Nasal colonization by *Staphylococcus aureus*

To the editor:

The primary habitat of *Staphylococcus aureus* is the moist squamous epithelium of the anterior nares. Where it colonizes a significant proportion of the human population either transiently or permanently. Surprisingly little is known about the molecular basis of nasal colonization, considering that carriage is a risk factor for infection.

A recent paper by Weidenmaier *et al.*[1] reported that a mutant that eliminates cell wall–associated teichoic acid (WTA) impairs the ability of bacteria to colonize the nares of cotton rats. Beads coated with WTA adhered strongly to primary cultures of epithelial cells, and pure WTA inhibited colonization in the animal model. However, one should use caution when interpreting *in vitro* assays with growing epithelial and endothelial cells, as *S. aureus* seems to adhere to terminally differentiated squamous cells *in vivo*[2].

While WTA may have an important role in nasal colonization, Weidenmaier *et al.* did not comment on the role of cell surface–associated proteins in colonization. We have shown that the surface protein clumping factor B (ClfB) promotes *S. aureus* attachment to human squamous nasal epithelial cells by binding keratin-10 (ref. 3). In addition, a *clfB* mutant of *S. aureus* colonizes the nares of mice poorly compared with the wild-type strain (J. Lee, Harvard University Medical School, personal communication).

We have also shown that several other surface-associated proteins contribute to adherence to squames[4]. The ligands for these proteins are not known. It seems that the ability to bind to human desquamated nasal cells is multifactorial and involves specific protein receptor-ligand interactions, as well as interactions mediated by teichoic acid.

The observations of Weidenmaier *et al.* do not exclude the possibility that the loss of WTA reduced the expression of surface proteins or compromised their function. Differences in expression of low-copy-number, high-molecular-weight surface proteins are best assessed using specific antibodies. It would be interesting to measure binding of the WTA mutant to keratin-10 over a range of ligand concentrations.

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The author declares competing financial interests (see the *Nature Medicine* website for details).

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Peschel *et al.* reply:

Colonization of the anterior nares of healthy individuals by *S. aureus* leads to an increased risk of nosocomial infections. We have recently shown that WTA polymers on the staphylococcal cell surface are essential for nasal colonization in a cotton rat model and mediate specific interaction with human nasal epithelial cells[1]. A WTA-deficient mutant was rapidly and completely lost from the nares, and preinstillation with purified WTA interfered with nasal colonization.

Foster suggests that nasal colonization should be regarded as a multifactorial process, and that surface-exposed staphylococcal proteins such as the keratin-10 binding protein ClfB (ref. 2) might also have a significant role in the process. We agree with this possibility and would like to emphasize that the Brief Communications format of our paper did not allow a more detailed discussion of other studies and further factors contributing to nasal colonization.

Bacterial binding to human cells has been shown in several cases to rely on more than one interaction, and may involve loose initial attachment followed by tighter binding. Future experiments may explain how WTA and surface proteins contribute to nasal colonization. It will be very interesting to study nasal colonization of *clfB* or similar mutants in the cotton rat model.

We cannot rule out that WTA deficiency compromises the keratin-binding capacity of surface proteins such as ClfB, but our preliminary experiments do not support such a conclusion (data not shown). The inhibition of nasal colonization by preinstillation of cotton rat nares with purified WTA, and the dose-dependent binding of WTA-coated microspheres to nasal cells, instead point strongly toward a WTA-mediated attachment of *S. aureus* to human cells. Elucidating the cognate interaction partner and its role in nasal colonization will be an interesting subject for future research.

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