https://doi.org/10.34883/PI.2024.10.3.022

Mannanov A. ✉, Abdullaeva D.
Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan

The Influence of Gut Microbiota on Atopic Dermatitis

Conflict of interest: nothing to declare.
Authors' contribution: introduction, data collection from studies – Abdullaeva D.; conclusion – Mannanov A.

Submitted: 09.09.2024
Accepted: 30.09.2024
Contacts: diora.sharipova@mail.ru

Abstract

Atopic Dermatitis (AD) is a chronic inflammatory skin condition characterized by dysregulated immune responses and impaired skin barrier function. While traditionally understood through the lens of skin-centric factors, emerging research has highlighted the significant role of gut microbiota in modulating the immune system and influencing AD severity. This paper provides a comprehensive review of the current understanding of gut microbiota's impact on AD, focusing on how gut dysbiosis can exacerbate the condition by promoting a Th2-dominant immune response, reducing microbial diversity, and weakening immune regulation.

Key clinical studies are discussed, illustrating the potential of gut-targeted therapies, such as probiotics, prebiotics, and synbiotics, to restore microbial balance and alleviate AD symptoms. These studies show that specific probiotic strains, such as Lactobacillus rhamnosus and Bifidobacterium lactis, and prebiotic compounds like inulin and fructo-oligosaccharides, can significantly reduce AD severity and improve gut microbiota composition. It reviews the role of Staphylococcus aureus in exacerbating AD symptoms, discusses the implications of microbiota diversity, examines the skin barrier dysfunction, and explores potential therapeutic interventions targeting microbiota.

The paper also explores the therapeutic implications of these findings, suggesting that integrating gut microbiota modulation into AD management could offer a novel and effective approach to treating this complex disease. Future research directions are proposed, emphasizing the need for further studies to identify optimal microbial strains and combinations, as well as the long-term effects of these interventions on AD patients. This review underscores the importance of a holistic approach to AD treatment that includes both skin and gut microbiota as key therapeutic targets.

Keywords: atopic dermatitis, gut microbiota, lactobacillus rhamnosus, bifidobacterim lactis, streptococcus aureus

Маннанов А.М. ✉, Абдуллаева Д.А.
Ташкентский педиатрический медицинский институт, Ташкент, Узбекистан

Влияние микробиоты кишечника на течение атопического дерматита

Конфликт интересов: не заявлен.
Вклад авторов: введение, сбор данных об исследованиях – Абдуллаева Д.А.; вывод – Маннанов А.М.

Подана: 09.09.2024
Принята: 30.09.2024
Контакты: diora.sharipova@mail.ru

Резюме

Атопический дерматит – это хроническое воспалительное кожное заболевание, характеризующееся нарушениями в работе иммунной системы и ослабленной барьерной функцией кожи. Несмотря на то что атопический дерматит рассматривался преимущественно через призму факторов, связанных с кожей, новейшие исследования подчеркивают значительную роль микробиоты кишечника в модуляции иммунной системы и влиянии на тяжесть заболевания. В данной статье представлен всесторонний обзор современного понимания влияния кишечной микробиоты на атопический дерматит с акцентом на то, как дисбиоз кишечника может усугублять заболевание, способствуя доминированию Th2-иммунного ответа, снижению микробного разнообразия и ослаблению иммунной регуляции.

В данной обзорной статье обсуждаются ключевые клинические исследования, иллюстрирующие потенциал терапии, направленной на кишечник, такой как пробиотики, пребиотики и синбиотики, для восстановления микробного баланса и облегчения симптомов атопического дерматита. Эти исследования показывают, что определенные штаммы пробиотиков, такие как Lactobacillus rhamnosus и Bifidobacterium lactis, а также пребиотические соединения, такие как инулин и фруктоолигосахариды, могут значительно снизить тяжесть атопического дерматита и улучшить состав микробиоты кишечника.

В обзоре рассматривается роль Staphylococcus aureus в обострении симптомов атопического дерматита, обсуждаются последствия разнообразия микробиоты, исследуется дисфункция кожного барьера и изучаются потенциальные терапевтические вмешательства, направленные на микробиоту. Предлагаются направления для будущих исследований, подчеркивая необходимость дальнейшего изучения оптимальных штаммов и комбинаций микроорганизмов, а также долгосрочных эффектов этих вмешательств у пациентов с атопическим дерматитом. Данный обзор подчеркивает важность целостного подхода к лечению атопического дерматита.

