, variable efficacy of BCG vaccine among others contribute to the mortality due to tuberculosis.

New advances in understanding the biology of *Mycobacterium tuberculosis (Mtb)* and availability of functional genomic tools, such as microarray and proteomics, in combination with modern approaches have not resulted in new drug in the past 30 yr. The problem is compounded by the appearance and persistence of resistance strains. Therefore, there is an urgent need to identify new drug targets in *Mycobacteria* leading to new drugs. In general, gene products involved in mycobacterial metabolism, persistence, transcription, cell wall synthesis and virulence could be possible and atractive targets for the development of new drugs.

The completion of the *Mtb* genome sequence allowed the identification of genes that were predicted to encode enzymes for most central metabolic pathways, however no fructose 1,6 -bisphosphatase was assigned. In a previous study, we had identified *Rv1099c* to encode this missing link [1], showing that *Rv1099c* encodes a major FBPase in *M. tuberculosis.* The corresponding gene has been shown to be attenuated *in vivo* in a Transposon Site Hybridization screen (TraSH) [2] which makes *Mtb* FBPase an attractive drug target.

We have previously reported the cloning, expression and purification to homogeneity of the purified enzyme and present the initial biochemical characterization [3]. MtFBPase displayed Michaelis-Menten kinetics for the substrate fructose 1, 6-bisphosphate. Further characterization of the enzyme has shown that FBPase activity is absolutely dependent on the divalent cations Magnesium or Manganese, where replacing with other bivalent metal ions resulted in loss of activity..

Mtb FBPase has been crystallized in the apo form by hanging-drop vapour diffusion method. Crystals diffracted to a resolution of 2.7Å and belonged to the hexagonal space group $P6_122$, with unit-cell parameters a=b= 131.3, c=143.2Å. The structure has been solved by molecular replacement using *E. coli* GlpX as a probe (PDBID: *3d1r*) [4]. The structure of the GlpX-F6P complex has also been solved and both structures have been refined. Structural results can be related to the other available structures of class II FBPases.

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Crystal structure of SmeT bound to the biocide Triclosan

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The wide utilization of biocides for different purposes, including toothpastes, soaps, house-hold compounds surfaces' disinfectants and even their use as additives of different materials to avoid their colonization by micro-organisms, poses a concern on the impact of these compounds on natural bacterial populations. In recent years, the possibility that widely-used biocides might co-select for antibiotic resistance has been suggested to pose a potential risk to the successful treatment of infectious diseases. I*n vitro* experiments have shown that exposure of bacterial populations to certain biocides, such as triclosan, indeed leads to selection for mutants with reduced susceptibility to antibiotics. On most occasions this resistance has been acquired as a consequence of the stable de-repression of MDR efflux pumps.

We have explored the possibility that the widely used biocide triclosan might induce antibiotic resistance using as a model the opportunistic pathogen *Stenotrophomonas maltophilia*. Biochemical,