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THROUGH A MICROSCOPIC LENS: SKIN MICROBIOME AS THE CONFEDERATE IN ATOPIC DERMATITIS

Catharina Clarissa Ursia ¹, Patricia Dian Putri ²

ABSTRACT

*Reciprocity between the skin microbiome and the host underlies the occurrence, exacerbation, and severity of atopic dermatitis (AD). However, the role of the skin microbiome in the pathogenesis of AD is yet to be depicted. This review highlights the host–microbiome interactions which rely on barrier status, microbiome composition, and microbe–microbe interactions. A microbiome shift, with an abundance of *S. aureus* and lower microbial diversity, compromises the skin barrier function.*

It shows that epidermal barrier defect depletes the protective commensal skin bacteria and demonstrates how dysbiosis of the skin microbiome can lead to AD.

Keyword: atopic dermatitis, skin microbiome, dysbiosis.

ABSTRAK:

Interaksi antara mikrobiota kulit dan kulit pejamu memiliki peran di balik manifestasi, tingkat keparahan, dan eksaserbasi dermatitis atopik (DA). Akan tetapi, peranan mikrobiota kulit dalam patogenesis DA masih belum sepenuhnya dijabarkan. Ulasan ini berfokus pada interaksi kulit pejamu-mikroba kulit yang bergantung pada keadaan sawar kulit, keanekaragaman mikrobiota, serta interaksi antar mikroba-mikroba kulit. Perubahan komposisi mikrobiota, dengan adanya peningkatan *S. aureus* dan penurunan keragaman mikrobiota menurunkan fungsi sawar kulit. Hal ini membuktikan bahwa mikrobiota komensal yang ditemukan pada kulit berperan penting dalam melindungi kulit terhadap patogen, serta menunjukkan bagaimana disbiosis mikrobiota tersebut dapat menyebabkan DA.

Kata kunci: dermatitis atopi, mikrobiota kulit, dysbiosis

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INTRODUCTION

The atopic dermatitis (DA) is a prevalent chronic skin disease, affecting about 20% of children and 5% of adults.^{1,2} A substantial number of patients suffer from severe or persistent AD and experience a devastating impact on their well-being.³ Furthermore, persons with AD renders an onerous financial implications.⁴

The epidermis functions as a functional and physical interface between the body and the environment. Epidermal disruption is a central pathologic process in AD.⁵ With such compromise, AD skin is associated with marked changes in the composition of the skin microbiome (dysbiosis), forming part of a complex interplay with skin barrier integrity and giving rise to the waxing and waning course AD.⁶ This review illustrates how abnormalities of the epidermal barrier in AD generate dysbiosis, which results in increased inflammatory cytokines and disease exacerbation.

SKIN MICROBIOME DEFINITION

Skin microbiota is an interrelated ecosystem comprising not only bacteria but also symbiotic fungi and viruses. The equilibrium and wholeness of these microbial diversity plays a pivotal role in preventing pathogens from pervading the

skin.^{7,8}

Healthy human skin commonly harbors several bacteria genera, including: *Staphylococcus*, *Corynebacterium* and *Cutibacterium*. Each genera has its topographical assortment.⁹ For example, *Staphylococcus* and *Corynebacterium* species more commonly reside in moist areas, while *Propionibacterium* species (recently renamed *Cutibacterium*) generally inhabited sebaceous areas. The *Malassezia* fungus is mostly found on the truncal area and upper extremities.¹⁰

Although the majority of these microbiome are harmless and even advantageous, some are potentially pathogenic under certain conditions and are referred to as “pathobionts”. Marked changes (dysbiosis) in the configuration of the skin bacterial microbiome, as found in AD, afflicts the skin barrier integrity.¹¹