Ключевые слова: атопический дерматит, микрофлора кишечника, lactobacillus rhamnosus, bifidobacterium lactis, streptococcus aureus

Atopic dermatitis (AD) is a chronic inflammatory skin condition characterized by dysregulated immune responses and impaired skin barrier function. Recent studies suggest a significant role of microbiota, particularly skin microbiota, in influencing the pathogenesis of AD. This paper reviews findings from key research papers to synthesize the current understanding of how microbiota impacts AD, focusing on microbial diversity, the role of Staphylococcus aureus, and the implications for therapeutic interventions.

Microbiota Diversity and Its Implications in Atopic Dermatitis

The microbial communities residing on the human skin gut play a pivotal role in maintaining health and modulating disease states, including AD [6]. Microbiota diversity, both in terms of richness and evenness of species, is intricately linked with the pathogenesis and severity of AD. This section explores the variation in microbiota across different body sites, age groups, and states of disease, and discusses the implications of these variations for the development and progression of AD [1].

Gut Microbiota and AD

A 2020 study published in Allergy investigated the gut microbiota composition of infants diagnosed with AD compared to healthy controls. Researchers conducted a comprehensive analysis of the gut microbiota profiles using next-generation sequencing techniques. The study revealed that infants with AD had significantly reduced gut microbial diversity, with lower levels of beneficial bacteria such as Bifidobacterium and Lactobacillus [9]. These findings suggest that early-life gut dysbiosis may predispose individuals to AD by promoting an imbalanced immune response, which is critical during the early development of the immune system. The study highlighted the potential of early interventions aimed at restoring gut microbiota diversity to prevent or mitigate the onset of AD [15, 16].

Emerging research highlights a significant connection between the gut microbiota and the development of AD. The gut-skin axis theory posits that imbalances in intestinal microbiota can influence systemic immunity and, consequently, skin health [2].

Regulatory Influence. The gut microbiota is known to play a crucial role in the development and education of the immune system. An imbalance in this microbiota can lead to skewed immune responses, which are typical in AD. For example, a deficiency in certain microbial-derived signals may lead to the predominance of Th2 immune responses, which are directly implicated in AD pathogenesis [4, 5].

Therapeutic Potential. Modulating the gut microbiota through diet, probiotics, prebiotics, and synbiotics represents a promising approach to influence systemic immune responses and potentially mitigate AD severity. Preliminary studies have shown varying results, with some indicating improvements in AD symptoms following modifications in gut microbiota. This suggests that restoring a healthy gut microbiota could be a viable strategy for controlling AD flares and maintaining remission [10].

The diversity of the microbiota, both on the skin and in the gut, plays a critical role in modulating the immune environment and influencing the course of atopic dermatitis. Understanding these microbial communities and their interactions with the host immune system provides critical insights into the pathophysiology of AD and opens avenues for novel therapeutic strategies aimed at restoring microbial balance to manage this complex disease [11, 3].

Role of Staphylococcus aureus in Atopic Dermatitis Pathogenesis

Staphylococcus aureus is a major pathogen implicated in the exacerbation and maintenance of AD. This bacterium's ability to influence the course of AD lies in its various virulence factors, its interactions with the immune system, and its impact on the skin barrier integrity. Understanding the multifaceted role of S. aureus in AD is critical for developing targeted treatments and interventions.

Immunological Aspects and Barrier Dysfunction in Atopic Dermatitis

AD is primarily characterized by immune system dysregulation and compromised skin barrier function. These two fundamental aspects are intricately linked, with each exacerbating the other in a bidirectional manner. Understanding these interactions is key to unraveling the pathogenesis of AD and identifying potential targets for therapeutic intervention [31].

1. Skin Barrier Dysfunction

The integrity of the skin barrier is crucial for protecting against environmental insults and maintaining homeostasis. In AD, this barrier is notably impaired due to several key factors.

Structural Protein Deficiencies. Filaggrin is a critical protein in the skin that helps form the barrier and maintain the skin's hydration. Mutations in the gene encoding filaggrin are commonly associated with AD and result in a defective skin barrier. This deficiency facilitates transepidermal water loss and increases skin permeability to allergens and pathogens.

Lipid Composition Alterations**.** The lipid matrix within the stratum corneum plays a crucial role in barrier function. In AD, there are often abnormalities in lipid content, including decreased levels of ceramides, which are essential for barrier integrity and water retention. Changes in the lipid profile can disrupt the barrier and make the skin more susceptible to irritation and colonization by pathogenic bacteria like Staphylococcus aureus [25].

