accessible faces and the three four-stranded ß-sheets. One therefore might characterize this fold as an inside-out α/β barrell. The present structure reflects the open conformation of the enzyme. We assume that large conformational changes upon catalysis are mediated mainly through two residues, a lysin and an arginine, which are located in the cleft between the two domains. These residues assure the open conformation of the native enzyme by the repulsive force between the positive charges of two amino groups. The binding of one of the two substrates probably results in neutralizing the repulsion between the two domains thereby allowing the movement of a catalytically active cystein toward the cleft.

PS04.07.20 PROGRESS IN DETERMINING THE STRUCTURE OF FRAGMENT D FROM HUMAN FIBRINOGEN. G. Spraggon, S. J. Everse, R. F. Doolittle, Center for Molecular Genetics, Univ. Calif. San Diego, La Jolla, CA, USA 92093-0634

Fragment D is a complex, large molecular weight (86,000 Da) fragment derived from vertebrate fibrinogen by limited proteolysis with plasmin or trypsin. Its three constituent polypeptide chains have long been supposed to form a coiled-coil at their amino-terminal ends and to be cemented by a ring-shaped triple set of disulfide bonds. The carboxyl-terminal portions of two of the chains make up two homologous globular domains. Recently we reported the crystallization of fragment D from human fibrinogen and some preliminary characterization (Everse *et al.* Prot. Sci., 4:101316,1995). The space group is $P2_1$, unit cell dimensions a = 107.7, b = 48.0, c = 167.6, beta = 105.7 In the interim, we have identified several isomorphous derivatives and have been able to calculate preliminary low resolution phases. The molecular envelope determined by solvent flattening of an initial fourier map has revealed an silhouette in which the boundaries of the distal domains and coiled coil are reasonably delineated. It also reveals, in contrast to our initial finding, that there is only one molecule per asymmetric unit. The solvent flattened map itself contains several features which can be attributed to secondary structure, including portions of the coiled-coil. Efforts to improve the phasing are under way.

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PS04.07.21 CRYSTALLOGRAPHIC STUDIES OF THE HUMAN PENTRAXINS, SERUM AMYLOID P COMPONENT AND C-REACTIVE PROTEIN. D. Thompson, I. J. Tickle, T. L. Blundell, M. B. Pepys[1] & S. P. Wood[2]. Department of Crystallography, Birkbeck College, Malet Street, London, [1]Immunological Medicine unit, Hammersmith Hospital, London, [2]Department of Biochemistry, University of Southampton, Southampton

The crystal structure of the two major human pentraxins have been determined to medium resolution. The pentraxins are a protein family which exhibit five fold symmetry of subunits and are capable of calcium dependent binding. The two major human pentraxins are Human Serum Amyloid P Component (SAP), which is found bound to amyloid deposits in amyloidosis and Alzheimer's disease, and C-reactive protein (CRP), which is believed to have a role during the immune response. SAP and CRP share 52% sequence identity. SAP exists in the plasma as a decamer, two pentameric rings interacting face to face, each subunit consisting of 204 amino acids, whereas CRP exists as a single pentameric ring made up of subunits consisting of 206 amino acids.

Two CRP crystal forms have been grown. Both are tetragonal. One has a unit cell of a=b=275.81 and c=94.21, and contains 3 pentamers per asymmetric unit and the other is of unit cell a=b=190.31 and c=132.12, space group $P4_32_12$, and contains two pentamers per asymmetric unit. A complete data set has been collected on this crystal form to a resolution of 3.0Å. Crystals have also been grown of decameric SAP. These are of spacegroup $P2_1$ and unit cell a=103.37 b=112.711 c=121.499 and β=91.87 and contains 1 decamer per asymmetric unit. A complete data set has been collected on this crystal form to 2.5Å.

Both structures have been solved by molecular replacement using the pentameric structure of SAP (Emsley, J. *et al.* (1994) Nature vol. 367, p338-345) as a model.

