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CURRENT USE OF "HEALTHY" BACTERIA (PROBIOTICS) IN ALLERGY (A NARRATIVE REVIEW)

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რეზიუმე

ადამიანის მიკრობიოტა მნიშვნელოვან როლს ასრულებს იმუნური სისტემის რეგულაციაში, ხოლო მისი დისბალანსი ასოცირებულია ალერგიულ დაავადებებთან, როგორებიცაა ატოპიური დერმატიტი, ალერგიული რინიტი და ასთმა. პრობიოტიკები განიხილება, როგორც მიკრობიოტას აღდგენისა და იმუნური პასუხების მოდულირების პერსპექტიული საშუალება. განხილულ იქნა 2010–2025 წლების პერიოდში გამოქვეყნებული 34 კვლევა, მათ შორის რანდომიზებული კონტროლირებადი კვლევები, კლინიკური კვლევები და სისტემური მიმოხილვები, ფოკუსით ბავშვთა პოპულაციაზე. შედეგებმა აჩვენა, რომ კონკრეტულ პრობიოტიკულ საშუალებებს შეუძლიათ შეამცირონ ალერგიული სიმპტომები, დააქვეითონ Th2 ტიპის ციტოკინები (IL-4, IL-5, IL-13), გაზარდონ IFN-γ, გააუმჯობესონ კლინიკური სიმპტომების ქულები (SCORAD, TNSS, C-ACT) და მოახდინონ ანთებითი miRNA-ების მოდულაცია. ბავშვები პრობიოტიკებზე უფრო მაღალი მგრძნობელობით გამოირჩევიან, რაც, სავარაუდოდ, იმუნური სისტემის პლასტიკურობითა და მიკრობიოტას განვითარების ეტაპებით აიხსნება. პრობიოტიკების გამოყენებისას სერიოზული გვერდითი მოვლენები არ დაფიქსირებულა. მიუხედავად იმისა, რომ პრობიოტიკები ვერ ჩაანაცვლებს ტრადიციულ სამკურნალო საშუალებებს, ისინი წარმოადგენს პერსპექტიულ და უსაფრთხო დანამატს ალერგიული დაავადებების პრევენციისა და მართვისთვის, განსაკუთრებით ბავშვებში. აუცილებელია დამატებითი კვლევები ეფექტური შტამების, დოზირების სქემებისა და სამიზნე პოპულაციების დასადგენად.

Introduction. A variety of studies have begun highlighting the significance of the microbiome in relation to health and illness since its identification. The microbiome can be divided into categories based on specific areas, including gut, oral, respiratory, and skin microbiota. These microbial communities coexist with their host, aiding in the maintenance of homeostasis and the modulation of immune responses. An imbalance in the microbiome can lead to dysfunctions within the body and contribute to a range of diseases like cardiovascular issues, cancers, respiratory diseases, and notably, allergic diseases such as asthma, atopic dermatitis, and allergic rhinitis. Investigating variations in the microbiome presents considerable promise for disease prediction, as longitudinal changes - particularly concerning functional genetic pathways instead of merely taxonomic composition - have been observed to precede the onset of numerous metabolic, autoimmune, and neuropsychiatric conditions [1]. The composition and resilience of the microbiome are intricately influenced by host genetic and environmental factors, including diet,

antibiotic use, and contemporary hygiene practices. With advancements in DNA sequencing technology becoming faster and more affordable, there is a potential for individualized microbiome assessments to become a standard diagnostic approach, allowing for preventive measures tailored to an individual's unique microbial and genetic characteristics [2].

Acknowledging the microbiome's crucial role in health and illness, there has been a growing interest in strategies to modify its composition for maintaining or restoring microbial equilibrium. Among these strategies, probiotics - live microorganisms that provide health benefits to the host - are extensively researched. Probiotics typically consist of gram-positive bacteria (such as Lactobacillus and Bifidobacterium) or yeasts (like Saccharomyces), and they are present in both dietary supplements and fermented foods, including yogurt, kefir, and Matsoni [3,4]. They are thought to exert positive effects by improving gastrointestinal function, enhancing mucosal immunity, and restoring balance to dysbiotic microbial communities. Probiotics have been studied for various conditions, such as Clostridium difficile-associated diarrhea, inflammatory bowel disease, atopic dermatitis, and other allergic diseases, although some uses lack conclusive evidence. Their effectiveness is significantly influenced by the strain, dosage, and viability of the microorganisms [5].

