

retained in the class II MHC peptide binding pocket until it is replaced by an antigen in the endosome. CLIP serves to stabilize the MHC heterodimer and also prevents binding of endogenous peptides. CLIP-to-antigen exchange, mediated by HLA-DM, is a key determinant of subsequent immunological events. HLA-CLIP stability is thought to be an important factor for triggering autoimmunity [1,2]. We have analyzed the non-covalent interaction between HLA-DQ2.5 and CLIP in order to determine the molecular basis for the unusually long half-life of the HLA-DQ2.5-CLIP complex. This is the first HLA-DQ-CLIP structure to be reported.

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**Keywords:** HLA-DQ2.5, autoimmunity, CLIP

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### Structure, function and evolution of the serum pentraxins

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Wide-ranging studies on the serum pentraxins C-reactive protein (CRP) and serum amyloid P component (SAP) are aimed at the investigation of the structural, functional and evolutionary relationships, and of the humoral and cellular recognition properties, of the pentraxins from species ranging from invertebrate to man. Recognition properties of the pentraxins, homologues of which have been found in mammals, fish, amphibians, and invertebrates, include cell wall phospholipids and fungal and bacterial polysaccharides. In the absence of highly developed adaptive immunity, a diverse array of humoral components, such as the pentraxins, provides an essential and effective strategy for recognising and destroying disease-causing pathogens. In humans CRP, when bound to a suitable physiological ligand, binds C1q and efficiently activates classical complement.

The structures of pentraxins from man [1,2] and *Limulus polyphemus* [3] reveal variable aggregation of the conserved protomer fold. Unusually LimSAP displays two distinct molecular aggregations for the same molecule, a doubly stacked octamer and a doubly stacked heptamer. Although sequence homology with human SAP is relatively low, structural homology is high. This is due in part to a "topological" equivalence of side chain position. Upon binding phosphoethanolamine, LimSAP binds a third calcium in each subunit, with all three calcium ions contributing to the binding and orientation of the ligand. New structural studies of mammalian, fish and horseshoe crab pentraxins provide further unique insights into not only the evolutionary conservation of an important functional role in immunity, but also into the diversity of molecular aggregation built from a phylogenetically conserved protomer fold.

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### Structural basis of recognition of pathogen-associated molecular patterns by pgrp-s

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Peptidoglycan recognition proteins (PGRPs) are involved in the recognition of pathogen-associated molecular patterns (PAMPs). The well known PAMPs include lipopolysaccharide (LPS) from Gram-negative bacteria and lipoteichoic acid (LTA) from Gram-positive bacteria. PGRP-short (PGRP-S) has been isolated from the mammary secretions of camel (CPGRP-S). It binds LPS and LTA with affinities of  $1.6 \times 10^{-9}$  M and  $2.4 \times 10^{-8}$  M respectively. The crystal structures of CPGRP-S complexes with LPS and LTA revealed that both compounds were held tightly inside the CPGRP-S tetrameric complex consisting of molecules A, B, C and D. The binding cleft is formed at the interface of molecules C and D which is extendable to the interface of A and C. The interface of molecules A and B is tightly packed while that between B and D forms an open channel. The hydrophilic moieties of these compounds occupy a common region while hydrophobic chains interact with distinct regions in the binding site. The flow cytometry studies showed that both LPS- and LTA-induced expressions of pro-inflammatory cytokines, TNF- $\alpha$  and IL-6 were inhibited by CPGRP-S. The results of animal studies using mice models indicated that both LPS- and LTA-induced mortality rates decreased drastically when CPGRP-S was administered. The recognition of both kinds of PAMPs from Gram-negative and Gram-positive bacteria, their high binding affinities to CPGRP-S, the significant decrease in the productions of LPS- and LTA-induced TNF- $\alpha$  and IL-6 on introduction of CPGRP-S and the drastic reductions in mortality rate in mice models by CPGRP-S suggest that CPGRP-S may be exploited as a common antibiotic agent for the welfare of mankind. This is particularly significant as there is an alarming rise in the incidence of bacterial resistance to known antibiotics. This also brings the amino acid sequence of CPGRP-S in focus particularly the presence of residues, Pro96 and Pro151 at one of the interfaces and the absence of three N-terminal residues and Cys8 as compared to human PGRP-S. So far in the family of PGRP-S, such a homotetrameric complex has been observed only for CPGRP-S.

**Keywords:** PGRP, PAMPs, LPS

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### Structural studies of macrophage proteins using UQSG pipeline

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Macrophages are cells differentiated from circulating blood monocytes that represent the first line of defense against pathogen invasion. Macrophages are widely distributed throughout the body and are particularly abundant at the route of pathogen entry. They play a critical role in immune defense by initiating, promoting, preventing, suppressing or terminating immune responses.

We established a high-throughput pipeline at the University of Queensland to investigate the structures and functions of novel macrophage proteins [1]. My project began with the selection of 12