PS04.07.22 CRYSTALS OF THE AUGMENTOR OF LIVER REGENERATION. C.-K. Wu[1,2], J.P. Rose[1], A. Francavilla[3], J.G. Prelich[3], A. Iacobellis[3], M. Hagiya[4], A. Rao[3], T. Starzl[3] and B.C. Wang[1], [1]Dept. of Biochemistery and Molecular Biology, Univ. of Georgia, Athens GA 30602, USA, [2]Dept. of Crystallography, Univ. of Pittsburgh, Pittsburgh, PA 15260, USA, [3]Pittsburgh Transplant Inst., Univ. of Pittsburgh School of Medicine, Pittsburgh, PA 15260, USA and [4]Pharmaceuticals Res. Ctr., Toyobo Co. Ltd., Ohtsu, Shiga 520-02, Japan

Almost every school child knows that chameleons can regenerate a lost tail. This interesting phenomenon of regrowth of lost body parts common in lower animals is generally rare in mammals. The liver however, is an unique organ in that it is capable of regeneration.

A new cellular growth factor termed augmentor of liver regeneration (ALR) shown to have a proliferative effect on liver cells while at the same time producing an immunosuppressive effect on liver-resident natural killer cells and liver-resident mononuclear leukocytes has been crystallized. The crystals diffract to beyond 2 Å resolution and belong to space group $P2_12_12_1$, with a=35.5Å, b=108.1Å and c=125.1Å. Based on 4 molecules per asymmetric unit, the Matthews coefficient is calculated to be 2.16 Å3/Da which corresponds to a solvent content of 43%.

Rat ALR has two related forms, "short" ALR which has 125 amino acid residues and "long" ALR, (ALR198), which contains 73 additional residues in the N-terminal segment of ALR . The long ALR is the result of an additional inframe ATG initiation site which is 5' to the initiation site used to code the 125 residue protein. The ALR cDNA sequence shows 50% homology with the sequence of the dual-function gene ERV1 (Essential for Respiration and Viability) of "baker's yeast", *Saccharomyces cerevisiae*. The ERV1 gene products are part of the mitochondrial respiratory chain, are essential for oxidative phosphorlyation and vegetative growth and also play a critical role in cell growth and regulation. Deletion of this gene has been shown to cause a severe growth defect and irreversible cessation of cell division after 3-4 days. The ALR gene could represent the mammalian equivalent of the ERV1 gene.

Details of the structure analysis will be presented.

PS04.07.23 CRYSTAL STRUCTURE ANALYSIS OF BOVINE HEART CYTOCHROME C OXIDASE. H. Yamaguchi, T. Tsukihara, H. Aoyama, E. Yamashita, T. Tomizaki, K. Shinzawa-Itoh*, R. Nakashima,* R. Yaono* and S. Yoshikawa*. Institute for Protein Research, Osaka University, Suita, Osaka565, Japan; and *Faculty of Science, Himeji Institute of Technology, Kamigohori, Ako-gun, Hyogo678-12, Japan

Bovine cytochrome c oxidase is a large membrane protein complex with molecular size of 200KDa comprising 13 different subunits and six metal centers, heme a, heme a_3, Cu_A, Cu_B, Mg and Zn. As the terminal enzyme of biological oxidation, the enzyme catalyzes O_2 reduction to H_2O at an active site with the four redox active transition metals coupling to a proton pumping process across the mitochondrial inner membrane.

The structure of the enzyme has been determined at 2.8Å resolution. Electron transfer pathway has been elucidated by the structural study. A clear electron density map at 2.8Å resolution was obtained by m.i.r. method followed by a density modification method. Out of 3606 amino acid residues in an asymmetric unit composed of a dimmer, structural models of 3560 residues as well as those of metal centers were successfully built.

The electron density map indicates a dinuclear copper center of Cu_A with an unexpected structure of [2Cu-2Sγ] similar to a [2Fe-2S] center. Zinc site is located at a nuclear encodes subunit on the matrix side