Current Trends in Biotechnology and Pharmacy
Vol. 20 (Supplementry Issue 1A), March 2026, ISSN 0973-8916 (Print)., 2230-7303 (Online)
10.5530/ctbp.2026.1s.20

Mapping Scientific Contributions to Gut Microbiota and Dairy Allergy Research: A Bibliometric Perspective

Suma Yashwitha Koduru[1], and Palanisamy Suresh Babu[2]*

[1]Department of Bioinformatics, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha Nagar, Thandalam, Chennai - 602 105, Tamil Nadu, India
[2]Department of Biotechnology, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha Nagar, Thandalam, Chennai - 602 105, Tamil Nadu, India
*Corresponding author: sureshbabup.sse@saveetha.com

Abstract

The gut microbiota plays a crucial role in dairy allergy development through immune modulation involving genes like IL-10 and IL-22. This study presents a comprehensive Bibliometric analysis of gut microbiota and dairy allergy research across PubMed, Web of Science, and Scopus (2015-2025). This analysis examined publication trends, Research hotspots, and collaborations among various countries, organisations, and authors. A total of 784 documents were analysed using co-occurrence networks for thematic mapping and co-authorship networks for collaborative patterns by employing VOS viewer and Biblioshiny in R Studio. Three dominant research clusters were related to immunological mechanisms involving IL-10/IL-22 regulation, diagnostic advancements using metagenomics, and therapeutic and dietary interventions using probiotics. The USA, China, and European nations emerged as leading contributors with exponential growth post-2020. Current trends highlight the microbiome-targeted therapies, including longitudinal microbiome studies and personalized nutrition approaches. The overall analysis provides a roadmap for future research, emphasizing the need for clinical trials combining multi-omics data with microbiota modulating strategies. The bibliometric framework provides a way for future research prioritization and policy development.

Keywords: Milk allergy, microbiota, gut microbiome, metagenomics, dysbiosis

Introduction

The interplay between gut microbiota and dairy allergies is a crucial area of research in immunology, microbiology, and nutrition science. In recent years, scientific attention has increasingly turned toward the gut microbiota as a key player in modulating immune function and allergic sensitivity (1). Disruptions to the microbial balance, often referred to as dysbiosis, have been linked to increased allergic susceptibility, while certain beneficial bacterial strains appear to offer protective effects. It is also a rapidly evolving field of study. There are therapeutic interventions, such as the use of probiotics, prebiotics, and dietary modulation, to manage or even prevent dairy-related allergic responses.(2)

Gut Microbiota and the Immune System Modulation

The gut microbiome consists of a varied assembly of bacteria, viruses, fungi, and other microorganisms that inhabit the digestive system. It plays a pivotal role in training and regulating the immune system. When balanced, it helps the body recognize the difference between harmful invaders and harmless substances, like the proteins found in food.(3) However, when dysbiosis (an imbalance in microbial composition) occurs, this immune tolerance can be disrupted, making us more prone to allergic reactions, such as those to dairy. This community significantly influences immune functions by maintaining both innate and adaptive immune cell activity, shaping the body's overall defense (4).

Dairy allergy mechanisms

The incidence of milk allergies is increasing due to the false identification of milk proteins as a harmful substance by the immune system, and the release of chemicals like histamine, causing symptoms such as skin rashes, stomach issues, breathing problems, or even a severe reaction called anaphylaxis (5). This occurs due to IgE antibodies, which trigger allergic responses when milk is consumed. Some reactions happen quickly (IgE-mediated), while others are delayed (non-IgE-mediated). Unlike lactose intolerance, which is a digestive problem caused by the inability to break down milk sugar (lactose), a dairy allergy is an immune response to milk proteins and can be life-threatening (6).

Common milk proteins involved in triggering allergies include casein, beta-lactoglobulin, and alpha-lactalbumin (7). Symptoms can range from mild, like itching and swelling, to severe conditions termed "anaphylaxis". In non-IgE-mediated reactions, symptoms may take longer to appear and usually affect the digestive system (8). Infants and in young children dairy allergies are most common, though some may outgrow them with age. Proper diagnosis and management, including avoiding dairy and carrying emergency medication (EpiPen), are essential for those with severe allergies (9).

Immune System Misidentification

In individuals with a dairy allergy, the immune system perceives milk proteins (like casein, beta-lactoglobulin, and alpha-lactalbumin) as dangerous invaders, leading to an overreaction. A casein allergy arises when the immune system mistakenly identifies the protein as a threat, leading to the production of allergic (IgE) antibodies for defense (10). Within minutes, the interaction between these antibodies and the specific protein causes the release of chemicals in the body, such as histamine, which results in symptoms like swelling in the lips, mouth, tongue, face, or throat, skin reactions including hives, rashes, or red, itchy skin, as well as nasal congestion, sneezing, a runny nose, itchy eyes, coughing, or wheezing. It is crucial to pay attention to situations associated with allergic reactions.

Role of Gut Microbiota in Dairy Allergy Development

The microbes in a baby's gut (microbiome) play a big role in lifelong health, especially in preventing allergies. When a baby has less diverse gut bacteria, they may be more likely to develop food allergies and other allergic diseases as they grow. Factors such as mode of delivery (vaginal vs caesarean), breastfeeding, antibiotic use, and diet can influence microbial composition. However, scientists believe that the specific types of bacteria presents are more important than just having many different kinds (11). Changes in gut bacteria during early life have been linked to allergic diseases. For example, babies with an imbalance in certain bacteria (measured as an increased E/B ratio, meaning more of one type of bacteria than another) were more likely to develop food allergies later on (12). Beneficial gut bacteria produce SCFAs (e.g., butyrate, acetate, propionate) through the fermentation of dietary fibers. SCFAs (short-chain fatty acids) play a key role in maintaining gut barrier integrity and promoting regulatory T cells, which help suppress allergic responses (13).

Genes Responsible

Human Interleukin-22 Gene

The IL22 gene in humans is situated on chromosome 12q15, close to the genes that code for IFN-γ and IL-26. This gene produces a protein called IL-22, which is made up of 179 amino acids that share 79% homology between a mouse and a human. When IL-22 is secreted from cells, it becomes active and is slightly shorter, with 146 amino acids. It usually works as a single protein, also a monomer, but in high numbers, it can form pairs, which are dimers or groups of four (tetramers) (14). Initial research indicated that IL-22 was consistently expressed solely in the thymus and brain; however, later investigations have revealed that its expression can also be induced in several other tissues, such as the gut, liver, lung, skin, pancreas, and spleen.

