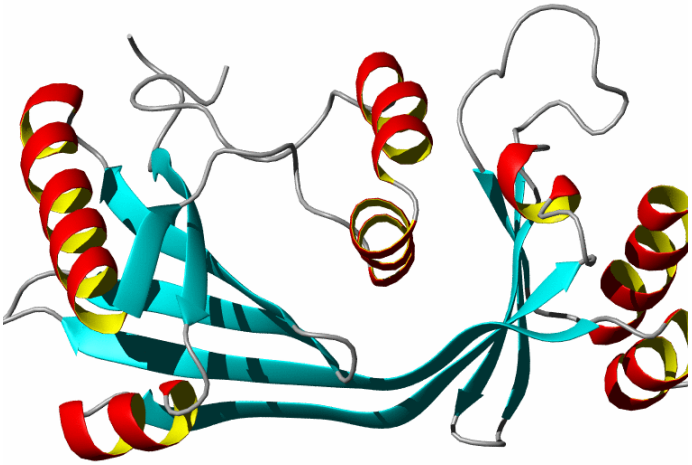
Center for Eukaryotic Structural Genomics

Protein Structure Initiative

Target ID	GO.34517	
Source Organism	*Mus Musculus*	
Target Name	BC025562	
PDB Entry	2JMU	Deposition: 05-Dec-2006
BMRB Entry	15063	Deposition: 19-Dec-2006
Function	mouse thiamine triphosphatase	
Produced From	*E. coli*	
Structure by NMR	Restraints/Residue: 20.9	Subunits/Molecule: 1
	No. of Residues: 224	Molecular Weight: 25.0kDa
	Backbone RMSD(5-213): 1.06 Å	All Heavy Atoms RMSD(5-213): 1.43 Å
Data Collected At	Nuclear Magnetic Resonance Facility at Madison (NMRFAM)	
Authors	Song, J., Markley, J.L.	



Structural Features

Mammalian soluble thiamine triphosphatase (ThTPase) is a 25-kDa cytosolic enzyme that specifically catalyzes the conversion of thiamine triphosphate (ThTP) to thiamine diphosphate (ThDP) and has an absolute requirement for divalent cations. We have investigated the kinetic properties of recombinant mouse thiamine triphosphatase (mThTPase) and determined its solution structure by NMR spectroscopy. Residues responsible for binding Mg(2+) and ThTP were determined from NMR titration experiments. The binding of Mg(2+) induced only a minor local conformational change, whereas ThTP binding was found to cause a more global conformational change. We derived a structural model for the mThTPase:ThTP:Mg(2+) ternary complex and concluded from this that, whereas free mThTPase has an open cleft fold, the enzyme in the ternary complex adopts a tunnel fold. Our results provide a functional rationale for a number of conserved residues and suggest an essential role for Mg(2+) in catalysis. We propose a mechanism underlying the high substrate specificity of mThTPase and discuss the possible role of water molecules in enzymatic catalysis.

References: (1) Song, J., Bettendorff, L., Tonelli, M., Markley, J.L. (2008) Structural basis for the catalytic mechanism of mammalian 25 kDa thiamine triphosphatase. *J Biol Chem* (epub ahead of print).

Percent Identity with Nearest PDB Structure at Time Solved	10% coverage (2FHZ)
Pfam Cluster	CYTH
Sequence Family Size	28

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