

## E0011

**Structural Insights into the Function of the Thiamin Biosynthetic Enzyme Thi4 from *Saccharomyces cerevesiae*.** C. T. Jurgenson, A. Chatterjee, T. P. Begley, S. E. Ealick, Department of Chemistry and Chemical Biology, Baker Lab, Cornell Univ., Ithaca, NY 14853 USA.

The structure of thiazole synthase (Thi4) from *Saccharomyces cerevesiae* has been solved by molecular replacement to 1.8 Å resolution. Thi4 exists as an octamer with one dimer in the asymmetric unit. The structure has the bound molecule adenosine diphosphate 5-(β-ethyl)-4-methyl-thiazole-2-carboxylic acid (AHZ), which has been characterized by NMR and ESI-MS. The overall fold resembles that of a flavoenzyme and displays a characteristic dinucleotide binding domain, suggesting that a dinucleotide precursor such as NAD<sup>+</sup> or FAD is the substrate for this enzyme. A cis-proline (Pro121) is located after the second β-strand of the dinucleotide binding fold and is believed to be involved in release of the small molecule for further catalysis upon isomerization through a cyclophilin known to bind to Thi4. The product that is present when Thi4 is overexpressed in bacteria and has been shown to react with 4-amino-5-hydroxymethyl-2-methylpyrimidine (HMP-PP) through the enzyme Thi6 to give thiamin phosphate. The evidence presented here allows for the unequivocal assignment of Thi4 as being responsible for thiazole biosynthesis in yeast, as well as the reaction pathway utilized in yeast to biosynthesize thiamin phosphate.