Trends in Microbiology

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Review

Host–Bacterial Crosstalk Determines *Staphylococcus aureus* Nasal Colonization

Michelle E. Mulcahy[1] and Rachel M. McLoughlin[1,*]

Staphylococcus aureus **persistently colonizes the anterior nares of approximately one fifth of the population and nasal carriage is a significant risk factor for infection. Recent advances have significantly refined our understanding of *S. aureus*–host communication during nasal colonization. Novel bacterial adherence mechanisms in the nasal epithelium have been identified, and novel roles for both the innate and the adaptive immune response in controlling *S. aureus* nasal colonization have been defined, through the use of both human and rodent models. It is clear that *S. aureus* maintains a unique, complex relationship with the host immune system and that *S. aureus* nasal colonization is overall a multifactorial process which is as yet incompletely understood.**

Staphylococcus aureus Carriage

Staphylococcus aureus is an opportunistic pathogen that is responsible for a multitude of hospital- and community-acquired infections. In contrast to its invasive infectious potential, *S. aureus* also forms part of the human microbiome, persistently and asymptomatically colonising the nasal vestibule of ~20% of the human population [1]. The remainder of the population is potentially intermittently colonised, and most individuals will be exposed to the organism transiently throughout their lifetime (Box 1). The evolution of *S. aureus* as an efficient coloniser is the result of complex interplay between a multitude of host and bacterial factors (Figure 1). *S. aureus* has evolved a highly specific relationship with the human host; persistent carriers artificially colonised with a mixed culture will specifically re-acquire their autologous strain [1]. Consistent with other opportunistic pathogens inhabiting the nasopharyngeal environment, such as *Streptococcus pneumoniae*, it has long been established that nasal carriage of *S. aureus* is a significant risk factor for infection, with infection often attributed to a resident strain [2,3]. A vaccine protecting against *S. pneumoniae* colonization has proven beneficial for the

Box 1. Incidence and Carriage Sites

Historically, *Staphylococcus aureus* nasal carriage has been separated into three classes: persistent (~20%), intermittent (~30%), and noncarriers (~50%) based on the prevalence of *S. aureus* in an individual's nasal swab culture [89]. However, a more recent study has re-classified *S. aureus* nasal carriage types as persistent and 'other' based on antistaphylococcal antibody profiles and the ability to eliminate *S. aureus* strains from the nose [1].

The moist squamous epithelium of the anterior nares has been traditionally defined as the principal habitat for *S. aureus*, and *S. aureus* adheres to desquamated epithelial cells isolated from this area [22,47]. New evidence, however, obtained from sampling of posterior sites within the nasal cavities of defined persistent carriers indicates that 100% of individuals sampled carried *S. aureus* in the posterior nares compared to 75% positive samples from the anterior nares, suggesting that the organism colonises the entire nasal vestibule [90]. *S. aureus* has been found at other sites in the nasopharyngeal cavity, including the inner nasal cavity, hair follicles, and throat [74,90–92]. Colonization of secondary sites on the body can occur and *S. aureus* is also found in the axillae, perineum, skin, and intestine [74,91,93]. However, it appears that nasal carriage is often the source of inoculation for other sites; the greater the bacterial load in the nose, the higher the likelihood that other body sites are colonised persistently [94].

Trends

A lower prevalence of mortality during *Staphylococcus aureus* bacteraemia in carriers compared to noncarriers implies that bacterial crosstalk with the immune system occurs during nasal colonization and that nasal carriers may have an immunological advantage over noncarriers.

Novel interactions between bacterial adhesins and host surface factors during colonization have been identified.

Staphylococcal ligand expression in the nose may be directly regulated by proinflammatory cytokine signalling pathways.

Emerging evidence suggests that adaptive cellular immune responses are a critical determinant of *S. aureus* nasal carriage.

Carrier strains may have an increased capacity to delay and/or manipulate the local immune response in the nose by manipulating innate signalling pathways.

[1]Host–Pathogen Interactions Group, School of Biochemistry and Immunology, Trinity Biomedical Sciences Institute, Trinity College Dublin, Dublin, Ireland

*Correspondence: rachel.mcloughlin@tcd.ie (R.M. McLoughlin).

