three-dimensional intensity data were collected by imaging plate diffractometer of RIGAKU RAXIS IIc. The average figure of merit at 3.0 Å resolution is 0.43, using "mlphare" in CCP4 program package. The phase improvement was carried out by "dm" in CCP4, resulting in a 2.2 Å resolution density map. The density modification includes histogram-mapping, constraint of Sayer formula, non-crystallographic averaging and solvent flattening, with assumption of 41% solvent content. The final free-R-value was 0.27 at 2.2 Å resolution. Two identical molecules are in the crystallographic asymmetric unit. The two molecules are related by 143 degree rotation around an axis almost parallel to the crystallographic z axis with some translation. Each molecule consists of two domains. The N-terminal domain has five helices and seven β-strands (α/β structure) with two additional long helices in N-terminus. The C-terminal domain is mainly composed of left-handed β-helix similar to the structure of UDP-N-acetylglucosamine-acyltransferase[1]). The protein structure is under refinement with program X-PLOR.

1) C. R. H. Raetz and S. L. Roderick, Science, 270, 997-1000(1995)

PS04.01.60 CALF SPLEEN PURINE NUCLEOSIDE PHOSPHORYLASE IN COMPLEX WITH AN N(7)-ACYCLOGUANOSINE INHIBITOR. Gertraud Koellner, Marija Luic, Agnieszka Bzowska, David Shugar & Wolfram Saenger, Institut fur Kristallographie, Freie Universitat Berlin, Takustr. 6, D-14159 Berlin, Germany

The complex of calf spleen purine nucleoside phosphorylase with an N(7)- acycloguanosine inhibitor was crystallized in the cubic space group $P2_13$ with an unit cell dimension a=94.02Å and one monomer in the asymmetric unit. The biologically active trimer is formed by the crystallographic three-fold axis. The structure was solved by molecular replacement using the model of the human erythrocyte enzyme [Ealick et al., Proc. Nat. Acad. Sci. USA 88, 11540 11544 (1990)]. The complexed calf spleen PNP crystallizes at pH 8.2-8.5 from PEG, which is almost optimal for enzyme activity [Kulikowska et al., Biochim. Biophys. Acta 874, 355- 363 (1986)]. N(7)-acycloguanosine binds in an inverted ('upside-down') orientation with respect to guanosine in the human PNP. The acyclic chain is engaged in several hydrogen bonds. Since the crystals were grown at pH 8.2-8.5. the secondary nitrogen of the acyclic chain (pKa~9.5) should be protonated. It follows that it is the acyclic chain which is predominantly responsible for binding of the inhibitor.

Agnieszka Bzowska, Marija Luic, Werner Schröder, David Shugar, Wolfram Saenger, Gertraud Koellner. (1995) FEBS Letters, 367, 214-218.

PS04.01.61 CRYSTAL STRUCTURE OF ISOZYME 4-4 & MOLECULAR MODELING OF ISOZYME 3-4 OF CLASS MU GLUTATHIONE S-TRANSFERASES FROM RAT LIVER. Gaoyi Xiao,[1] Xinhua Ji,[1,2] Richard Armstrong,[3] and Gary L. Gilliland[1]. [1]Center for Advanced Research in Biotechnology of the University of Maryland Biotechnology Institute and the National Institute of Standards and Technology, 9600 Gudelsky Drive, Rockville, MD 20850. [2]NCIFCRDC, P.O. Box B, Frederick, MD 21702. [3]Department of Biochemistry and the Center in Molecular Toxicology, Vanderbilt University School of Medicine, Nashville, TN 37232

Glutathione S-transferases (GST) are a family of phase-II detoxification enzymes that may also play a role as transport proteins. To date, five different gene classes, alpha, mu, pi, theta and sigma, of this dimeric enzyme have been identified. Several subunit types have been found for the different gene classes in many different organisms. Heterodimers composed of different subunits of the same gene class are commonly isolated. Interclass heterodimers, however, have not been observed [1]. We report here the crystal structure of the 50 kDa 4-4 isozyme of the rat liver mu GST. The three-dimensional structure was determined at 3.5 Å resolution by the molecular replacement method using the 3-3 isozyme of the rat liver mu GST [2]. This represents the first example of the structure of a second GST subunit type from the same gene class. Details of the 4-4 mu GST structure, results of an analysis of the interface interactions of the two homodimeric structures, and results of molecular modeling of the heterodimeric 3-4 mu GST isozyme to learn what features at the dimer interface allow heterodimer formation will be presented.

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[2] Ji, X., Zhang, P., Armstrong, R. N. and Gilliland, G. L. (1994) *Biochemistry* 31, 10169-10184.

PS04.01.62 HIGH RESOLUTION CRYSTAL STRUCTURE OF ORNITHINE AMINOTRANSFERASE COMPLEXED WITH THE NEUROTOXIN GABACULINE. Sapan A. Shah, Betty W. Shen and A.T. Brunger. The Howard Hughes Medical Institute and Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT 06520, USA.

Ornithine aminotransferase (OAT) is a 45kD pyridoxal phosphate-dependent enzyme that catalyzes the transfer of the delta amino group of ornithine to an alpha ketoglutarate substrate. OAT and gamma aminobutyric acid transaminase (GABA-AT) belong to the same subgroup of transaminases, and in addition to sharing high sequence homology, are inactivated by common inhibitors. One such inhibitor is the neurotoxin gabaculine (5-amino- 1,3-cyclohexadienylcarboxylic acid), a cyclic analogue of the inhibitory neurotransmitter GABA. We present here a 2.3 angstrom structure of the OAT/gabaculine complex, solved using phases from the native structure (Shen et al, manuscript in preparation). The complex reveals the structural basis for the "suicide" binding of gabaculine to the active site. Gabaculine is positioned in the active site through a hydrogen bond between its carboxyl group and Tyr55. Following binding to the PLP cofactor and aromatization of the cyclohexadienyl ring, the inhibitor is sandwiched in a favorable stacked arrangement between two aromatic residues, Tyr85 and Phe177.

PS04.01.63 THE CRYSTAL STRUCTURE OF THE HGXPRTASE FROM THE PROTOZOAN PARASITE T. FOETUS. John R. Somoza, Marian Chin, Pamela J. Focia, Ching C. Wang and Robert J. Fletterick, Dept. of Biochemistry & Biophysics, University of California at San Franscisco, CA 94143-0448

The crystal structure of the hypoxanthine-guanine-xanthine phosphoribosyltransferase from Tritrichomonas foetus has been determined and refined against data to 1.9 angstrom resolution. T. foetus HGXPRTase crystallizes as an asymmetric dimer, with GMP bound to only one of the two molecules that form the asymmetric unit. Each molecule of HGXPRTase is formed by two lobes joined by a short "hinge" region, and the GMP binds in a cavity between the two lobes. A comparison of the two molecules in the asymmetric unit shows that the hinge region is flexible, and that ligand binding affects the relative positions of the two lobes. The binding of GMP brings the two lobes closer together, rotating one lobe by about 5 degrees relative to the other.

T. foetus appears to depend on HGXPRTase for its supply of GMP, making this enzyme a target for anti-parasite drug design. A comparison of the structures of T. foetus HGXPRTase and human HGPRTase reveals that, while these enzymes retain a similar polypeptide fold, there are substantial differences between the active sites of these two homologs. These differences suggest that it will be possible to find compounds that selectively inhibit the parasite enzyme.