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The Role of the Gut Microbiome in Immune Regulation and Autoimmune and Allergic Diseases: Implications of Probiotics, Prebiotics, and Fecal Microbiota Transplantation

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Abstract:

Autoimmune and allergic diseases are systemic conditions caused by immune dysregulation, affecting millions globally. Autoimmune disorders, such as rheumatoid arthritis and systemic lupus erythematosus, involve autoreactive lymphocytes attacking host tissues, while allergic diseases like asthma and atopic dermatitis stem from exaggerated immune responses to environmental antigens. Emerging evidence highlights the critical role of the gut microbiome in maintaining immune homeostasis and its dysregulation (dysbiosis) in the pathogenesis of these diseases. This systematic review, adhering to PRISMA 2020 guidelines, examined studies published in the last decade to explore microbiota-mediated immune regulation and the therapeutic potential of probiotics, prebiotics, and fecal microbiota transplantation (FMT). A total of 145 records were identified, with 16 studies meeting inclusion criteria after rigorous screening and quality assessment. Results reveal that dysbiosis, marked by reduced microbial diversity and shifts in bacterial composition, contributes to immune dysfunction and disease progression. Probiotics and prebiotics were shown to enhance regulatory T-cell activity, restore gut barrier integrity, and reduce inflammatory cytokines, while FMT demonstrated efficacy in conditions such as ulcerative colitis and type 1 diabetes, improving clinical outcomes. Despite promising short-term results, challenges including variability in methodologies, accessibility, and long-term safety remain. This review highlights the gut microbiome as a crucial therapeutic target in autoimmune and allergic diseases. Integrating microbiome-based interventions with personalized approaches could revolutionize immune regulation and disease management, paving the way for innovative, accessible, and effective treatment strategies to improve patient outcomes worldwide.

Introduction

Autoimmune diseases encompass a range of persistent, systemic conditions in which the immune system mistakenly targets the body's tissues, leading to chronic inflammation and the accumulation of immune complexes in various organs [1]. In autoimmune diseases, a loss of self-tolerance leads to the activation of autoreactive lymphocytes, resulting in immune-mediated damage to the body's cells and tissues [1,2]. Epidemiological data suggest that autoimmune diseases are prevalent in approximately 5-8% of the global population, with limited therapeutic options. With over 80 recognized disorders, they present a substantial global challenge, severely affecting patient lives and imposing considerable societal strain [3]. The American Autoimmune Related Disease Association (AARDA) reports that autoimmune disorders impact over 20 million individuals in the United States. The incidence of these conditions is projected to grow significantly shortly [4].

Allergic diseases like allergic rhinitis, asthma, atopic dermatitis, food allergies, and eczema are systemic conditions caused by immune system dysfunction, with rising incidence rates driven by various factors including genetics, environment, and immune status[5]. In allergic diseases, immune dysregulation manifests as an exaggerated immune response to harmless environmental antigens (allergens). This involves a Th2-dominant immune pathway, with excessive production of IgE antibodies, mast cell degranulation, and the release of inflammatory mediators like histamine [6,7]. Allergic diseases including anaphylaxis, food allergies, asthma, allergic rhinitis, eczema, and drug allergies affect millions of individuals worldwide. Asthma impacts approximately 300 million people globally, food allergies affect an estimated 200 to 250 million individuals, and allergic rhinitis affects nearly 400 million people. These conditions often coexist, requiring an integrated diagnostic and treatment approach and greater awareness among physicians and patients [7].

John Donne's quote, "No man is an island," reflects the interconnectedness between humans and society. From birth, humans are colonized by microbes, particularly in the gastrointestinal tract (GIT), which hosts a diverse microbiota of bacteria, fungi, viruses, and parasites. This gut microbiota acts as a "superorganism," aiding digestion, producing essential metabolites, protecting against infections, maintaining intestinal health, and regulating immunity [2]. Dysbiosis, or an imbalance in gut microbiota, is increasingly recognized as a key factor in the development of autoimmune and allergic

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diseases. The cross-talk between gut microbiota and host immunity is a key factor in maintaining physiological stability and plays a significant role in the etiology of diseases [8]. Historically, before Koch's postulates established microbes as agents of disease, the miasma theory, which proposed that "bad air" caused illness, was widely accepted in Europe and China in ancient times and was loosely linked to microbial presence. Attention was initially focused on the characteristics of microorganisms that disrupted the host's homeostasis. In recent years, however, advancements in technology have led to a paradigm shift, now focusing on the intricate role that microbes play in the pathogenesis of autoimmune and allergic diseases, highlighting their impact on immune regulation and disease development [9].