SKIN MICROBIOME DISRUPTION IN AD

The species *S. aureus* colonizes AD skin and is only found in a small proportion of healthy control skin.^{12,13} In AD skin, there is a difference in microbiome composition between lesional and nonlesional skin. For example, there is a lower bacterial diversity in AD flexures, with an abundance of *S. aureus* and *S.*

epidermidis species.^{14,15} The abundance of *staphylococcus* progressively increase from non-lesional skin samples over acute to chronic lesions; with a significantly higher abundance of *staphylococci* in chronic lesions compared to nonaffected skin.¹⁶

This dysbiosis is positively correlated with AD flares, proven by a temporal relationship linking microbiome shift and AD exacerbations; and recovery of microbial diversity following treatment.^{17,18}

Not only does colonization of *S. aureus* leads to AD flares, but it is also associated with more severe exacerbation of AD.^{19,20} As a matter of fact, the clinical link between *S. aureus* burden and AD severity has been proven through cultural studies; with an inverse correlation between the abundance of the protective commensals, *S. epidermidis* and *Corynebacterium*, relative to *S. aureus*.^{15,21–23} These commensals can induce antimicrobial peptides (AMP) which inhibit *S. aureus* colonization on human skin. Thus, the depletion of these commensal species consequently depletes the likely regulatory or protective commensals.^{15,24,25}

Methicillin-resistant *Staphylococcus aureus* (MRSA) colonization in AD is associated with a more profound change in the composition of commensal bacteria²⁶ and gives rise to an

oppressive inflammatory reaction, as opposed to skin that is populated by Methicillin-resistant *Staphylococcus aureus* (MSSA) establishment.^{27,28}

A systematic review showed that there is also a reduced number of *Malassezia* species and greater diversity of other fungal genera (excluding *Malassezia*, *Aspergillus*, *Candida*, and *Cryptococcus* genera).²²

ROLE OF EACH MICROBIOTA IN AD

One way the host responds to abundantly colonized *S. aureus* in AD lesion is via antimicrobial defense mechanism. This may be done by commensal bacteria, such as *S. epidermidis* through the production of AMP, and by *C. acnes* through lipid utilization.²⁹

A recent study confirmed that *S. Epidermidis* can specifically limit *S. aureus* growth³⁰ and suppress inflammation via activation of APC and secretion of anti-inflammatory IL-10.³¹ In addition, *S. epidermidis* also secretes a lipoteic acid which suppresses both keratinocytes inflammatory cytokines and inflammation through a TLR2-dependent mechanism.³¹

A study was done by Nakatsuji found that *Coagulase-negative Staphylococcus* (CoNS), a commensal bacteria, protects normal skin from *S.*

aureus colonization. Conversely, deficiency in commensal bacteria is associated with establishing *S. aureus* in AD skin.²⁵ The growth of *C. acnes*, which particularly depends on the presence of fatty substrate in the skin, might be restricted in AD.¹⁶ One study demonstrated that a higher quantity of *C. acnes* is inversely correlated to the number of *S. aureus* colonization.³² It has been confirmed that *C. acnes* is capable of producing propionic acid, a short-chain fatty acid (SCFA), through the fermentation of glycerol which restricts *S. aureus* growth.³³

It is still controversial whether

Malassezia plays a role in AD. Perhaps it is associated with its pathogenicity, as seen in AD patients with more prominent symptoms on the head and neck. Nevertheless, studies identified a decrease in *Malassezia* in AD.^{34,35} One of the studies was done in a group with previous AD exacerbation, not on antifungus medication.³⁴ In short, dry AD skin and deprivation of *C. acnes* which produces substances essential for *Malassezia* growth, creates a poor growing condition for *Malassezia*.^{34,3}

