Should the Microbiome Be Treated as a Therapeutic Target for Non-infectious Skin Diseases?

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AT THE European Academy of Dermatology and Venereology (EADV) Congress 2026, more than 20,000 experts from across the globe came together to share insights, collaborate, and showcase the latest research in dermatology. As part of the 'Controversies II' session, speakers debated the question: 'Is the microbiome a relevant therapeutic target in non-infectious diseases?'. This pro-and-con debate explored the potential of the microbiome as a therapeutic target in non-infectious dermatological diseases, bringing together contrasting perspectives to encourage critical discussion of the current evidence and its clinical implications.

INTRODUCTION

The debate was introduced by Tilo Biedermann, LMU Munich, Germany, who set the scene for the later arguments by highlighting the significance of the cutaneous microbiome, for which research was advanced by initiatives such as the Human Genome Project (HGP) and Human Microbiome Project (HMP). Atopic dermatitis (AD) was shown to serve as an important example of how microbial diversity can recover following anti-inflammatory treatment, whilst *Staphylococcus aureus*, the dominant species in AD-associated dysbiosis, was shown to decline following treatment.[1] Further studies have demonstrated the immunomodulatory effects of *Roseomonas mucosa* in mouse and cell culture models of AD. *R. mucosa* isolates taken from individuals with AD worsened outcomes in these models, while isolates from individuals without AD improved outcomes.[2]

However, translating these findings into clinical benefit has proved challenging. A therapeutic product containing three combined strains of *R. mucosa* failed to achieve its primary endpoint in a Phase II trial: a reduction of at least 50% in disease severity measured using the Eczema Area and Severity Index (EASI50).[3] Biedermann therefore framed the central question for the session: can the microbiome serve as a relevant therapeutic target?

AGAINST: THE MICROBIOME IS NOT YET A RELIABLE THERAPEUTIC TARGET

Carsten Flohr, King's College London, UK, opened the debate by challenging the clinical utility of the microbiome as a therapeutic target. He emphasised how microbial diversity varies by site, age, and environment, and acknowledged the role of dysbiosis in AD, psoriasis, and acne. However, he pointed out that association does not necessarily equate to causation, and microbiome signatures are highly variable, non-specific, and unstable. The lack of reproducibility reflects weak causal evidence, high inter-individual variability, environmental confounders, and limited evidence of sustained clinical benefit. Flohr highlighted that AD is driven by Type 2 inflammation, barrier dysfunction, and genetics, but questioned whether microbiome changes are primary drivers of disease or secondary to these processes.

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Although *S. aureus* colonisation correlates with severity, reducing its abundance does not necessarily lead to disease remission.[4-6]

Flohr then returned to the seemingly promising *R. mucosa* research, which failed to meet the primary endpoint in a Phase II trial.[2,3] Although microbiome-related mechanisms have been demonstrated, they have not consistently translated into clinical efficacy. He stressed that mechanistic activity alone does not replace established anti-inflammatories. Instead, Flohr argued, the environmental axis must be considered, given that efficacy depends on interactions between microbes and their environment. Factors including UV, pollution, and humidity may influence the activity of live therapies *in vivo*. He referred back to the research by Callewaert et al.,[1] initially introduced by Biederman, which reported a decline in *S. aureus* following skin barrier restoration by dupilumab, highlighting that dysbiosis may also arise as a consequence of skin barrier damage.[1]

Flohr extended his argument beyond atopic dermatitis to psoriasis, highlighting inconsistent microbiome signatures, with changes potentially occurring alongside or following cytokine-driven inflammation.[7] Similarly, he argued that acne is not driven by bacterial overgrowth, as *C. acnes* abundance can be similar in healthy skin. Instead, acne is influenced by strain-level differences, sebum, hormones, and inflammation.[8-10] Flohr emphasised that the clinical efficacy of microbiome-targeted therapies, including probiotics and bacteriophages, remains insufficiently established in acne. Standard therapies, such as retinoids, benzoyl peroxide, and isotretinoin, instead work by targeting host biology.[8-10]

Flohr also highlighted potential safety concerns associated with live therapeutics, which can replicate within host systems. Potential risks include unintended microbial persistence, adverse immune effects, and the transfer of undesirable genetic material.