The human interleukin-22 gene plays a role in cow's milk allergy, with IL-22 levels correlating with blood eosinophil numbers and being reduced by elimination diet (15). IL-22 is involved in training the whole immune system to tolerate harmless substances. If IL-22 function is disrupted, then the immune system may wrongly see milk proteins as dangerous, leading to an allergic reaction instead of tolerance.IL-22 helps maintain the gut lining, preventing harmful substances (like allergens in milk) from entering the bloodstream. In people with a milk allergy, IL-22 levels may be altered, leading to a weaker gut barrier and increased immune sensitivity to milk proteins (16).

Human Interleukin-10 Gene

The IL10 gene is responsible for producing interleukin-10 (IL-10), an important anti-inflammatory cytokine that helps regulate the immune system. It is located on chromosome 1 (1q32). L-10 is a protein (cytokine) that helps control the immune system and reduce inflammation. It is mainly made by monocytes (a type of white blood cell) and some immune cells. Normally, IL-10 levels are low, but the body produces more IL-10 when immune cells are activated by bacteria, viruses, or other immune signals (17). IL-10 helps stop the production of inflammatory molecules (like IFN-γ, IL-2, and TNF-α), preventing excessive immune reactions. It suppresses Th1 cells (which promote inflammation) but stimulates Th2 cells, which are more involved in allergic reactions. IL-10 is produced by mast cells, which are involved in allergic reactions. It can reduce inflammation at the site of an allergic reaction. It helps balance the immune system, preventing damage from overactive inflammation while allowing necessary immune responses to continue (18). IL-10 plays a crucial role in milk allergy, and its gene (IL-10) and its polymorphisms are associated with the development and persistence of cow’s milk allergy. IL-10 is present in human milk and may have immunomodulating effects on the infant’s digestive system (19). These genetic changes can alter IL-10 production, potentially reducing its ability to suppress excessive immune reactions to milk proteins. Lower IL-10 levels might lead to an overactive immune response, increasing the risk of developing and maintaining CMA (20)

Symbiotic Therapy with Microbes and Lactulose Reduces Food Allergy:

Cow’s milk allergy (CMA) is one of the earliest food allergies seen in infants and has been linked to differences in gut bacteria (Table 1). Researchers found that mice given

Table 1: CMA-Linked Gut Pathobionts and Their Mechanistic Role

Microbe (s)	Negative Effects	Contributing Factors	Ref.
Clostridium difficile	Overrepresented in CMA; disrupts the gut barrier and promotes inflammation	Often arises after antibiotic use, which depletes healthy bacteria and allows overgrowth	(23)
Escherichia coli (some strains)	Found in higher abundance in CMA infant	Dysbiosis due to a lack of protective microbe and early in life	(24)
Klebsiella pneumoniae	Linked to inflammation and impaired immune tolerance in allergic infants	Can thrive in oxygen-exposed environments; imbalance due to reduced anaerobes like *A. caccae*	(25)
Enterococcus faecalis	Associated with gut barrier damage and immune system overactivation in CMA	Overgrowth in disrupted microbiota, often antibiotic-resistant, thrives in an imbalanced gut	(26)
Bacteroides fragilis (some strains)	Alters immune signaling and gut environment; may worsen allergic symptoms in CMA	Overrepresented or lacking balancing species like Bifidobacteria	(27)

gut bacteria from CMA infants developed allergic reactions, while those given bacteria from healthy infants did not. One helpful bacterium, *Anaerostipes caccae* (*A. caccae*), was more common in healthy infants and could prevent allergic responses by itself, likely due to its ability to produce butyrate, a compound known to support immune balance (21). To help *A. caccae* grow in the gut without needing antibiotics, scientists paired it with a prebiotic called lactulose. This combination, called a synbiotic, increased levels of helpful gut compounds, boosted beneficial bacteria like Bifidobacteria, and reduced allergic symptoms in mice. It was effective against both milk and peanut allergies. These results suggest that *A. caccae* with lactulose may offer a safe, natural way to prevent or treat food allergies (22).

Diagnostic Methods for Milk Allergy

To evaluate a suspected milk allergy, a healthcare provider may recommend a skin test and/or a blood test.

1. Skin test: In this test, the skin is introduced to a small amount of milk protein through a tiny prick. If an allergic reaction occurs, such as a raised, itchy bump, it may indicate a milk allergy. However, this test isn't completely reliable and should be conducted by an allergy specialist (28)

2. Blood test: This test measures the level of immunoglobulin E (IgE) antibodies specific to milk in the bloodstream. While useful, it also has limitations in accurately diagnosing milk allergy. (29) If neither test provides a definitive diagnosis, an oral food challenge may be performed under strict medical supervision. This procedure involves gradually consuming increasing amounts of foods that may or may not contain milk to observe for adverse reactions. Due to the potential risk of severe allergic responses, oral challenges should only be conducted by trained allergists.(30)

Formula Alternatives and Management Strategies for CMA in Infants

When infants are formula-fed, either exclusively or in combination with breastfeeding, paediatricians often consider changing the formula if symptoms of intolerance or allergy arise. A variety of alternatives to standard cow's milk-based formulas are available, including amino acid-based formulas (AAF), partially hydrolyzed formulas (pHF), extensively hydrolyzed formulas (eHF), rice-based hydrolysates, soy formulas, and milk from other mammals such as goats, sheep, or camels (31). These formulas vary in their degree of protein breakdown and intended use. pHFs are designed to reduce allergenicity while preserving some protein fragments to promote oral tolerance, making them suitable for allergy prevention but not treatment. eHF is more extensively hydrolyzed to eliminate allergenic epitopes and is appropriate for both prevention and treatment of cow's milk allergy (CMA). (32) AAF, composed of free amino acids, is intended solely for treatment and is typically tolerated by over 95% of infants with CMA. While soy formulas are generally safe and effective in 85–90% of affected infants, other mammalian milks are not recommended for CMA treatment due to nutritional inadequacy and a high degree of cross-reactivity with cow's milk proteins. For example, despite being available as infant formula in some regions, goat's milk has a cross-reactivity rate of approximately 80% and is therefore not advised (33). The choice of formula should be guided by the severity of the allergy, the clinical response, and established guidelines aimed at harmonizing diagnosis and management practices(34).

