

THE ROLE OF THE SKIN MICROBIOME IN ATOPIC DERMATITIS: NEW
THERAPEUTIC PERSPECTIVES

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Abstract: Background: Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by intense pruritus and eczematous lesions. Its pathogenesis is increasingly linked to a profound dysbiosis of the skin microbiome, notably the overabundance of *Staphylococcus aureus*. Objective: This review synthesizes the current understanding of the skin microbiome's role in AD pathogenesis and critically evaluates emerging microbiome-targeted therapeutic strategies. Main Body: The review highlights that the AD skin microenvironment is characterized by a significant reduction in microbial diversity and the pathogenic dominance of *S. aureus*, which contributes to barrier dysfunction and inflammation. Consequently, therapeutic strategies aimed at restoring eubiosis—including the use of probiotics, prebiotics, and skin microbiota transplantation—are emerging as promising approaches to disease management. Conclusion: Targeting the skin microbiome represents a paradigm shift in dermatology, offering a novel and promising frontier for developing more effective, personalized, and long-lasting treatments for atopic dermatitis.

Keywords: atopic dermatitis, skin microbiome, *Staphylococcus aureus*, dysbiosis, therapeutic strategies, probiotics.

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by intense pruritus (itching), eczematous lesions, and significant skin barrier dysfunction. It is one of the most common dermatological disorders, affecting up to 20% of children and 3-5% of adults globally, and it substantially impairs the quality of life for patients and their families. The pathophysiology of AD is complex and multifactorial, involving a combination of genetic predisposition, immune system dysregulation, and environmental factors [1].

The human skin is colonized by a diverse community of microorganisms, collectively known as the skin microbiome, which plays a crucial role in maintaining cutaneous homeostasis and educating the immune system. In recent years, compelling evidence has emerged highlighting the profound impact of microbial dysbiosis—an imbalance in the composition and function of the skin microbiome—on the development and exacerbation of AD. Healthy skin typically harbors a balanced ecosystem of diverse bacteria, whereas the skin of AD patients is frequently characterized by a marked reduction in microbial diversity and a significant overabundance of *Staphylococcus aureus*.

S. aureus colonization in AD is not merely a consequence of the disease but is an active contributor to its pathology. This bacterium exacerbates skin inflammation through the secretion of toxins and superantigens, disrupts the skin barrier, and triggers a pathological immune response, creating a vicious cycle of inflammation and infection. Consequently, understanding the intricate interplay between the host and the skin microbiome is paramount for developing more effective and targeted therapeutic strategies [2].

Despite advancements in treatment, current therapies for AD, such as topical corticosteroids and calcineurin inhibitors, primarily focus on suppressing the immune response and often have limitations, including potential side effects and high relapse rates upon cessation. Therefore, there is a critical need for novel therapeutic approaches that address the underlying microbial

imbalance. This review aims to summarize the current understanding of the skin microbiome's role in the pathogenesis of AD and to explore emerging microbiome-targeted therapeutic perspectives, including the use of probiotics, prebiotics, and bacteriotherapy, that hold promise for the future management of this challenging disease.

The skin microbiome: From homeostasis to ad pathogenesis

The microbiome of healthy skin: A state of eubiosis - in a state of health, the skin is colonized by a diverse and stable microbial community that exists in a symbiotic relationship with the host. This state, known as eubiosis, is crucial for maintaining the integrity of the skin barrier and modulating local immune responses. The composition of this microbiome varies depending on the skin site (e.g., oily, moist, or dry areas) but is generally dominated by commensal bacteria such as *Cutibacterium acnes*, coagulase-negative staphylococci (e.g., *Staphylococcus epidermidis*), and various species of *Corynebacterium*. These commensals play a protective role by competing with potential pathogens for nutrients and space, and by producing antimicrobial peptides (AMPs) that inhibit the growth of harmful microorganisms. For instance, *S. epidermidis* has been shown to produce AMPs that selectively inhibit *S. aureus* colonization [5].

The dysbiotic shift in atopic dermatitis - The hallmark of the skin microbiome in AD is a profound state of dysbiosis, most notably characterized by a dramatic loss of microbial diversity and the subsequent dominance of *Staphylococcus aureus*. During disease flares, *S. aureus* can constitute over 90% of the total skin microbiome in affected areas, whereas it is found in much lower abundance on the skin of healthy individuals. This reduction in diversity is not limited to lesional (affected) skin; even non-lesional skin of AD patients often shows a subclinical dysbiotic signature, suggesting that this microbial imbalance precedes and contributes to the clinical manifestation of flares.

The pathogenic role of staphylococcus aureus in AD - the overwhelming presence of *S. aureus* is a key driver of AD pathology. Its virulence factors actively contribute to the disease's vicious cycle. *S. aureus* secretes a range of exotoxins, including superantigens like Staphylococcal enterotoxin B (SEB), which trigger a massive, non-specific T-cell activation and subsequent release of pro-inflammatory cytokines, thereby amplifying the inflammatory response. Furthermore, *S. aureus* can form biofilms, which are structured communities of bacteria encased in a protective matrix. These biofilms enhance bacterial adherence to the skin, provide resistance to host immune defenses and antimicrobial treatments, and further impair skin barrier function. This sustained microbial assault perpetuates barrier damage and chronic inflammation, which are central features of AD.

