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# Mycobiome and Microbiome in Seborrheic Dermatitis

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Seborrheic dermatitis (SD) is a chronic inflammatory skin disease in which scaling and erythema occur on various body parts, such as the scalp, eyebrows, nasolabial folds, and ears. Although it is a common skin disease, its pathogenesis remains unclear. It has various causes, including microorganisms and immune and nervous system abnormalities that act in a complex manner. The skin mycobiome/microbiome, an important factor in SD occurrence, is being actively studied. Among the skin microorganisms related to SD, *Malassezia* and *Cutibacterium* have been extensively studied. Recently, it was revealed that various microorganisms are related in several ways. The study of changes in mycobiome/microbiome involves comparing types and abundances of microorganisms and degrees of microbial diversity; patients and healthy individuals; the lesion and nonlesion areas; and affected body parts. Several studies on the mycobiome/microbiome associated with SD have shown relatively consistent results; however, some have revealed different outcomes. These variations occur because of differences in individuals, study groups, and sampling/study methodology. Therefore, further research is needed for the application the results of these studies in the treatment of SD.

**Key Words:** Microbiome, Mycobiome, Seborrheic dermatitis

## INTRODUCTION

Seborrheic dermatitis (SD) is a chronic inflammatory skin disease that causes flakes and erythema on the scalp, eyebrows, nasolabial folds, glabella, and ears. Although it is a common skin disease, its cause is still unclear[1]. Previous studies have reported on the associations between immune response and inflammation, microorganisms, abnormal skin lipids, epidermal hyperkeratosis, and neurotransmitter abnormalities. Climate, medications, malnutrition, and genetic factors may also cause SD[1].

SD pathogenesis due to *Malassezia*, a fungi, and *Cutibacterium*, a bacteria, have been well studied. Several studies have reported that *Malassezia furfur* weakens the skin barrier function by producing indoles, which are ligands for aryl hydrocarbon receptors, or using oleic and arachidonic acids generated as sebum metabolites[2]. *Cutibacterium acnes* and *Malassezia* have lipolytic ability, converting triglycerides into free fatty acids[3]. Recently, with the development of the microbiome concept in all fields of dermatology, SD research has expanded to investigate the involvement of mycobiome/microbiome.

## SEBORRHEIC DERMATITIS MYCOBIOME

Several studies have confirmed the α- and β-mycobiome diversity in patients with SD. The patient's Shannon index of α diversity has been reported to decrease as well as increase[4,5]. Several reports have stated that no difference exists between the lesion and nonlesion areas and according to the body

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**Table 1.** α and β diversity in seborrheic dermatitis

| Subject | | | Mycobiome | Microbiome |
|---|---|---|---|---|
| Lin et al. (2020)[4] | Scalp SD/healthy Lesional/ non-lesional | α | Decreased Shannon diversity in SD<br>No significant changes in lesional/non-lesional | No significant changes between SD/healthy<br>No significant changes in lesional/ non-lesional |
| | | β | PCoA could distinguish SD/healthy<br>No significant changes in lesional/non-lesional | PCoA could distinguish SD/healthy<br>No significant changes in lesional/ non-lesional |
| Grimshaw et al. (2019)[9] | Scalp SD/healthy Lesional/ non-lesional | α | N/A | N/A |
| | | β | NMDS plots showed no distinct community clustering between SD/heathy | NMDS plots showed distinct community clustering between lesional/non-lesional |
| Saxena et al. (2018)[5] | Scalp SD/healthy | α | Significantly higher Shannon diversity in SD | No significant changes between SD/healthy |
| | | β | N/A | UniFrac distances showed significant difference between SD/healthy |
| Park et al. (2017)[11] | Scalp SD/healthy | α | Significantly lower richness (Chao1) and lower evenness (Simpson's index) in SD | Significantly higher richness (Chao1) and lower evenness (Simpson's index) in SD |
| | | β | PCoA and MDS plots showed distinct community clustering between SD/healthy | PCoA and MDS plots showed distinct community clustering between SD/healthy |
| Soares et al. (2016)[8] | Scalp, Forehead SD/healthy Lesional/ non-lesional | α | Significantly increased Shannon diversity in SD | Significantly increased Shannon diversity in SD scalps and forehead compared to healthy controls |
| | | β | ANOSIM and NMDS plots showed distinct community clustering Scalp/Forehead lesional/non-lesional in SD | ANOSIM and NMDS plots showed distinct community clustering according to body sites and between lesional and non-lesional |
| Tanaka et al. (2016)[15] | Scalp Lesional/ non-lesional | α | N/A | No significant changes between lesional/non-lesional |
| | | β | N/A | PCoA showed clear separation between lesional/non-lesional |

