**s8a.m4.p5** **Crystal Structure of the First Three Domains of the Type-1 Insulin-like Growth Factor Receptor.** T.P.J. Garrett[1], N.M. McKern[2], M. Lou[1], M.J. Frenkel[2], J.D. Bentley[2], G.O. Lovrecz[2], T.C. Elleman[2], L.J. Cosgrove[2] and C.W. Ward[2]. *Biomolecular Research Institute[1] and CSIRO Division of Molecular Science[2],343 Royal Parade, Parkville, Victoria, 3052, Australia.*
Keywords: membrane proteins, receptors.

The type I insulin-like growth factor (IGF-1R) belongs to a family of vertebrate cell surface receptors which include insulin receptors. Homologues have also been found in many invertebrates including some of the simplest multicellular animals. Ligands for this family are protein hormones which induce a variety of metabolic and mitogenic responses in humans. The growth hormones, IGF-I and IGF-II are essential for normal growth and development but also appear necessary in malignant transformation of some cells. Insulin is a major mediator of glucose homeostasis in a variety of tissues. A peculiar feature of these receptors is that they pre-exist on the cell surface as disulfide-linked dimers and the hormone binding event is thought to trigger a structural change in the receptor which transmits the signal into the cell.

We have determined the first structure of an extra-cellular fragment (L1-cys rich-L2 domains) of IGF-1R to 2.6 Å resolution. L1 and L2 are homologous and they adopt a fold which represents a new type of structural domain. The cys-rich region also shows unique structural features, being composed of disulfide-bonded modules which are associated in a novel manner. The three domains surround a central space which is just large enough to accommodate a ligand molecule. Although this fragment does not bind ligand, many of the determinants for ligand-binding and specificity map to the lining of this central site.

**s8a.m4.p6** **The 22kDa endo-specific membrane-bound lytic transglycosylase EmtA.** F.I. Gliubich[a], A.M.W.H Thunnissen and B.W. Dijkstra. *Laboratory of Biophysical Chemistry and Groningen Biomolecular Sciences and Biotechnology Institute University of Groningen, Nijenborgh 4, 9474 AG Groningen - The Netherlands. a: Current address: Molecular Simulations Inc, 235/250 The Quorum, Barnwell Road Cambridge, U.K.*
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Lytic transglycosylases are bacterial enzymes that catalyse the breakdown of peptidoglycan cleaving the β-1,4-glycosidic bond between N-acetylmuramic acid (MurNAc) and N-acetylglucosamine (GlcNAc) residues with concomitant production of 1,6-anhydromuropeptides. Different functions have been proposed for these enzymes, including a role in the enlargement and division of the cell wall during bacterial growth and division or in the localised opening of the peptidoglycan net to allow the export of bulky compounds such as DNA, toxins and flagella.

Our studies aim at the structural and functional characterisation of the lytic transglycosylase family using X-ray crystallography and biochemical methods. The structures of the 70-kDa and 35-kDa soluble lytic transglycosylases (Slt70 and Slt35) from *E. coli* were solved previously [1-2]. EmtA is a novel, unique member of the *E. coli* lytic transglycosylase family which shows endo-specific substrate cleavage whereas all the others are exo-lytic enzymes [3].

The crystal structure of a soluble form of EmtA, with its N-terminal lipoprotein tail replaced by a poly-histidine tag, was solved at 2.2 Å resolution using the MAD phasing technique. The positions of the 30 selenium atoms in the asymmetric unit were determined using SnB [5] and phases refined with SHARP [6] and Warp [7].

The structure of EmtA enabled us to better understand functional properties of the endo-lytic transglycosylase and define its relationships with the other enzymes in the Slt family.

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