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binding (lectin) characteristics of this particular pentraxin. Significantly the structure reveals an arrangement of beta strands very similar to the subunit fold of the legume lectins Concanavalin A and pea lectin.

Possible clinical applications and rational drug design:

Amyloidosis is defined as a group of biochemically diverse conditions in which normally innocuous soluble proteins polymerize to form insoluble fibrils. This growing mass of amyloid fibrils is universally bound by SAP to form amyloid deposits which persist and invade the extracellular spaces of organs destroying normal tissue architecture and function. One of our aims is to try and disperse these deposits by designing drugs to remove bound SAP allowing normal in vivo clearance mechanisms to act upon the fibrils. Further possiblities are to use the specificity of SAP in designing magic bullets. This idea is well founded in the use of radiolabelled SAP as the only means of imaging amyloid in vivo using whole body scans.

DS-05.03.04 A STRUCTURAL COMPARISON OF BACTERIAL AND VIRAL NEURAMINIDASES G.L. Taylor*, S.J. Crennell, , E.F. Garman§, W.G. Laver† and E. Vimr‡, Department of Biochemistry, University of Bath, Claverton Down, Bath, BA2 7AY, U.K.

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We have determined the structure of *S. Typhimurium* LT2 neuraminidase/sialidase using MIR techniques to 1.6Å, and have obtained inhibitor complexes to 1.6Åand 2.2Å. This is the first bacterial sialidase whose structure has been determined, and despite only 16% sequence homology shares the same fold as the influenza virus enzyme. The viral enzyme requires Ca^{2+} for optimal activity; the bacterial enzyme does not. The viral enzyme possesses at least 8 conserved disulphides; the bacterial only one. The fold of six four-stranded antiparallel β-sheets is very similar, but the strand and loop lengths vary considerably. The active site shares features with the viral enzyme: an arginine triad, a hydrophobic pocket, and a tyrosine which most probably stabilizes a carbonium ion intermediate in the catalysis similar to β-galactosidase. There are differences, however, which explain the differential binding of various substituted sialic acids. The structure provides valuable information for those designing inhibitors targeted at this enzyme against various pathogens.

DS-05.03.05 STRUCTURAL, FUNCTIONAL AND EVOLUTIONARY IMPLICATIONS OF THE THREE-DIMENSIONAL CRYSTAL STRUCTURE OF MURINE INTERFERON-β. By Y.Mitsui* and T.Senda, Nagaoka University of Technology, Nagaoka, Niigata, 940-21, Japan

Interferons (IFN) are proteins showing antiviral, antitumor and immunomodulator activities with significant therapeutic value for Type C hepatitis and other diseases. The IFN's have been classified into two categories on the basis of their biological and physical properties. Type I IFN's include fibroblast interferon (IFN-β) and the leukocyte family of interferons (IFN-α) which is composed of at least 10 subspecies. Each member of Type I IFN's contain ~165 amino acid residues exhibiting considerable sequence homology to each other, and competes for the same receptors. In contrast, Type II IFN (IFN-γ) is produced in response to mitogens and antigenic stimuli, contains ~146 amino acid residues exhibiting no significant sequence homology to Type I IFN's and displays no measurable binding to Type I interferon receptors.

The first and still the only three-dimensional structure of Type I IFN, the crystal structure of recombinant murine interferon-β, was elucidated by T.Senda *et al.* (*Proc.Japan Acad.*, 1990, **66B**, 77 - 80; *The EMBO J.*, 1992,**11**, 3193 - 3201). It appears to represent the basic structural framework of all Type I IFN's including IFN-β and all subtypes of IFN-α of various mammalian origin. The huge accumulated data on the structure activity relationship of Type I IFN's using various chemical and genetical techniques have been systematically evaluated in terms of the three-dimensional structure. Several intriguing observations have also been made through 1) structural comparison with other cytokines, for which three-dimensional structure has been established, including interferon-γ (Ealick,S.E. *et al.*, *Science*, 1991, **252**, 698 - 702; Samudzi,C.T. *et al.*, *J. Biol. Chem.*, 1991, **266**, 21791 - 21797), and 2) considerations on evolution of cytokines and cytokine receptors (Mitsui,Y., Senda,T., Shimazu,T., Matsuda,S. and Utsumi,J., *Pharmacology and Therapeutics*, 1993, in press; also see the poster presented by T.Senda and Y.Mitsui). Some of the results follow. a) Basic structural framework of Type I IFN is a four-α-helix bundle with 2 overhand inter-helical connections as in the case of growth hormone, GM-CSF and (the revised structure of) IL-2. b) Type II IFN (IFN-γ) exhibits only a topological (if any) structural similarity with Type I IFN's (IFN-α and IFN-β). c) Functionary important sites on the Type I IFN molecules are located on the two separate polypeptide chain segments which, however, form an apparently one contiguous receptor-binding site. d) Comparisons between human and murine amino-acid sequences for various cytokines and their cognate receptor proteins show that 1) the speed of their evolutionary variation is generally much faster than in other proteins (*e.g.* enzymes) and 2) amino acid substitution rate of cytokines correlates with that of their cognate receptors. "Coupled evolution" shared by a cytokine and its cognate receptor protein(s) may well be an explanation for this phenomenon.

DS-05.03.06
STRUCTURAL IMMUNOLOGY OF MOUSE MHC CLASS I
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Structures of murine MHC class I H-2K^b have been determined in complex with three different peptide antigens at 2.3 - 2.5Å resolution. The structures reveal, when compared with the corresponding human HLA structures of B27, Aw68.1 and A-2 from the Wiley laboratory, a general mechanism for peptide binding. The peptides are embedded deeply within the 25Å binding groove and specific hydrogen bonds to the peptide backbone as well as the amino carboxyl terminal provide specificity for peptides of 8 to 9 residues in length. This mode of binding explains the higher affinity but low sequence specificity of the MHC interaction. Comparison of the three H-2K^b peptide complexes has revealed small but significant changes in the MHC structure itself which may affect T-cell recognition. Such sequence changes are synergistic in as much as different peptide sequences can cause different changes in the MHC so that the information content of the peptide is enhanced. The question of whether the empty MHC class molecule has the same conformation as in the peptide complex is being addressed.

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