Crystal Structure of Catalase-Peroxidase from *Mycobacterium tuberculosis*

Katherine A. Brown, Thomas Bertrand, Nigel A.J. Eady and Jamie N. Jones

Department of Biological Sciences, Centre for Molecular Microbiology and Infection, Flowers Building, Imperial College London, London SW7 2AZ UK

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The *Mycobacterium tuberculosis* CP (*mt*CP) has been the subject of numerous studies as this heme-dependent enzyme is known to activate isoniazid (INH), a core compound used to treat tuberculosis. In particular, it has long been observed that INH resistance in tuberculosis-causing mycobacteria has often been correlated with reduced levels of catalase activity. Subsequently, it was confirmed that the presence of an active CP, encoded by a single gene, *katG*, is sufficient to confer INH sensitivity in *M. tuberculosis*, the organism principally responsible for tuberculosis. Studies using *mt*CP obtained either from the organism or in a recombinant form demonstrated that the enzyme is capable of oxidizing INH; however, the mechanism of oxidation and the precise mode of action of the drug are still subjects for debate. We have crystallized the enzyme and now report its crystal structure refined to 2.4-Å resolution. The structure reveals new information about dimer assembly and provides information about the location of residues which may play a role in catalysis including candidates for protein-based radical formation. Comparative computational and NMR studies have been used to predict a binding site for INH. ana a proposed enzyme-catalyzed reaction mechanism for activation of the drug .