

Structural Basis of Ligand Recognition by the Collectins

Annette Shrive¹, Chris Martin¹, Ian Burns¹, Jenny Paterson¹, Jackie Martin¹, Uday Kishore^{2,3}, Ken Reid² and Trevor Greenhough¹, ¹ School of Life Sciences, Keele University, UK. ² MRC Immunochemistry Unit, University of Oxford, UK. ³ John Radcliffe Hospital, University of Oxford, UK. E-mail: a.k.shrive@keele.ac.uk

The biological activity of collectins is exerted through Ca-dependent binding of the terminal monosaccharide of, for example, cell surface lipopolysaccharide and phospholipids, peptidoglycans and glycosaminoglycans. The residues in the carbohydrate-binding pocket which coordinate to both the calcium ion and the ligand are highly conserved. Variability in other binding determinants in the binding pocket is, however, evident throughout the family. One of these determinants has been shown to influence bound ligand orientation in rat MBP [1], but there is, as yet, no explanation of the variability of orientation and relative affinity for the variety of ligands.

Our high resolution structures of recombinant collectin fragments, including a biologically and therapeutically active fragment of hSP-D, in both unliganded and ligand-complexed forms [2], provide preliminary data towards an understanding of the ligand specificity of the collectins. They also raise questions regarding the interaction of hSP-D with natural ligands, the regulation of its activity by calcium, and its interaction with receptors on immune effector cells.

[1] Ng K.K.S., Kolaktar A.R., Park-Snyder S., Feinberg H., Clark D.A., Drickamer K., Weis W.I., *J. Biol. Chem.*, 2002, **277**, 16088-16095. [2] Shrive A.K., Tharia H.A., Strong P., Kishore U., Burns I., Rizkallah P.J., Reid K.B.M., Greenhough T.J., *J. Mol. Biol.*, 2003, **331(2)**, 509-523.

Keywords: lectin, immune system, ligand-protein interactions