Recent studies have increasingly investigated the role of probiotics in preventing and modulating allergic diseases. The ways in which probiotics affect allergic responses are multifaceted and involve the modulation of both innate and adaptive immunity. For instance, strains of Lactobacillus can decrease pro-inflammatory responses by influencing the NF-κB signaling pathway and promote anti-inflammatory effects by triggering IL-10 production through the maturation of dendritic cells [6]. Specific probiotic species, such as Bifidobacterium animalis and B.longum, have been shown to increase the production of IFN-γ and TNF-α, while B. bifidum stimulates Th17 cells through IL-17 secretion. Furthermore, probiotics might assist in rebalancing the Th1/Th2 immune axis, which is frequently altered in allergic conditions. In vitro experiments with PBMCs from allergic individuals exposed to L. plantarum, L. lactis, L. casei, and Lactobacillus GG have shown decreases in Th2 cytokines like IL-4 and IL-5, while murine asthma models indicate that LGG and B. lactis alleviate allergic symptoms by inducing TGF-β [7]. Additional mechanisms include enhanced secretion of mucosal IgA and the modulation of allergen-specific T and B cell responses [8]. These immunological interactions encompass a complex network of genes, receptors, signaling molecules, and gut-associated lymphoid tissue, suggesting that probiotics have potential not only as a treatment but also for the prevention of allergic diseases.

Nevertheless, significant questions persist: Is it possible to reestablish microbial balance through specific interventions like probiotics and fecal microbiota transplantation? Could probiotics one day serve as a replacement for or a complement to conventional treatments such as antihistamines and corticosteroids in managing allergies? Regardless of the outcomes, it is evident that we are entering a groundbreaking period in the fields of microbiology and immunology - one that has the potential to transform our approaches to predicting, preventing, and treating allergic and immune-related conditions.

Methods: A thorough search of the literature was performed utilizing the following electronic databases: PubMed, PMC (PubMed Central), ScienceDirect. The purpose of the search was to find studies that assess the effectiveness of probiotics in managing allergic conditions, specifically atopic dermatitis, allergic rhinitis, and asthma in children.

The criteria for inclusion included: Human studies published from 2010 to 2025, Study designs that encompassed randomized controlled trials (RCTs), clinical trials, and systematic reviews or meta-analyses. The criteria for exclusion consisted of: Studies focused solely on animals, articles that were not fully accessible or published in a language other than English. The search strategy utilized combinations

of keywords such as "probiotics," "allergy," "children," "atopic dermatitis," "asthma," and "allergic rhinitis." After screening and eligibility assessment, a total of 34 studies were selected for inclusion, consisting of 12 randomized controlled trials, 6 clinical trials, and 6 systematic reviews or meta-analyses. This methodological framework enabled a focused evaluation of the clinical impact of probiotics on allergic disorders.

Results. To evaluate the therapeutic potential of probiotics in allergic disorders, numerous clinical studies have investigated their effects on symptom severity, immune modulation, and overall quality of life in atopic dermatitis (AD), allergic rhinitis, and asthma. The results concerning atopic dermatitis are summarized below.

Atopic dermatitis (AD) is a long-lasting inflammatory skin disorder that is especially common among infants and young children. Traditional treatments often involve the use of topical corticosteroids and immunosuppressants; however, recent research has underscored the potential role of probiotics as supplementary therapies owing to their effects on immune regulation and the gut-skin connection [9]. Numerous randomized controlled trials (RCTs) have shown the effectiveness of particular probiotic strains in pediatric patients. In a significant investigation by Cukrowska et al., which included 151 children under the age of two with AD and a cow's milk protein allergy, participants who received L. rhamnosus and L. casei strains for three months, in conjunction with an elimination diet, experienced marked reductions in SCORAD scores in both treatment groups ($p < 0.0001$), with the probiotic group demonstrating quicker improvement [10]. Likewise, a 12-week study conducted in Spain involving 50 children (ages 4–17) that utilized a blend of B. lactis, B. longum, and L. casei found a notably greater decrease in SCORAD scores (–19.2 points) in those given probiotics compared to a placebo [11]. Another study that investigated L. paracasei, L. fermentum, and their combination exhibited improvements in SCORAD and quality of life (QoL) scores ($p = 0.02$ - 0.03), along with significant reductions in IL-4 and IgE levels [12]. In adults, a meta-analysis encompassing six RCTs ($n = 241$) indicated noteworthy enhancements in SCORAD and QoL following the use of probiotics. However, no changes were observed in itch intensity, DLQI, IL-4, IFN-γ, or IgE levels [13]. This implies that probiotics may be more beneficial for treating pediatric AD.

