POSTBIOTICS AS A NOVEL THERAPEUTIC STRATEGY IN THE PREVENTION AND MANAGEMENT OF FOOD ALLERGY: MECHANISTIC INSIGHTS AND CLINICAL PERSPECTIVES

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ABSTRACT

Food allergy (FA) is a growing global health concern, particularly in pediatric populations, and is closely linked to disruptions in gut microbial balance. Mounting evidence highlights the crucial role of the gut microbiota in immune system development and in modulating allergic sensitization. While probiotics have traditionally been employed to restore microbial equilibrium, recent studies suggest that their non-viable derivatives—postbiotics—offer comparable or even superior health benefits without the associated safety risks of live microbes. Postbiotics are bioactive compounds, including short-chain fatty acids (SCFAs), bacteriocins, and lipoteichoic acids, produced by probiotic microorganisms either during fermentation or after cell lysis. These molecules have demonstrated immunomodulatory, anti-inflammatory, and barrier-protective properties in various preclinical and clinical models. Mechanistically, postbiotics act by enhancing gut epithelial integrity, promoting regulatory T cell (Treg) development, modulating cytokine signaling, and inhibiting dysbiosis-related inflammatory responses. This review explores the biological role of postbiotics in the prevention and treatment of FA, elucidating their molecular mechanisms, therapeutic potential, and clinical relevance. Emphasis is placed on their interaction with the gut-immune axis and their role in restoring immune tolerance. Given their stability, safety, and multifunctional benefits, postbiotics represent a promising new class of functional agents for allergy management, particularly in infants and immunocompromised populations.

Keywords

Postbiotics; Food Allergy; Gut Microbiota; Immune Tolerance; Short-Chain Fatty Acids (SCFAs); Regulatory T Cells (Tregs); Epithelial Barrier; Microbiota-Derived Metabolites; Dysbiosis; Functional Foods

INTRODUCTION

Food allergy (FA) is one of the most prevalent immune disorders globally, often resulting from a breakdown in immune tolerance (Lopez-Fandiño, 2019). It poses a significant public health challenge, particularly in developed countries, where it adversely affects patients' quality of life (Iweala and Nagler, 2019). Over the past two decades, both the prevalence and severity of FA have increased markedly, with considerable health and economic impacts, especially in pediatric populations. These include higher medical visits, increased need for treatments, and additional healthcare expenditures (Gupta et al., 2011; Paparo et al., 2019).

To date, more than 170 food items have been identified as potential allergens. The most serious allergic reactions are commonly triggered by the consumption of fish, shellfish, peanuts, milk, tree nuts, soy, wheat, seeds, and eggs. However, the prevalence of specific food allergens may vary across individuals, populations, and geographical regions (Gupta et al., 2011; National Academies of Sciences and Medicine, 2017; Panel, 2010; Sicherer et al., 2010).

The development of FA is influenced by various risk factors, including genetic predispositions, environmental exposures, and their interactions, which contribute to immune tolerance failure (Canani, Gilbert, and Nagler, 2015; Paparo et al., 2017). Emerging evidence highlights the critical role of the gut microbiota in immune development. Gut microbial composition and diversity, particularly in early life, are now recognized as key modulators of immune responses and the onset of food allergies (Prince et al., 2015). Thus, establishing and maintaining gut microbial eubiosis is considered essential for the prevention and management of FA.

NON-ALLERGEN SPECIFIC THERAPIES AND THE ROLE OF PROBIOTICS

In recent years, a variety of therapeutic strategies have been developed to address FA, encompassing both allergen-specific and non-allergen-specific approaches. These include:

