Acta Cryst. (2002). A**58** (Supplement), C102

THE X-RAY CRYSTAL STRUCTURE OF FORMALDEHYDE DISMUTASE AT 2.3Å RESOLUTION

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Formaldehyde dismutase (FDM) exhibits the catalysis of the dismutation of aldehydes and alcohol: aldehyde oxdoreduction in the absence of an exogenous electron acceptor. The crystal structure of FDM was determined at 2.3 Å resolution by multi-wavelength anomalous dispersion method. FDM is composed of four identical subunits with a molecular weight of 44,000. Each subunit contains 2 zinc atoms. Preliminary intensity data were collected using CuKα radiation from a rotating-anode X-ray generator (Rigaku ultraX 18HF) operated at 40kV 100mA. Crystals of FDM belong to the space group *I*41 with unit-cell dimensions of a = b = 89.74 Å, c = 226.77 Å and there are two molecules per asymetric unit. Intensity data of native crystal and anomalous dispersion data were collected using Synchrotron Radiation at SPring-8 BL38B1. Experimental phases were obtained with MAD method using 3 wavelengths.

Keywords: CRYSTAL STRUCTURE FORMALDEHYDE DISMUTASE OXIDOREDUCTASE

Acta Cryst. (2002). A**58** (Supplement), C102

STRUCTURES OF THE TWO POLYMORPHIC FORMS OF HUMAN HISTAMINE METHYLTRANSFERASE

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Histamine is an important messenger in cell-to-cell communication: it mediates allergy and inflammation, regulates gastric acid secretion, and is a neurotransmitter that affects several (patho)physiological processes. Histamine methyltransferase (HNMT) inactivates histamine by transferring a methyl group from S-adenosyl-L-methionine (AdoMet) to the ring nitrogen atom $N\varepsilon_2$ of its substrate's imidazole yielding methylhistamine and S-adenosyl-L-homocysteine. The less frequent polymorphic form (allozyme) of human HNMT (Ile105) has a lower activity (84%) when compared to the Thr105 variant. The 10% of the population with the Ile105 allozyme have a greater risk for asthma.
The structure of HNMT has two domains: the larger is a consensus AdoMet-binding domain found in many other AdoMet-dependent methyltransferases, and a smaller domain reminiscent of the β-subdomain found in the bacterial CheR protein MTase involved in protein-protein interactions. The position of the allozyme variation is not near the active site but at the carboxyl end of a helix whose amino end is involved with binding AdoMet. HNMT has a deep catalytic cavity located at the domain interface. This cavity allows HNMT to be very selective for histamine while permitting it to accommodate inhibitors diverse in chemical structure as well as clinical pharmacology. Besides several antimalarial drugs such as amodiaquine and quinacrine, the anticholinesterase tacrine and the oncolytic agent metoprine are very potent inhibitors. Other inhibitors include the compound SKF-91488 and first generation antihistamines such as diphenhydramine. Structures of complexes of both human allozymes of HNMT, with many of these inhibitors, have been determined. These structures show several modes of binding to and inhibition of HNMT, and have implications for design of drugs for histamine-related diseases.

Keywords: **METHYLTRANSFERASES, DRUG INTERACTION, SINGLE NUCEOTIDE POLYMORPHISMS**

Acta Cryst. (2002). A**58** (Supplement), C102

CRYSTAL STRUCTURE OF THE SMALL FORM OF GLUCOSE-INHIBITED DIVISION PROTEIN A *FROM THERMUS THERMOPHILUS* HB8

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The gene of the glucose-inhibited division protein A (GidA) was first isolated in association with a glucose-inhibited division phenotype by Meyenburg and Hansen. The gidA genes are well conserved among wide range of prokaryotes and generally localized near the chromosomal replication origin. GidA is therefore proposed to have a role in the control of cell division, but its function remains unclear. A subset of organisms have a second smaller GidA. For example, *Thermus thermophilus* HB8 has GidA consisting of 597 amino acids and second one consisting of 232 amino acids (GidA2). Both GidA and GidA2 have a conserved dinucleotide-binding motif at N-terminus. We report here the crystal structure of GidA2 from *Thermus thermophilus* HB8 with a bound FAD cofactor at 1.8 Å resolution. The GidA protein (prepared by 'Structurome Project' of RIKEN Harima Institute) was crystallized using PEG4000 as a precipitant. Diffraction data were collected at BL44B2 and BL45XU, SPring-8. The crystals belonged to the trigonal *P*3221 with unit-cell dimensions of a = b = 78.70 and c = 66.14 Å. Phases were determined from the MAD data using an Hg derivative and the structure was finally refined to R = 0.189 (Rfree = 0.214). Although FAD was not added to the crystallization solvent, FAD is still bound to the GidA2 at high occupancy. The N-terminal domain of the determined structure contains six parallel β-strands interspersed by α-helices that appear on both sides of the six-stranded β-sheet, which is characteristic of a dinucleotide binding fold, the so-called the Rossman fold.

Keywords: **CELL DIVISION, FLAVOPROTEIN, PROTEIN STRUCTURE**

Acta Cryst. (2002). A**58** (Supplement), C102

CRYSTAL STRUCTURE OF A BACTERIAL TRNA-PRECURSOR PROCESSING ENZYME: RNase PH FROM *BACILLUS SUBTILIS*

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In *Escherichia coli*, the maturation of precursor tRNA molecules is carried out by multiple ribonucleases showing overlapping activities [1]. The exoribonuclease RNase PH is found to be involved in processing at the 3' end, cleaving the +2 nucleotide following the well-characterized tRNA-CCA sequence. A homologous protein has been detected in *Bacillus subtilis*, which has also been assigned RNase PH. *In vitro*, RNase PH catalyses the phosphorolysis of polyadenylate and the polymerization of nucleotide diphosphates into a tRNA chain. The phosphorolysis reaction has a requirement of inorganic phosphate and Mg^{2+}, whereas the synthetic reaction only requires Mg^{2+}. RNase PH from *Bacillus subtilis* has been crystallized with ammonium sulphate at pH 8.5 in the presence of Cd^{2+}. It crystallizes in space group $P2_12_12_1$ with cell dimensions: a = 100, b = 146, c = 152 Å. The structure has been solved by isomorphous replacement using 5 derivatives containing from 2 to 6 Hg-sites. The crystal contains a 32 hexamer in the asymmetric unit. 242 residues of 245 in the monomer have been modeled. The C-terminal Glu243-Lys245 is disordered. Residual electron density showed the presence of two sulphate ions per monomer. The hexamer of RNase PH is to be considered as a trimer of dimers. The dimer is structural homologous to the monomer of polynucleotide phosphorylase[2].
References
[1] Li & Deutsher (1996) Cell 86, 503-512.
[2] Symmons, Jones & Luisi (2000) Structure 8, 1215-1226.

Keywords: **RNASE PH EXONUCLEASE TRNA PROCESSING**