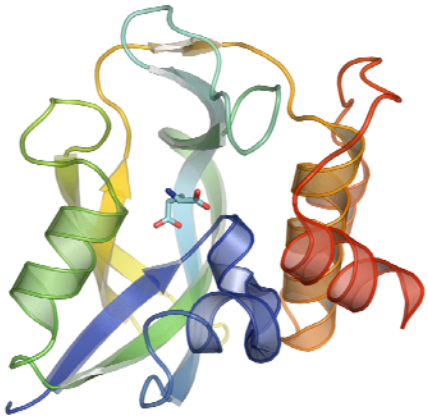
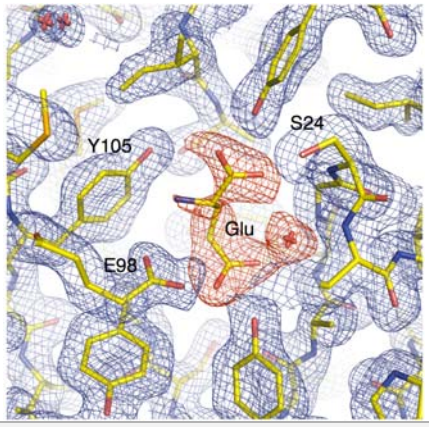
Center for Eukaryotic Structural Genomics

Protein Structure Initiative

Target ID	GO.35223	
Source Organism	*Homo sapiens*	
Target Name	BC000625	
PDB Entry	2I5T	Deposition: 25-Aug-2006
Function	hypothetical protein LOC79017 (FF/Refine: 2Q53)	
Produced From	*E. coli* B834(DE3) p(RARE2) pVP-30	
Structure by X-ray	Resolution: 2.01 Å	R-value (R-free): 18.6% (23.4%)
	No. of Residues/ASU: 338	Monomers/ASU: 2
Data Collected At	Advanced Photon Source 22-ID 23-ID-D 18-Jun-2006	
Authors	E. Bae, G.E. Wesenberg, G.N. Phillips, Jr., E. Bitto, C.A. Bingman	





Structural Features

Human gene C7orf24 encodes a protein recently annotated as γ-glutamyl cyclotransferase (GGC). GGC is an enzyme involved in a metabolic cycle implicated in transport of certain amino acid across the cell membranes in kidneys. This so-called γ-glutamyl cycle uses glutathione (GSH) as a carrier. The first step of the pathway is catalyzed by γ-glutamyl transpeptidase that conjugates γ-glutamyl moiety of GSH to a particular amino acid. The conjugate is translocated across the plasma membrane and converted to free amino acid and 5-oxoproline by GGC. GSH is then regenerated and translocates across the membrane where it can be utilized in another round of transport. The crystal structure of GGC reveals an α/β protein fold with novel topology. The N-terminal part of the protein consists of a five-stranded β-barrel flanked by three α-helices. The C-terminal part made of three long α-helices packs against one side of the central β-barrel. The putative active site lies in a deep cavity in the center of the protein. The structural highlight of the active site is a loop with crown ether-like arrangement of backbone nitrogens that might stabilize the substrate by hydrogen bonding. Conserved active site residues Ser24, Glu98, and Tyr105 likely play an important role in substrate binding and/or catalysis. They are positioned in the vicinity of an electron density found in the active site of GGC. This density has been tentatively modeled as L-glutamate, which may act as an inhibitor of GGC. The search for the structural homologs of GGC revealed a similarity of this protein to several hypothetical proteins of the UPF0131 family with closest homolog YkqA from *Bacillus subtillis* (PDB ID 2GIK). The active site loop and the putative catalytic residues are strictly conserved among these homologs. However, the C-terminal domain has diversified, probably to accommodate a different function of each protein.

Referemces: (1) Bae, E., Bingman, C.A., Aceti, D.J., Phillips, G.N., Jr. (2008) Crystal structure of *Homo sapiens* protein LOC79017. *Proteins* 70(2):588-91.

Percent Identity with Nearest PDB Structure at Time Solved	none
Pfam Cluster	AIG2
Sequence Cluster Size	167

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