Probiotic Use in Allergy Prevention and Management of CMA

Recent studies indicate that taking probiotics during pregnancy and breastfeeding may enhance the composition of breast milk by altering microbial contents and immune factors, which could be advantageous for the infant's gut health and lower the likelihood of allergies (35). The World Allergy Organization (WAO) advises the use of probiotics for pregnant and breastfeeding women, as well as for high-risk infants who are not exclusively breastfed.

Conversely, other expert organizations, such as the Academy of Allergy and Clinical Immunology and the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition, do not endorse the use of probiotics or prebiotics for preventing allergies because the evidence is of low quality and inconclusive (36). In relation to the therapeutic application of probiotics for infants with cow's milk allergy (CMA), a number of randomized controlled trials have explored the use of Lactobacillus rhamnosus GG (LGG). Findings suggest that LGG might alleviate gastrointestinal symptoms, decrease intestinal inflammation, and support the establishment of tolerance to cow's milk proteins. (37). Additionally, some studies observed a reduction in eczema severity measured by the Scoring Atopic Dermatitis(SCORAD index) in probiotic-treated infants (37). However, findings across studies remain inconsistent and imprecise, limiting the ability to draw definitive conclusions. While probiotics are generally considered safe for pregnant women and infants, isolated effects such as transient reductions in hemoglobin levels have been reported. Importantly, the clinical benefits of probiotics are strain-specific, meaning results from one product cannot be generalized to another without precise strain identification (38). Therefore, improved regulation, including mandatory disclosure of strain-level details and manufacturing processes, is essential for evaluating probiotic safety and efficacy in allergy prevention and management.(39)

Bibliometric Analysis

The statistical method for analyzing data from book chapters, articles, reviews, editorial papers, and other sources, known as bibliometric analysis. The trends, characteristics, and research status in the particular field are understood. This method's main purpose is to explore the structure, understand the evolution, citations are usually assessed as an impact, and finally, to shed light on the emerging topics in a specific field(40, 41). A literature search was carried out using the keywords "gut microbiota AND milk allergy" to collect relevant research articles. The search was conducted in three major databases: Scopus, PubMed, and Web of Science, covering the period from 2015 to 2025. The search results were exported on March 4, 2025, in the following formats: Common Separated Value (.CSV) from Scopus, PubMed format for PubMed, and plain text (.txt) for Web of Science. The total number of documents retrieved was 232 from Scopus, 232 from PubMed, and 320 from Web of Science.

The collected data was analyzed using VOSviewer (version 1.6.20) and RStudio with R version 4.4.3. All required packages for bibliometric analysis were installed following the method described by (42). The Biblioshiny interface was used to generate key outputs such as co-occurrence and co-authorship networks, bibliographic coupling, document types, annual publication trends, tree maps, country-wise scientific output, and factorial analysis.

Results

Publication Type

The pie chart (Fig. 1) depicts the distribution of document types related to milk allergy research from 2015 to 2025, compiled from Web of Science, Scopus, and PubMed databases, and reveals a predominant focus on original research articles. As illustrated in the pie chart, articles constitute the majority at

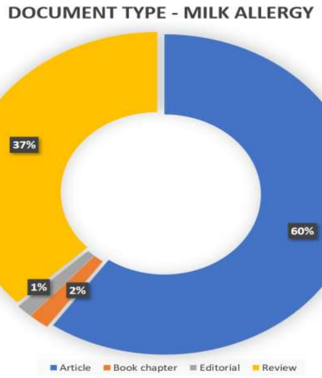

Fig 1: Document Type

60%, underscoring the emphasis on empirical studies in this field. Review articles follow at 37%, highlighting a strong interest in synthesizing existing knowledge and summarizing evidence. Book chapters account for approximately 2%, suggesting limited academic textbook contributions on the subject. Editorials represent the smallest share at 1%, indicating minimal editorial commentary or opinion pieces. The predominance of original articles and reviews reflects an active and evolving research landscape focused on understanding and addressing milk allergy from clinical, nutritional, and immunological perspectives. Duplicate articles were included during the compilation.

Annual Scientific Production

The Figure 2 entitled "Scientific Production per Year – Milk Allergy" illustrates the annual number of scientific literatures from 2014 to 2025 published in PubMed, Web of Science (WoS), and Scopus. As a whole, there is a definite increasing trend in milk allergy research across the three databases as an indication of increasing scientific interest in the topic. Scopus presents the highest number of publications, with the greatest number occurring around 2024 at about 46 articles, while WoS and PubMed also record significant upticks, with their all-time highs occurring around that year. Of particular interest is the steep increase in Scopus publications between the years 2016 and 2018, followed by a small dip, then a rise again after 2020. WoS has a linear increase with a decline in 2020, whereas PubMed demonstrates a steadier but linear increase. There is a drastic decline in all databases in 2025, which most probably accounts for missing data for the current year and not for a real fall in research activity. These trends indicate a growing interest in milk allergy within the scientific community, presumably fueled by heightened awareness of food allergies and technological advances in associated biomedical sciences.

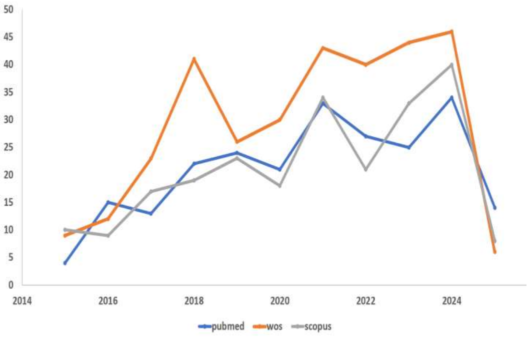

Fig 2: Annual Scientific Production

Corresponding Authors Countries

The Table 2 emphasizes the top 10 contributing nations to milk allergy literature in science, as indexed in the three prominent databases, Scopus, Web of Science (herein WoS), and PubMed. The USA dominates both Scopus and WoS with 35 and 93 papers, respectively, emphasizing its dominant

Table 2: Number of Articles Published by Different Countries

Rank	Scopus		WoS		PubMed	
	Country	NOA	Country	NOA	Country	NOA
1	USA	35	USA	93	China	32
2	Italy	30	Italy	41	Italy	31
3	China	28	Canada	30	USA	29
4	Netherlands	13	China	22	Netherlands	11
5	UK	11	Spain	18	Spain	11
6	Australia	10	Netherlands	14	Australia	9
7	Japan	9	Australia	12	Japan	7
8	Spain	9	Poland	9	France	5
9	Canada	8	UK	9	Switzerland	5
10	Korea	5	Germany	7	Canada	4

*NOA- Number of Articles

position in milk allergy research. China dominates PubMed with 32 papers, followed by Italy and the USA, ranking in the top three in all databases. Italy demonstrates robust output across all databases, ranking second in all three databases, emphasizing its vibrant research environment in allergy research. China also demonstrates a robust ranking, ranking third in Scopus and WoS and leading on PubMed. The Netherlands, Spain, and Australia are also prominent contributors, ranking in the top ten in all databases, emphasizing their sustained investment in allergy-related health research. Notably, some nations, such as France, Switzerland, and Germany, are only present in particular databases, emphasizing differences in the coverage of indexing or regional publication patterns. Overall, the data emphasize a geographically diverse contribution to milk allergy literature with a cluster of output in North America, Europe, and Asian regions, emphasizing the global significance of understanding and managing milk allergy.