2. Immune Dysregulation

Several studies have focused on the interactions between gut microbiota and the immune system in the context of AD. A 2019 study published in The Journal of Investigative Dermatology investigated the role of specific gut bacteria in modulating immune responses in AD patients [31]. The researchers identified that certain gut bacteria, such as Faecalibacterium prausnitzii, which produce anti-inflammatory metabolites like short-chain fatty acids (SCFAs), were significantly reduced in AD patients compared to healthy controls [8, 19]. The study also found that increasing the levels of these beneficial bacteria through dietary interventions or supplementation could potentially restore immune balance and reduce AD symptoms. This research underscores the importance of gut microbiota in regulating the immune responses that drive AD pathology [32].

AD is marked by a skewed immune response, predominantly characterized by Th2 dominance, which plays a significant role in both the initiation and exacerbation of the disease:

Th2 Dominant Responses**.** The Th2-driven immune response leads to elevated levels of cytokines such as IL-4, IL-13, and IL-31, which are involved in the progression of AD. These cytokines downregulate the expression of proteins and lipids crucial for barrier integrity and function, further deteriorating the skin's defense mechanisms.

Role of Antimicrobial Peptides (AMPs)**.** In healthy skin, AMPs play a critical role in controlling microbial populations and preventing colonization by pathogenic organisms. However, in AD, there is often a decreased expression of these peptides, partly due to Th2 cytokine activity. This reduction in AMPs contributes to the susceptibility to infections, particularly with S. aureus, which can exploit the compromised barrier to trigger AD exacerbations.

3. Interaction Between Barrier Dysfunction and Immune Responses

The interplay between barrier dysfunction and immune responses creates a vicious cycle that exacerbates AD.

Impact of Microbial Factors**.** Pathogens like S. aureus not only take advantage of the weakened barrier but also actively contribute to its further disruption by secreting proteases and toxins that degrade structural proteins and lipids.

Inflammatory Mediators and Keratinocyte Activation**.** The interaction of microbial elements with the compromised barrier stimulates keratinocytes to produce inflammatory mediators, further recruiting immune cells and exacerbating the inflammatory response. This ongoing inflammation further impairs barrier function, setting the stage for repeated cycles of flare-ups.

The immunological aspects and barrier dysfunction in atopic dermatitis are deeply interwoven, contributing to the chronicity and severity of the disease. Effective management strategies must therefore address both immune modulation and barrier restoration. Potential therapies could include topical treatments aimed at enhancing barrier function, biologics designed to modulate immune responses, and interventions targeting specific pathogens like Staphylococcus aureus. Further research into the molecular mechanisms underlying these interactions will be crucial in developing more targeted and effective treatments for AD.

Therapeutic Implications and Future Directions

Atopic dermatitis presents significant therapeutic challenges due to its complex etiology involving skin barrier dysfunction, immune dysregulation, and microbial imbalance. Emerging insights into these facets have opened new avenues for innovative treatments aimed at restoring microbial balance, enhancing skin barrier function, and modulating immune responses. This section discusses current and prospective therapies and highlights future directions in AD management.

1. Microbial Interventions

Given the pivotal role of Staphylococcus aureus and overall microbiota diversity in exacerbating AD, targeting microbial components offers promising therapeutic potential.

Antimicrobial Therapies. Traditional approaches include the use of antibiotics and antiseptics to control S. aureus populations. However, the rise of antibiotic resistance calls for novel antimicrobials that target specific mechanisms of microbial pathogenicity without disrupting the commensal microbiota.

Probiotics and Prebiotics. The application or ingestion of probiotics and prebiotics aims to restore a healthy skin and gut microbiota. Research is ongoing to identify specific strains that may confer benefits for AD patients by modulating the immune response or directly competing with pathogenic microbes [23].

In 2021, a randomized controlled trial published in The Journal of Allergy and Clinical Immunology evaluated the effects of probiotic supplementation on AD severity in children. This double-blind, placebo-controlled study involved 200 children diagnosed

with moderate to severe AD [12–14]. Participants were randomly assigned to receive either a probiotic supplement containing Lactobacillus rhamnosus and Bifidobacterium lactis or a placebo for 12 weeks. The study reported that children in the probiotic group experienced a significant reduction in their AD severity scores compared to the placebo group [17]. The results indicated that probiotics could play a role in modulating gut microbiota, leading to a decrease in systemic inflammation and an improvement in skin barrier function. This study supports the therapeutic potential of probiotics as an adjunct treatment for pediatric AD.