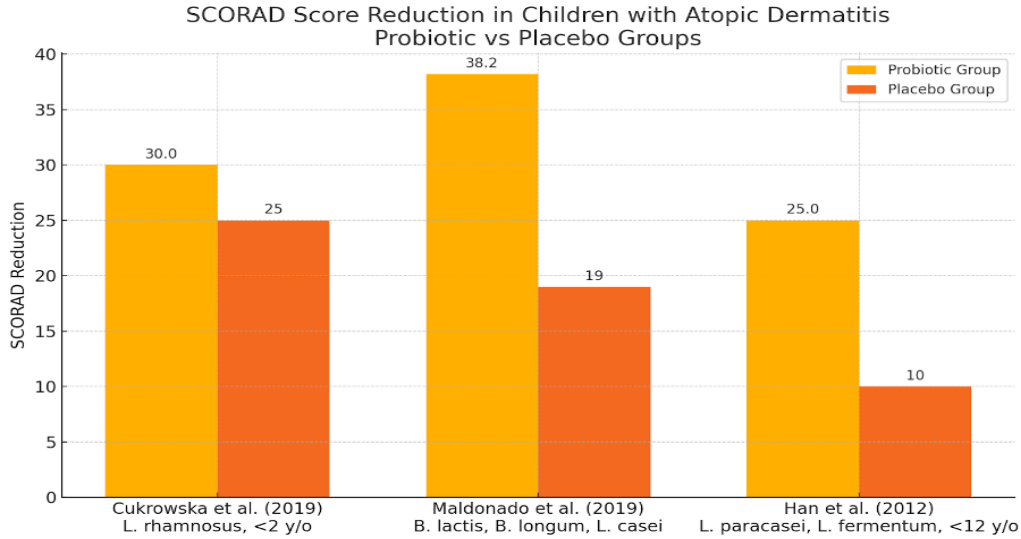

Figure 1. SCORAD score reduction in children with atopic dermatitis across three RCTs

Allergic rhinitis (AR) is a prevalent inflammatory disorder affecting the nasal mucosa, initiated by exposure to allergens. Recent clinical studies indicate that probiotics may act as a valuable supplementary therapy by influencing immune responses and easing symptoms, especially in children. In a four-week double-blind, placebo-controlled study, children aged 6 to 19 years who were administered

Bifidobacterium longum and Lactobacillus plantarum (NVP-1703) demonstrated significant decreases in total nasal symptom score (TNSS) when compared to the placebo group ($p = 0.011$), with enhancements noted in both morning and evening symptoms, along with reduced ratios of IL-4/IL-22 and IL-5/IL-22 [14]. A six-week investigation conducted in Karachi, involving 212 children (aged 6 to 60 months), evaluated Lactobacillus paracasei LP-33 against cetirizine. Both groups experienced symptom relief, but the probiotic group reported no side effects, indicating a positive safety profile [15]. In a year-long study with children aged 2 to 5 years suffering from allergic rhinitis or asthma, those consuming fermented milk containing L. casei encountered fewer rhinitis episodes (mean difference –1.6; 95% CI: –3.15 to –0.05) and shorter durations of diarrhea compared to those on placebo [16]. For adults, a five-week multicenter trial investigated the effects of ATOPRIN (L. paracasei LP-33) in conjunction with loratadine in a cohort of 425 individuals. The probiotic group reported notable enhancements in quality of life ($p = 0.0255$) and ocular symptoms ($p = 0.0029$) relative to placebo [17]. Together, these studies suggest that certain strains such as L. paracasei, L. plantarum, B. longum, and L. casei may enhance AR symptoms and overall quality of life, while also demonstrating a strong safety profile in both pediatric and adult populations.