Countries' Scientific Production

Global scientific production on milk allergy and gut microbiome demonstrates decisive regional patterns on PubMed, Web of Science (WOS), and Scopus. The United States and China uniformly dominate on all three platforms, an indicator of their robust research infrastructure. PubMed emphasizes biomedical research centres such as the US, China, Italy, and Australia, whereas WOS demonstrates a similar trend with slightly wider academic coverage. Scopus shows broader global involvement, with contributions from India, Brazil, and Europe (Figure 3). This suggests increased global interest in the knowledge of milk allergy, gut microbiota interactions, and the creation of alternative therapies like probiotics and plant-based alternatives.

Countries' Scientific Collaboration

Figure 4 illustrates a dynamic landscape of worldwide scientific alliances focused on gut microbiota and food allergy studies. Crafted with VOSviewer, this visualization portrays the geographic breadth and collaborative strength of research ties using bibliometric analysis. Node dimensions signify the volume of scholarly work, while connecting lines represent the vigor of international cooperation. The United States stands out as a pivotal player, acting as the nexus for numerous cross-border partnerships, notably with Canada, China, England, and Australia. This emphasizes America's prominent role in advancing global scientific progress in this area. Across Europe, nations such as Italy, Germany, the Netherlands, France, and England forge cohesive clusters, reflecting strong regional bonds and aligned research priorities. Asian countries, including China, Japan and Iran are increasingly woven into this intricate network, marking a surge in their scientific influence. The map also delineates distinctive regional communities, Southern and Central Europe (green), Western Europe (blue), and North America with its affiliates (red), each symbolizing unique yet interconnected circles of collaboration. The pattern of dispersion and cross-linking reveals a flourishing environment of international teamwork, predominantly led by affluent regions, but with a rising presence of emerging contributors. Ultimately, this analysis offers valuable insights into the spatial distribution of research activity and highlights avenues for strengthening global collaboration in the field of microbiota-allergy investigations.

Co-Occurrence

Figure 5 illustrates a network visualization of major terms identified within the reviewed literature, presenting an in-depth conceptual map of how gut microorganisms relate to hypersensitivity disorders. Created with VOSviewer, this diagram organizes terms into unique theme-based groups according to their frequency of co-mention and the strength of their associations (represented in Table 3). Three main groupings stand out: the first centers on infant microbial establishment and immune system development, the second emphasizes interventions using beneficial microbes, and

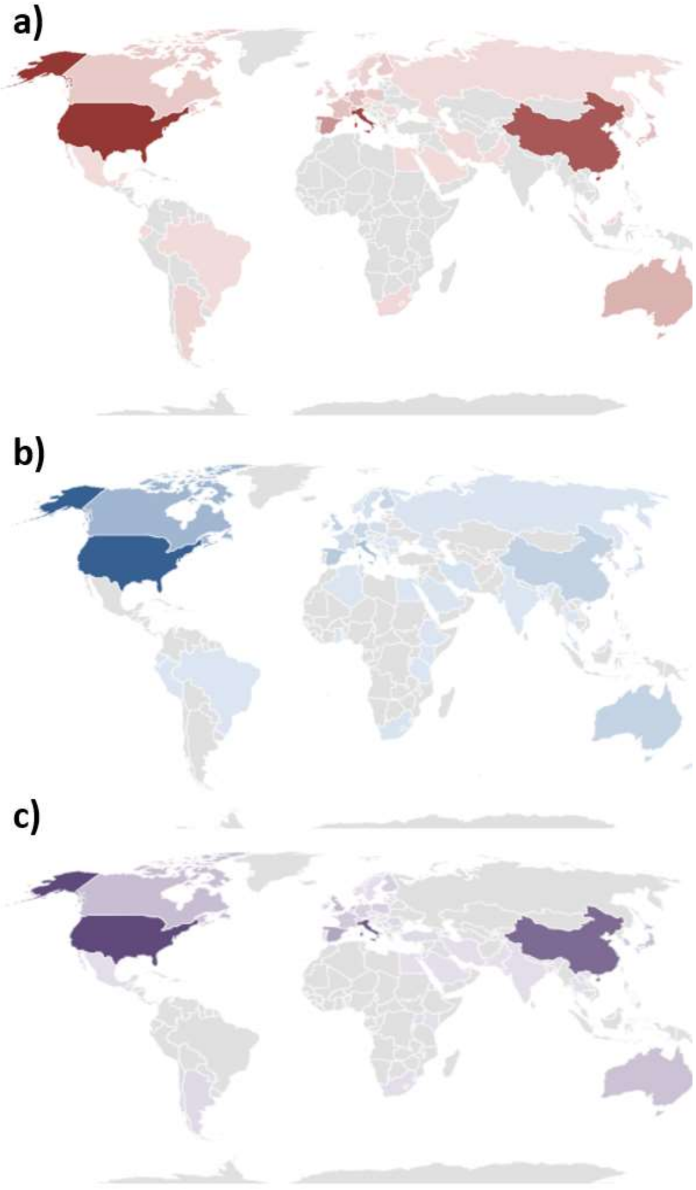

Fig 3: Country’s Scientific Production (a) PubMed (b) WOS (c) Scopus

the third addresses patient outcomes and methods for detecting allergies. The pronounced links among these groupings highlight the collaborative and cross-disciplinary character of ongoing investigations. Central nodes such as those referring to intestinal flora, allergic responses, and microbial communities feature prominently, underscoring their influence throughout the field. This thematic analysis not only captures prevailing directions in the literature but also points toward emerging

