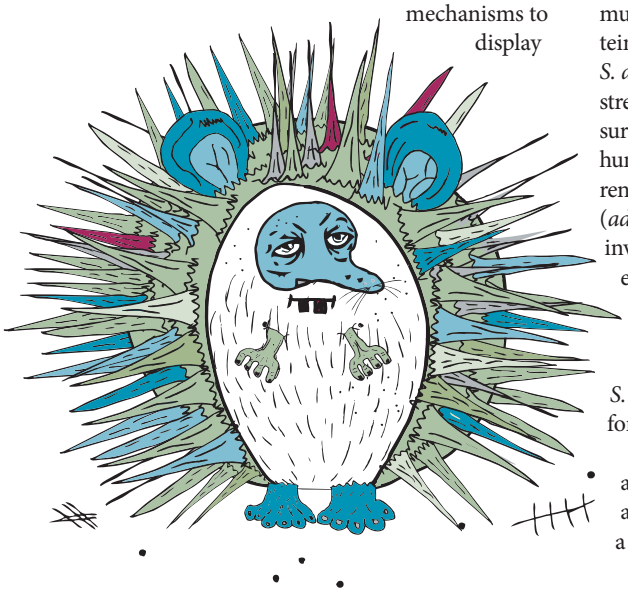
BACTERIAL IMMUNE EVASION

An evasive surface

Gram-positive bacterial pathogens can evade the host innate immune response by using a cell surface protein to synthesize adenosine, a potent suppressor of inflammation, according to a new report in the *Journal of Experimental Medicine*.

Gram-positive pathogens such as *Staphylococcus aureus* use various mechanisms to display proteins on their cell surfaces, including covalent attachment to peptidoglycan by a sortase protein. Thammavongsa *et al*. were interested in the contribution of sortase-anchored cell surface proteins to staphylococcal immune evasion. They began by screening a transposon insertion library to identify mutations in sortase-anchored proteins that impaired the ability of *S. aureus* to survive in the bloodstream. One mutation that decreased survival in blood from mice, rats and humans was in *sasH*, which the authors renamed adenosine synthase A (*adsA*). The importance of AdsA for invasive staphylococcal disease was examined using a mouse renal-abscess model of *S. aureus* infection, and it was shown that AdsA was necessary for *S. aureus* replication and abscess formation *in vivo*.



What is the mechanism of action of AdsA? Sequence analysis revealed the presence of a 5′-nucleotidase domain, which indicated that AdsA might be able to catalyse the synthesis of adenosine from 5′-adenosine monophosphate. This activity was confirmed both *in vitro* and in an *in vivo* infection model, and was shown to be essential for *S. aureus* virulence *in vivo*. The authors went on to show that many other Gram-positive bacteria contain AdsA homologues and that *Bacillus anthracis* also uses adenosine synthesis as an immune evasion mechanism.

Adenosine has a variety of anti-inflammatory effects, which include inhibiting neutrophil degranulation and impairing the phagocytic activity of macrophages. This work reveals that Gram-positive pathogens use a cell surface protein to synthesize adenosine, thus downregulating the innate immune response and promoting bacterial survival within host tissues.

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