Abbreviations: ANOSIM, analysis of similarities; MDS, metric multidimensional scaling; N/A, not available; NMDS, non-metric multidimensional scaling; PCoA, principal coordinates analysis; SD, seborrheic dermatitis

parts[4,6]. Another study reported a decrease in the Chao and Simpson indexes[7].

Regarding β diversity, study results indicating that it is possible to distinguish between the patient and healthy individual as well as those indicating that they cannot be distinguished exist. Further, results regarding the lesion and nonlesion areas are heterogenous[4,7-10]. A previous report stated the absence of any difference in diversity according to disease severity[10] (Table 1).

Among the fungi constituting the mycobiome, the most well-known is *Malassezia*. Additionally, it has been reported that fungi, such as *Mycosphaerella*, *Candida*, *Filobasidium*, *Aspergillus*, *Ganoderma*, *Exidia*, *Pilatoporus*, and *Engyodontium*, vary in SD. Currently, heterogeneous results indicate the increase or decrease of each species, but the increase in *Malassezia*, especially *M. restricta*, and the decrease in *M. golbossa*, reveal similar results[4-14].

## SEBORRHEIC DERMATITIS MICROBIOME

The α-diversity of the SD microbiome showed inconsistent results. Thus, among the outcomes obtained, the relatively consistent one states that no difference between the lesion and nonlesion areas exist[7-9]. Regarding the β-diversity, the main opinion is that the sample distance is higher in healthy individuals[4,5,7-9,15] (Table 1). The members of the microbiome include *Staphylococcus*, *Cutibacterium*, *Streptococcus*, *Pseudomonas*, *Actinobacteria*, and *Firmicutes*. It is considered that *Staphylococcus* and *Streptococcus* increase while *Cutibacterium* and *Pseudomonas* decrease[4-9,12,13,15].

## CAUSES OF DISCREPANCIES BETWEEN STUDY RESULTS

Differences between study results arise due to differences between individuals. Moreover, factors such as residence and race of the population, sampling method, and sequencing techniques differ among studies. Sequencing results also vary depending on the target gene, and there are various methods for sequencing, such as cloning and Sanger sequencing, quantitative polymerase chain reaction, amplicon sequencing, and whole metagenome sequencing; however, currently no standardized sampling or experimental method exists. Therefore, the results are bound to be affected[2].

## THE RELATIONSHIP BETWEEN MYCOBIOME/MICROBIOME AND SEBORRHEIC DERMATITIS SYMPTOMS

For clinically meaningful microbiome changes, it should be confirmed that changes are significantly related to clinical symptoms. However, research is limited on this topic. According to a study by Saxena et al.[5], *M. globosa*, known to decrease mainly in SD, showed a negative correlation with total dandruff and itching and a positive correlation with total *Malassezia*. Also, a decrease in *Pseudomonas* and an increase in *Staphylococcus* were positively correlated with dandruff and itch[5]. A positive correlation of *Staphylococcus* and *Cutibacterium* with TEWL and water content indicates their potential role in skin barrier function[12]. Moreover, researchers have analyzed the functional pathways of the mycobiome/microbiome. The mycobiome are enriched in pathways involved in cell-host adhesion in the dandruff. Contrastingly, the microbiome was enriched in pathways related to the synthesis and metabolism of amino acids, biotin, and other B-vitamins, which have been reported to be essential for hair growth[5].