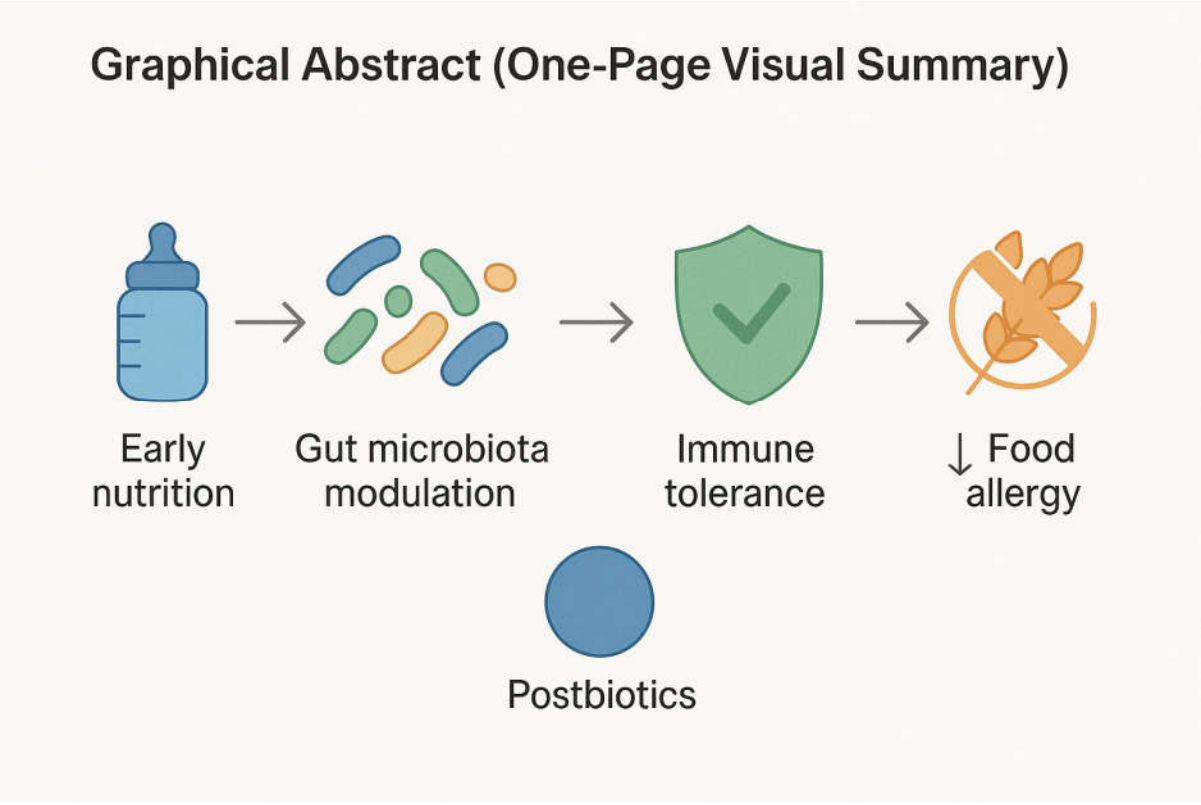
1. Enhancing specific IgG or IgA levels,
2. Inhibiting Th2 effector cells,
3. Promoting regulatory T cell responses, and
4. Reducing allergen-specific IgE levels (Berin, 2014).

Among non-allergen-specific strategies, the use of probiotics has gained substantial interest. Probiotics are defined as live microorganisms that, when administered in adequate

amounts, confer health benefits to the host (Adams, 2010; Hill et al., 2014). Preclinical and clinical studies suggest that probiotics may alleviate FA by promoting immune tolerance (Lunjani et al., 2018). These beneficial effects are primarily attributed to their interaction with the innate immune system. Key mechanisms include:

- Inducing the secretion of regulatory cytokines,
- Enhancing mucosal IgA responses,
- Modulating gut barrier integrity and mucus layer thickness,
- Stimulating the synthesis of secretory IgA (sIgA) and β-defensins, and
- Regulating gut microbial communities and their postbiotic outputs (Canani et al., 2016; Iweala and Nagler, 2019; Paparo et al., 2019).

However, the effectiveness of probiotics is highly dependent on specific strains, the quantity administered, and the type of carrier used (Heine, 2018). Importantly, the health-promoting properties of probiotics are increasingly linked not only to the viable cells but also to their non-viable components and metabolic byproducts—referred to as *postbiotics* (Homayouni et al., 2012).



POSTBIOTICS: A PROMISING ALTERNATIVE

Postbiotics refer to non-viable microbial cells, cell components, or metabolites that, when administered in adequate amounts, confer health benefits to the host. These include soluble factors such as vitamins, bacteriocins, organic acids, enzymes, short-chain fatty acids (SCFAs), hydrogen peroxide, ethanol, diacetyl, peptides, cell surface proteins, teichoic acids, peptidoglycan-derived muropeptides, endo- and exopolysaccharides, lactocepins, plasmalogens, polyphosphates, and quorum-sensing molecules. These bioactive compounds may be naturally produced during fermentation or synthesized under controlled laboratory conditions (de la Rosa et al., 2019; Homayouni Rad et al., 2020; Rai, Pandey, and Sahoo, 2018).

Postbiotics offer several advantages, including enhanced safety, stability, and reproducibility. They may exert various health effects similar to probiotics, including immunomodulatory, anti-inflammatory, antioxidant, and antimicrobial activities (Figure 1 illustrates the major classes of postbiotics).

CONCERNS REGARDING LIVE PROBIOTIC ADMINISTRATION

While probiotics are traditionally defined as live microbial cells (Mohamadshahi et al., 2014; Sanaie et al., 2013), growing evidence suggests that viability is not always required to achieve health benefits. Non-viable probiotic fractions—such as cell-free extracts, purified cell walls, or culture supernatants—have demonstrated bioactivity (Gueniche et al., 2010; Raman, Ambalam, and Doble, 2016). In commercial preparations, the proportion of non-viable cells can exceed that of viable cells, suggesting that postbiotics may be the primary contributors to the observed health effects (Adams, 2010; Dash et al., 2015).

Nevertheless, certain probiotic strains (e.g., *Lactobacillus buchneri*, *L. helveticus*, *L. hilgardii*, *Bifidobacterium*, *Bacillus*, and *Streptococcus thermophilus*) used in foods and supplements have been associated—albeit rarely—with adverse events. These include horizontal gene transfer of antibiotic resistance, expression of virulence factors, translocation to sterile tissues, aberrant colonization patterns, and immunopathological responses such as bacteremia, sepsis, peritonitis, urogenital infections, meningitis, pneumonia, and infective endocarditis, particularly in immunocompromised individuals or severely ill patients (Cohen, 2018; Imperial and Ibana, 2016; Kothari, Patel, and Kim, 2019; Netzker et al., 2015).