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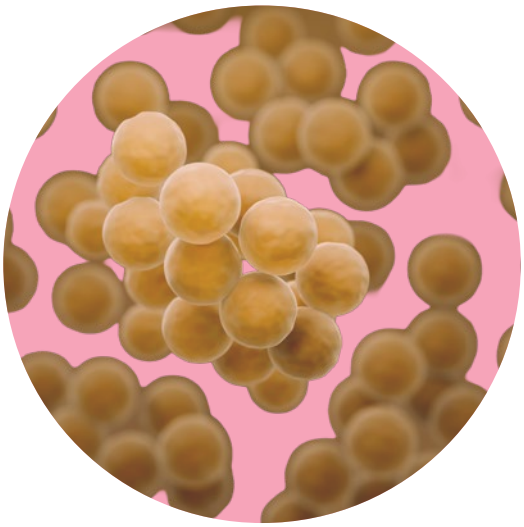


He suggested that microbiome therapies face mechanistic challenges because host immunity can reshape microbial communities, whilst barrier dysfunction may prevent introduced organisms from establishing durable colonisation.[10-12]

Turning his attention to the future, he outlined where the focus should lie: restoring the host environment and epidermal barrier to suppress inflammation and stop secondary bacterial entry.[13,14] He also suggested that microbiome strategies should look beyond live biotherapeutics to non-viable postbiotics and metabolites, which may offer alternatives that avoid some risks associated with live cells. He further advocated genomic profiling of strains to better understand host–microbe interactions before intervening.

IN FAVOUR: THE MICROBIOME COULD SERVE AS A VALUABLE TARGET IN NON-INFECTIOUS DISEASE

Ellen van den Bogaard, Radboud University, Nijmegen, the Netherlands, presented the opposing perspective. She began by highlighting the range of immune-mediated inflammatory diseases associated with dysbiosis, including acne vulgaris, psoriasis, cutaneous T cell lymphoma, and atopic dermatitis. She argued that although many studies focus on potentially pathogenic microbes, less abundant commensal organisms may also hold therapeutic potential.[15] Various options are available for microbiome-targeted therapies: prebiotics, which support beneficial microbes; postbiotics, which comprise inanimate microorganisms and/or their components that confer a health benefit; and probiotics, the provision of live beneficial bacteria. Next-generation probiotics include engineered live biotherapeutics, which may provide barrier support, modulate the immune response, and promote competition with pathogenic bacteria.[5]



Van den Bogaard then addressed the challenges in translating microbiome research into clinical interventions. She described how the microbiome may contribute to disease without necessarily being its primary driver. Additionally, microbiome dysbiosis is highly heterogeneous, and therefore current therapies may lack the biological precision and durability required for consistent clinical benefit. She described the gap between extensive preclinical studies and clinical interventions as a 'translational graveyard'. To address these challenges, she suggested using microbiome-targeting therapies as adjuncts to established anti-inflammatory drugs. She also suggested that patient populations should be stratified, microbial engineering could be utilised to improve therapeutic persistence, and postbiotics could offer a potentially safer means of modulating commensal communities, rather than relying solely on antibiotics or probiotics. Bottlenecks between preclinical studies and clinical impact could be addressed through improved human skin models and readout systems, as well as *in silico* modelling to complement experimental data.

Taking a closer look at patient stratification, van den Bogaard highlighted findings from the BIOMAP consortium, which identified two endotypes of AD, one of which was characterised by *S. aureus*-associated dysbiosis, while the other was not. Endotype 2 was characterised by a 108-gene innate-inflammatory signature, including IL-1β and IL-6, increased myeloid infiltration, and *S. aureus*-associated dysbiosis.[16] The findings suggested a lower

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clinical response to dupilumab at Week 16 in this subgroup. Van den Bogaard highlighted how functional experiments suggested a synergistic inflammatory response involving Th2 cytokines and *S. aureus*-associated signalling in keratinocytes.[16] These findings suggest that microbiome-associated inflammatory pathways may be particularly relevant in certain patient subgroups, supporting further investigation of endotype-guided treatment strategies.

