

Novel Cell Wall-Associated Glycosylated Proteins and Their Role In Host Pathogen Interaction

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Characterisation of novel glycosylated cell wall-associated proteins

Glycosylation of proteins in eukaryotes has been well studied but only recently has its importance being recognized in prokaryotes (archaea and bacteria). Bacterial glycoproteins are present in many archaeobacteria and eubacteria and based on their localization, prokaryotic glycoproteins are classified as crystalline surface layer (S-layer), membrane-associated glycoproteins, surface-associated glycoproteins as well as secreted glycoproteins and exoenzymes. The glycosylation of these proteins contributes to several functions including maintenance of protein conformation and stability, protection against proteolytic activity, surface recognition and cell adhesion. Studies on the IDG-60 glycoprotein of *Streptococcus* mutants revealed that glycosylation is required for maintaining the integrity of the cell wall and the uniformity of cell shape.

Glycosylation is also required by some enzymes for their activity such as in the glycosylated anchor endopeptidase (LPXTGase) that cleaves the LPXTG sequence motif of cell surface proteins of Gram-positive bacteria. More interesting is the role of glycosylation in cell adhesion. Adhesion of *Streptococcus parasanguis* to the tooth surface is mainly mediated by glycosylated Fap1. Platelet binding by *Streptococcus gordonii* is determined by the heavily glycosylated cell wall anchored protein, GspB. *S. aureus* has a GspB homolog called SraP, which also mediates the direct binding of *S. aureus* to platelets.

The role of sdr family in host pathogen interaction

The Sdr family of proteins is MSCRAMMs related to ClfA and ClfB and are present in *S. aureus* and *S. epidermidis*. The structure of SdrG of *S. epidermidis* has been solved in the presence of a peptide derived from its cognate ligand, fibronectin. This has given rise to the dock, lock and latch model for ligand binding by these adhesins. In *S. aureus*, strains either contain SdrC and SdrD or SdrC, SdrD and SdrE. All show significant homology to each other with a distinct domain structure (Figure 1.1). The LPXTG motif links the proteins to the cell wall. The B repeats of SdrD have been shown to bind Ca²⁺ and have been proposed to modulate the distance of the A region from the cell surface. The A region has been proposed to be involved in ligand binding as in SdrG and ClfB. However no ligands have been described for SdrC or SdrD. It has been shown that recombinant SdrC or SdrD does not bind keratin or induce platelet aggregation. However an sdrCD mutant has reduced binding to human nasal epithelial cells (F. Roche and T. J. Foster, unpublished). Thus the role of the Sdr family of proteins is still mostly obscure.

Results

The Knock-out of the *sdrC*, *sdrD*, and Glycosyltransferases A and Genes Results show that these genes are not affecting the bacteria growth. Analysis of the cell wall associated glycosylated proteins in *S. aureus* using SDS-PAGE and Shift staining assay gave an extremely strong 98 kDa band which N-terminal sequencing revealed to be SdrC. In addition Western blot analysis using human sera react strongly with many *S. aureus* proteins among them SdrC. These results show that Glycosylation though it's rare in bacteria but can have a very important role and in this case we believe that glycosylation is playing a key role in host pathogen interaction.