ADVANTAGES OF POSTBIOTICS

Beneficial gut microorganisms produce a range of low molecular weight bioactive metabolites that play a crucial role in modulating the growth, reproduction, and activity of other beneficial microbes, as well as in maintaining gut cell integrity and protecting the host from environmental stressors (Tomar et al., 2015; Zhang et al., 2010). These soluble compounds—either secreted directly by viable probiotic cells or released following microbial lysis—accumulate in the intestinal lumen, where they interact with host cells to regulate various cellular processes and metabolic pathways, ultimately contributing to improved health outcomes (Aguilar-Toala et al., 2018).

Postbiotics exhibit several functional advantages, including efficient absorption, metabolism, and excretion, along with the ability to signal and elicit biological responses across multiple organs and tissues in the host. As a promising alternative to live probiotics, postbiotics address key safety concerns while maintaining or enhancing therapeutic efficacy.

They possess several attractive characteristics such as:

- Defined and stable chemical structures,
- A favorable safety profile with non-toxic nature,
- Enhanced shelf life and storage stability,
- Resistance to enzymatic degradation in the mammalian gastrointestinal tract, and
- Functional stability under diverse physiological conditions (Kataria et al., 2009; Paparo et al., 2019).

BIOLOGICAL ROLE OF POSTBIOTICS IN THE PREVENTION AND TREATMENT OF FOOD ALLERGY

Food allergy (FA) has been increasingly associated with disruptions in the composition and function of the gut microbiota. The epithelial interfaces of the gastrointestinal tract are frequent sites of allergic inflammatory responses (Park, Lee, and Hong, 2018; Savage et al., 2018). The gut microbiome not only plays a vital role in digestion and resistance to pathogen invasion but also produces a range of bioactive metabolites that are critical for maintaining epithelial barrier function and modulating immune responses (Riiser, 2015).

Various endogenous and exogenous factors—such as host genetics, diet, environmental exposures, psychosocial stress, medication, and infections—can influence the structure and

functionality of the gut microbiota (Honda and Littman, 2012). Epidemiological data and in vivo studies suggest that alterations in gut microbial composition, particularly in early life, contribute to dysbiosis, which may disrupt immune homeostasis and predispose individuals to allergic disorders (Fujimura et al., 2016; Ho and Bunyavanich, 2018). Notably, microbial disturbances within the first 1,000 days of life—especially during the first 100 days—can significantly affect inflammatory pathways and the development of immune-mediated diseases such as FA (Dominguez-Bello et al., 2011; Arrieta et al., 2015).

A dysbiotic gut environment is often characterized by a shift in microbial populations toward pathogenic strains. These pathogenic microbes can outcompete beneficial species, disrupt colonization of protective microbiota, and produce harmful secondary metabolites (e.g., toxins), ultimately impairing host health (Odenwald and Turner, 2019). In such scenarios, the consumption of postbiotic-enriched functional foods or nutraceuticals may offer a protective strategy by directly inhibiting pathogen growth and toxin production (Homayouni Rad et al., 2020). The antimicrobial actions of postbiotics are primarily attributed to compounds such as short-chain fatty acids (SCFAs) and bacteriocins (Aguilar-Toala et al., 2018).

MECHANISMS OF ACTION

One critical mechanism by which postbiotics contribute to gut homeostasis is through the modulation of oxygen availability in the colon. Butyrate, a well-known SCFA, activates PPAR-γ signaling pathways in colonocytes, promoting β-oxidation and establishing a hypoxic environment that favors anaerobic, butyrate-producing microbes while inhibiting the expansion of potentially pathogenic species (Byndloss et al., 2017). Additionally, dietary fiber—fermented by beneficial gut microbes—results in a diverse pool of postbiotic compounds that interact with host epithelial and immune cells to maintain gastrointestinal homeostasis.