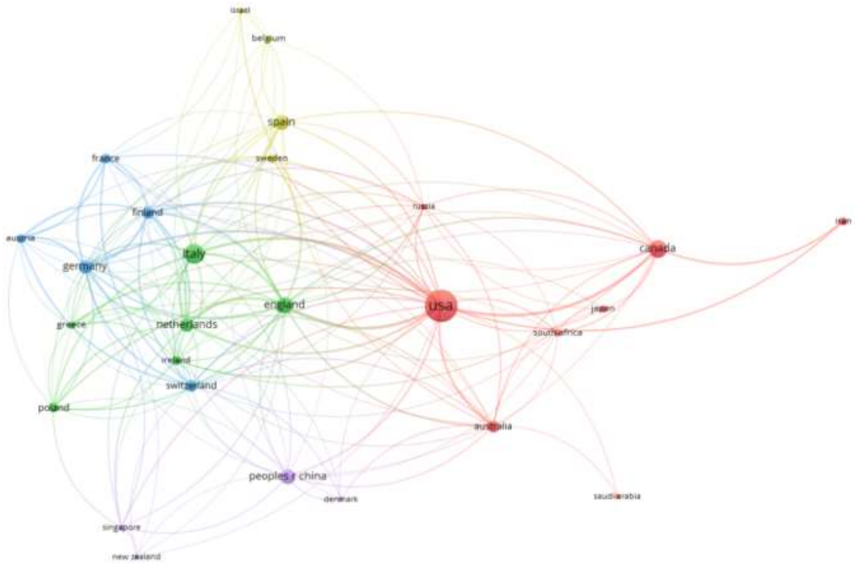

Fig 4: Countries' Scientific Collaboration

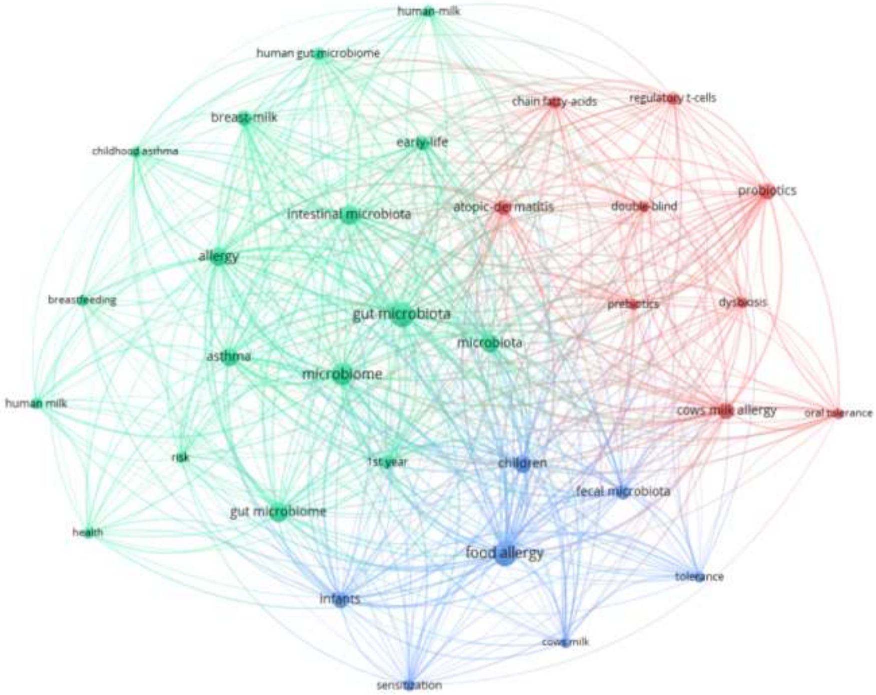

Fig 5: Co-Occurrence

Table 3: Differentiation of Cluster Colours

Cluster	Primary Research Focus	Emerging Direction	Conceptual Core
Green	Microbial colonization in early life	Longitudinal studies on maternal-infant microbiota transfer	Developmental immunity
Red	Probiota or prebiotic interventions and immune tuning	Personalized microbiome-based therapies for allergy prevention	Immune modulation
Blue	Clinical and diagnostic dimensions of allergy	Biomarker discovery, tolerance profiling, infant allergy screening	Translational allergy research

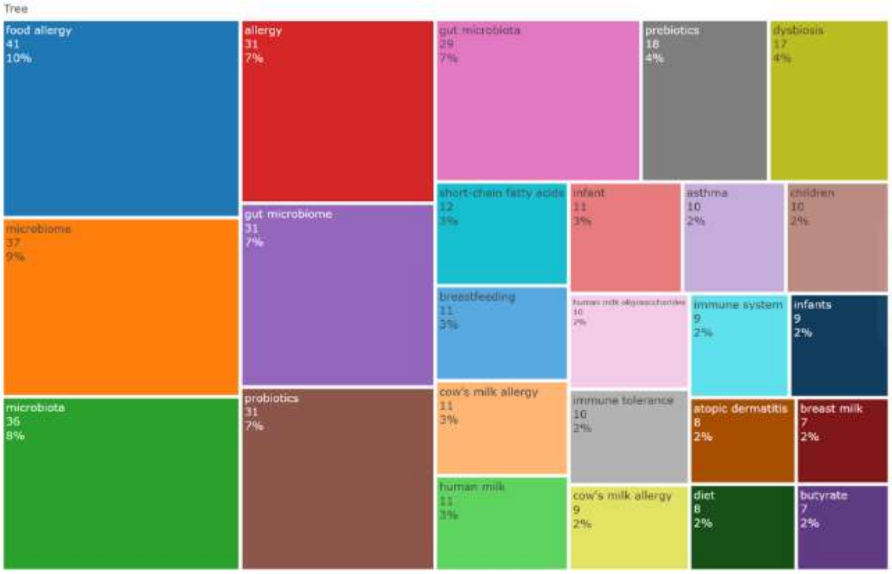

Fig 6: Tree map

topics for subsequent study, such as building immune tolerance, adjusting microbial ecosystems, and tracking changes from infancy onward.

Tree Map

The tree maps from WoS, Scopus, and PubMed reveal important areas of research based on the links between milk allergy and the gut microbiome (Figure 6). The continued emphasis on commonly recurring terminology such as "food allergy", "microbiota", "gut microbiome", and "probiotics" shows that understanding the role of microbes in the development of allergies remains a fundamental aspect of that research. The focal points of WoS explicitly mandate life-stage aspects of inquiry by using "breast milk" and "infants", while the language of Scopus includes microbes and adds terminology related to clinical (e.g., "prebiotics") and dietary aspects (e.g., "immune tolerance"). The addition of the terminology used in PubMed expands the current inquiry areas, while also including children, development, and clinical studies, thereby showing a strong emphasis on pediatric and experimental areas of overlap. Overall, these maps show that there exists a shared interest in understanding early microbially-mediated exposure and exploring microbially-mediated approaches for milk allergy management.