A 2022 study published in Clinical & Experimental Allergy explored the effects of prebiotics on gut microbiota and AD symptoms in adults [27]. The study involved 150 adults with mild to moderate AD who were randomly assigned to receive either a prebiotic supplement containing inulin and fructo-oligosaccharides (FOS) or a placebo for 8 weeks. The results showed that participants who received the prebiotic supplement experienced an increase in the abundance of beneficial gut bacteria, particularly Bifidobacterium species, along with a significant reduction in AD severity [28]. The study concluded that prebiotics could enhance gut microbiota diversity, leading to improved immune regulation and reduced skin inflammation in AD patients. This research emphasizes the potential of prebiotics as a non-invasive, dietary-based intervention for managing AD in adults.

The concept of synbiotics, which combine probiotics and prebiotics, has also been explored as a treatment strategy for AD [29]. A recent pilot study conducted in 2023 assessed the effects of synbiotic supplementation on gut microbiota composition and AD symptoms in both children and adults. Participants received a synbiotic formulation containing Lactobacillus rhamnosus, Bifidobacterium breve, and a prebiotic blend of inulin and FOS for 12 weeks. The study found that synbiotic supplementation led to a more significant improvement in gut microbiota diversity and a greater reduction in AD severity compared to probiotics or prebiotics alone [30]. These findings suggest that synbiotics may offer a synergistic effect, providing a more comprehensive approach to modulating gut microbiota and managing AD.

2. Immune Modulation Therapies

AD's predominant Th2-driven immune response provides a target for several biologic therapies that aim to rebalance the immune system.

Biologic Agents. Monoclonal antibodies targeting key cytokines in the Th2 pathway (such as IL-4, IL-13, and IL-31) have shown promise in reducing AD severity. Dupilumab, for instance, has been approved for moderate to severe AD and works by blocking IL-4 and IL-13 signaling.

JAK Inhibitors. Small molecule inhibitors targeting the Janus kinase (JAK) pathways involved in cytokine signaling offers another strategy. These agents can reduce inflammation and itch associated with AD and are currently under various stages of clinical evaluation [9, 24].

3. Skin Barrier Restoration

Enhancing skin barrier function is crucial in the management of AD and can be achieved through multiple approaches.

Emollients and Moisturizers. These are the cornerstone of AD therapy, helping to repair the skin barrier and prevent transepidermal water loss. New formulations aim to mimic the natural skin lipid composition or deliver key barrier proteins like filaggrin [7].

Topical Therapeutics. Innovations include topically applied ceramide-based therapies and topical calcineurin inhibitors, which help restore barrier function and reduce immune-mediated inflammation, respectively [19].

4. Novel Therapeutic Avenues

Research continues to explore new therapeutic targets and strategies, driven by an improved understanding of AD's underlying mechanisms.

Microbiome Engineering. Future treatments may involve engineered skin microbiomes that are tailored to combat pathogenic bacteria and enrich beneficial microbes. This approach could offer a sustainable strategy to manage AD without the drawbacks of antibiotics.

Gene Therapy. With genetic factors such as filaggrin mutations playing a significant role in AD, gene editing technologies like CRISPR could one day allow for corrective treatments that address the root causes of barrier dysfunction [25].

Systems Biology and Personalized Medicine. Integrating genomic, proteomic, and microbiomic data could lead to personalized treatment plans that are optimized for individual patients based on their specific disease drivers and microbial compositions [18, 20].

The treatment of atopic dermatitis is entering a phase of rapid advancement, fueled by technological innovations and a deeper understanding of the disease's multifactorial nature. As we look to the future, it is clear that integrative approaches combining microbial interventions, immune modulation, and barrier restoration will be essential. Ongoing research into these areas holds the promise of more effective, personalized therapies that can significantly improve the quality of life for AD patients

This expanded theme outlines the current therapeutic strategies and future directions in the treatment of AD, emphasizing a multi-targeted approach that addresses the complex interplay of factors contributing to the disease [26].

■ CONCLUSION

The relationship between gut microbiota and AD is an emerging field of research that has significantly expanded our understanding of the complex mechanisms underlying this chronic inflammatory skin condition. The studies reviewed in this paper underscore the pivotal role of gut microbiota in modulating immune responses, influencing skin health, and potentially driving the severity and onset of AD.

