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Structure of the Thiazole Synthase/ThiS Complex, an Essential Component of Thiamin Biosynthesis in *Bacillus subtilis*. Ethan C. Settembre, Pieter C. Dorrestein, Huili Zhai, Abhishek Chatterjee, Fred W. McLafferty, Tadhg P. Begley, Steven E. Ealick, Dept. of Chem. and Chem. Biol., Cornell Univ., Ithaca, NY 14853.

Thiazole synthase is essential for the final formation of the thiazole moiety of thiamin pyrophosphate (vitamin B1). Humans cannot synthesize thiamin and so this required cofactor must be received from an exogenous source. The chemical pathway for thiamin metabolism is complicated and, as such, the mechanisms of many enzymes are unknown. We have determined the structure of thiazole synthase in complex with ThiS, the sulfur donor protein for thiazole formation, at 3.15 Å resolution. Thiazole synthase is a tetramer with 222 symmetry. The monomer is a $(\beta\alpha)_8$ barrel with similarities to the aldolase class 1 and flavin mononucleotide dependent oxidoreductase and phosphate binding superfamilies. ThiS is a compact protein with a fold similar to ubiquitin. The structure allowed us to model the substrate deoxy-D-xylulose 5-phosphate (DXP) in the active site and to identify Lys96, Glu98 and Asp182 as key active site residues. The structure was used to propose a mechanism, which was tested by a series of mutagenesis and biochemical studies. Analysis of the structure of the thiazole synthase/ThiS complex revealed the nature of the protein:protein interactions and suggested that a previously undetected surface of ubiquitin and ubiquitin like proteins may be involved in complex formation.