PATHOGENESIS

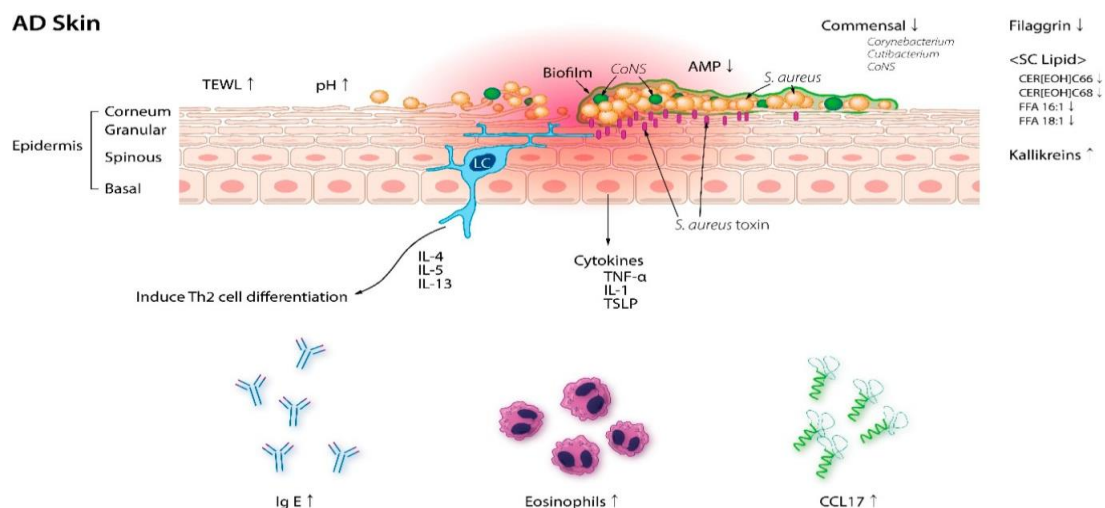


Figure 1: Pathogenesis of dysbiosis and AD ³⁶

There are three critical factors in the pathogenesis of AD: epidermal barrier dysfunction, changes in the microbiome composition, and abnormalities of the skin

immunity related to T-helper 2 (Th-2). These factors may reciprocate and retaliate against each other.³⁷

Impaired Skin Barrier

The interplay between multiple risk factors increases the risk of skin barrier impairment, thus favoring *S. aureus* colonization on AD skin. These factors include the reduction of filaggrin and filaggrin degradation products (FDPs), altered lipid profiles, the strength of *S. aureus*-corneocyte adhesion, microbial dysbiosis resulting in the deficiency of AMPs, and overexpressed Th2 cytokines.^{38,39}

Pyrrolidone carboxylic acid and urocanic acid are examples of filaggrin and FDP. Both have the ability to maintain skin pH and inhibit the growth of *S. aureus* on the skin⁴⁰. The lack of filaggrin in AD results in a higher pH, a condition approbative for *S. aureus* growth, therefore inducing more skin barrier impairment.^{24,41,42}

In AD skin, reduced filaggrin and FDP increases the adherence of *S. aureus* to epidermal cells.^{43,44} Other factors that favors *S. aureus* adhesion (to bronectin, loricrin and cytokeratin 10) are deformed corneocyte and presence of clumping factor B and fibronectin- binding proteins.⁴³

The fatty substrate of the skin; such as free fatty acid, ceramides, and sphingosine; essentially maintains the integrity of the skin barrier and prevents

pathologic colonization of *S. aureus*.⁴⁵ An in vitro study proposes that exogenous FFA 16:1 also has a potent bacterial inhibiting features.⁴⁶ Unfortunately, this lipid metabolism and composition is altered by the highly conveyed Th2 in AD.³⁸

At a physiologic state, the skin's pH is preserved at a level of < 5,5. This protective acidity is maintained by anaerobic bacteria, such as *Finegoledia spp.* and *Lactobacillus spp.*, through the fermentation of FDP which generates short chain fatty acids, lactic acid, and propionic acid. Not only do they conserve a favorable pH for the skin ecosystem, but these substances also have a role in the activation of AMP at the time of skin injury. However, this protective role may be ablated in AD, as there is enhanced oxygenation, thus decreasing the quantity of these anaerobic bacteria. This (menjelaskan kalimat yang mana?) creates a good environment for *S. aureus* colonization.⁴⁷

