visualize ambiguous bonding electrons between aplyronine A and actin.

Keywords: aplyronine A, antitumor effect, maximum entropy method

P.04.19.6

Acta Cryst. (2005). A**61**, C254

Crystal Structure of SSL11, a Superantigen-related Toxin from *Staphylococcus Aureus*

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The pathogenic bacterium *Staphylococcus aureus* expresses a large number of protein toxins, which contribute to serious human disease. Analysis of the s. aureus genome identified a cluster of genes, encoding what are now called "staphylococcal superantigen-like" (SSL) proteins [1]. We report structural and functional studies on one of these proteins, SSL11.

SSL11 was expressed in *E. coli*, purified and crystallized from 0.2M NaH_2PO_4, 20% PEG3350. The crystals are monoclinic, space group $P2_1$, with a=52.2, b=100.9, c=79.6 Å, β=91.2°, with 4 molecules in the asymmetric unit. The crystal structure was solved by molecular replacement, using the structure of the related SET3 (SSL5) [2] as search model, and is being refined at 2.2 Å resolution (R=0.308, R_{free}=0.337). The fold of SSL11 very closely resembles that of SSL5 and shows that it belongs to the wider superantigen family.

Functional studies show that SSL11 does not have superantigen activity, but instead binds with high affinity to the human IgA receptor. This suggests a role in human disease. Intriguingly, SSL11 forms a dimer in the crystal that closely resembles that formed by SSL5 (but not by superantigens), suggesting a functional importance.

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Keywords: bacterial toxin, crystal structure, dimerisation

P.04.19.7

Acta Cryst. (2005). A**61**, C254

Crystal Structure of 5-Aminolevulinate Synthase of *Rhodobacter capsulatus*

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5-Aminolevulinate synthase (ALAS) is the first and rate-limiting enzyme of heme biosynthesis in humans, animals, other non-plant eukaryotes and α-proteobacteria. It catalyzes the synthesis of 5-aminolevulinic acid, the first common precursor of all tetrapyrroles, from glycine and succinyl-coenzyme A.

eALAS (e for erythroid) is one of two isoforms of ALAS expressed in mammals and is responsible for approximately 90 % of body heme production. Naturally occurring mutations in human eALAS directly cause a hereditary disease known as X-linked sideroblastic anemia (XLSA). These disorders are characterized by inadequate formation of heme and accumulation of iron in erythroblast mitochondria.

We solved the crystal structure of ALAS of *Rhodobacter capsulatus*, 50 % identical by sequence to its human counterpart, at a resolution of 2.1 Å. Additional structures with each of the substrates glycine and succinyl-CoA reveal the active site organization and provide new insight into the enzyme mechanism.

We can now locate most naturally occurring XLSA mutations with high precision and interpret the clinical XLSA-cases in terms of the three-dimensional structure of the enzyme involved. Thus new impetus is given to finding ways of treating XLSA.

In addition the structure of ALAS completes the structural analysis of enzymes in heme biosynthesis.

Keywords: heme biosynthesis, pyridoxal 5'-phosphate, anemia

P.04.19.8

Acta Cryst. (2005). A**61**, C254

Structures of *B. burgdorferi* OspB Alone, and in Complex with a Bactericidal Fab

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Certain antibody Fab fragments directed against the C-terminus of outer surface protein B (OspB), a major lipoprotein of the Lyme disease spirochete, *Borrelia burgdorferi*, have the unusual property of being bactericidal even in the absence of complement. We report here X-ray crystal structures of a C-terminal fragment of *B. burgdorferi* outer surface protein B (OspB) both alone and in a complex with the bactericidal Fab H6831. The H6831 epitope is topologically analogous to the LA-2 epitope of OspA and is centered around OspB Lys 253, a residue essential for H6831 recognition. A 8-sheet present in the free OspB fragment is either disordered or removed by proteolysis in the H6831-bound complex. In both crystal structures, OspB C-terminal fragments form artificial dimers connected by *inter*molecular 8-sheets. OspB structure, stability, and possible mechanisms of killing by H6831 and other bactericidal Fabs are discussed in light of the structural results.

Keywords: Lyme disease, antibody antigen interactions, cell surfaces

P.04.19.9

Acta Cryst. (2005). A**61**, C254

Crystal Structure of Botulinum Neurotoxin Type G Light Chain

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The seven serotypes (A-G) of botulinum neurotoxins (BoNTs) block neurotransmitter release through their specific proteolysis of one of the three proteins of the soluble N-ethylmaleimide-sensitive-factor attachment protein receptor (SNARE) complex, which is essential for membrane vesicle fusion. BoNTs have stringent substrate specificities that are unique for metalloprotease in that they require exceptionally long substrates. In order to understand the molecular reasons for the unique specificities of the BoNTs, it is essential to expose the molecular differences in their structures that give rise to their unique characteristic. Therefore, structures of all serotypes are required, and toward achieving this goal here is reported the crystal structure of the catalytic light chain of *Clostridium botulinum* neurotoxin type G (BoNT/G-LC) that has been determined to 2.35 Å resolution. The structure of BoNT/G-LC reveals a C-terminal β-sheet, which is critical for LC oligomerization, is unlike that seen in the other LC structures. Serotype structural differences observed in the pool of LC structures reveal residues in BoNT/G-LC that are likely to be involved in substrate recognition of the P1' residue and a second remote exosite for recognition of a SNARE motif.

Keywords: botulinum neurotoxin, light chain, substrate recognition

P.04.20.1

Acta Cryst. (2005). A**61**, C254-C255

Integration of XAS and NMR Techniques for the Structure Determination of Metallo-proteins. Examples from the Study of Copper Transport Proteins

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NMR is a powerful technique for protein structure determination in solution. However, when dealing with metallo-proteins, NMR