## P04.19.405

*Acta Cryst*. (2008). A**64**, C357

### Two staphylococcal sialic acid binding proteins from the superantigen superfamily

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Staphylococcus aureus is a significant human pathogen. Among its large repertoire of secreted toxins is a group of staphylococcal superantigen-like proteins (SSLs). These are homologous with superantigens (SAgs) but do not have the same activity. We have shown that two of these proteins, SSL5 and SSL11, bind to human granulocytes and to the cell surface receptors for human IgA (FcaRI) and P-selectin (PSGL-1) in a sialic acid-dependent manner. We co-crystallized both SSL5 and SSL11 with the tetrasaccharide sialyl-Lewis X (sLeX), a key determinant of PSGL-1 binding to P-selectin. The structures of the SSL5-sLeX and SSL11-sLeX complexes were refined at resolutions of 1.65 Å and 1.6 Å, respectively. Both SSLs share the same SAg-like fold and both show a similar tendency to form dimeric structures in the crystal. In both complex structures, sLeX binds to a specific site on the surface of the C-terminal domain, in a conformation identical to that bound by P-selectin. Conservation of the key carbohydrate-binding residues indicates that this ability to bind human glycans is shared by a substantial sub-group of the SSLs. This indicates that the ability to target human glycans is an important property of this group of toxins. Structural comparisons also show that the sialic acid binding site in SSL5 contains a substructure that is shared by other sialic acid binding proteins from bacteria and viruses and represents a common binding motif.

Keywords: superantigen-like toxins, microbial pathogenesis, staphylococcus aureus

## P04.19.406

*Acta Cryst*. (2008). A**64**, C357

### Crystal structure of the extracellular protease of the nosocomial pathogen stenotrophomonas maltoph

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Stenotrophomonas maltophilia is a multiresistant pathogen increasingly emerging in the hospital environment. In immunosuppressed patients these bacteria may cause severe infections associated with tissue lesions like pulmonary haemorrhage. This indicated proteolysis as a possible pathogenic mechanism in these infections. Indeed, a new protease with broad specificity has been found to be secreted by S. maltophilia [Windhorst et al., J Biol Chem 277, 11042]. The gene, termed StmPr1, was analyzed; it codes for a 63 kDa precursor, which is processed to the mature protein of 47 kDa. The enzyme is an alkaline serine protease which, by sequence homology and enzymic properties, can be further classified as a new member of the family of subtilases. However biochemical studies with the purified protein indicated that the StmPr1 protease differs substantially from so far known subtilisins in molecular size and in substrate specificity. In order to gain insights into the structure-function-relationship the StmPr1 gene was overexpressed in E. coli and processed to the active enzyme. Crystals of the native and inhibited enzyme could be grown after the protease was allowed to truncate from the C-terminus to a 36 kDa active core protein. Diffraction data sets of the native and inhibited enzyme were collected to 1.5 Angstrom resolution applying synchrotron-radiation, and the 3D-structure was solved. Compared to known baterial proteases it revealed a new overall fold and architecture of the active site. The high resolution structure can serve to develop specific agents for a targeted therapy of St. maltophilia infections.

Keywords: crystal structure, bacterial, protease

## P04.19.407

*Acta Cryst*. (2008). A**64**, C357

### Crystal structure of a sigma28-regulated non-flagella virulence protein *from campylobacter jejuni*

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Campylobacter jejuni, a Gram-negative motile bacterium, is a leading cause of human gastrointestinal infections. The mechanism of C. jejuni mediated enteritis appears to be multi-factorial. The flagella of C. jejuni play complex roles in virulence of this human pathogen. Of note, in the absence of a specialized type III secretion system, the C. jejuni flagella filament secretes several non-flagellar proteins to the extracellular milieu, some of which are involved in virulence. Cj0977 is a recently identified virulence factor in C. jejuni, and is expressed by a sigma28 promoter which controls late genes in the flagellar regulon. A Cj0977 mutant was fully motile but significantly reduced in invasion of intestinal epithelial cells in vitro. In an effort to gain insight into the structural basis of C. jejuni virulence, we set out to solve the crystal structure of Cj0977. The crystal structure reveals that Cj0977 adopts the 'hot-dog' fold, which is characterized by 6 beta-stranded antiparallel beta-sheet wrapping around an alpha-helix. The characteristic hot-dog fold proteins are found in certain coenzyme A compound binding proteins with numerous oligomeric states. Structural comparison with other known hot-dog fold proteins suggest a possible link between virulence and membrane lipid biosynthesis. This work was supported by Robert A. Welch Foundation grant # E-1616 to H.J.Y.

Keywords: bacterial pathogenesis, hot-dog fold, virulence

## P04.20.408

*Acta Cryst*. (2008). A**64**, C357-358

### Allostery in p38-docking-peptide interaction-an NMR study

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