## THE RELATIONSHIP BETWEEN MYCOBIOME/MICROBIOME AND SD TREATMENT

For the application of microbiome research in actual clinical practice, it is necessary to check whether dysbiosis improves after treatment and whether this improvement leads to symptom progression, besides examining the relationship between microorganisms and clinical symptoms. However, there is limited research on this field. Leong et al.[16] confirmed the changes in *M. restricta* and *M. globosa* in 35 healthy subjects before and after using antifungal zinc pyrithione shampoo. On the one hand, *M. restricta* temporarily decreased after shampooing, but the variation among individuals was large. However, it soon returned to the original state, thus failing to maintain a meaningful change. On the other hand, *M. globosa* was unaffected by the use of zinc pyrithione shampoo[16]. The following results confirmed the changes in patients with SD using selenium-disulfide shampoo. The participants used 2% ketoconazole shampoo for 1 month. The outcomes showed beneficial results, such as the reduction of dandruff and erythema, restoration of *Malassezia* diversity, reduction of total *Malassezia* count, and reduction of *Staphylococcus*. The participants were classified into two groups. The first group maintained treatment using 1% $SeS_2$-based shampoo, and the other group used a vehicle. It was confirmed that the significant response after using ketoconazole shampoo was well maintained in the group using the selenium shampoo[17].

Rather than regulating existing microbes, some treatments involve supplementation with beneficial microorganisms. Hence, strains known to be helpful against atopic dermatitis in patients with SD can be used, as patients with SD also suffer from barrier damage and skin immune abnormalities, such as atopic dermatitis[18]. *Vitreoscilla filiformis* is a gram-negative bacterium that stimulates regulatory T cells and does not affect the survival of microorganisms constituting the microbiome[19]. It has been reported that when applied to patients with atopic dermatitis, it helps to moisturize the skin[20]. Therefore, when vitreoscilla biomass was applied to SD patients, symptom improvement, such as itching, was observed[21]. The application of the *Lactobacillus* biomass (*Lactobacillus sporogene* or *Lactobacillus rhamnosus*) also appeared to be beneficial in the improvement of both psor-

iasis and SD[22,23]. Furthermore, another study investigated the reaction after oral ingestion rather than microbial application. SD symptoms, such as dandruff, improved when *Lactobacillus paracasei* NCC 2461 ST11 was taken once daily[24].

## CONCLUSION

In conclusion, SD mycobiome/microbiome diversity can be considered controversial, and presently, this research has relatively decreased. It is possible that the difference between the lesion and nonlesion areas is not significant, and there is a change in species and quantity. *Malassezia* (esp., *restricta*), *Staphylococcus*, and *Streptococcus* increased in abundance, whereas *M. globosa*, *Cutibacterium*, and *Pseudomonas* decreased. There are possible correlations between SD symptoms and changes in the microbiome and its metabolic pathways.

However, there is no definitive conclusion regarding the SD mycobiome/microbiome. For future research, a consensus on sampling and sequencing methods is required. Further studies on the relationship between microbes and SD symptoms or treatment using microbes are warranted.

## CONFLICT OF INTEREST

In relation to this article, we declare that there is no conflict of interest.