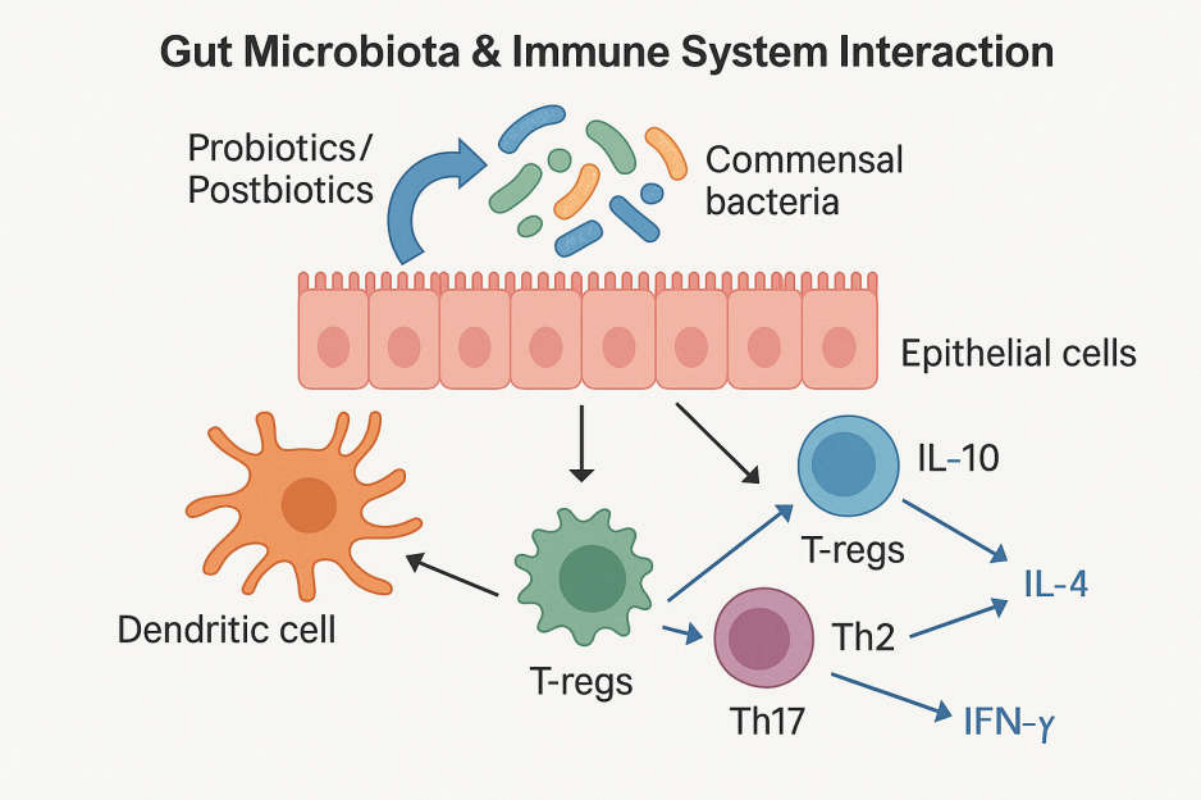
Regular intake of postbiotics enhances mucosal barrier integrity, limits allergen translocation into systemic circulation, and reduces allergic sensitization. These effects occur through both direct and indirect interactions with immune cells such as dendritic cells (DCs) and macrophages (Stefka et al., 2014; Wesemann and Nagler, 2016). Unlike probiotics, which introduce foreign microbial strains into the gut, postbiotics support the function of the host's native microbiota, offering a safer and more targeted intervention for restoring immune tolerance and managing FA (Iweala and Nagler, 2019; Homayouni Rad et al., 2020).

The gastrointestinal tract's core functions—digestion, absorption, and immune defense—are mediated by gut-associated lymphoid tissues (GALT), mucosal immune cells (e.g., Th1, Th2, Th17, and Treg cells), antimicrobial peptides (AMPs), secretory IgA, and the metabolic byproducts of gut microbiota, including postbiotics (Kurashima and Kiyono, 2017). GALT plays a pivotal role in inducing immune tolerance, especially in response to dietary proteins encountered by antigen-presenting cells (APCs) in the gut mucosa (Fu et al., 2019). The use of postbiotics is a promising strategy to reinforce epithelial barrier function and modulate immune responses favorably (Aguilar-Toala et al., 2018).

Experimental studies have identified several key mechanisms by which postbiotics support gut barrier function and suppress inflammation:

- Upregulation of genes involved in tight junction protein synthesis,
- Activation of transcription factors such as STAT3 and SP1,
- Enhanced transepithelial electrical resistance in intestinal epithelial cell models (e.g., Caco-2, T84, IPEC-J2),
- Stimulation of AMP production by intestinal epithelial cells (IECs),
- Restoration of epithelial integrity in inflammatory conditions, such as inflammatory bowel disease (IBD) (Miao et al., 2016; Valenzano et al., 2015; Yan and Ajuwon, 2017; Zhao et al., 2018).

Moreover, commensal microbes such as *Clostridia* and their SCFA metabolites (e.g., butyrate) stimulate type 3 innate lymphoid cells (ILC3s) in the colonic lamina propria to produce IL-22, a cytokine that enhances epithelial defense by inducing AMP secretion from Paneth cells and mucus release from goblet cells. This immunological cascade reduces dietary antigen penetration into the bloodstream and mitigates allergic sensitization (Sabat, Ouyang, and Wolk, 2014; Stefka et al., 2014).



Postbiotics and Immune Tolerance in FA

Preclinical and clinical studies highlight the role of SCFAs, particularly butyrate, in promoting immune tolerance by inducing regulatory T cells (Tregs) and reducing inflammatory responses to dietary antigens (Di Costanzo et al., 2016; Nowak-Wegrzyn and Chatchatee, 2017). SCFAs serve as energy sources for colonocytes and act through G-protein-coupled receptors (GPRs) such as GPR43 and GPR109A to stimulate IL-10 production by DCs and macrophages, supporting Treg development in mesenteric lymph nodes (Paparo et al., 2019).