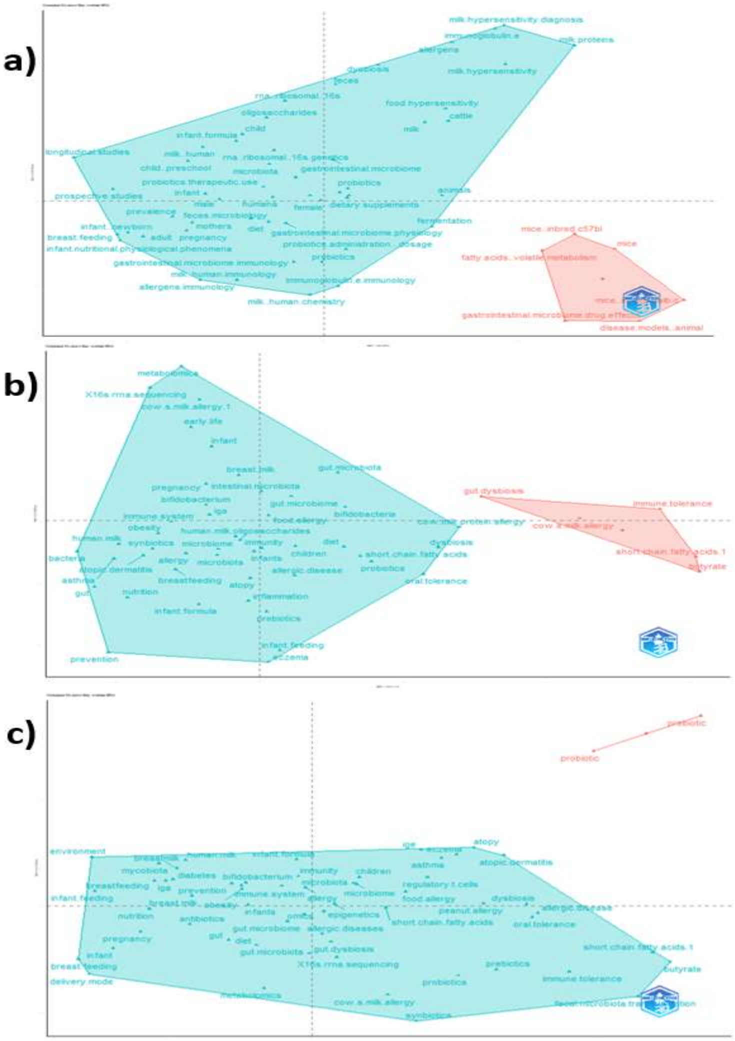

Fig 7: Factorial Analysis (a) PubMed (b) Scopus (c) WOS

Factorial Analysis

Upon comparing the two clusters throughout the various databases, some significant differences become apparent (Table 4). In PubMed, the primary (blue) cluster focuses on clinical subjects, specifically symptoms and treatment options, whereas the secondary (red) cluster goes deeper into immune system functions and molecular causes (Fig 7a). In Scopus, the blue cluster has a broader reach, including the microbiome and dietary patterns, whereas the red cluster focuses on specific dietary strategies and host-related physiology (Fig 7b). On the other hand, the WOS database shows the predominant cluster, encompassing considerable research on systemic and developmental themes, while the secondary cluster investigates more niche and emerging topics, such as particular allergies and long-term health effects (Fig 7c). These observations highlight that the blue

Table 4: Comparison of Factorial Analysis

Database	Blue Cluster (Main Cluster)	Red Cluster (Secondary Cluster)
PubMed	Focuses on clinical and biomedical terms: infants, cow's milk protein allergy, gut microbiota, probiotics	Focuses on immune-related mechanisms: immune tolerance, inflammation, and allergic response
Scopus	Covers interdisciplinary research: microbial diversity, diet, prebiotics, metagenomics	Includes intervention strategies: host-microbe interaction, dietary modulation, gut barrier
WOS	Focuses on systemic and developmental aspects: early-life colonization, immune development, inflammation	Sparse cluster with niche or emerging topics: specific allergens, pathways, long-term effects

clusters generally represent a wider and more established research base, while the red clusters are more focused on targeted mechanisms and emerging scientific trends.

Discussion

The field of gut microbiota and dairy allergy research has seen rapid growth from 2015 to 2025, with notable increases in publications since 2020 and significant contributions from the USA, China, and European nations (43). Much of the research centres on how the gut microbiome influences immune responses, particularly through cytokines like IL-10 and IL-22, in both the development and management of cow's milk allergy(44). Thematic analysis reveals that the field is primarily focused on understanding immunological mechanisms, developing new diagnostic tools such as metagenomics, and exploring potential therapeutic strategies, including probiotic and dietary interventions(45). Although the interest in microbiome-based therapies, especially for children, continues to rise, the actual clinical effectiveness of probiotics remains uncertain, stressing the need for more robust and standardized studies (46). The research landscape is gradually shifting from foundational discovery toward personalized prevention and treatment strategies, but bringing these advances into clinical practice is challenged by inconsistencies in research design and insufficient regulatory guidance (47). This overall analysis highlights the need for greater international cooperation, standardized research methods, and integrated approaches combining immunology, nutrition, and microbiome science to better address dairy allergies (48).

Future Scope

- Future research on gut microbiota and dairy allergy is shifting towards precision medicine, where treatments are made specific to a person's unique genetics and microbial composition.
- This includes tailored interventions like specific probiotics, symbiotic, and diet changes designed especially for the individual.
- Utilizing advanced multi-omics technologies, along with long-term studies, will deepen our understanding of how to safely and effectively modulate the gut microbiome to prevent or manage dairy allergies.
- There's a real need for well-designed, standardized clinical trials to ensure that the results we get are reliable and comparable.
- Greater international collaboration will be crucial to produce strong evidence and help bring microbiome-based treatments into everyday medical practice.