Dysbiosis

The leaky epidermal skin barrier in AD permits the entry of environmental and cutaneous pathogens and immunogens, causing skin dysbiosis.⁴⁸ Skin dysbiosis, and vice versa, disrupts the epidermal barrier, either directly or indirectly.^{49,50} Altogether, this propels an endless loop of

1 inflammation, itch, and more skin barrier breakdown.⁴⁸

Decreased number of commensals, thus decreased expression of AMP, including cathelicidins and β -defensins, causes skin dysbiosis and skin barrier defects.^{23,24} It also creates an advantageous environment for *S. aureus* colonization.⁵¹ Despite that, higher expression of interleukin (IL)-4 and IL-13 in AD down-regulates LL-37 and HBD-3.^{51,52}

S. aureus colonization is strongly associated with an even worse barrier dysfunction. Perhaps, this is due to the assembly of biofilm, which can induce more profound skin inflammation.³⁶ A biofilm is a bacterial product that is enclosed in an extracellular matrix and adheres to the corneocyte. This biofilm formation produces immune deterrence, precipitating AD recurrences and causing difficult-to-treat infection.⁵³

The colonizing *S. aureus* then generates offending factors, notably: enzyme, toxin, and protein, that promotes skin barrier dysfunction and inflammation in AD. These include: phenol-soluble modulins δ -toxin, superantigens, protein A, proinflammatory lipoproteins, and proteases.⁴³

Serine proteases from *S. aureus* are also involved in barrier disruption and type 2 inflammation.⁵⁴ Additionally, α -toxin, a fundamental *S. aureus* toxin, induces the death of skin cells and further epidermal defect.⁵⁵

T-Helper 2 Immunity

Colonization of *S. aureus* in AD results in a more intense hapten sensitization, more pronounced Th-2 expansion, and dire skin impairment.^{23,43}

The greater inflammatory reaction has recently been recognized to correspond to *S. aureus* colonization. This is mainly due to the initiation and expansion of Th-2 cytokine shift prompted by *S. aureus*. Other mechanisms involved in this grueling inflammatory response include: deliberation of chemokines and proinflammatory substrates, production of IL (for instance IL-31) following degranulation of mast cell, as well as augmentation of B cell (independent of T cell).^{43,56}

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REFERENCES

1. Ahn K. The prevalence of atopic dermatitis in Korean children. *Allergy Asthma Immunol Res.* 2016;8:1–2.
2. Mortz CG, Andersen KE, Dellgren C, Barington T, Bindslev-Jensen C. Atopic dermatitis from adolescence to adulthood in the TOACS cohort: Prevalence, persistence and comorbidities. *Eur. J. Allergy Clin Immunol.* 2015 Jul 1;70(7):836–45.
3. Eckert L, Gupta S, Gadkari A, Mahajan P, Gelfand JM. Burden of illness in adults with atopic dermatitis: analysis of National Health and Wellness Survey data from France, Germany, Italy, Spain, and the United Kingdom. *J Am Acad Dermatol.* 2019;81:187–95.
4. Ariëns LFM, van Nimwegen KJM, Shams M, de Bruin DT, van der Schaft J, et al. Economic burden of adult patients with moderate to severe atopic dermatitis indicated for systemic treatment. *Acta Derm Venereol.* 2019;99(9):762–8.
5. Leung DYM, Berdyshev E, Goleva E. Cutaneous barrier dysfunction in allergic diseases. *J Allergy Clin Immunol.* Mosby Inc. 2020;45: 1485–97.
6. Yamazaki Y, Nakamura Y, Núñez G. Role of the microbiota in skin immunity and atopic dermatitis. *Allergology International. JSA.* 2017;66: 539–44.
7. Erin Chen Y, Fischbach MA, Belkaid Y. Skin microbiota-host interactions. *Nature.* Nature Publishing Group. 2018;553: 427–36.
8. Byrd AL, Belkaid Y, Segre JA. The human skin microbiome. *Nature Reviews Microbiology.* Nature Publishing Group; 2018;16:143–55.
9. Grice EA, Kong HH, Conlan S, Deming CB, Davis J, et al. Topographical and Temporal Diversity of the Human Skin Microbiome. *Science AAAS.* 2009;324:1190-1192..
10. Findley K, Oh J, Yang J, Conlan S, Deming C, et al. Topographic diversity of fungal and bacterial communities in human skin. *Nature.* 2013;498:367–70.
11. Tsakok T, Woolf R, Smith CH, Weidinger S, Flohr C. Atopic dermatitis: the skin barrier and beyond. *Br J Dermatol.* Blackwell Publishing Ltd. 2019;180:464–74.
12. Kim BS, Kim JY, Lim HJ, Lee WJ, Lee SJ, et al. Colonizing features of

