Poster Presentations

[MS5-P19] Structural Studies of Innate Immune Proteins <u>R. da Silva</u>, I. Burns, T.J. Greenhough, A. K. Shrive

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Innate immune defence proteins interact with a variety of different organisms such as bacteria, fungi allergens and viruses. Collectins and Pentraxins are two examples of innate immune protein families. Collectins, a group of C-type lectins which include Mannosebinding Lectin and Surfactant Proteins, are multimeric assemblies of polypeptides, cysteine rich N-terminus containing a domain, a collagen like region, an α -helical neck region and a C-terminal carbohydrate recognition domain (CRD) [1]. Collectins recognise and bind a variety of pathogens in a calcium-dependent manner and are part of the immune system clearance mechanism of invading pathogens. A link between collectin levels and disease, inflammation, allergy and asthma has been noted. Collectins are present in various organs such as the lungs, heart, prostate and kidney. In the lungs the surfactant proteins hSP - D and hSP-A recognise a wide range of microbial targets, such as viruses, bacteria, yeasts and fungi, promoting microbial aggregation and enhanced uptake and killing by immune cells. [1,2]. Biologically active recombinant fragments of lung collectins thus present themselves as a potential therapy in treating inflammatory and infectious diseases in the lung. Structural studies of surfactant proteins with natural ligands such as the lipopolysaccharide (LPS) from Haemophilus influenzae will allow an increased knowledge of the molecular mechanisms of recognition and binding of different pathogens, and how the clearance of those pathogens is effected. The **Pentraxins**, a family of proteins which includes C-reactive protein (CRP),

are evolutionarily conserved serum proteins found in mammals, fish, amphibians and invertebrates. Pentraxins have the ability to recognise and bind to phosphocholine and phosphoethanolamine groups present in cell wall phospholipids and polysaccharides, and in fungal and bacterial LPS. [3][4]. Structural studies of CRP from a variety of sources, complexed with natural ligands including the LPS and teichoic acid from Gram negative and Gram positive bacteria respectively, will provide an increased understanding of how pentraxins recognise their physiological ligands and effect immune clearance. Limulus polyphemus pentraxins provide an ideal basis not only for the study of bacterial recognition by CRP but also the evolution of the immune system, molecular phylogeny and protein evolution, since invertebrates lack an adaptive immune system and pentraxins are central to host defence and innate immunity.

References:

[1]- Crouch, E., Wright, J. (2001 Surfactant Proteins A and D and pulmonary host defence. *Annual Review of Physiology*.63: 521-554
[2]- Wright, R. (2005)
Immunoregulatory functions of surfactants proteins. *Nat Rev Immunol.* 5(1):58-68.
[3]- Shrive, A.K., Metcalfe, A., Cartwright, J., Greenhough, T. (1999). C-Reactive protein and SAP-like pentraxins are both present in *Limulus polyphemus* Haemolyph: Crystal

Structure of *Limulus* SAP. J. Mol. Biol. 290: 997-1008.

[4]- Shrive, A. K., Cheetham, G. M. T.,

Holden, D., Myles, D. A. A., Turnell, W.

G., Volanakis, J. E., Pepys, M. B.,

Bloomer, A. C. & Greenhough, T. J. (1996). Three dimensional structure of human C-reactive protein. *Nature Struct. Biol.* **3**: 346-354.

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