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## REFERENCES

1. Wikramanayake TC, Borda LJ, Miteva M, Paus R. Seborrheic dermatitis-Looking beyond *Malassezia*. Exp Dermatol 2019;28:991-1001
2. Tao R, Li R, Wang R. Skin microbiome alterations in seborrheic dermatitis and dandruff: A systematic review. Exp Dermatol 2021;30:1546-1553
3. Adalsteinsson JA, Kaushik S, Muzumdar S, Guttman-Yassky E, Ungar J. An update on the microbiology, immunology and genetics of seborrheic dermatitis. Exp Dermatol 2020;29:481-489
4. Lin Q, Panchamukhi A, Li P, Shan W, Zhou H, Hou L, et al. *Malassezia* and *Staphylococcus* dominate scalp microbiome for seborrheic dermatitis. Bioprocess Biosyst Eng 2021;44:965-975
5. Saxena R, Mittal P, Clavaud C, Dhakan DB, Hegde P, Veeranagaiah MM, et al. Comparison of healthy and dandruff scalp microbiome reveals the role of commensals in scalp health. Front Cell Infect Microbiol 2018;8:346
6. Clavaud C, Jourdain R, Bar-Hen A, Tichit M, Bouchier C, Pouradier F, et al. Dandruff is associated with disequilibrium in the proportion of the major bacterial and fungal populations colonizing the scalp. PLoS One 2013;8:e58203
7. Park T, Kim HJ, Myeong NR, Lee HG, Kwack I, Lee J, et al. Collapse of human scalp microbiome network in dandruff and seborrhoeic dermatitis. Exp Dermatol 2017;26:835-838
8. Soares RC, Camargo-Penna PH, de Moraes VC, De Vecchi R, Clavaud C, Breton L, et al. Dysbiotic bacterial and fungal communities not restricted to clinically affected skin sites in dandruff. Front Cell Infect Microbiol 2016;6:157
9. Grimshaw SG, Smith AM, Arnold DS, Xu E, Hoptroff M, Murphy B. The diversity and abundance of fungi and bacteria on the healthy and dandruff affected human scalp. PLoS One 2019;14:e0225796
10. Soares RC, Zani MB, Arruda AC, de Arruda LH, Paulino LC. *Malassezia* intra-specific diversity and potentially new species in the skin microbiota from Brazilian healthy subjects and seborrheic dermatitis patients. PLoS One 2015;10:e0117921
11. Park HK, Ha MH, Park SG, Kim MN, Kim BJ, Kim W. Characterization of the fungal microbiota (mycobiome) in healthy and dandruff-afflicted human scalps. PLoS One 2012;7:e32847
12. Wang L, Clavaud C, Bar-Hen A, Cui M, Gao J, Liu Y, et al. Characterization of the major bacterial-fungal populations colonizing dandruff scalps in Shanghai, China, shows microbial disequilibrium. Exp Dermatol 2015;24:398-400
13. Xu Z, Wang Z, Yuan C, Liu X, Yang F, Wang T, et al. Dandruff is associated with the conjoined interactions between host and microorganisms. Sci Rep 2016;6:24877
14. Tajima M, Sugita T, Nishikawa A, Tsuboi R. Molecular analysis of *Malassezia* microflora in seborrheic dermatitis patients: comparison with other diseases and healthy subjects. J Invest Dermatol 2008;128:345-351
15. Tanaka A, Cho O, Saito C, Saito M, Tsuboi R, Sugita T. Comprehensive pyrosequencing analysis of the bacterial microbiota of the skin of patients with seborrheic dermatitis. Microbiol Immunol 2016;60:521-526

16. Leong C, Wang J, Toi MJ, Lam YI, Goh JP, Lee SM, et al. Effect of zinc pyrithione shampoo treatment on skin commensal *Malassezia*. Med Mycol 2021;59:210-213
17. Massiot P, Clavaud C, Thomas M, Ott A, Guéniche A, Panhard S, et al. Continuous clinical improvement of mild-to-moderate seborrheic dermatitis and rebalancing of the scalp microbiome using a selenium disulfide-based shampoo after an initial treatment with ketoconazole. J Cosmet Dermatol 2021;doi:10.1111/jocd.14362
18. Mottin VHM, Suyenaga ES. An approach on the potential use of probiotics in the treatment of skin conditions: acne and atopic dermatitis. Int J Dermatol 2018;57:1425-1432
19. Benyacoub J, Bosco N, Blanchard C, Demont A, Philippe D, Castiel-Higounenc I, et al. Immune modulation property of *Lactobacillus paracasei* NCC2461 (ST11) strain and impact on skin defences. Benef Microbes 2014;5:129-136
20. Guéniche A, Dahel K, Bastien P, Martin R, Nicolas JF, Breton L. *Vitreoscilla filiformis* bacterial extract to improve the efficacy of emollient used in atopic dermatitis symptoms. J Eur Acad Dermatol Venereol 2008;22:746-747
21. Guéniche A, Cathelineau AC, Bastien P, Esdaile J, Martin R, Queille Roussel C, et al. *Vitreoscilla filiformis* biomass improves seborrheic dermatitis. J Eur Acad Dermatol Venereol 2008;22:1014-1015
22. Vijayashankar M, Raghunath N. Pustular psoriasis responding to probiotics-a new insight. Our Dermatol 2012;3:326-329
23. Navarro-López V, Martínez-Andrés A, Ramírez-Boscá A, Ruzafa-Costas B, Núñez-Delegido E, Carrión-Gutiérrez MA, et al. Efficacy and safety of oral administration of a mixture of probiotic strains in patients with psoriasis: A randomized controlled clinical trial. Acta Derm Venereol 2019;99:1078-1084
24. Reygagne P, Bastien P, Couavoux MP, Philippe D, Renouf M, Castiel-Higounenc I, et al. The positive benefit of *Lactobacillus paracasei* NCC2461 ST11 in healthy volunteers with moderate to severe dandruff. Benef Microbes 2017;8:671-680