Oral administration of dietary fiber and SCFA-rich postbiotics (acetate, butyrate) has been shown to enhance retinal dehydrogenase activity in $CD103^{+}$ dendritic cells—an essential component of vitamin A metabolism—thereby enhancing IgA responses and promoting oral tolerance in murine models (Tan et al., 2016). Similarly, butyrate administration has demonstrated suppression of acute allergic reactions in vivo (Aitoro et al., 2017).

Lipoteichoic acid (LTA), a postbiotic component derived from *Lactobacillus plantarum*, exhibits anti-inflammatory effects by downregulating TNF-α-induced cytokine expression via a TLR-2-dependent pathway. This results in the inhibition of NF-κB and MAPK signaling pathways in intestinal epithelial cells (Kim et al., 2012).

Key mechanisms underlying the therapeutic action of postbiotics in FA include:

1. Modulation of Treg activity via histone deacetylase (HDAC) inhibition,
2. Signaling through GPRs,
3. Provision of metabolic energy for intestinal epithelial cells,
4. Induction of anti-inflammatory cytokines (e.g., IL-10, IFN-γ), and
5. Reduction of DNA methylation rates, contributing to immune regulation (Paparo et al., 2019; Iweala and Nagler, 2019).

FUTURE PERSPECTIVES

The effectiveness of postbiotics is influenced by several variables, including the parent microbial strain, production and purification methods, the diversity of bioactive molecules, dosage, and delivery systems (Heine, 2018; Wegh et al., 2019). Current evidence supports the use of postbiotics as a safe and promising adjunct or alternative therapy for preventing and managing FA—particularly in vulnerable populations such as infants and young children—without the risks associated with live probiotics (Castan et al., 2020).

Despite these advances, further research is essential to fully understand the mechanisms of action, optimize delivery methods, and confirm clinical efficacy in large-scale human studies targeting chronic allergic diseases such as food allergy.

CONCLUSION

Food allergy continues to pose a major public health challenge, with increasing incidence worldwide. The interplay between the gut microbiota and the host immune system plays a pivotal role in the pathogenesis of allergic diseases. Postbiotics—non-viable microbial-derived compounds—have emerged as safe, stable, and effective alternatives to live probiotics. They exert their health-promoting effects by enhancing epithelial barrier function, modulating host immune responses, suppressing inflammation, and promoting immune tolerance through well-defined molecular pathways.

REFERENCES

Adams, C. A. (2010). The probiotic paradox: Live and dead cells are biological response modifiers. *Nutrition Research Reviews,* *23*(1), 37–46. https://doi.org/10.1017/S0954422410000090

Aguilar-Toala, J., Garcia-Varela, R., Garcia, H., Mata-Haro, V., Gonzalez-Cordova, A., Vallejo-Cordoba, B., and Hernandez-Mendoza, A. (2018). Postbiotics: An evolving term within

the functional foods field. *Trends in Food Science and Technology, 75*, 105–114. https://doi.org/10.1016/j.tifs.2018.03.009

Aitoro, R., Simeoli, R., Amoroso, A., Paparo, L., Nocerino, R., Pirozzi, C., di Costanzo, M., Meli, R., De Caro, C., Picariello, G., et al. (2017). Extensively hydrolyzed casein formula alone or with *L. rhamnosus* GG reduces β-lactoglobulin sensitization in mice. *Pediatric Allergy and Immunology, 28*(3), 230–237. https://doi.org/10.1111/pai.12687

Arrieta, M.-C., Stiemsma, L. T., Dimitriu, P. A., Thorson, L., Russell, S., Yurist-Doutsch, S., Kuzeljevic, B., Gold, M. J., Britton, H. M., Lefebvre, D. L., et al. (2015). Early infancy microbial and metabolic alterations affect risk of childhood asthma. *Science Translational Medicine, 7*(307), 307ra152. https://doi.org/10.1126/scitranslmed.aab2271

Berin, M. C. (2014). Future therapies for IgE-mediated food allergy. *Current Pediatrics Reports, 2*(2), 119–126. https://doi.org/10.1007/s40124-014-0041-0

Byndloss, M. X., Olsan, E. E., Rivera-Chavez, F., Tiffany, C. R., Cevallos, S. A., Lokken, K. L., Torres, T. P., Byndloss, A. J., Faber, F., Gao, Y., et al. (2017). Microbiota-activated PPAR-γ signaling inhibits dysbiotic *Enterobacteriaceae* expansion. *Science, 357*(6351), 570–575. https://doi.org/10.1126/science.aam9949

Canani, R. B., Gilbert, J. A., and Nagler, C. R. (2015). The role of the commensal microbiota in the regulation of tolerance to dietary allergens. *Current Opinion in Allergy and Clinical Immunology, 15*(3), 243. https://doi.org/10.1097/ACI.0000000000000157

Canani, R. B., Sangwan, N., Stefka, A. T., Nocerino, R., Paparo, L., Aitoro, R., Calignano, A., Khan, A. A., Gilbert, J. A., and Nagler, C. R. (2016). *Lactobacillus rhamnosus* GG-supplemented formula expands butyrate-producing bacterial strains in food allergic infants. *The ISME Journal, 10*(3), 742. https://doi.org/10.1038/ismej.2015.151

