The dynamic change of the skin microbiome in severe hidradenitis suppurativa after short term treatment with adalimumab
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Background: The composition and diversity of microbiome community has been implicated in inflammatory skin disorders. Adalimumab, an anti-tumor necrosis factor (TNF)-α monoclonal antibody, recovered along with clinical symptoms after treatment. The involvement of bacteria in the pathogenesis of hidradenitis suppurativa has been postulated, although the roles of bacteria remain unclear. In the present study, we aimed to investigate the skin microbiome in severe HS patients and the dynamic change after adalimumab treatment. Methods: We prospectively recruited 13 severe HS patients and 10 healthy controls from September 1st, 2019 to April 10th, 2020 in Chang Gung Memorial Hospital, Kaohsiung branch and Chiayi branch. Samples were collected in HS patients and healthy controls were recruited. Regular supply of HS patients and healthy controls for 20 weeks, and compared these parameters after treatment. Results: A total of 13 HS patients, 10 healthy controls and 6 post-treatment HS patients were included in the final analysis. Corynebacteria and Staphylococcus were frequently identified in healthy controls, while Prevotella, Peptostreptococcus, Firmicutes, Acanthococcus, and Eukerkella were significantly dominated in HS patients (P<0.05). Although alpha diversity was similar across 3 groups, there were significant differences in the composition of bacteria between healthy control group and HS group, and in that between healthy control group and post-treatment group (P<0.05). However, there was no difference between the HS group and post-treatment HS group despite successful clinical responses (P=0.56). Conclusion: Severe HS patients featured with characteristic skin microbiome on the lesional surface that differed significantly from healthy controls. After successful treatment with adalimumab, the composition of the distinct skin microbiome did not alter significantly despite evident clinical improvement.

Isolevulin disrupts skin microbiome composition and metabolic function after 20 weeks of therapy
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Despite being the gold standard treatment for severe acne for nearly 40 years, how isoleuvinin influences the entire microbiome, the strain level composition of C. acnes, and the metabolic function of the microbiome throughout treatment is still not clear. We collected cyanoacrylate glue follicular casts from the cheek of acne patients (14 M, 4 F; ages 14-29 yrs.) throughout isoleuvinin treatment (0wk, 1wk, 4wks, 8wks, 20wks and 6 months after cessation) followed by whole genome sequencing to determine how the skin microbiome and strain composition of C. acnes is influenced by isoleuvinin. As expected, isoleuvinin significantly decreased sebum levels by 4wks of treatment and disease severity scores significantly decreased by 20wks of treatment. 5 diversity (Shannon Diversity Index) was not significantly impacted by isoleuvinin treatment. However, β-diversity (VAST) was significantly altered at both 8wks and 20wks (p<0.05) of isoleuvinin compared to pretreatment. The relative abundance of C. acnes significantly decreased after 20wks of treatment (p<0.03) and analysis of C. acnes strains showed that SLST cluster A strains (phytotype IA) were most affected and decreased by 20wks (p<0.05). We identified 989 KEGG orthology (KO) terms enriched at 20wks compared to 0wks. Pathway analyses revealed significant decreases in 3 pathways: amino acid biosynthesis (q=0.0055), peptidoglycan biosynthesis (q=0.0143), and folate biosynthesis (q=0.05). Down regulation of these three pathways likely reflects the change in energy sources (decreased sebum) and decreased levels of C. acnes. Six months after isoleuvinin, sebum and C. acnes levels, microbial composition and metabolic pathways returned to pretreatment levels, indicating that isoleuvinin does not permanently alter the skin microbiome. In sum, 20 weeks of isoleuvinin treatment is necessary to induce significant changes in the critical factors of acne pathogenesis.

Pharmacological properties of Myrtacine and Celastrol extracts on Cathelicidin and inflammatory cascade involved in acne
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Acne vulgaris is a chronic and recurring skin disease affecting many adolescents and adults throughout their lifetimes. The pathogenesis of acne involves an interplay of several factors including sebum production increase and follicular hyperkeratinization. More recently, another key factor has been identified: the microbiome, and more particularly Cathelicidin acnes (C. acnes) species, and its impact on the local Th17-mediated immune-inflammation. In this study, the pharmacological properties of Myrtacine®, Myrtus communis extract, and Celastrol, in particular, were evaluated for their ability to inhibit the proliferation and promoting their differentiation. Furthermore, Myrtacine® had an anti-virulence effect by the significant inhibition of several virulence factor gene expression. Myrtacine® (0.001%), C. acnes (0.0025%) significantly and synergistically inhibited the inflammatory activities of IL-8, IL-1α, IL-1β, IL-18 and TNFα produced in response to IA1 C. acnes. Myrtacine®. Moreover, an inhibitory effect of Celastrol, in solution of formulation at 0.3%, was demonstrated specifically on IL17 released by immune cells in vitro but also by Th17-symphocytes integrated in a 3-dimensional skin model. Our results clearly indicated the regulatory properties of Myrtacine® and Celastrol on Th17-mediated immune-inflammation. Therefore, it shows the real interest of these two active ingredients for a targeted therapy of inflammatory acne disease.

Neutrophil-specific defense receptors that prevent skin dryness and bacterial infection
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Defensins are a large family of positively-charged antimicrobial peptides that have been implicated in innate immune defense. Although defensins are present on the skin and the oral mucosa, they are also present in the lungs, where they protect against bacterial infection. Defensins play a critical role in innate immune defense, and disruption of defensin expression has been shown to lead to increased susceptibility to bacterial infections. In this study, we determined the role of defensins in skin dryness and bacterial infection. We first measured the level of defensins in the skin of mice with different strains and found that defensins are significantly higher in the skin of mice with the dry skin phenotype compared to the normal skin phenotype. We then used a transgenic mouse model to overexpress defensins in the skin and found that this resulted in a significant decrease in the number of bacteria in the skin. These results suggest that defensins play a crucial role in skin dryness and bacterial infection and provide a potential target for the development of novel treatments for skin dryness and bacterial infection.