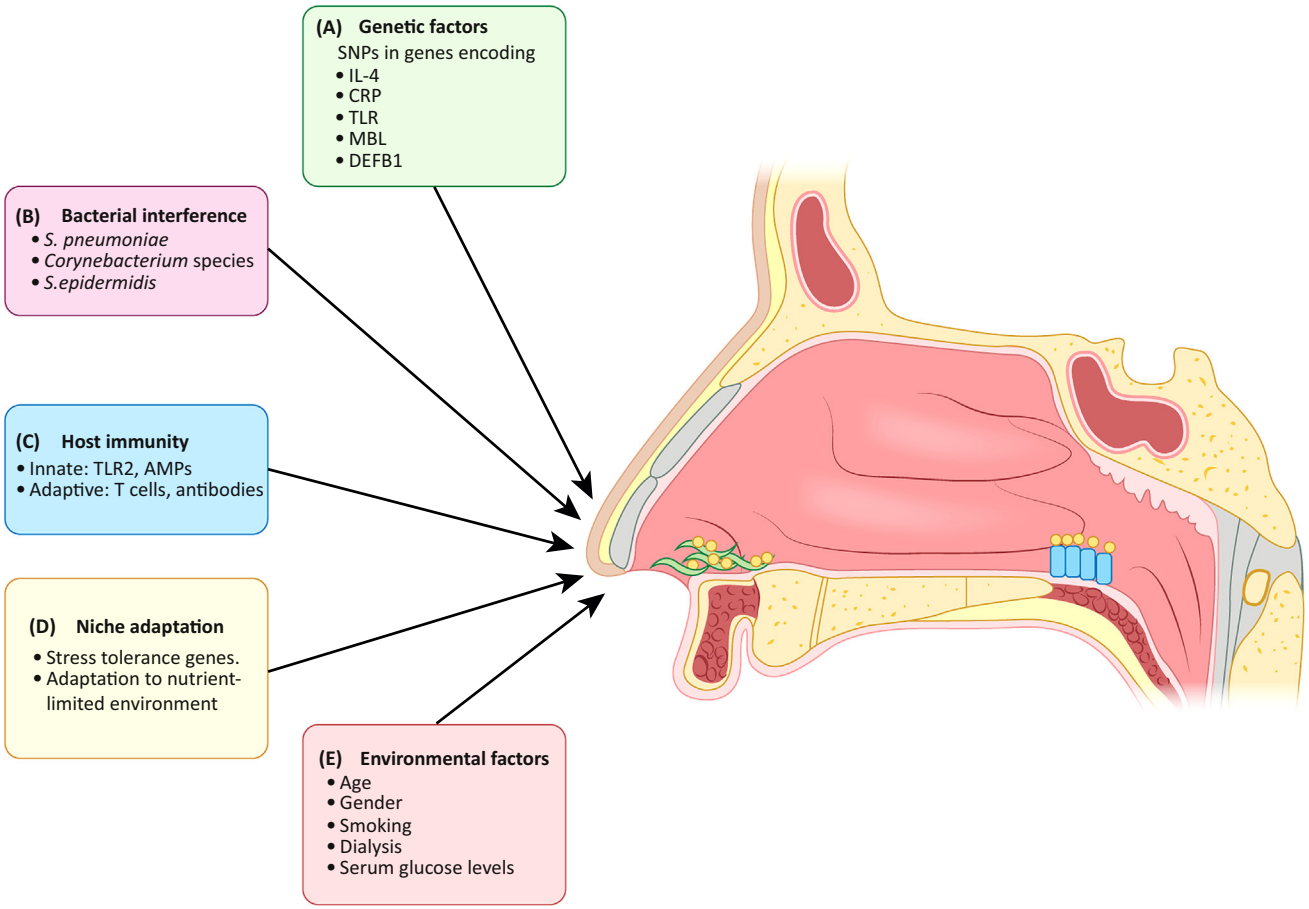

Figure 1. Host and Bacterial Influences on Nasal Carriage. This figure depicts the nasal cavity and nasal epithelium. *Staphylococcus aureus* (yellow circle) adheres to the squamous epithelium of the anterior nares (green cells) as well as the cells of the inner nasal cavity (blue). The evolved relationship between *S. aureus* and the host has led to several specific and complex interactions that are known to influence nasal carriage. (A) Genetic factors. Single nucleotide polymorphisms (SNPs) in several genes that encode factors involved in local immunity correlate with persistent carrier status. (B) Bacterial interference. The presence of other bacterial species in the nasopharyngeal cavity can exert an antagonistic influence on *S. aureus* nasal carriage. (C) Host immunity. Impairment in TLR2 expression and the production of AMPs by keratinocytes can cause a reduction in colonization. T cell-mediated adaptive immunity facilitates clearance of *S. aureus* from the nose in murine models. Distinct patterns of humoral adaptive responses are observed between *S. aureus* nasal carriers and noncarriers. (D) Niche adaptation. *S. aureus* utilizes specific mechanisms to adapt to the nasal niche. Genes involved in stress tolerance are important for colonization *in vivo*. (E) Environmental factors. Correlations between age, gender, smoking, serum glucose level, dialysis use and persistent carriage have been recorded.

prevention of pneumococcal disease, prompting a discussion on whether vaccination against *S. aureus* carriage may prove beneficial in at-risk individuals. However, lower cases of mortality from *S. aureus* bacteraemia in nasal carriers imply an immunological advantage to carriage and suggests that carriers may be immunologically adapted to their own strain [3]. Insufficient knowledge on the impact that *S. aureus* carriage has on the immune system currently precludes a true assessment of the benefits or disadvantages of nasal carriage. However, it is clear that *S. aureus* has evolved a unique relationship with the immune system and that bacterial crosstalk with the immune system may be the critical factor underpinning colonization.

Immune Determinants of *S. aureus* Carriage

There is significant direct and indirect evidence for an association between host immunity and *S. aureus* nasal carriage (Table 1). Polymorphisms in immune genes encoding mannose-binding