Castan, L., Bøgh, K. L., Maryniak, N. Z., Epstein, M. M., Kazemi, S., O'Mahony, L., Bodinier, M., Smit, J. J., Bilsen, J. H. M., Blanchard, C., et al. (2020). Overview of in vivo and ex vivo endpoints in murine food allergy models: Suitable for evaluation of the sensitizing capacity of novel proteins? *Allergy, 75*(2), 289–301. https://doi.org/10.1111/all.13943

Cohen, P. A. (2018). Probiotic safety—No guarantees. *JAMA Internal Medicine, 178*(12), 1577–1578. https://doi.org/10.1001/jamainternmed.2018.5403

Dash, G., Raman, R. P., Prasad, K. P., Makesh, M., Pradeep, M., and Sen, S. (2015). Evaluation of paraprobiotic applicability of *Lactobacillus plantarum* in improving the immune response and disease protection in giant freshwater prawn, *Macrobrachium rosenbergii*

(de Man, 1879). *Fish and Shellfish Immunology, 43*(1), 167–174. https://doi.org/10.1016/j.fsi.2014.12.007

de la Rosa, C., Flores-Gallegos, A. C., Muñiz-Marquez, D., Nobre, C., Contreras-Esquivel, J. C., and Aguilar, C. N. (2019). Fructooligosaccharides production from agro-wastes as alternative low-cost source. *Trends in Food Science and Technology, 91*, 139–146. https://doi.org/10.1016/j.tifs.2019.06.013

Di Costanzo, M., Amoroso, A., and Canani, R. B. (2016). Gut microbiota as a target for food allergy. *Journal of Pediatric Gastroenterology and Nutrition, 63*(1S), S11–S13. https://doi.org/10.1097/01.mpg.0000489618.97688.b8

Dominguez-Bello, M. G., Blaser, M. J., Ley, R. E., and Knight, R. (2011). Development of the human gastrointestinal microbiota and insights from high-throughput sequencing. *Gastroenterology, 140*(6), 1713–1719. https://doi.org/10.1053/j.gastro.2011.02.011

Fu, L., Cherayil, B. J., Shi, H., Wang, Y., and Zhu, Y. (2019). Food allergy and the microbiota: Implications for probiotic use in regulating allergic responses. In *Food Allergy* (pp. 179–194). Springer. https://doi.org/10.1007/978-981-13-7510-3_11

Fujimura, K. E., Sitarik, A. R., Havstad, S., Lin, D. L., Levan, S., Fadrosh, D., Panzer, A. R., LaMere, B., Rackaityte, E., Lukacs, N. W., et al. (2016). Neonatal gut microbiota associates with childhood multisensitized atopy and T cell differentiation. *Nature Medicine, 22*(10), 1187–1191. https://doi.org/10.1038/nm.4176

Gueniche, A., Bastien, P., Ovigne, J. M., Kermici, M., Courchay, G., Chevalier, V., Breton, L., and Castiel-Higounenc, I. (2010). *Bifidobacterium longum* lysate, a new ingredient for reactive skin. *Experimental Dermatology, 19*(8), e1–e8. https://doi.org/10.1111/j.1600-0625.2009.00932.x

Gupta, R. S., Springston, E. E., Warrier, M. R., Smith, B., Kumar, R., Pongracic, J., and Holl, J. L. (2011). The prevalence, severity, and distribution of childhood food allergy in the United States. *Pediatrics, 128*(1), e9–e17. https://doi.org/10.1542/peds.2011-0204

Heine, R. G. (2018). Food allergy prevention and treatment by targeted nutrition. *Annals of Nutrition and Metabolism, 72*(3), 33–45. https://doi.org/10.1159/000487380

Hill, C., Guarner, F., Reid, G., Gibson, G. R., Merenstein, D. J., Pot, B., Morelli, L., Canani, R. B., Flint, H. J., Salminen, S., et al. (2014). Expert consensus document: The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nature Reviews Gastroenterology and Hepatology, 11*(8), 506–514. https://doi.org/10.1038/nrgastro.2014.66

Ho, H.-E., and Bunyavanich, S. (2018). Role of the microbiome in food allergy. *Current Allergy and Asthma Reports, 18*(4), 27. https://doi.org/10.1007/s11882-018-0780-z

Homayouni, A., Alizadeh, M., Alikhah, H., and Zijah, V. (2012). Functional dairy probiotic food development: Trends, concepts, and products. In *Probiotics* (pp. 3–31). Rijeka, Croatia: InTech.