- Staphylococcus aureus in early childhood atopic dermatitis and in mothers: A cross-sectional comparative study done at four kindergartens in Daegu, South Korea. *Ann Allergy Asthma Immunol.* 2011;106(4):323–29.
13. Park HY, Kim CR, Huh IS, Jung MY, Seo EY, et al. Staphylococcus aureus colonization in acute and chronic skin lesions of patients with atopic dermatitis. *Ann Dermatol.* 2013;25(4):410–16.
 14. Bjerre RD, Holm JB, Palleja A, Sølberg J, Skov L, et al. Skin dysbiosis in the microbiome in atopic dermatitis is site- specific and involves bacteria, fungus and virus. *BMC Microbiol.* 2021;21(1):1-10.
 15. Fyhrquist N, Muirhead G, Prast-Nielsen S, Jeanmougin M, Olah P, et al. Microbe-host interplay in atopic dermatitis and psoriasis. *Nat Commun.* 2019;10(1):1-12.
 16. Baurecht H, Rühlemann MC, Rodríguez E, Thielking F, Harder I, et al. Epidermal lipid composition, barrier integrity, and eczematous inflammation are associated with skin microbiome configuration. *J Allergy Clin Immunol.* 2018;141(5):1668-76.
 17. Kong HH, Oh J, Deming C, Conlan S, Grice EA, Beatson MA, et al. Temporal shifts in the skin microbiome associated with disease flares and treatment in children with atopic dermatitis. *Genome Res.* 2012;22(5):850–59.
 18. Kim J, Kim BE, Leung DYM. Pathophysiology of atopic dermatitis: Clinical implications. AAP. OceanSide Publications Inc.2019;40(2): 84–92.
 19. Pothmann A, Illing T, Wiegand C, Hartmann AA, Elsner P. The Microbiome and Atopic Dermatitis: A Review. *Am J Clin Dermatol.* Adis; 201;20:749–61.
 20. Williams MR, Gallo RL. Evidence that Human Skin Microbiome Dysbiosis Promotes Atopic Dermatitis. *J Invest Dermatol.* Elsevier B.V.; 2017;137:2460–63.
 21. Tay ASL, Li C, Nandi T, Chng KR, Andiappan AK, et al. Atopic dermatitis microbiomes stratify into ecologic dermatypes enabling microbial virulence and disease severity. *J Allergy Clin Immunol.* 2021;147(4):1329–40.
 22. Bjerre RD, Bandier J, Skov L, Engstrand L, Johansen JD. The role of the skin microbiome in atopic dermatitis: a systematic review. *Br J*

