**Structural Basis for the Induced Fit, Substrate Recognition, and Mechanism of Threonine Synthase**

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Threonine synthase, which is a pyridoxal 5'-phosphate dependent enzyme, catalyzes the β, γ-replacement reaction of an *O*-phospho-L-homoserine to give a threonine and an inorganic phosphate. The three-dimensional structures of the enzyme from *Thermus thermophilus* HB8 in its native form and complexed with the substrate analogue (2-amino-5-phosphonopetanoic acid) have been determined at 2.15 and 2.0 Å resolution, respectively. The enzyme is a homo dimer, with the polypeptide chain of the subunit folded into large, small, and swap domains. The complexed form of the enzyme assigned as an enamine uncovered the interactions of the cofactor-analogue conjugate with the active-site residues. The binding of the substrate analogue induces the large conformational change at the domain level to close the active-site. The small domain rotates by about 25° and approaches the large domain to shield the substrate analogue from the solvent region. The complicated catalytic process of the enzyme has been elucidated based on the complex structure to reveal the stereochemistry of the reaction and present the released inorganic phosphate as the possible catalyst to carry a proton to Cγ atom of the substrate.

[1] Omi R., Goto M., Miyahara I., Mizuguchi H., Hayashi H., Kagamiyama H., Hirotsu K., *J Biol Chem*., 2003, **14**, 278(46), 46035.

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