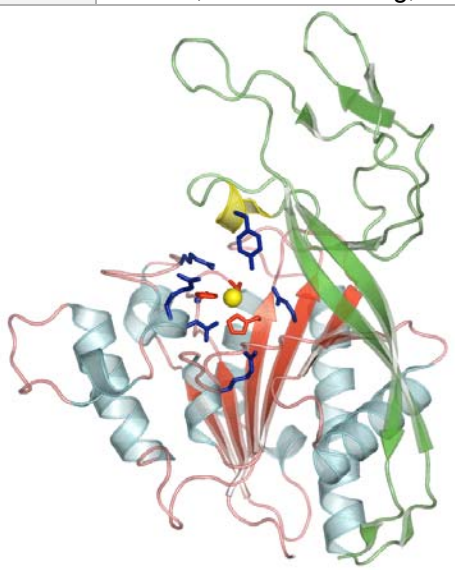
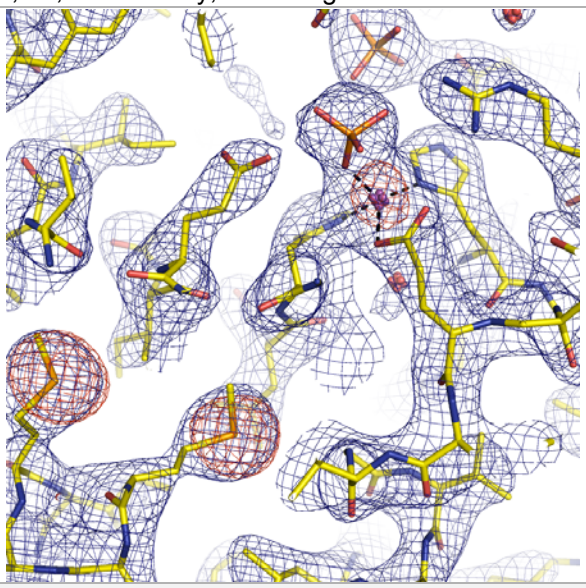
Center for Eukaryotic Structural Genomics

Protein Structure Initiative

Target ID	GO.79368	
Source Organism	*Homo sapiens*	
Target Name	BC029128	
PDB Entry	2I3C	Deposition: 17-Aug-2006
Function	aspartoacylase (FF/Refine: 2Q51)	
Produced From	*E. coli* B834 pRARE-2	
Structure by X-ray	Resolution: 2.8Å	R-value (R-free): 19.5 % (24.3%)
	No. of Residues/ASU: 624 (604)	Monomers/ASU: 2
Data Collected At	Advanced Photon Source 22-ID 05-Aug-2006	
Authors	E. Bitto, G.E. Wesenberg, G.N. Phillips, Jr., J.G. McCoy, C.A. Bingman	





Structural Features

Aspartoacylase catalyzes hydrolysis of N-acetyl-L-aspartate to aspartate and acetate in the vertebrate brain. Deficiency in this activity leads to spongiform degeneration of the white matter of the brain and is the established cause of Canavan disease, a fatal progressive leukodystrophy affecting young children. The crystal structures of recombinant human and rat aspartoacylase were solved refined to 2.8Å and 1.8Å resolution, respectively. The structures revealed that the amino-terminal domain of aspartoacylase adopts a protein fold similar to that of zinc-dependent hydrolases related to carboxypeptidase A. The catalytic site of aspartoacylase shows close structural similarity to those of carboxypeptidases despite only 10-13% sequence identity between these proteins. About one hundred carboxy-terminal residues of aspartoacylase form a globular domain with a 2-stranded β-sheet linker that wraps around the amino-terminal domain. The long channel leading to the active site is formed by the interface of the amino- and carboxy-terminal domains. The carboxy-terminal domain is positioned in a way that prevents productive binding of polypetides in the active site. We hypothesize that the catalytic mechanism of aspartoacylase is closely analogous to that of carboxypeptidases. The structures also provide a structural framework necessary for understanding the deleterious effects of the missense mutations of human aspartoacylase.

References: (1) Bitto, E., Bingman, C.A., Wesenberg, G.E., McCoy, J.G., Phillips, G.N., Jr. (2007) Structure of aspartoacylase, the brain enzyme impaired in Canavan disease. *PNAS* 104(2):399-400.

Percent Identity with Nearest PDB Structure at Time Solved	84% 2GU2 (CESG)
Pfam Cluster	AstE_AstA
Sequence Cluster Size	78 NR at e<0.1

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