- Dermatol.* Blackwell Publishing Ltd. 2017;177: 1272–78.
23. Angulo EL, Gern JE. Staphylococcus aureus and staphylococcus epidermidis strain diversity underlying pediatric atopic dermatitis. *Pediatrics*. 2018;142:229–30.
 24. Czarnecki T, Krueger JG, Guttman-Yassky E. Novel concepts of prevention and treatment of atopic dermatitis through barrier and immune manipulations with implications for the atopic march. *J Allergy Clin Immunol*. Mosby Inc. 2017;139:1723–34.
 25. Teruaki Nakatsuji, Tiffany H. Chen, Saisindhu Narala. Antimicrobials from human skin commensal bacteria protect against Staphylococcus aureus and are deficient in atopic dermatitis. *Sci. Transl. Med.* 2017;9:1–11.
 26. Shi B, Leung DYM, Taylor PA, Li H. Methicillin-Resistant Staphylococcus aureus Colonization Is Associated with Decreased Skin Commensal Bacteria in Atopic Dermatitis. *J Invest Dermatol.* 2018;138(7):1668–71.
 27. Ong PY, Leung DYM. Bacterial and Viral Infections in Atopic Dermatitis: a Comprehensive Review. *Clin Rev Allergy Immuno.* Humana Press Inc.; 2016;51:329–37.
 28. Kobayashi T, Glatz M, Horiuchi K, Kawasaki H, Akiyama H et al. Dysbiosis and Staphylococcus aureus Colonization Drives Inflammation in Atopic Dermatitis. *Immunity*. 2015;42(4):756–66.
 29. Nakatsuji T, Chen TH, Two AM, Chun KA, Narala S, et al. Staphylococcus aureus Exploits Epidermal Barrier Defects in Atopic Dermatitis to Trigger Cytokine Expression. *J Invest Dermatol.* 2016;136(11):2192–2200.
 30. Wollenberg A, Christen-Zäch S, Taieb A, Paul C, Thyssen JP, et al. ETFAD/EADV Eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. *J Eur Acad Dermatol Venereol.* 2020;34(12):2717–44.
 31. Lai Y, di Nardo A, Nakatsuji T, Leichtle A, Yang Y, et al. Commensal bacteria regulate toll-like receptor 3-dependent inflammation after skin injury. *Nat Med.* 2009;15(12):1377–82.
 32. Francuzik W, Franke K, Schumann RR, Heine G, Worm M. Propionibacterium acnes abundance correlates inversely with staphylococcus aureus: Data from atopic dermatitis skin microbiome. *Acta Derm Venereol.*

- 2018;98(5):490–95.
33. Wang Y, Dai A, Huang S, Kuo S, Shu M, et al. Propionic acid and its esterified derivative suppress the growth of methicillin-resistant *Staphylococcus aureus* USA300. *Benefic Microbes*. 2014;5(2):161–68.
 34. Chng KR, Tay ASL, Li C, Ng AHQ, Wang J, et al. Whole metagenome profiling reveals skin microbiome-dependent susceptibility to atopic dermatitis flare. *Nat Microbiol*. 2016;1(9):1-9.
 35. Moosbrugger-Martinz V, Hackl H, Gruber R, Pilecky M, Knabl L, Orth-Höller D, et al. Initial Evidence of Distinguishable Bacterial and Fungal Dysbiosis in the Skin of Patients with Atopic Dermatitis or Netherton Syndrome. *J Invest Dermatol*. 2021;141(1):114–23.
 36. Kim JE, Kim HS. Microbiome of the skin and gut in atopic dermatitis (Ad): Understanding the pathophysiology and finding novel management strategies. *J Clin Med*. 2019;8(4):1-5.
 37. Iwamoto K, Moriwaki M, Miyake R, Hide M. *Staphylococcus aureus* in atopic dermatitis: Strain-specific cell wall proteins and skin immunity. *International. JSA*. 2019;68:309–15.
 38. Berdyshev E, Goleva E, Bronova I, Dyjack N, Rios C, et al. Lipid abnormalities in atopic skin are driven by type 2 cytokines. *JCI Insight*. 2018;3:1-13.
 39. Goleva E, Berdyshev E, Leung DYM. Epithelial barrier repair and prevention of allergy. *Journal of Clinical Investigation*. *J Clin Invest*. 2019;129:1463–74.
 40. Leung DYM, Guttman-Yassky E. Deciphering the complexities of atopic dermatitis: Shifting paradigms in treatment approaches. *J Allergy Clin Immunol*. Mosby Inc.; 2014;134:769–79.
 41. Clausen ML, Edslev SM, Andersen PS, Clemmensen K, Kroghfelt K, et al. *Staphylococcus aureus* colonization in atopic eczema and its association with filaggrin gene mutations. *Br J Dermatol*. 2017;177(5):1394–400.
 42. Miajlovic H, Fallon PG, Irvine AD, Foster TJ. Effect of filaggrin breakdown products on growth of and protein expression by *Staphylococcus aureus*. *J Allergy Clin Immunol*. 2010;126(6):1184-88.
 43. Geoghegan JA, Irvine AD, Foster TJ. *Staphylococcus aureus* and Atopic Dermatitis: A Complex and Evolving Relationship. *Trends in Microbiology*. Elsevier Ltd; 2018;26: 484–97.

