Status: structure completed

Three publications have resulted from visits to ESRF

EMBO J. 2001 Aug 1;20(15):3910-6.

Structure of human cystathionine beta-synthase: a unique pyridoxal 5'-phosphate-dependent heme protein.
Meier M, Janosik M, Kery V, Kraus JP, Burkhard P.

Cystathionine beta-synthase (CBS) is a unique heme- containing enzyme that catalyzes a pyridoxal 5'-phosphate (PLP)-dependent condensation of serine and homocysteine to give cystathionine. Deficiency of CBS leads to homocystinuria, an inherited disease of sulfur metabolism characterized by increased levels of the toxic metabolite homocysteine. Here we present the X-ray crystal structure of a truncated form of the enzyme. CBS shares the same fold with O-acetylserine sulfhydrylase but it contains an additional N-terminal heme binding site. This heme binding motif together with a spatially adjacent oxidoreductase active site motif could explain the regulation of its enzyme activity by redox changes.

Biochim Biophys Acta. 2003 Apr 11;1647(1-2):206-13.

Structural insights into mutations of cystathionine beta-synthase.
Meier M, Oliveriusova J, Kraus JP, Burkhard P.

Cystathionine beta-synthase (CBS) is a unique heme-containing enzyme that catalyses a pyridoxal 5'-phosphate (PLP)-dependent condensation of serine and homocysteine to give cystathionine. Deficiency of CBS leads to homocystinuria, an inherited disease of sulfur amino acid metabolism characterised by increased levels of homocysteine and methionine and decreased levels of cysteine. Presently, more than 100 CBS mutations have been described which lead to homocystinuria with different degrees of severity in the patients. We have recently solved the crystal structure of a truncated form of this enzyme, which enables us to correlate some of these mutations with the structure.

Acta Crystallogr D Biol Crystallogr. 2001 Feb;57(Pt 2):289-91.

Crystallization and preliminary X-ray diffraction analysis of the active core of human recombinant cystathionine beta-synthase: an enzyme involved in vascular disease.
Janosik M, Meier M, Kery V, Oliveriusova J, Burkhard P, Kraus JP.

Cystathionine beta-synthase (CBS) is a unique heme enzyme that catalyzes a PLP-dependent condensation of serine and homocysteine to give cystathionine. Deficiency of CBS leads to homocystinuria, an autosomal recessively inherited disease of sulfur metabolism. A truncated form of CBS in which the C-terminal amino-acid residues have been deleted has been prepared. The truncated CBS subunits form a dimer, in

contrast to the full-length subunits which form tetramers and higher oligomers. The truncated CBS yielded crystals diffracting to 2.6 A which belong to space group P3(1) or P3(2). This is the first comprehensive structural investigation of a PLP and heme-containing enzyme.