Emerging microbiome-targeted therapeutic perspectives

The growing understanding of the skin microbiome's role in AD has paved the way for novel therapeutic strategies aimed at correcting dysbiosis. These approaches move beyond traditional immunosuppression to restore a healthy microbial ecosystem.

Probiotics, prebiotics, and postbiotics - Modulating the microbiome through beneficial bacteria and their substrates is a highly promising avenue.

Probiotics: These are live microorganisms that, when administered in adequate amounts, confer a health benefit. In the context of AD, both oral and topical probiotics are being investigated. Oral probiotics, such as certain strains of *Lactobacillus* and *Bifidobacterium*, are thought to exert their effects by modulating the systemic immune system via the gut-skin axis. Topical probiotics, on the other hand, aim to directly reintroduce beneficial bacteria to the skin to compete with *S. aureus* and improve barrier function. For example, strains of *Roseomonas mucosa* and *Staphylococcus epidermidis* have shown promise in clinical trials.

Prebiotics: These are substrates that are selectively utilized by host microorganisms, conferring a health benefit. Topically applied prebiotics, such as certain oligosaccharides, can promote the growth of beneficial commensal bacteria over pathogens like *S. aureus*.

Postbiotics: This refers to the application of inanimate microorganisms or their components, such as lysates or metabolites. These can directly modulate skin immunity and barrier function without the challenges of keeping bacteria alive in a formulation. Lysates of bacteria like *Vitreoscilla filiformis* have been incorporated into emollients and shown to reduce AD severity.

Bacteriotherapy skin microbiota transplantation - a more direct approach to restoring a healthy microbiome is bacteriotherapy, also known as skin microbiota transplantation (SMT). This involves the transfer of the complete microbial community from a healthy donor to the skin of an AD patient. The goal is to re-establish a diverse and stable ecosystem. Early-phase clinical trials have demonstrated that topically applying a solution containing commensal bacteria from a healthy donor can significantly reduce *S. aureus* colonization and improve AD symptoms, with effects lasting for several months after treatment. While promising, this approach requires further research to optimize donor screening, application methods, and long-term safety.

Phage therapy - bacteriophage (phage) therapy is an innovative strategy that uses viruses to specifically target and kill bacteria. Given the central role of *S. aureus* in AD, phages that exclusively infect and lyse this bacterium are being explored as a highly targeted treatment. This approach has the advantage of eliminating the pathogen without harming the beneficial commensal bacteria, thereby preserving microbial diversity. Preclinical studies and early case reports have shown the potential of phage therapy to reduce *S. aureus* load on the skin, but larger clinical trials are needed to confirm its efficacy and safety in AD patients.

Discussion

The paradigm for understanding and treating atopic dermatitis is undergoing a significant shift, moving from a purely immune-centric view to a more holistic, ecosystem-based approach that places the skin microbiome at the center of its pathogenesis. This review has synthesized the evidence demonstrating that the dysbiotic state, particularly the proliferation of *S. aureus*, is a critical driver of AD. The emerging therapeutic strategies—ranging from probiotics to skin microbiota transplantation and phage therapy—represent a logical and exciting evolution in dermatological care. They offer the potential for more targeted, effective, and safer long-term management of AD by addressing a root cause of the disease rather than merely suppressing its symptoms.

However, the translation of these promising concepts into standard clinical practice faces several challenges. First, the definition of a "healthy" skin microbiome is not universal and can vary significantly between individuals. Second, the efficacy of probiotic and prebiotic therapies can be highly strain-specific and dependent on the formulation and delivery method. For bacteriotherapy, key questions regarding optimal donor selection, long-term engraftment of the transplanted microbiome, and safety remain to be fully addressed.

Future research should focus on several key areas. Large-scale, randomized controlled trials are essential to validate the efficacy and safety of these novel therapies. Longitudinal studies that track the skin microbiome of AD patients over time will provide deeper insights into the dynamics of dysbiosis and treatment response. Furthermore, developing personalized treatment strategies based on an individual's specific microbial signature ("personalized microbiome medicine") could represent the ultimate goal in AD management. Combining microbiome-targeted therapies with traditional treatments may also offer synergistic benefits.

Conclusion

In conclusion, the skin microbiome plays a pivotal and undeniable role in the pathogenesis of atopic dermatitis. The dysbiotic dominance of *S. aureus* perpetuates a cycle of barrier

dysfunction and inflammation that is central to the disease. Microbiome-targeted therapies are no longer a futuristic concept but an active and rapidly advancing field of research that holds immense promise to revolutionize AD management. By aiming to restore microbial balance, these novel strategies offer a path towards more durable disease control and an improved quality of life for the millions of patients affected by this chronic condition.

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