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Ecology of eczema

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Abstract

Patients with atopic dermatitis have fundamentally different skin microbial populations compared with people with healthy skin. Bacteria associated with atopic dermatitis express genes for survival in dry conditions and for ammonia production, modulating the pH of this distinct environment and driving complex ecological interactions.

Atopic dermatitis, colloquially known as eczema, is an increasingly common inflammatory skin disease that mostly affects children, but also some adults. It has long been known that patients with eczema have higher colonization with the pathogenic bacteria *Staphylococcus aureus*, and flares of atopic dermatitis coincide with increased staphylococcal abundance¹. Only recently has the technology existed to measure the entire microbial community on the skin, and intensive efforts have been made to catalogue the variation in microbial populations at different sites on the body and between different people over time^{2,3}. In this issue of *Nature Microbiology*, Chng *et al.*⁴ provide a detailed analysis of microbial differences between people with atopic dermatitis and healthy controls. By using whole metagenome DNA sequencing (in contrast to 16S rDNA), they were able to explore the genetic capabilities of the microorganisms to provide insight into their specialization to different host environments.

In the Western world, atopic dermatitis is 2–3 times more common in children, but in Asia there is a relatively higher prevalence in adults⁵. Chng *et al.* measured the microbiomes of young Singaporean adults who were distinguished as having atopic dermatitis or healthy skin by the well-established ISAAC questionnaire⁶. This questionnaire is designed for children, but likely correctly identified the subjects in this study. They then performed detailed control experiments to identify the best methods for reliable DNA acquisition with the most ease of use. Tape-stripping, in which the researcher applies and peels a piece of tape about 50 times from the skin provided the best results. Importantly, Chng *et al.* measured the trans-epidermal water loss and skin pH to establish that their subjects, while having positive history of atopic dermatitis, were not actively having a flare of disease.

Chng *et al.* found that people with atopic dermatitis have increased *Streptococcus*, *Gemella*, and *Corynebacterium*, but decreased *Dermacoccus* (Fig. 1). The findings were more apparent in male subjects, perhaps related to less topical-cream usage. Remarkably, the same genera of bacteria were found in atopic dermatitis patients in a previous study⁷, which

targeted children from the Washington D.C. area of the US, emphasizing the generalizability of the results.

However, the question remained whether the bacteria in atopic dermatitis have any causal effect on skin health. Chng *et al.* used an agar-diffusion assay to show that atopic dermatitis-associated streptococcal species have an inhibitory effect on *S. aureus* growth, in apparent contradiction to its increased abundance¹. Previous reports have shown inhibitory effects of *S. epidermidis* on *S. aureus* growth via secretion of bactericidal proteins in an *in vivo* setting on mouse skin⁸, which was not reproduced in the agar-diffusion experiment, so the contradictory findings may be refined by *in vivo* experiments. It is also possible that higher abundance of *S. aureus* in atopic dermatitis selects for species that can compete with their virulence by producing antagonizing factors of their own. The bacteria in atopic dermatitis appear to be selected by their ability to antagonize *S. aureus* growth, which would be interesting to examine in future studies.

In addition to microorganism–microorganism interactions, Chng *et al.* analysed microbial interactions with their environment. Through use of whole metagenome DNA sequencing, they were able to measure the abundance of specific genes in the population. They found that atopic dermatitis-associated *S. aureus* expresses a lipase gene variant associated with a dry environment, suggesting adaptation to atopic skin. Second, they found more genes involved in ammonia production, most probably affecting the observed increase in skin pH. The findings above show a complex interplay between the bacteria themselves as well as alteration and adaptation to the skin environment.

The findings by Chng *et al.* highlight a complex ecology with interactions between microbial organisms and the host environment, but many questions remain. Since the skin immune system of people with atopic dermatitis is tolerant to *Staphylococcus* colonization and growth, is the rise of anti-staphylococcal *Streptococcus* species a direct consequence? Are there protective effects of certain microorganisms in atopic dermatitis that are as yet unappreciated, and could therefore be targeted therapeutically? And in addition to their antagonistic effects on *Staphylococcus*, is there synergy in the growth of *Streptococcus*, *Gemella* and *Corynebacterium*, or is their concurrent growth merely correlative? To distinguish correlative events from causal interactions, current technology requires use of germ-free mouse models. For example, competition assays in the presence and absence of *S. aureus* may reveal a growth advantage of *Streptococcus*, *Gemella* and *Corynebacterium* compared with *Demacoccus* or other commensals. Colonization with certain combinations of bacteria may also show a growth advantage and unique metabolic signatures. Detection of weak interactions between microorganisms and differentiation of microorganism–microorganism interactions from those with their environment may require statistical models that have been developed for complex ecosystems. There is still much to understand about the numerous microorganisms that inhabit our skin and our interactions with them. □

References

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Figure 1.

A comparison between the microbiomes of healthy patients and those who have atopic dermatitis. A healthy skin microbial community (left) is characterized by a polymicrobial community high in *Dermacoccus*, with few anti-staphylococcal bacteria and no *S. aureus*. In patients with atopic dermatitis, non-flare microbial communities (centre) have more anti-staphylococcal bacteria, which produce *S. aureus* growth inhibition factors. During an atopic dermatitis flare (right), *S. aureus* dominates the bacterial community.