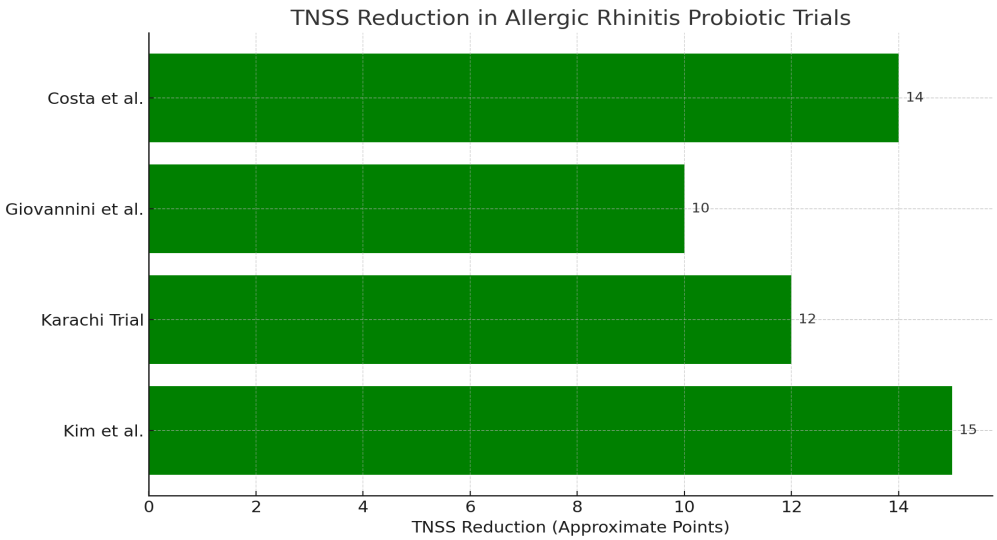

Figure 2. Approximate Total Nasal Symptom Score (TNSS) reduction reported in four randomized controlled trials assessing the efficacy of probiotics in allergic rhinitis.

Preventing allergic rhinitis, especially through microbiome-related approaches like probiotics, may significantly contribute to protecting both respiratory and oral health. Allergic rhinitis is linked to a higher likelihood of oral health issues, such as tooth decay, gum inflammation, and irregularities in orofacial development [21,22,23]. These connections are primarily due to nasal blockage that results in mouth breathing, which modifies salivary flow, pH levels, and the makeup of the oral microbiome. Young children with allergic rhinitis, particularly those under the age of six, seem to be especially susceptible to these impacts [24]. Considering these relationships, approaches designed to prevent or adjust allergic rhinitis may also assist in reducing related oral health problems.

Asthma is a long-term inflammatory disease of the airways characterized by reversible airflow limitation and immune system imbalance. Recent research indicates that probiotics could enhance clinical outcomes by influencing immune responses. In a double-blind randomized controlled trial, 40 adults with mild to moderate asthma were assigned either a multi-strain probiotic (composed of L. casei, L. acidophilus, L. rhamnosus, B. breve, B. longum, and S. thermophilus) or a placebo for a duration of eight weeks. Those in the probiotic group exhibited improvements in FEV_1 and FVC, a decrease in IL-4 levels, an increase in IFN-γ, and beneficial alterations in inflammatory miRNAs (↓ miR-146a, miR-16; ↑ miR-

133b). Some mild gastrointestinal symptoms were noted, but no serious adverse events occurred [18]. Research involving children yields comparable advantages. In one study, 49 children who received L. gasseri A5 demonstrated enhanced PEFR and lower symptom scores and cytokine levels (TNF-α, IL-12, IL-13) after 8 weeks [19]. Another investigation involving 160 children indicated that L. paracasei, L. fermentum, and their combination led to improved asthma management (↓ severity scores, ↑ C-ACT, ↓ IgE, ↑ PEFR) over a period of 3 months [20]. These results imply that probiotics may act as beneficial adjuncts in managing asthma, particularly in pediatric cases, although further extensive and prolonged studies are necessary to validate long-term effectiveness and ideal formulations.

