Daniel Lavin 32970735 dlav447@aucklanduni.ac.nz 38 Middleton Rd

Maybe you were born with it or maybe it's your skin and gastrointestinal microbiome.

Our skin is the largest organ of the body and plays a major role in protecting us from the outside world while helping maintain our internal environment. Skin disease remains arguably one of the most common of human illness affecting up to 70% of the population(1). Dermatological conditions range from mild to life threatening and have a marked psychological impact (2). Importantly, with the rise of antibiotic resilient bacteria and treatment resistant conditions there remains a need for therapeutic development (3). Interestingly, we share our skin with billions of bacteria, fungi, and viruses termed the skin microbiome (4,5). Additionally, the gut also houses billions of bacteria reported to have a dynamic relationship with the skin (6,7). A recent body of evidence has indicated the skin and gut microbiomes may play a key role in the pathophysiology underpinning a plethora of skin diseases. Here is discussed how the skin and gut microbiomes may promote or prevent skin disease.

The skin microbiome

The skin microbiome is a significant constituent of the human skin ecosystem, primarily comprised of a diverse array of bacteria, typically exceeding 1000 distinct species in an individual. Traditionally, the majority of skin-dwelling bacteria are characterized as commensal or mutualistic in their relationship with the host (4,5). Mutualistic bacteria offer a range of potential advantages, including the regulation of skin pH, the metabolism of sebum, and the modulation of immune responses (8,9). For instance, Staphylococcus epidermidis, a commonly found bacterium on healthy skin, is known to counteract the pathological colonization of Staphylococcus aureus. In an in vitro study, it was demonstrated that Staphylococcus epidermidis promotes the production of the antimicrobial compound human β-defensin 2 when interacting with undifferentiated human keratinocytes (10) . The heightened levels of human β-defensin 2 subsequently inhibit the growth of S. aureus (10). Thus, it is plausible that Staphylococcus epidermidis attenuates the proliferation of S. aureus by inducing the production of antimicrobial compounds from epithelial cells.

Additionally, certain Micrococcus bacteria exhibit the capability to metabolize skin oils, particularly sebum, which is a natural oily substance generated by sebaceous glands within the skin (11,12). Sebum plays a pivotal role in preserving skin moisture and safeguarding the skin. Nonetheless, excessive sebum production can contribute to skin issues like acne. Micrococcus bacteria aid in regulating sebum levels by breaking down and utilizing its components, thereby maintaining an optimal balance (11,12). Furthermore, Bifidobacterium is believed to have a role in curbing excessive inflammatory responses in the skin (13,14). Excessive inflammation can lead to skin conditions such as eczema and psoriasis (12). Beneficial bacteria like Bifidobacterium contribute to maintaining a harmonious immune response, diminishing the likelihood of skin inflammation (13,14). Consequently, the skin microbiome represents a multifaceted ecosystem consisting of various organisms that could have a pivotal impact on the health of the skin. However, it is well-established that an imbalance in the skin microbiota, known as skin dysbiosis, can predispose individuals to various skin diseases.

Skin microbiome in disease

While the human skin plays host to a multitude of bacteria as part of its natural microbiota, the interactions between these microorganisms and their host can yield various health outcomes. Certain conditions, such as folliculitis, acne, and cellulitis, can manifest when the delicate equilibrium within the skin's microbial community is disrupted. For instance, Staphylococcus aureus, a commonly occurring skin bacterium, has been extensively implicated in the etiology of cellulitis. A meta-analysis

revealed that Staphylococcus aureus was the predominant causative agent in over 50% of cases of cellulitis, as evidenced by positive cultures (15).

