is grown on acetate, IDH is in its inactive phosphorylated form, thus inhibiting Krebs' cycle. Alternatively, a change of carbon source to glucose or pyruvate results in the activation of IDH by dephosphorylation, and the initiation of Krebs' cycle. The function of AceK and its involvement in the regulation of Krebs' cycle and the glyoxylate bypass is well-characterized, but its structural and mechanistic qualities have remained relatively unknown. The determination of the crystal structure could provide confirmation of the function of AceK by identifying the various kinase, phosphatase and ATPase domains and insights into the coordination of the kinase and phosphatase activity of AceK. Of note, it is currently unknown how, or if at all, the active site changes conformation as it switches between kinase and phosphatase activity. Three Acek crystal forms were obtained and SAD datasets were collected at CHESS and BNL synchrotron source. The AceK structure is determined at 2.6 Å. The overall AceK structure displays a typical eukaryotic kinase folding.

Keywords: kinase, phosphatase, isocitrate dehydrogenase

P04.02.70

Acta Cryst. (2008). A**64**, C252

Structure of decameric PLP-dependent acid induced arginine decarboxylase from *Escherichia coli*

Juni Andrell[1], Megan J Maher[2], Matthew G Hicks[3], Tracy Palmer[4], So Iwata[1]

[1]Imperial College of Science, Technology and Medicine, Division of Biomolecular Sciences, MPC group, Level 1, Biochemistry building, Exhibition Road, London, London, SW7 2AZ, UK, [2]Centenary Institute of Cancer Medicine and Cell Biology, Sydney, Australia, [3]Biological Sciences, University of East Anglia, Norwich, UK, [4]Division of Environmental and Applied Biology, University of Dundee, Dundee, UK, E-mail：juniandrell@gmail.com

In order to infect a human host, enteric *Escherichia coli* must pass through the stomach, which has a pH of around 2.0, and survive there for approximately two hours before the stomach is emptied. *E. coli* is capable of surviving in the highly acidic environment of the stomach since it possesses systems that make it acid resistant. Three such systems have been identified, one of which is the arginine-dependent acid resistance system (AR3). AR3 requires the presence of arginine and is dependent on the acid induced arginine decarboxylase (AdiA) and the arginine-agmatine antiporter (AdiC). AdiA converts one molecule of arginine into agmatine and AdiC transports the agmatine out of the cell in exchange for arginine. Through this enzymatic cycle, AR3 acts to protect the organism by preventing the accumulation of protons inside the cell. In order to investigate the enzymatic mechanism involved in AR3, we have determined the structure of the acid induced arginine decarboxylase, AdiA, by X-ray crystallography. The AdiA structure, solved by multiple isomorphous replacement (MIR), revealed a ca. 800 kDa decameric assembly with unusual five-fold non-crystallographic symmetry. Presented here is the structure of AdiA from E. coli refined to 2.4 Å resolution, its pyridoxal-5'-phosphate (PLP) containing active site and its large macromolecular assembly.

Keywords: arginine decarboxylase, macromolecular proteins, acid resistance

P04.02.71

Acta Cryst. (2008). A**64**, C252

The substrate recognition and the catalytic reaction mechanisms of D-3-hydroxybutyrate dehydrogenase

Md. Mominul Hoque[1], Satoru Shimizu[1], Md. Tofazzal Hossain[1,2], Tamotsu Yamamoto[3], Shigeyuki Imamura[3], Kaoru Suzuki[5], Masaru Tsunoda[5], Hitoshi Amano[4], Takeshi Sekiguchi[5], Akio Takenaka[1,5]

[1]Tokyo Institte of Technology, Graduate School of Bioscience and Biotechnology, 5249 Nagatsuta, Midori-ku, Yokohama, Kanagawa, 226-8501, Japan, [2]Department of Biochemistry and Molecular Biology, University of Rajshahi, Rajshahi-6205, Bangladesh, [3]Asahi Kasei Pharma Corporation, Tagat-gun, Shizuoka 410-2323, Japan, [4]Fukushima National College of Technology, Taira-kamiarakawa, Iwaki 970-8034, Japan, [5]College of Science and Engineering, Iwaki Meisei University, Chuodai-iino, Iwaki 970-8551, Japan, E-mail：mominbio@yahoo.com

D-3-Hydroxybutyrate dehydrogenase (HBDH) is an NAD$^+$-dependent enzyme for reversible conversion between D-3-hydroxybutyrate and acetoacetate. These ketone bodies are important energy sources, but their excess level causes ketoacidosis. HBDH can be used as a marker in the assay of diabetes mellitus, and/or ketoacidosis. To reveal the reaction mechanism, the crystal structures of *Alcaligenes faecalis* HBDH in the *apo* form and two different *holo* forms, one with a substrate analogue, acetate (HBDH-NAD-AC) and the other with the reaction product, acetoacetate (HBDH-NAD-AA), have been determined by X-ray crystallography. The physiologically active enzyme is a homo tetramer assembled according to the non-crystallographic 222 point symmetry. Each subunit has a principal domain with a typical Rossmann fold. The two helices, H6 and H7 of the small domain, move to the principal domain to trap NAD$^+$ in a cavity. In HBDH-NAD-AC complex, an acetate ion is directly bound to the residues Q94, H144, K152 and Q196 through hydrogen bonds. A water molecule is bound to S142 and Y155, mimicking the hydroxyl group of the substrate D-3-hydroxybutyrate. The position of the water oxygen atom is near the methyl group of the acetate. These structural features strongly suggest the binding scheme of the true substrate in the enzyme-NAD complex. In the HBDH-NAD-AA crystal, obtained by adding the substrate, the reaction product acetoacetate has been found in the active site. This structure is consistent to our proposed reaction mechanism [1]. The basic structural architecture of the enzyme is highly conserved as a member of the SDR family with the catalytic triad of S142, Y155 and K159.

[1] Hoque *et al*., *Acta Cryst* . D **64**, In press (2008).

Keywords: hydroxybutyrate dehydrogenase, ketone bodies, X-ray structure

P04.02.72

Acta Cryst. (2008). A**64**, C252−253

Using natural variations among shikimate dehydrogenases to study modes of substrate selectivity

James Peek[1], Sasha Singh[2], John Stavrindes[3], David S Guttman[1,4], Dinesh Christendat[1]

[1]University of Toronto, Department of Cell and Systems Biology, 25 Willcocks Street, Toronto, Ontario, M5S3B2, Canada, [2]Children's Hospital Boston, Department of Pathology, John F. Enders Research Laboratories, 320 Longwood Avenue, Boston, Massachusetts, 02115, USA, [3]Department of Biochemistry and Molecular Biophysics, University of Arizona, 1007 E Lowell Street, Tucson, Arizona, 85721, USA, [4]Centre for the Analysis of Genome Evolution and Function, University of Toronto, 25 Willcocks Street, Toronto, Ontario, M5S3B2, Canada, E-mail：james.peek@utoronto.ca