Homayouni Rad, A., Aghebati Maleki, L., Samadi Kafil, H., Fathi Zavoshti, H., and Abbasi, A. (2020). Postbiotics as novel health-promoting ingredients in functional foods. *Health Promotion Perspectives, 10*(1), 3–4. https://doi.org/10.15171/hpp.2020.02

Honda, K., and Littman, D. R. (2012). The microbiome in infectious disease and inflammation. *Annual Review of Immunology, 30*(1), 759–795. https://doi.org/10.1146/annurev-immunol-020711-074937

Imperial, I. C., and Ibana, J. A. (2016). Addressing the antibiotic resistance problem with probiotics: Reducing the risk of its double-edged sword effect. *Frontiers in Microbiology, 7*, 1983. https://doi.org/10.3389/fmicb.2016.01983

Iweala, O. I., and Nagler, C. R. (2019). The microbiome and food allergy. *Annual Review of Immunology, 37*(1), 377–403. https://doi.org/10.1146/annurev-immunol-042718-041621

Kataria, J., Li, N., Wynn, J. L., and Neu, J. (2009). Probiotic microbes: Do they need to be alive to be beneficial? *Nutrition Reviews, 67*(9), 546–550. https://doi.org/10.1111/j.1753-4887.2009.00226.x

Kim, H., Jung, B. J., Jung, J. H., Kim, J. Y., Chung, S. K., and Chung, D. K. (2012). *Lactobacillus plantarum* lipoteichoic acid alleviates TNF-α-induced inflammation in the HT-29 intestinal epithelial cell line. *Molecules and Cells, 33*(5), 479–486. https://doi.org/10.1007/s10059-012-2266-5

Kothari, D., Patel, S., and Kim, S.-K. (2019). Probiotic supplements might not be universally effective and safe: A review. *Biomedicine and Pharmacotherapy, 111*, 537–547. https://doi.org/10.1016/j.biopha.2018.12.104

Kurashima, Y., and Kiyono, H. (2017). Mucosal ecological network of epithelium and immune cells for gut homeostasis and tissue healing. *Annual Review of Immunology, 35*(1), 119–147. https://doi.org/10.1146/annurev-immunol-051116-052424

Lopez-Fandiño, R. (2019). Role of dietary lipids in food allergy. *Critical Reviews in Food Science and Nutrition*, 1–18. https://doi.org/10.1080/10408398.2019.1602025

Lunjani, N., Satitsuksanoa, P., Lukasik, Z., Sokolowska, M., Eiwegger, T., and O'Mahony, L. (2018). Recent developments and highlights in mechanisms of allergic diseases: Microbiome. *Allergy, 73*(12), 2314–2327. https://doi.org/10.1111/all.13634

Miao, W., Wu, X., Wang, K., Wang, W., Wang, Y., Li, Z., Liu, J., Li, L., and Peng, L. (2016). Sodium butyrate promotes reassembly of tight junctions in Caco-2 monolayers involving inhibition of MLCK/MLC2 pathway and phosphorylation of PKCβ2. *International Journal of Molecular Sciences, 17*(10), 1696. https://doi.org/10.3390/ijms17101696

Mohamadshahi, M., Veissi, M., Haidari, F., Shahbazian, H., Kaydani, G.-A., and Mohammadi, F. (2014). Effects of probiotic yogurt consumption on inflammatory biomarkers in patients with type 2 diabetes. *BioImpacts: BI, 4*(2), 83–88. https://doi.org/10.5681/bi.2014.020

National Academies of Sciences, Engineering, and Medicine. (2017). *Finding a path to safety in food allergy: Assessment of the global burden, causes, prevention, management, and public policy*. Washington, DC: National Academies Press. https://doi.org/10.17226/23658

Netzker, T., Fischer, J., Weber, J., Mattern, D. J., König, C. C., Valiante, V., Schroeckh, V., and Brakhage, A. A. (2015). Microbial communication leading to the activation of silent fungal secondary metabolite gene clusters. *Frontiers in Microbiology, 6*, 299. https://doi.org/10.3389/fmicb.2015.00299

Nowak-Wegrzyn, A., and Chatchatee, P. (2017). Mechanisms of tolerance induction. *Annals of Nutrition and Metabolism, 70*(2), 7–24. https://doi.org/10.1159/000457915

Odenwald, M. A., and Chapman, C. G. (2019). Gut dysbiosis and its epigenomic impact on disease. In S. Mathers, and L. Ferguson (Eds.), *Nutritional epigenomics* (pp. 409–422). Elsevier.

Panel, N.-S. E. (2010). Guidelines for the diagnosis and management of food allergy in the United States: Report of the NIAID-sponsored expert panel. *Journal of Allergy and Clinical Immunology, 126*(6), S1–S58.

Paparo, L., Aitoro, R., Nocerino, R., Di Scala, C., Di Costanzo, M., Cosenza, L., Granata, V., and Canani, R. B. (2017). Epigenetic regulation of early nutrition on immune system. In *Handbook of Nutrition, Diet, and Epigenetics* (Vol. 2, pp. 1–12). Cham: Springer International Publishing.

Paparo, L., Nocerino, R., Di Scala, C., Della Gatta, G., Di Costanzo, M., Buono, A., Bruno, C., and Berni Canani, R. (2019). Targeting food allergy with probiotics. In S. Guandalini

and F. Indrio (Eds.), *Probiotics and child gastrointestinal health: Advances in microbiology, infectious diseases and public health* (Vol. 10, pp. 57–68). Cham: Springer International Publishing.

