THE SKIN MICROBIOME IN CANINE ATOPIC DERMATITIS

Charles Bradley, VMD, Diplomate ACVP
Pathobiology, School of Veterinary Medicine
University of Pennsylvania, Philadelphia, PA, USA

Elizabeth Grice, PhD
Dermatology, Perelman School of Medicine
University of Pennsylvania, Philadelphia, PA, USA

The microbiome:

The microbiota is the sum of bacteria, fungi, viruses, and parasites living in and on a given habitat or host. Though the terms are often used interchangeably, the microbiome refers to the genetic component of these microbes, and unless otherwise specified often refers to bacterial communities. All of our experiences in health and disease are altered by either the microbiota or their metabolites, including but not limited to smell, taste, touch, energy metabolism, nutrient absorption and barrier and immune function. The shared microbiota between people is also influenced by their environment and strongly influenced by their pets.

Advances in high-throughput (“next generation”) sequencing have allowed for culture-independent evaluation of these communities. The methods most commonly utilized to examine the microbiome include targeted amplicon sequencing, whole genome metagenomics and other downstream analyses: transcriptomics or proteomics. Statistical methods used in ecology studies are often employed, examining both intraindividual (alpha diversity) and interindividual (beta) diversity metrics and changes in community composition/structure.

The skin microbiome

Our understanding of the skin microbiome is limited, but rapidly evolving. Microbiomic studies of the skin face many challenges. Samples are generally procured from surface swabs with low biomass. As such contaminants can have a dramatic effect on the study outcome necessitating careful collection and processing of samples along with numerous positive and negative controls. Regions of the 16s rRNA gene evaluated can also influence study outcome, making comparison across studies difficult. For example, the V4 region of the 16s rRNA gene has been demonstrated to underestimate the relative proportion of Propionibacterium acnes and Staphylococcus aureus in the skin microbiome compared to the V1-V3 region.

There are very few studies surveying the bacterial skin microbiome of dogs, and most of these characterize normal skin communities, with fewer examining disease states. Microbiome studies of human skin are slightly more abundant, and both differences and similarities with the companion animal microbiome have been elucidated. In people there are dry, moist and oily (sebaceous) microenvironments across the skin associated with differing microbial communities. In contrast, the microbiome of the haired skin of dogs is much more homogenous. Interindividual variability in both people and dogs is significant, influenced by the individual, environment and life-style. The most abundant phyla in healthy dogs are similar to people and include Proteobacteria, Firmicutes, Actinobacteria, and Bacteroides. In health, there is generally a higher level of microbial diversity compared to disease states. Cutaneous diseases most commonly studied in the human microbiome field include atopic dermatitis (AD), acne, psoriasis.

Dogs as a model for atopic dermatitis

Studies of AD often rely on mice as animal models to highlight specific genetic changes. However, mice do not recapitulate the complexity of human disease and lack clinical similarity to human AD. Canine atopic dermatitis (cAD) occurs spontaneously and exhibits similar immunological and clinical features of human AD. Similarities include prevalence (approximately 10% of the general population), environmental triggers, immunologic profiles, genetic predispositions, lesion distribution and frequent colonization by Staphylococcus spp. Furthermore, dogs share the same environment with their owners.

The skin microbiome in canine atopic dermatitis
The most common isolates associated with bacterial folliculitis in dogs are *Staphylococcus* spp. During flare states of cAD, commonly with bacterial folliculitis, there is decreased microbial diversity, with *S. pseudintermedius* and *S. schleiferi* overrepresented, both via culture and culture-independent methods. A similar progression has been documented in human AD with increased abundance of *S. aureus* and *S. epidermitis*. Following culture-directed systemic antimicrobial therapy for bacterial microbial diversity is restored, with a decreased levels of *Staphylococcus* present (Figure 1). However, the recurrence of folliculitis/dermatitis in some dogs four to six weeks following treatment is accompanied by reduction in diversity (Figure 2). Epidermal barrier function (as measured by transepidermal water loss) is also inversely correlated with the abundance of *Staphylococcus* and is restored following treatment and lower levels of *Staphylococcus*. Mechanisms of staphylococcal perturbation of the epidermal barrier not well defined may be through direct or indirect (immunostimulatory) means. With the strong similarities in microbial shifts during flare and resolution, cAD represents a near-perfect model to study host-microbiome interactions of AD.

![Figure 1](image1.png) **Figure 1**: During flare states of cAD with bacterial folliculitis (Visit 1) the relative abundance of Staphylococcus is greater than control populations and following 4-6 weeks of antimicrobial therapy (Visit 2) the relative abundance of Staphylococcus is reduced with some lasting effect at a post treatment follow up visit (Visit 3).

![Figure 2](image2.png) **Figure 2**: Microbial diversity in cAD with bacterial folliculitis is lower than in the skin of normal dogs. Diversity increases following antimicrobial therapy, but decreases again after cessation of treatment, corresponding with a recrudescence of pyoderma in some cases. ***p<0.001  **p<0.01 Wilcoxon rank-sum test

### References and Further Reading