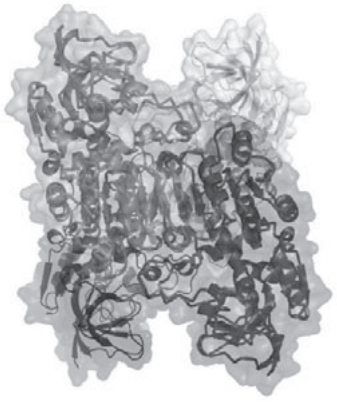
diet L-Threonine is an indispensable amino acid and under normal conditions is synthesised by microbes from oxaloacetate. Threonine degradation occurs by two major pathways: -either it is converted by TDH to 2-amino-3-ketobutyrate, which by the action of 2-amino-3-oxobutyrate CoA ligase produces glycine and acetyl CoA. -or alternatively L-serine/ threonine dehydratase converts threonine to NH_4^+ and 2-ketobutyrate and the latter is further metabolized by way of acetyl CoA.



Keywords: threonine dehydrogenase, enzyme, zinc

P04.02.67

Acta Cryst. (2008). A**64**, C251

Structural studies of acyl-CoA thioesterase 7 and its role in inflammation

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Acyl-CoA thioesterases (Acots) are important enzymes involved in the hydrolysis of acyl-CoA to free fatty acids and coenzyme A. The enzyme can be found in a large range of organisms from bacteria to humans and in all mammalian tissues and cells. The mammalian full length acyl-CoA thioesterase (Acot7) enzyme is comprised of two hotdog fold domains. The crystal structures of both the N- and C-terminal domains were determined separately at 1.8 and 2.5 Å resolution, respectively, and the structure of full length enzyme was inferred by a combination of chemical cross-linking, mass spectrometry, and molecular modeling. We have shown using functional and biochemical assays that both the domains are required for activity of enzyme and mutational studies have shown that out of the two possible actives sites, only one is functional. This is in contrast with the acyl-CoA thioesterases from the primitive organisms, in which the active form of the enzyme can be achieved from one single domain copy. Because, Acot7 is highly expressed in macrophages, up-regulated by LPS (lipoploysacchrides), has a strong affinity towards arachidonyl-CoA and its over expression in macrophages alters the D2 and E2 prostaglandin production, we propose that it plays an important role in inflammation. Collectively, our results link the molecular and cellular functions of Acot7 and identify it as a candidate drug target in inflammatory disease.

Keywords: X-ray crystallography, protein structure, acyl CoA thioesterase

P04.02.68

Acta Cryst. (2008). A**64**, C251

Structural proteomics of secreted proteases from the ovine footrot pathogen, *Dichelobacter nodosus*

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Dichelobacter nodosus is the primary cause of ovine footrot, a contagious disease that causes severe economic loss to the sheep industry. The severity of the infection can range from virulent to benign depending upon the causative *D. nodosus* isolate. Virulent footrot is characterised by the separation skin horn junction whilst benign isolates cause a mild inflammation of this tissue. Virulent isolates of *D. nodosus* secrete three subtilisin-like serine proteases, the acidic proteases AprV2 and AprV5 and the basic protease BprV. It is postulated that these proteases play an essential role in the pathogenesis of virulent footrot due to their ability to degrade components of the extracellular matrix at the site of infection. Benign isolates of *D. nodosus* secrete the closely related proteases AprB2 and BprB which differ from AprV2 and BprV by one amino acid (Y92R) and ten amino acids respectively. In this study, X-ray crystallography has been used to elucidate the structural differences between the proteases secreted by virulent and benign isolates. The crystal structures of AprV2, AprB2, BprV and BprB have been determined to 2 Å, 1.7 Å, 2 Å and 1.8 Å respectively. The structures revealed a conserved subtilisin domain with a unique disulphide tethered, solvent exposed loop that partially occluded the active site. The single amino acid difference between AprV2 and AprB2 is located at the tip of this loop. Amino acid variations between BprV and BprB are located throughout the structure including surface residues and residues in the substrate binding site and the active site occluding loop of the protease. This study provides an insight into the structure of the secreted proteases from *D.nodosus* and the role of these proteases play in the pathogenesis of ovine footrot.

Keywords: enzyme structure determination, proteases, infectious diseases

P04.02.69

Acta Cryst. (2008). A**64**, C251-252

Structure determination of *E. coli* isocitrate dehydrogenase kinase/phosphatase

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The study of bacterial phosphorylation systems was advanced by the discovery of a phosphorylating activity in *E. coli* which regulates isocitrate dehydrogenase (IDH). This was the first prokaryote phosphorylation system to be identified in bacteria, and is the only known serine/threonine (Ser/Thr) phosphorylation system/pathway in E. coli. This phosphorylation-dephosphorylation system modifies the Ser-113 residue on IDH. It is this modification that regulates the amount of isocitrate going through the glyoxylate bypass. IDH competes with isocitrate lyase in directing isocitrate through the Krebs' cycle or glyoxylate bypass, respectively. When the organism