Probiotics cause abovementioned potentially beneficial effects in the host via several mechanisms, which are divided into physiological and immunological sections [25]. Physiologically, probiotics impact the body by competing with harmful bacteria for attachment points on the mucosal surface, which helps to prevent their colonization. They strengthen the integrity of the epithelial barrier and enhance barrier function, partly by stimulating goblet cells that boost mucus production through the activation of mucin gene expression. These modifications contribute to a less favorable environment for the persistence of pathogens. On the immunological front, probiotics adjust epithelial signaling pathways, resulting in decreased NF-κB activation and lower expression of pro-inflammatory cytokines. A crucial mechanism includes restoring the balance between Th1 and Th2 cytokines, marked by an increase in regulatory cytokines such as IL-4, IL-5, and IL-13. Probiotics also activate dendritic cells, fostering the differentiation of $CD4^+$ $Foxp3^+$ regulatory T cells (Tregs) and the release of TGF-β and IL-10, which play key roles in immune tolerance. Additionally, they influence B cell activity, boosting the production of secretory IgA and IgG4 while decreasing allergen-specific IgE levels. In certain instances, the effects are mediated by short-chain fatty acids (SCFAs) interacting with G-protein coupled receptors (GPRs) and engaging TLR-2/TLR-4, subsequently activating downstream immunoregulatory pathways [26]

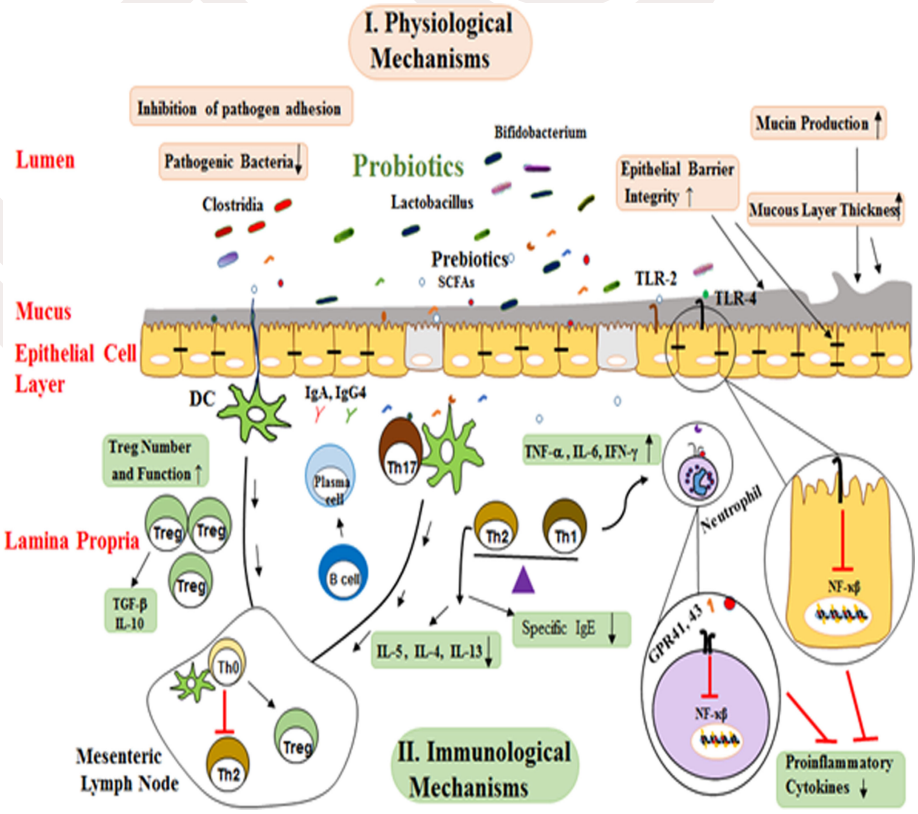

Figure 3. Possible mechanisms where probiotics affect allergic diseases. Adapted from Eslami, M., Bahar, A., Keikha, M., Karbalaei, M., Kobyliak, N. M., & Yousefi, B. (2020). *Probiotics function and modulation of the immune system in allergic diseases. Allergologia et Immunopathologia*, 48(6), 771–788.

Discussion: By analyzing the outcomes of the reviewed research papers, it can be concluded that the therapeutic strategies involving immunotherapy and the mitigation of side effects in the treatment of allergic diseases are still crucial objectives. The primary aim remains to foster long-term immune tolerance and facilitate individual recovery.