Conclusion

This study presents a detailed overview of global scientific efforts exploring the relationship between gut microbiota and dairy allergy, with a focus on cow's milk allergy (CMA). Research output from 2015 to 2025 shows a clear increase in studies addressing this topic (49), reflecting the growing recognition of the gut microbiome's role in immune regulation and allergic disease development. The analysis of articles from Scopus, PubMed, and Web of Science reveals that original research dominates the literature, supported by a substantial number of review papers synthesizing current knowledge (50). Three major research themes emerged: the influence of early-life microbial exposure on allergy risk, intervention strategies such as probiotics and symbiotic, and the involvement of immune-modulating genes like IL-10 and IL-22. Countries such as the United States, China, and Italy lead in publication volume, supported by strong collaborative networks that span multiple continents (51). The findings emphasize that microbial imbalance in early life may contribute to increased susceptibility to allergic responses, while specific beneficial bacteria and dietary approaches show promise in reducing symptoms and promoting immune tolerance (52). For example, therapies combining *Anaerostipes caccae* with lactulose have demonstrated potential in managing food allergies in experimental models. Overall, this work highlights the global research momentum in understanding how gut microbes influence dairy allergy mechanisms and management. It provides a foundation for future research aimed at developing targeted, microbiome-based therapies for preventing and treating CMA and related allergic conditions.

References

1. Wiertsema SP, van Bergenhenegouwen J, Garssen J, Knippels LMJ (2021) The interplay between the gut microbiome and the immune system in the context of infectious diseases throughout life and the role of nutrition in optimizing treatment strategies. Nutrients 13:886
2. Zhao M, Chu J, Feng S, Guo C, Xue B, He K, Li L (2023) Immunological mechanisms of inflammatory diseases caused by gut microbiota dysbiosis: A review. Biomed Pharmacother 164:114985
3. Wu H-J, Wu E (2012) The role of gut microbiota in immune homeostasis and autoimmunity. Gut Microbes 3:4–14
4. Shao T, Hsu R, Rafizadeh DL, et al (2023) The gut ecosystem and immune tolerance. J Autoimmun 141:103114
5. Hochwallner H, Schulmeister U, Swoboda I, Spitzauer S, Valenta R (2014) Cow's milk allergy: from allergens to new forms of diagnosis, therapy and prevention. Methods 66:22–33
6. Walsh J, Meyer R, Shah N, Quekett J, Fox AT (2016) Differentiating milk allergy (IgE and non-IgE mediated) from lactose intolerance: understanding the underlying mechanisms and presentations. Br J Gen Pract 66:e609-11
7. Edwards CW, Younus MA (2025) Cow milk allergy. StatPearls
8. Zhang S, Sicherer S, Berin MC, Agyemang A (2021) Pathophysiology of non-IgE-mediated food allergy. ImmunoTargets Ther 10:431–446
9. Dribin TE, Waserman S, Turner PJ (2023) Who needs epinephrine? Anaphylaxis, autoinjectors, and parachutes. J Allergy Clin Immunol Pract 11:1036–1046
10. Chen F-M, Lee J-H, Yang Y-H, Lin Y-T, Wang L-C, Yu H-H, Chiang B-L (2014) Analysis of α-lactalbumin-, β-lactoglobulin-, and casein-specific IgE among children with atopic diseases in a tertiary medical center in Northern Taiwan. J Microbiol Immunol Infect 47:130–136
11. Rey-Mariño A, Francino MP (2022) Nutrition, gut Microbiota, and allergy development in infants. Nutrients 14: 4316
12. Yan X, Yan J, Xiang Q, Dai H, Wang Y, Fang L, Huang K, Zhang W (2023) Early-life gut microbiota in food allergic children and its impact on the development of allergic disease. Ital J Pediatr 49:148
13. Zhang Y-W, Wu Y, Liu X-F, Chen X, Su J-C (2024) Targeting the gut microbiota-related metabolites for osteoporosis: The inextricable connection of gut-bone axis. Ageing Res Rev 94:102196
14. Dudakov JA, Hanash AM, van den Brink MRM (2015) Interleukin-22: immunobiology and pathology. Annu Rev Immunol 33:747–785

15. Li J, Xiao C, Li C, He J (2025) Tissue-resident immune cells: from defining characteristics to roles in diseases. Signal Transduct Target Ther 10:12

16. Barros KV, Flor Silveira VL, Laranjeira MS, Wandalsen NF, Passeti S, de Oliveira R, Munekata RV, Noakes PS, Miles EA, Calder PC (2017) Evidence for involvement of IL-9 and IL-22 in cows' milk allergy in infants. Nutrients. https://doi.org/10.3390/nu9101048

17. Cieśla D, Nowak T (2025) The influence of immune system-related genes on the development of atopic dermatitis. Postepy Dermatol Alergol 42:232–242

18. Cope A, Le Friec G, Cardone J, Kemper C (2011) The Th1 life cycle: molecular control of IFN-γ to IL-10 switching. Trends Immunol 32:278–286

19. Noh J, Lee JH, Noh G, Bang SY, Kim HS, Choi WS, Cho S, Lee SS (2010) Characterisation of allergen-specific responses of IL-10-producing regulatory B cells (Br1) in Cow Milk Allergy. Cell Immunol 264:143–149

20. Kim A-R, Kim HS, Kim DK, et al (2016) Mesenteric IL-10-producing CD5+ regulatory B cells suppress cow's milk casein-induced allergic responses in mice. Sci Rep 6:19685

21. Mauras A, Wopereis H, Yeop I, et al (2019) Gut microbiota from infant with cow's milk allergy promotes clinical and immune features of atopy in a murine model. Allergy 74:1790–1793

22. Hesser LA, Puente AA, Arnold J, Ionescu E, Mirmira A, Talasani N, Lopez J, Maccio-Maretto L, Mimee M, Nagler CR (2024) A synbiotic of Anaerostipes caccae and lactulose prevents and treats food allergy in mice. Cell Host Microbe 32:1163-1176.e6

23. Vasilescu I-M, Chifiriuc M-C, Pircalabioru GG, Filip R, Bolocan A, Lazăr V, Diţu L-M, Bleotu C (2021) Gut Dysbiosis and Clostridioides difficile Infection in Neonates and Adults. Front Microbiol 12:651081

24. Fieten KB, Totté JEE, Levin E, Reyman M, Meijer Y, Knulst A, Schuren F, Pasmans SGMA (2018) Fecal microbiome and food allergy in pediatric atopic dermatitis: A cross-sectional pilot study. Int Arch Allergy Immunol 175:77–84