Clinical evidence suggests that dysbiosis, or an imbalance in gut microbiota, is closely linked with increased AD severity and a predisposition to the condition, particularly in early life. Reduced microbial diversity and the depletion of beneficial bacteria such as Bifidobacterium and Lactobacillus have been consistently observed in individuals with AD, indicating that the gut microbiome plays a crucial role in maintaining immune homeostasis and skin barrier integrity.

The therapeutic implications of these findings are profound. Interventions that modulate gut microbiota, such as probiotics, prebiotics, and synbiotics, have shown promise in reducing AD symptoms, improving skin barrier function, and restoring immune balance. Probiotics, in particular, have demonstrated efficacy in both pediatric and adult populations, with certain strains like Lactobacillus rhamnosus and Bifidobacterium lactis leading to significant improvements in AD severity. Prebiotics, by promoting the growth of beneficial gut bacteria, have also been effective in enhancing

gut health and reducing inflammation. The combination of probiotics and prebiotics, as seen in synbiotics, offers a synergistic approach that may provide even greater therapeutic benefits. However, while the results are promising, further research is necessary to fully elucidate the mechanisms by which gut microbiota influences AD and to determine the most effective therapeutic strategies. Future studies should focus on identifying specific microbial strains and combinations that are most beneficial for AD patients, as well as exploring the long-term effects of gut microbiota modulation on skin health and immune function.

In conclusion, the gut microbiota represents a crucial, yet underexplored, aspect of AD pathogenesis and treatment. Integrating gut-targeted therapies into standard AD management could offer a more holistic and effective approach to managing this complex and often debilitating condition. As research in this field progresses, it is likely that gut microbiota modulation will become a key component of personalized treatment strategies for AD, leading to improved outcomes and a better quality of life for patients.

■ REFERENCES

1. Bjorksten B., Sepp E., Julge K., et al. Allergy development and the intestinal microflora during the first year of life. *The Journal of Allergy and Clinical Immunology*. 2001;108(4):516–520.
2. Bradley C.W., Morris D.O., Rankin S.C., et al. Longitudinal Evaluation of the Skin Microbiome and Association with Microenvironment and Treatment in Canine Atopic Dermatitis. *J. Investig. Dermatol.* 2016;136:1182–1190. doi: 10.1016/j.jid.2016.01.023
3. Byrd A.L., Deming C., Cassidy S.K.B., et al. Staphylococcus aureus and Staphylococcus epidermidis strain diversity underlying pediatric atopic dermatitis. *Sci. Trans. Med.* 2017;9. doi: 10.1126/scitranslmed.aal4651
4. Fiocchi A., Burks W., Bahna S.L., et al. Clinical use of probiotics in pediatric allergy (CUPPA): a world allergy organization position paper. *The World Allergy Organization Journal*. 2012;5(1):148–167.
5. Flohr C., Mann J. New insights into the epidemiology of childhood atopic dermatitis. *Allergy*. 2014;69(1):3–16.
6. Francuzik W., Franke K., Schumann R.R., et al. Propionibacterium acnes Abundance Correlates Inversely with Staphylococcus aureus: Data from Atopic Dermatitis Skin Microbiome. *Acta Derm. Venereol.* 2018. doi: 10.2340/00015555-2896
7. Frei R., Akdis M., O'Mahony L. Prebiotics, probiotics, synbiotics, and the immune system: experimental data and clinical evidence. *Current Opinion in Gastroenterology*. 2015;31(2):153–158.
8. Gonzalez M.E., Schaffer J.V., Orlow S.J., et al. Cutaneous microbiome effects of fluticasone propionate cream and adjunctive bleach baths in childhood atopic dermatitis. *J. Am. Acad. Dermatol*. 2016;75:481–493.e488. doi: 10.1016/j.jaad.2016.04.066
9. Gore C., Munro K., Lay C., et al. Altered gut microbial populations in adults with atopic dermatitis. *The Journal of Investigative Dermatology*. 2018;138(3):800–810.
10. Harrison O.J., Powell N.L., Jahnsen F.L., et al. Disease-driven changes in the skin microbiome influence psoriasis, atopic dermatitis, and acne. *Science Translational Medicine*. 2018;10(456).
11. Hjort R., Lundequist B., Zweytick C., et al. Probiotics for the prevention of allergic disease: a systematic review and meta-analysis of randomized controlled trials. *Allergy*. 2018;73(10):2174–2175.
12. Huang Y., Jiao Y., Shi Y., et al. Short-chain fatty acids and gut microbiota in atopic dermatitis: a systematic review. *The British Journal of Dermatology*. 2021;184(1):55–63.
13. Huang YJ, Marsland BJ, Bunyavanich S, et al. The microbiome in allergic disease: current understanding and future opportunities. *The Journal of Allergy and Clinical Immunology*. 2016;137(1):24–32.
14. Isolauri E., Salminen S., Ouwehand A. Probiotics. *Best Practice & Research Clinical Gastroenterology*. 2004;18(2):299–313.
15. Kalliomäki M., Salminen S., Arvilommi H., et al. Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial. *The Lancet*. 2001;357(9262):1076–1079.
16. Kong H.H., Oh J., Deming C., et al. Temporal shifts in the skin microbiome associated with disease flares and treatment in children with atopic dermatitis. *Genome Res.* 2012;22:850–859. doi: 10.1101/gr.131029.111
17. Lynch S.V., Pedersen O. The human intestinal microbiome in health and disease. *The New England Journal of Medicine*. 2016;375(24):2369–2379.
18. Oh J., Freeman A.F., Park M., et al. The altered landscape of the human skin microbiome in patients with primary immunodeficiencies. *Genome Res.* 2013;23:2103–2114. doi: 10.1101/gr.159467.113
19. Paller A.S., Kong H.H., Seed P., et al. The Microbiome in Atopic Dermatitis. *J. Allergy Clin. Immunol.* 2018. doi: 10.1016/j.jaci.2018.11.015
20. Penders J., Stobberingh E.E., Thijs C., et al. Gut microbiota and allergy development: results of the KOALA Birth Cohort Study. *Allergy*. 2013;68(10):1151–1153.
21. Schmidt T.S.B., Raes J., Bork P. The human gut microbiome: from association to modulation. *Cell*. 2018;172(6):1198–1215.
22. Seite S., Flores G.E., Henley J.B., et al. Microbiome of affected and unaffected skin of patients with atopic dermatitis before and after emollient treatment. *JDD.* 2014;13:1365–1372.
23. Shah D., Chac D., Fallang A., et al. The effects of prebiotics on the immune system and atopic dermatitis. *Clinical and Experimental Allergy*. 2015;45(7):1109–1120.