Similarly, acne vulgaris, a prevalent dermatological condition, is associated with the pathogenic proliferation of Propionibacterium acnes, a natural constituent of the skin's microbiota, particularly in regions rich in sebaceous glands like the face, neck, and back. The overabundance of Propionibacterium acnes has been linked to inflammation and the characteristic features of acne (12,16). One study highlighted its capacity to provoke a robust inflammatory response in animal models through Toll-like receptor activation and cytokine production, thereby implicating it in the pathophysiology of acne vulgaris (16). Moreover, conditions like psoriasis, a common chronic inflammatory skin disease, have also been linked to imbalances in skin bacterial colonies. Alekseyenko et al, 2013 demonstrated increased colonization of psoriatic lesions by Corynebacterium, Propionibacterium, Staphylococcus, and Streptococcus, in contrast to healthy skin (17). This suggests that dysregulation of the skin microbiota may be a contributing factor in the development of psoriasis. Hence, it is evident that certain bacteria may exert beneficial effects on skin health, while others can be detrimental. Notably, significant efforts have been dedicated to manipulating the skin microbiome to foster symbiosis and enhance overall skin health.

Skin microbiome and disease treatment

As previously mentioned, certain bacterial species may play a pivotal role in promoting skin health, while others can exacerbate dysbiosis and contribute to skin diseases. An enticing approach to addressing these issues involves nurturing the growth of beneficial bacteria while curbing the proliferation of detrimental ones. Various strategies have been explored for modifying the skin microbiome, encompassing antibiotics, probiotics, prebiotics, lifestyle adjustments, and even bacteriophages. For instance, a probiotic cream enriched with sonicated Streptococcus thermophilus enhanced ceramide production among patients afflicted with atopic dermatitis—an inflammatory skin condition (18). The results included a reduction in symptoms like erythema, scaling, and pruritus (18). This suggests that probiotics may indeed hold promise as a therapeutic tool for managing skin diseases.

Another intriguing avenue for manipulating the skin microbiome involves a procedure known as a skin microbiome transplant. This procedure entails transferring the skin microbiome of a healthy individual to the cleansed and disinfected skin area of another person with the aim of ameliorating the latter's skin condition. In a well-executed study, subjects were meticulously selected based on their high antimicrobial activity against S. aureus and subsequently cultured. When patients suffering from atopic dermatitis were treated with the cultured bacteria exhibiting potent antimicrobial properties against S. aureus, a significant reduction in S. aureus colonization was observed (10). Consequently, skin microbiome transplants emerge as a promising therapeutic avenue for managing skin conditions.

Additionally, another intriguing approach to regulating the skin microbiome is the deployment of bacteriophages, or simply phages. These viruses are specialized parasites that exclusively target and replicate within bacterial cells. Remarkably, phages possess the unique ability to selectively infect specific types of bacteria while leaving human cells unharmed, rendering them an ideal therapeutic candidate. In a notable study, the application of five common phages targeted against the bacterium Acinetobacter baumannii yielded favorable outcomes in a mouse wound infection model (19). This suggests the potential utility of phages in mitigating pathological bacterial colonization within an infective context.

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The gut microbiome and skin health

Similar to the skin microbiome, the gut microbiome hosts billions of microorganisms, including bacteria, viruses, and fungi. Yet, the gastrointestinal environment presents distinct challenges and selective pressures for these microbes compared to the skin (20,21). Research in the rapidly evolving field of gut microbiome science reveals its significant role in facilitating digestion, optimizing nutrient absorption, and regulating the immune system to defend against pathogens and inflammation (6,7). Importantly, emerging findings underscore its crucial connection to skin health (22). For example, one common bacteria of the microbiome Bifidobacterium have been reported to be reduced in patients with atopic dermatitis (12). Hence, it is possible that dysregulation of gut microbiome may be collated to certain bacteria in the microbiome (23). Similarly, another study showed that bacterial DNA in the plasma of patients was significantly increased in patients with psoriasis (24). The psoriasis patients with elevated bacterial plasma DNA also were recorded to have increased inflammatory markers such as IFN-γ, IL-1β, IL-6, IL-12, and TNF compared with the healthy controls (24). The researchers therefore concluded that gut microbiome dysregulation promoted increased bacterial DNA plasma in psoriasis patient increasing inflammation and possibly driving the disease. Further, the gut microbiome has also been shown to play a role in rosacea, an inflammatory facial skin disease. One study reported that patients with rosacea were colonized with helicobacter pylori up to 88% of the time. When helicobacter pylori patients were treated, the symptoms of rosacea improved significantly. Therefore, it is likely the microbiome may have a key role to play in skin pathologies such as rosacea.