She then turned her attention to low-abundance commensals, which often receive relatively little attention. Studies have identified Gram-positive anaerobic cocci that are potent in inducing host defence responses.[17] Their reduced abundance in AD has been proposed to create conditions that favour *S. aureus* colonisation. Heat-killed lysates from these organisms are being investigated as potential postbiotics that could stimulate host defence, including through aryl hydrocarbon receptor signalling and host–microbe interactions.[17]

Van den Bogaard concluded her talk by emphasising that although microbiome-targeted therapies are not yet ready to fulfil their full therapeutic potential, further research could help overcome the translational barriers. She highlighted the need to examine lower-abundance commensals, improve the relevance of human models, and refine prebiotics, probiotics, and postbiotics to support microbial homeostasis. Microbiome sequencing and *in silico* modelling should be utilised to provide data-driven insights and refine our understanding of the mechanisms underlying host–microbe interactions.

CONCLUSIONS

The debate highlighted a shared challenge: translating microbiome research into reproducible clinical benefit. While Flohr emphasised the limitations of current evidence and the importance of addressing host inflammation and barrier dysfunction, van den Bogaard argued that more precise, patient-specific approaches could unlock the microbiome's therapeutic potential. Ultimately, progress may depend on identifying the relevant microbes, mechanisms, and patient populations in which targeted interventions can deliver measurable clinical benefit.

References

1. Callewaert C et al. IL-4Rα blockade by dupilumab decreases Staphylococcus aureus colonization and increases microbial diversity in atopic dermatitis. J Invest Dermatol. 2020;140(1):191-202.e7.
2. Myles IA et al. First-in-human topical microbiome transplantation with Roseomonas mucosa for atopic dermatitis. JCI Insight. 2018;3(9):e120608.
3. Tham EH et al. The skin microbiome in pediatric atopic dermatitis and food allergy. Allergy. 2024;79(6):1470-84.
4. Boggio CMT et al. Skin microbiota in atopic dermatitis: victim or executioner? Clin Microbiol Rev. 2025;38:e00277-24.
5. van Hout NE et al. From prebiotics to engineered microbes: microbe-inspired treatments for atopic dermatitis. Br J Dermatol. 2026;194(3):420.
6. Simpson EL et al. Rapid reduction in Staphylococcus aureus in atopic dermatitis subjects following dupilumab treatment. J Allergy Clin Immunol. 2023;152(5):1179-95.
7. Zhong L et al. Microbiome dysbiosis and therapeutic restoration in atopic dermatitis. Front Cell Infect Microbiol. 2026;16:1693905.
8. Mias C et al. Change in Cutibacterium acnes phylotype abundance and improvement of clinical parameters using a new dermocosmetic product containing Myrtus communis and Celastrol enriched plant cell culture extracts in patients with acne vulgaris. J Eur Acad Dermatol Venereol. 2023;37(Suppl 2):20-5.
9. Niedźwiedzka A et al. The role of the skin microbiome in acne: challenges and future therapeutic opportunities. Int J Mol Sci. 2024;25(21):11422.
10. O'Neill AM, Gallo RL. Host-microbiome interactions and recent progress into understanding the biology of acne vulgaris. Microbiome. 2018;6(1):177.
11. Eisenstein M. The hunt for a healthy microbiome. Nature. 2020;577:S6-8.
12. Stefanovic N, Irvine AD. Filaggrin and beyond: new insights into the skin barrier in atopic dermatitis and allergic diseases, from genetics to therapeutic perspectives. Ann Allergy Asthma Immunol. 2024;132(2):187-95.
13. Silverberg JI et al. Efficacy and safety of upadacitinib versus dupilumab in adults and adolescents with moderate-to-severe atopic dermatitis: week 16 results of an open-label randomized efficacy assessor-blinded head-to-head phase IIIb/IV study (Level Up). Br J Dermatol. 2024;192(1):36-45.
14. Chatzigeorgiou I et al. Restoration of skin barrier abnormalities with IL4/13 inhibitors and Jak inhibitors in atopic dermatitis: a systematic review. Medicina (Kaunas). 2024;60(8):1376.
15. Ederveen THA et al. Skin microbiota in health and disease: from sequencing to biology. J Dermatol. 2020;47(10):1110-8.
16. Hübenthal M et al. Th2-primed innate immune amplification defines a distinct atopic dermatitis endotype. Gene Expression Omnibus (GEO). Accession no. GSE330551. Available at: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE330551. Last accessed: 26 October 2026.
17. van der Krieken DA et al. Gram-positive anaerobic cocci guard skin homeostasis by regulating host-defense mechanisms. iScience. 2023;26(4):106483.