Structural and functional studies of streptococcal surface adhesins

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av filosofie doktorsexamen framläggs till offentligt försvar i Sal D, plan 9, Tandläkarhögskolan, Norrlands Universitetssjukhus, Torsdagen den 12 september, kl. 10:00.
Avhandlingen kommer att förvaras på engelska.

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Abstract

The oral cavity is home to an array of microorganisms that are associated with dental plaque. Some Gram-positive bacteria are common inhabitants of the oral cavity and in order to colonize such a unique environment adhesion becomes essential and is accomplished by adhesins expressed on the bacterial surface. Adhesins can interact with host molecules or with structures on the resident oral microbial flora. Members of the antigen I/II (AgI/II) protein family are commonly found on the surface of oral streptococci and have the unique feature that their putative adhesin domain is located in the centre of the primary sequence. Crystal structures representing parts of the C-terminal domains from two AgI/II members, SpaP from *Streptococcus mutans* and AspA from *Streptococcus pyogenes*, were determined to 2.2 and 1.8 Å resolution respectively. The structures are very similar and consist of two domains with DEv-IgG folds. The proteins are stabilized by intramolecular isopeptide bonds and tightly coordinated metal ions. Another group of surface proteins is the microbial surface components recognizing adhesive matrix molecules (MSCRAMMs) that have their putative adhesin domain in the N-terminal, presented on a stalk formed by multiples of repeated C-terminal domains. *Sgo0707* from *Streptococcus gordonii* is an example of this group of proteins and its N-terminal domain was determined to 2.1 Å resolution. The structure consists of two domains, N1 and N2, both of which adopt β-sandwiches. In the *Sgo0707* structure no isopeptide bonds or metal ions were detected. A putative binding cleft is present in the N1 domain. Functional studies revealed collagen type-1 and keratinocytes as possible binding partners. In order to further characterize the AgI/II protein AspA from *S. pyogenes* a long form of the protein, AspA-AVPC, was expressed and purified. During the purification process it was observed that the protein fragmented into two major parts. This process could be inhibited by the addition of 0.5 mM EDTA during protein purification. In conclusion, these studies have resulted in adding to the knowledge of protein structures and function of streptococcal surface proteins.

Keywords
Oral cavity, dental plaque, surface protein, X-ray crystallography.