25. Azwai SM, Lawila AF, Eshamah HL, Sherif JA, Farag SA, Naas HT, Garbaj AM, Salabi AAE, Gammoudi FT, Eldaghayes IM (2024) Antimicrobial susceptibility profile of Klebsiella pneumoniae isolated from some dairy products in Libya as a foodborne pathogen. Vet World 17:1168–1176

26. Kim H-J, Youn H-Y, Kang H-J, Moon J-S, Jang Y-S, Song K-Y, Seo K-H (2022) Prevalence and virulence characteristics of Enterococcus faecalis and Enterococcus faecium in bovine mastitis milk compared to bovine normal raw milk in South Korea. Animals (Basel) 12:1407

27. Xu J, Sheikh TMM, Shafiq M, et al (2025) Exploring the gut microbiota landscape in cow milk protein allergy: Clinical insights and diagnostic implications in pediatric patients. J Dairy Sci 108:73–89

28. Castro Neves A, Romeira AM, Marques JG, Matos V, Leiria Pinto P (2020) Blood or skin: what is best in predicting cow's milk allergy diagnosis? Eur Ann Allergy Clin Immunol 52:160–164

29. Ciğerci Günaydın N, Eren Akarcan S, Gülen F, Bal CM, Tanaç R, Atasever M, Demir E (2022) Cut-Off values of specific IgE and skin prick test to predict oral food challenge positivity in children with cow's milk allergy. Turk Arch Pediatr 57:603–610

30. Chinthrajah RS, Tupa D, Prince BT, Block WM, Rosa JS, Singh AM, Nadeau K (2015) Diagnosis of food allergy. Pediatr Clin North Am 62:1393–1408

31. D'Auria E, Salvatore S, Acunzo M, Peroni D, Pendezza E, Di Profio E, Fiore G, Zuccotti GV, Verduci E (2021) Hydrolysed formulas in the management of cow's milk allergy: New insights, pitfalls and tips. Nutrients 13:2762

32. Maryniak NZ, Sancho AI, Hansen EB, Bøgh KL (2022) Alternatives to cow's milk-based infant formulas in the prevention and management of cow's milk allergy. Foods 11:926

33. Ribes-Koninckx C, Amil-Dias J, Espin B, Molina M, Segarra O, Diaz-Martin JJ (2023) The use of amino acid formulas in pediatric patients with allergy to cow's milk proteins: Recommendations from a group of experts. Front Pediatr 11:1110380

34. NIAID-Sponsored Expert Panel, Boyce JA, Assa'ad A, et al (2010) Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol 126:S1-58
35. Jiang L, Zhang L, Xia J, Cheng L, Chen G, Wang J, Raghavan V (2025) Probiotics supplementation during pregnancy or infancy on multiple food allergies and gut microbiota: a systematic review and meta-analysis. Nutr Rev 83:e25–e41
36. Fiocchi A, Pawankar R, Cuello-Garcia C, et al (2015) World Allergy Organization-McMaster university guidelines for allergic disease prevention (GLAD-P): Probiotics. World Allergy Organ J 8:4
37. Tan W, Zhou Z, Li W, Lu H, Qiu Z (2021) Lactobacillus rhamnosus GG for cow's milk allergy in children: A systematic review and meta-analysis. Front Pediatr 9:727127
38. Guo Y, Chen J, Qu Y, Wu X, Zhang S, Wang J, Yue X, Liu Z, Xie A, Li M (2025) Research progress on probiotics in alleviating cow's milk allergy: A review. Foods 14:1879
39. Binda S, Chow-Shi-Yée M, El Salti S, Auclair-Ouellet N, Oula M-L, Carton T, Leuillet S, Tomassi D, Hemmings R, Kadoch I-J (2025) The effect of probiotics on health in pregnancy and infants: A randomized, double-blind, placebo-controlled trial. Nutrients. https://doi.org/10.3390/nu17111825
40. Ishwarya RA, Anju R, Kamaraj M, Aravind J (2024) Recent advancements in pesticide mitigation using engineered Escherichia coli strains (2024). Applied Environmental Biotechnology 9:17–30
41. Kamaraj M, Kiruthika N, Naganathan T, Saranya T, Aravind J (2025) Bibliometric analysis and impact of heavy metals contamination in soils. Global Journal of Environmental Science and Management 11:321–342
42. N'goye KS, Soude H, Loko YLE (2022) Evolution and trend of deep learning in agriculture: A bibliometric approach. J Comput Commun 10:113–124
43. Ke H, Yao H, Wei P (2025) Advances in research on gut microbiota and allergic diseases in children. Curr Res Microb Sci 8:100362
44. Moriki D, Francino MP, Koumpagioti D, Boutopoulou B, Rufián-Henares JÁ, Priftis KN, Douros K (2022) The role of the gut microbiome in cow's milk allergy: A clinical approach. Nutrients 14:4537
45. Gyriki D, Nikolaidis C, Stavropoulou E, Bezirtzoglou I, Tsigalou C, Vradelis S, Bezirtzoglou E (2024) Exploring the gut microbiome's role in inflammatory Bowel Disease: Insights and interventions. J Pers Med 14:507
46. Maftei N-M, Raileanu CR, Balta AA, Ambrose L, Boev M, Marin DB, Lisa EL (2024) The potential impact of probiotics on human health: An update on their health-promoting properties. Microorganisms 12:234
47. Gulliver EL, Young RB, Chonwerawong M, et al (2022) Review article: the future of microbiome-based therapeutics. Aliment Pharmacol Ther 56:192–208
48. Andreou E, Papaneophytou C (2025) Boosting immunity through nutrition and gut health: A narrative review on managing allergies and multimorbidity. Nutrients. https://doi.org/10.3390/nu17101685
49. Bognanni A, Firmino RT, Arasi S, et al (2024) World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) guideline update - XI - Milk supplement/replacement formulas for infants and toddlers with CMA - Systematic review. World Allergy Organ J 17:100947
50. Aguilera AC, Dagher IA, Kloepfer KM (2020) Role of the microbiome in allergic disease development. Curr Allergy Asthma Rep 20:44
51. Sestito S, D'Auria E, Baldassarre ME, Salvatore S, Tallarico V, Stefanelli E, Tarsitano F, Concolino D, Pensabene L (2020) The role of prebiotics and probiotics in prevention of allergic diseases in infants. Front Pediatr 8:583946
52. Feehley T, Stefka AT, Cao S, Nagler CR (2012) Microbial regulation of allergic responses to food. Semin Immunopathol 34:671–688