

## **Structural basis for evasion of mucosal immune barriers by *Staphylococcus aureus* revealed in the complex of SSL7 with IgA-Fc**

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*Staphylococcus aureus* is an important human pathogen and is a major cause of septicemia, toxic shock, pneumonia, osteomyelitis and endocarditis. Up to 30% of the normal population has persistent asymptomatic infections of the nasal mucosa with *S. aureus*, which is the result of its ability to evade and modify the human immune system. The evasion of mucosal immune barriers by *S. aureus* is largely due to a member of a family of staphylococcal superantigen like (SSL) proteins called SSL7. This putative exotoxin recognizes and inhibits the function of human IgA and complement C5. We report here the 3D structure of the complex of SSL7 with IgA-Fc at 3.2 Å resolution. The oligonucleotide/oligosaccharide binding (OB) domain, instead of the β-grasp domain, of SSL7 primarily interacts with the Fc. Two SSL7 molecules bind the Fc (one per heavy chain) at the junction between the CH2 and CH3 domains. Interestingly, the OB-domains are also loosely draped around and shield most of the lateral surfaces of the two CH3 domains. The β-grasp domains extend beyond the end of IgA-Fc and are near the expected positions of the tail-pieces and J-chain that are involved in the formation of dimeric IgA. Nearly all IgA residues participating in interactions with SSL7 are also bound by the leukocyte IgA receptor CD89 (FcαRI), thereby explaining how SSL7 potently inhibits CD89-mediated cellular effector functions such as phagocytosis, degranulation and respiratory burst. The ability of *S. aureus* to subvert IgA mediated immunity is likely to facilitate its persistent survival in mucosal environments like the nasal passage.