The studies indicate that probiotics have shown effectiveness in various domains, such as lowering levels of IL-4, IL-5, IL-13 (Th2 cytokines), IgE, and clinical assessments like SCORAD, C-ACT, TNSS, and RQLQ; elevating IFN-γ (a Th1 cytokine); and modifying inflammatory miRNAs (decreasing miR-146a and miR-16 while increasing miR-133b). These actions contributed to the rebalancing of Th1/Th2 immune responses, minimizing systemic inflammation, and enhancing epithelial barrier function, all achieved with a positive safety profile and no serious adverse effects reported.

Nonetheless, these advantages were not consistently seen across all individuals. The research pointed out significant differences between adults and children, with much greater effectiveness noted in pediatric populations. Within children, outcomes varied based on age, history of breastfeeding, and allergic sensitization, as indicated in a study on atopic dermatitis. This variability prompts important inquiries: Why is the effectiveness of probiotics typically higher in children than in adults and what accounts for the differences observed among children? The most feasible explanations may include increased immunological flexibility during early development, a healthier gut-immune relationship due to extended breastfeeding, and a more vigorous Th2 response in children, making them more amenable to probiotic influence.

Collectively, the current data endorses the clinical advantages of particular probiotic strains in treating and possibly preventing allergic diseases, especially in children, while boasting a robust safety profile. This does not mean that probiotics lack effectiveness in adults; for instance, a study involving ATOPRIN combined with loratadine in adults showed considerable improvement, affirming its supplementary value.

Despite these encouraging results, certain limitations remain, including small sample sizes, insufficient randomization, and limited diversity of strains, with some studies not providing clear information on conditions and targeted probiotic species. According to the existing evidence, probiotics should not be viewed as replacements for standard symptomatic treatments like antihistamines, but they may function as beneficial supplements that can decrease drug reliance or improve outcomes, particularly in pediatric populations.

Conclusion. Probiotics offer a promising complementary strategy for preventing and managing allergic conditions, particularly in children. They can mitigate inflammation, enhance immune tolerance, and alleviate allergic symptoms through various physiological and immunological mechanisms, including: suppression of Th2 responses and shift response to Th1 [27], butyrate production and increased induction of tolerance [28], increase of IL-10 and decreased inflammation [29] , decreased eosinophil level and serum specific IgE levels [30], increasing the IFN-γ/IL-4 ratio [31], increasing Treg cells and inducing their responses [32], increasing TGF-β responses and inhibiting allergic responses; and reducing the expression of metalloproteinase 9 and cell infiltration [33]. Moreover, recent studies indicate that probiotics may also help in preventing complications related to allergies that extend beyond the immune system, such as oral health issues and modifications in orofacial development associated with allergic rhinitis [24]. While not all effects are definitively established and the efficacy can vary by strain, the safety of probiotics and their immunoregulatory traits position them as an important part of prevention and treatment approaches for allergic conditions [34]. Future extensive and rigorously controlled studies are crucial to pinpoint the most effective strains, dosage schedules, and target populations to achieve the greatest clinical advantages.

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CURRENT USE OF "HEALTHY" BACTERIA (PROBIOTICS) IN ALLERGY (A NARRATIVE REVIEW)

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SUMMARY

The human microbiome plays a crucial role in immune regulation, and its imbalance is associated with allergic diseases such as atopic dermatitis, allergic rhinitis, and asthma. Probiotics have emerged as a potential strategy for restoring microbial balance and modulating immune responses. This review evaluated 34 studies published between 2010 and 2025, including randomized controlled trials, clinical trials, and systematic reviews, focusing on pediatric populations. The findings indicate that specific probiotic strains can reduce allergic symptoms, decrease Th2 cytokines (IL-4, IL-5, IL-13), increase IFN-γ, improve clinical scores (SCORAD, TNSS, C-ACT), and modulate inflammatory miRNAs. Children showed higher responsiveness, likely due to greater immune plasticity and microbiome development. No serious adverse effects were reported. Although probiotics are not a replacement for conventional therapies, they represent a promising, safe adjunct in the prevention and management of allergic diseases, particularly in children. Further research is needed to define optimal strains, dosages, and treatment protocols.

Keywords: Probiotics, Allergies, Microbiome, Hygiene hypothesis, Immunomodulation