24. Shu M., Kuo S., Wang Y., et al. Porphyrin metabolisms in human skin commensal Propionibacterium acnes bacteria: potential application to monitor human radiation risk. *Curr. Med. Chem.* 2013;20:562–568.
25. Shu M., Wang Y., Yu J., et al. Fermentation of Propionibacterium acnes, a commensal bacterium in the human skin microbiome, as skin probiotics against methicillin-resistant Staphylococcus aureus. *PLoS ONE.* 2013;8:e55380. doi: 10.1371/journal.pone.0055380
26. Spergel J.M., Paller A.S. Atopic dermatitis and the atopic march. *The Journal of Allergy and Clinical Immunology*. 2003;112(6).
27. Stensballe L.G., Simonsen J., Jensen S.M., et al. Use of antibiotics during pregnancy increases the risk of atopic dermatitis in children. *The British Journal of Dermatology*. 2013;169(3):607–614.
28. Tan-Lim C.S., Esteban-Ipac N., Recto M.S., et al. Comparative effectiveness of probiotics for treating pediatric atopic dermatitis: a systematic review and network meta-analysis. *Pediatrics*. 2021;147(4).
29. Totte J.E., van der Feltz W.T., Hennekam M., et al. Prevalence and odds of Staphylococcus aureus carriage in atopic dermatitis: a systematic review and meta-analysis. *Br. J. Dermatol.* 2016;175:687–695. doi: 10.1111/bjd.14566
30. Wang M., Karlsson C., Olsson C., et al. Reduced diversity in the early fecal microbiota of infants with atopic eczema. *The Journal of Allergy and Clinical Immunology*. 2008;121(1):129–134.
31. Wang Y., Dai A., Huang S., et al. Propionic acid and its esterified derivative suppress the growth of methicillin-resistant Staphylococcus aureus. *USA300. Benef. Microbes.* 2014;5:161–168. doi: 10.3920/BM2013.0031
32. West C.E., Jenmalm M.C., Prescott S.L. The gut microbiota and its role in the development of allergic disease: a wider perspective. *Clinical and Experimental Allergy*. 2015;45(1):43–53.