[MS5-P50] Structural basis of bacterial recognition by surfactant protein D.

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The aim of our structural research is to characterise, at the molecular level, how innate immunemolecules, both native and in the form of potentially therapeutic recombinant fragments, both in their own right and in concert with other immune mechanisms, recognise their targets and effect clearance. Our high resolution structures of rfhSP-D, a biologically and therapeutically active fragment of human surfactant protein D (hSP-D) provide an understanding of the ligand specificity of the collectins [1,2]. New structural work on the interaction of lipopolysaccharide fragments of the lung pathogen Haemophilus influenzae with this recombinant hSP-D fragment reveals a novel mode of interaction and sheds light on variation in bacterial strain recognition [3]. By using this H. influenzae Eagan strain and mutants with well characterised LPS structures of varying complexity we have shown that pathogenicity in vivo in wild type and SP-D -/- mice is inversely related to their SP-D binding and opsonic susceptibility in vitro. The crystal structure of the rfhSP-D complexed with a delipidated Eagan 4A LPS suggests that efficient LPS recognition by SP-D requires multiple binding interactions utilising the three major ligand-binding determinants in the SP-D binding pocket, with 1) Ca-dependent binding of inner core heptose accompanied by interaction of Kdo with 2) Arg343 and 3) Asp325. This shows for the first time that SP-D does not only interact with surface carbohydrate moieties in LPS glycoforms but can also interact with carbohydrate moieties located in the very core of LPS molecules. Therefore, extended LPS structures are important in shielding more vulnerable sites in the LPS core, revealing a mechanism by which pathogens with complex LPS extensions efficiently evade a first-line mucosal innate immune defence.


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Figure. Bound Eagan 4A in the rfhSP-D – ligand complex showing the bound Hep and the Kdo(anhydro) ligand. The glucose is not visible in the electron density.