Crystal Structure of Dihydropteroate Synthase from *Streptococcus pneumoniae*

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Dihydropteroate synthase (DHPS) catalyses a key step in the biosynthesis of folic acid, joining *para*-aminobenzoic acid to hydroxymethylpterin pyrophosphate. It is also the target for the sulphonamide family of antimicrobial drugs [1], and hence a well-established target for anti-infectives. We have determined the crystal structure of DHPS from the respiratory pathogen *Streptococcus pneumoniae* [2], as a prelude to a study of the recognition of sulphonamides and mechanisms of drug resistance by the enzyme. Data was collected from DHPS crystals which diffracted to 1.90Å resolution: attempts to solve the structure by molecular replacement using DHPS structures from other organisms failed, however. A second crystal form was obtained from a DHPS preparation with selenomethionine incorporation. Data were collected to 2.32Å resolution (97% complete), and the structure was subsequently solved using a single wavelength SAD data set. This model was subsequently used to solve the structure of the first crystal form. *S. pneumoniae* DHPS has a TIM-barrel fold and the active site is surrounded by several extensive loop regions which appear to play an important part in substrate recognition and the compulsory order ternary complex mechanism of the enzyme [2].

[1] Bermingham A., Derrick J.P., *Bioessays*, 2002, **24**, 637. [2] Vinnicombe H.G., Derrick J.P., *Biochem Biophys Res Commun,* 1999*,* **258**, 752.

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