44. McAleer MA, Irvine AD. The multifunctional role of filaggrin in allergic skin disease. *J Allergy Clin Immunol.* 2013; 131: 280–91.
45. Kim BE, Leung DYM. Significance of skin barrier dysfunction in atopic dermatitis. *Allergy, Asthma and Immunology Research. Korean Academy of Asthma, Allergy and Clinical Immunology.* 2018;10: 207–15.
46. Li S, Villarreal M, Stewart S, Choi J, Ganguli-Indra G, et al. Altered composition of epidermal lipids correlates with *Staphylococcus aureus* colonization status in atopic dermatitis. *Br J Dermatol.* Blackwell Publishing Ltd. 2017;177:125–7.
47. Stalder JF, Fluhr JW, Foster T, Glatz M, Proksch E. The emerging role of skin microbiome in atopic dermatitis and its clinical implication. *J Dermatolog Treat.* Taylor and Francis Ltd. 2019;30:357–64.
48. Zhu TH, Zhu TR, Tran KA, Sivamani RK, Shi VY. Epithelial barrier dysfunctions in atopic dermatitis: a skin–gut–lung model linking microbiome alteration and immune dysregulation. *Br J Dermatol.* Blackwell Publishing Ltd. 2018;179:570–81.
49. Ljm Zeeuwen P, Boekhorst J, van den Bogaard EH, de Koning HD, Mc Van De Kerkhof P, et al. Microbiome dynamics of human epidermis following skin barrier disruption. *Genome Biol.* 2012; 13(11): 1-15.
50. Wollina U. Microbiome in atopic dermatitis. *Clin Cosmet Investig Dermatol.* Dove Medical Press Ltd. 2017;10:51–6.
51. Nakatsuji T, Gallo RL. The role of the skin microbiome in atopic dermatitis. *Ann Allergy Asthma Immunol. American College of Allergy, Asthma and Immunology;* 2019;122:263–69.
52. Mallbris L, Carlén L, Wei T, Heilborn J, Nilsson MF, et al. Injury downregulates the expression of the human cathelicidin protein hCAP18/LL-37 in atopic dermatitis. *Exp Dermatol.* 2010;19(5):442–49.
53. Tankersley A, Frank MB, Bebak M, Brennan R. Early effects of *Staphylococcus aureus* biofilm secreted products on inflammatory responses of human epithelial keratinocytes. *J Inflamm.* 2014; 11(17): 1-10.
54. Williams MR, Nakatsuji T, Gallo RL. *Staphylococcus aureus*: Master

- Manipulator of the Skin. *Cell Host Microbe*. Cell Press. 2017;22: 579–81.
55. Brauweiler AM, Goleva E, Leung DYM. Interferon- γ Protects from Staphylococcal Alpha Toxin-Induced Keratinocyte Death through Apolipoprotein L1. *J Invest Dermatol*. 2016;136(3):658–64.
 56. Leung DYM. The microbiome and allergic diseases: A struggle between good and bad microbes. *Ann Allergy Asthma Immunol*. 2019;122(3):231–2.