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Keywords: antibody structure, photophysics, protein dynamics

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Engineering Immune System Glycoproteins to form Uniform Crystalline Lattices
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Interactions of antibodies and Fc receptors (FcR) play a fundamental role in immunity. However, antibodies and FcR are heavily glycosylated, making it difficult to obtain strongly diffracting crystals. Consequently, most structures for these proteins have been determined at low to medium resolutions (<3.0-2.6 Å). Without modifying the carbohydrates, we are developing procedures for generating crystals of immune system glycoproteins that diffract to high resolutions.

A 2.0 Å structure was previously determined for FcγRIIa with a point mutation of Ser to Phe at position 88[1]. The Phe88 side chain is involved in a key lattice contact by completing a hydrophobic pocket that traps a proline "guest ligand" from a symmetry related receptor monomer. As a result the crystals are robust, allowing a variety of receptor glycoforms to be resolved and the structural analysis extended to 1.5 Å. The role of Phe88 in promoting uniform crystalline lattices has been shown by determining the 2.3 Å resolution structure of the "wild-type" (Ser88) FcγRIIa glycoprotein. The Ser88 receptor crystals were fragile with receptors arranged in a different and more loosely packed crystalline lattice compared to Phe88 receptor crystals.

The improved properties of FcγRIIa crystals containing the lattice forming Phe88 mutation may have profound implications for the field of macromolecular crystal engineering.

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Keywords: immune system proteins, cell surface receptors, crystal engineering

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Crystal Structure of Leukocyte Ig-like Receptor 9 (LIR9/ILT11 /CD85f)
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Leukocyte Immunoglobulin(Ig)-like receptors (LIRs) are human Ig-like receptors that have activating and inhibitory function in leukocytes. LIRs can be subdivided into three groups: inhibitory, activating and secreted molecules. LIR9 is mainly expressed on monocytes and neutrophils as both membrane bound and secreted forms. The membrane bound LIR9 is an activating receptor with arginine residue in its transmembrane region, and the cross-linking of LIR9 induces activation of monocytes. Whereas LIR1 and LIR2, the inhibitory receptors of LIR family, are known to bind to a broad range of human MHC class I molecules (MHCIs), the binding property of LIR9 is unknown. LIR9 shows less homology with LIR1/2/6 recognizing MHCIs (less than 60% amino acid identity with LIR1/2/6). Here we demonstrated that LIR9 had no or very weak affinities to MHCIs by biosensor analysis. Furthermore, we determined the crystal structure of extracellular domain of LIR9 at 1.9 Å resolution by MAD method. The structure showed large structural differences in the region corresponding to the MHCI binding site of LIR1, resulting in the disability of LIR9 to bind to MHCIs. These results raised the possibility that LIR9 recognizes a non-MHCI ligand.
Keywords: immune regulation, immunoglobulin-like receptor, structural immunology

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The Crystal Structure of Human CD1d with and without α-Galactosylceramide Bound
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The glycolipid α-galactosylceramide binds with high affinity to CD1d and stimulates NKT cells. Here we report the crystal structure of human CD1d in complex with synthetic α-galactosylceramide at 3.2 Å resolution. The structure reveals a tightly fit lipid in the CD1d hydrophobic binding groove, with the sphingosine chain bound in the C' pocket and the longer acyl chain anchored in the A' pocket. Pocket volumes and hydrogen bonds to the glycolipid head group optimize α-galactosylceramide binding to CD1d. The structure of CD1d without lipid is also presented which shows a more open conformation of the binding groove than is seen in lipid-bound CD1d, suggesting a dual conformation of CD1d in which the "open" conformation is more able to load lipids than the lipid-bound "closed" conformation.
Keywords: humanCD1d, empty MHC class I-like protein, α-galactosylceramide

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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 and serum amyloid P component 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.

The structures of pentraxins from man [1], rat, Mustelis canis and L. polyphemus [2,3,4] reveal variable aggregation of the conserved protomer fold, details of novel binding properties and insights in to the relationships between structural, functional and sequence homology.

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Keywords: pentraxin, innate immunity, evolution

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Structural Studies of Human CD81 Extracellular Domain
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CD81 is a four transmembrane protein of 236 amino acids, belonging to the tetraspanin protein family, involved in various