Park, H. J., Lee, S. W., and Hong, S. (2018). Regulation of allergic immune responses by microbial metabolites. *Immune Network, 18*(1), e15. https://doi.org/10.4110/in.2018.18.e15

Prince, B. T., Mandel, M. J., Nadeau, K., and Singh, A. M. (2015). Gut microbiome and the development of food allergy and allergic disease. *Pediatric Clinics of North America, 62*(6), 1479–1492. https://doi.org/10.1016/j.pcl.2015.07.007

Rai, A. K., Pandey, A., and Sahoo, D. (2018). Biotechnological potential of yeasts in functional food industry. *Trends in Food Science and Technology, 83*, 129–137. https://doi.org/10.1016/j.tifs.2018.11.016

Raman, M., Ambalam, P., and Doble, M. (2016). *Probiotics and bioactive carbohydrates in colon cancer management*. India: Springer.

Riiser, A. (2015). The human microbiome, asthma, and allergy. *Allergy, Asthma and Clinical Immunology, 11*(1), 35. https://doi.org/10.1186/s13223-015-0102-0

Sabat, R., Ouyang, W., and Wolk, K. (2014). Therapeutic opportunities of the IL-22–IL-22R1 system. *Nature Reviews Drug Discovery, 13*(1), 21–38. https://doi.org/10.1038/nrd4176

Sanaie, S., Ebrahimi-Mameghani, M., Mahmoodpoor, A., Shadvar, K., and Golzari, S. E. (2013). Effect of a probiotic preparation (VSL#3) on cardiovascular risk parameters in critically-ill patients. *Journal of Cardiovascular and Thoracic Research, 5*(2), 67.

Savage, J. H., Lee-Sarwar, K. A., Sordillo, J., Bunyavanich, S., Zhou, Y., O'Connor, G., Sandel, M., Bacharier, L. B., Zeiger, R., Sodergren, E., et al. (2018). A prospective microbiome-wide association study of food sensitization and food allergy in early childhood. *Allergy, 73*(1), 145–152. https://doi.org/10.1111/all.13232

Sicherer, S. H., Muñoz-Furlong, A., Godbold, J. H., and Sampson, H. A. (2010). US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. *Journal of Allergy and Clinical Immunology, 125*(6), 1322–1326. https://doi.org/10.1016/j.jaci.2010.03.029

Stefka, A. T., Feehley, T., Tripathi, P., Qiu, J., McCoy, K., Mazmanian, S. K., Tjota, M. Y., Seo, G. Y., Cao, S., Theriault, B. R., et al. (2014). Commensal bacteria protect against food allergen sensitization. *Proceedings of the National Academy of Sciences, 111*(36), 13145–13150. https://doi.org/10.1073/pnas.1412008111

Tan, J., McKenzie, C., Vuillermin, P. J., Goverse, G., Vinuesa, C. G., Mebius, R. E., Macia, L., and Mackay, C. R. (2016). Dietary fiber and bacterial SCFA enhance oral tolerance and protect against food allergy through diverse cellular pathways. *Cell Reports, 15*(12), 2809–2824. https://doi.org/10.1016/j.celrep.2016.05.047

Tomar, S. K., Anand, S., Sharma, P., Sangwan, V., and Mandal, S. (2015). Role of probiotics, prebiotics, synbiotics and postbiotics in inhibition of pathogens. In *The battle against microbial pathogens: Basic science, technological advances and educational programs*. Badajoz, Spain: Formatex.

Valenzano, M. C., DiGuilio, K., Mercado, J., Teter, M., To, J., Ferraro, B., Mixson, B., Manley, I., Baker, V., Moore, B. A., et al. (2015). Remodeling of tight junctions and enhancement of barrier integrity of the CACO-2 intestinal epithelial cell layer by micronutrients. *PLoS One, 10*(7), e0133926. https://doi.org/10.1371/journal.pone.0133926

Wegh, C. A., Geerlings, S. Y., Knol, J., Roeselers, G., and Belzer, C. (2019). Postbiotics and their potential applications in early life nutrition and beyond. *International Journal of Molecular Sciences, 20*(19), 4673. https://doi.org/10.3390/ijms20194673

Wesemann, D. R., and Nagler, C. R. (2016). The microbiome, timing, and barrier function in the context of allergic disease. *Immunity, 44*(4), 728–738. https://doi.org/10.1016/j.immuni.2016.02.002

Yan, H., and Ajuwon, K. M. (2017). Butyrate modifies intestinal barrier function in IPEC-J2 cells through a selective upregulation of tight junction proteins and activation of the Akt signaling pathway. *PLoS One, 12*(6), e0179586. https://doi.org/10.1371/journal.pone.0179586

Zhang, J., Du, G.-C., Zhang, Y., Liao, X.-Y., Wang, M., Li, Y., and Chen, J. (2010). Glutathione protects *Lactobacillus sanfranciscensis* against freeze-thawing, freeze-drying, and cold treatment. *Applied and Environmental Microbiology, 76*(9), 2989–2996.

Zhao, Y., Chen, F., Wu, W., Sun, M., Bilotta, A. J., Yao, S., Xiao, Y., Huang, X., Eaves-Pyles, T. D., Golovko, G., et al. (2018). GPR43 mediates microbiota metabolite SCFA regulation of antimicrobial peptide expression in intestinal epithelial cells via activation of mTOR and STAT3. *Mucosal Immunology, 11*(3), 752–762. https://doi.org/10.1038/mi.2017.118