The gut microbiome in Skin disease therapy

As aforementioned the gut microbiome likely plays a major role in maintaining skin health and when perturbed may contribute to disease. Thus, the gut microbiome has become an increasingly targeted avenue of therapeutic targets for skin disease. For instance, in a double-blind, placebo-controlled intervention trial including daily mixture of Lactobacillus rhamnoses and Bifidobacterium animalis, in infants, the incidence of atopic dermatitis was significantly reduced in the probiotic group compared to placebo. Therefore, probiotics may alter the risk of developing atopic dermatitis in infants. Another therapy is Synbiotics which are a combination of probiotics (live beneficial microorganisms) and prebiotics (non-digestible compounds that support microbial growth) designed to work together to enhance gut health. By providing probiotics with the necessary nutrients, synbiotics aim to promote the survival and activity of beneficial gut microorganisms. For example, in a double-blind, randomized, placebo-controlled trial, a synbiotic named Lactocare was administered to patients with psoriasis (25). After 12 weeks of treatment, psoriasis symptoms were significantly reduced in the treatment group compared to placebo (25). Therefore, it is likely synbiotic may be used to treat skin disease such as psoriasis. Further, another novel treatment in atopic dermatitis is faecel transplants. Fecal transplants, also known as fecal microbiota transplantation (FMT), are medical procedures in which fecal material from a healthy donor is transferred into the gastrointestinal tract of a recipient to restore or rebalance the recipient's gut microbiome. One study showed that atoptic dermatitis was reduced in mice sterilized with antibiotics when treated with healthy donor Fecal microbiota transplantation (16). Therefore, Fecal microbiota transplantation may be a possible therapeutic avenue for atopic dermatitis.

In conclusion, the gut microbiome, akin to the skin microbiome, is home to a diverse range of microorganisms and is pivotal for digestion, nutrient absorption, and immune system regulation. Recent research has revealed its connection to skin health, with links to conditions like atopic dermatitis, psoriasis, and rosacea. Furthermore, the gut microbiome is now a target for skin disease therapy.

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Probiotics such as Lactobacillus and Bifidobacterium show promise in reducing the risk of atopic dermatitis, while synbiotics, combining probiotics and prebiotics, are effective for conditions like psoriasis. Fecal microbiota transplantation is being explored as a potential therapy for atopic dermatitis, showing promise in experimental settings. In essence, the gut microbiome significantly influences skin health, and various therapeutic approaches, including probiotics, synbiotics, and FMT, are being investigated to manage skin diseases through gut microbiome modulation.

In conclusion, the intricate relationship between our skin and gastrointestinal microbiomes is a growing area of research with profound implications for our understanding of skin health and disease. Our skin microbiome, composed of a diverse array of bacteria, fungi, and viruses, can either promote or prevent skin diseases. The connection between the gut microbiome and skin health is equally significant. Dysregulation of the gut microbiome has been associated with skin conditions such as atopic dermatitis, psoriasis, and rosacea. Emerging research suggests that probiotics, synbiotics, and fecal microbiota transplantation may offer therapeutic solutions for these skin diseases by restoring gut microbial balance. These imbalances highlight the importance of maintaining a harmonious skin microbiota. To address these challenges, various strategies, including probiotics, skin microbiome transplants, and bacteriophages, offer promising avenues for managing skin diseases and promoting a balanced skin microbiome.

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