Microbiota based therapies such as probiotics, prebiotics, and fecal microbiota transplantation (FMT) are emerging as promising treatments for restoring immune balance and reducing inflammation. These therapies offer more personalized and effective options for managing these diseases [10]. Additionally, recent advancements in the treatment of these diseases include the development of targeted biologicals like monoclonal antibodies like omalizumab for allergies [7] that specifically modulate immune pathways. Recent advancements in autoimmune disease treatment, including CAR-T therapy, FcRn inhibitors, and ketogenic diets, emphasize targeted approaches. However, challenges such as accessibility, cost, and side effects highlight the need for ongoing research to improve and expand these therapies [11-13].

Probiotics and prebiotics help reshape the gut microbiome by promoting the growth of beneficial bacteria, which in turn stabilizes immune function, restores intestinal barrier integrity, and modulates inflammatory pathways, ultimately reducing disease flares and improving symptom management in autoimmune and allergic diseases [8,10]. Fecal microbiota transplantation (FMT) was first used in 1983 to treat Clostridium difficile (C. diff) infections, where it proved effective in restoring the balance of gut microbiota and resolving the infection. In 2010, the U.S. Food and Drug Administration recognized FMT as a promising treatment for recurrent C. diff infections. Since then, FMT has been explored for other conditions like inflammatory bowel disease (IBD) and chronic constipation, where it has shown potential in restoring gut health and improving symptoms. More recently, researchers are investigating FMT's potential in treating autoimmune and allergic diseases, as it may help modulate the immune system, reduce inflammation, and restore immune balance by re-establishing a healthy gut microbiome [10,14].

This systematic review will examine the intricate link between microbial dysbiosis and immune dysregulation, focusing on how imbalances in the microbiome and its metabolites drive immune flare-ups in autoimmune and allergic diseases. It will also explore the therapeutic potential of probiotics, prebiotics, and fecal microbiota transplantation in restoring immune stability, emphasizing personalized approaches to disease management and improving patient outcomes.

Methods

This systematic review examines the role of the gut microbiome in autoimmune and allergic diseases, with particular emphasis on immune regulatory mechanisms, the impact of dysbiosis on immune instability, and the therapeutic potential of prebiotics, probiotics, and fecal microbiota transplantation. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.

Eligibility criteria

The eligibility criteria for this review included studies involving human participants with autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus) or allergic conditions (e.g., asthma, eczema). Eligible studies examined gut microbiome dysbiosis in disease pathogenesis or immune regulation, or evaluated microbiome-based interventions such as probiotics, prebiotics, or fecal microbiota transplantation (FMT). Accepted study designs included clinical trials, cohort, case-control, cross-sectional studies, and systematic reviews or meta-analyses, with outcomes assessing immune markers, clinical improvement, or gut microbiota restoration. Only English-language studies published within the past 10 years were included; non-human studies, unrelated conditions, and articles lacking relevant microbiome or immune outcomes were excluded. Study selection was performed in a stepwise manner, with initial title and abstract screening followed by full-text assessment. Methodological quality was evaluated using AMSTAR 2, SANRA 2, and the Cochrane Collaboration Risk of Bias Tool, and only studies achieving ≥70% quality scores were included in the final analysis.

Databases and search strategy

We conducted a comprehensive search across multiple databases, including PubMed, PMC, Google Scholar, Cochrane Library, and ScienceDirect, to ensure a thorough review of relevant literature. Our search strategy utilized keywords such as "gut microbiome," "immune regulation," "autoimmune diseases," "allergic conditions," "probiotics," "prebiotics," "FMT," "microbiota dysbiosis," "Treg cells," and "short-chain fatty acids (SCFAs)" to identify relevant literature. A Boolean search approach was utilized to explore multiple databases by integrating relevant keywords and MeSH terms. The detailed search strategy for this systematic review is presented in Table 1.

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DATA BASE	SEARCH CRITERIA	FILTERS APPLIED	ARTICLES FOUND
Pubmed	("Gastrointestinal Microbiome/immunology"[Mesh]) AND ("Autoimmune Diseases/immunology"[Mesh] OR "Autoimmune Diseases/microbiology"[Mesh] OR "Autoimmune Diseases/physiopathology"[Mesh]) And	10 years publication date,free full text, English, Humans	60
	(("Dysbiosis/immunology"[Mesh] OR "Dysbiosis/microbiology"[Mesh])) AND ("Hypersensitivity/immunology"[Mesh] OR "Hypersensitivity/microbiology"[Mesh] OR "Hypersensitivity/physiopathology"[Mesh])	10 years publication date,free full text, English, Humans	30
Google scholar	gut dysbiosis and autoimmune disease and allergy and probiotics or prebiotics or fecal transplant	Include citations, last 10 years	30
PMC	("dysbiosis"[MeSH Terms] OR "dysbiosis"[All Fields]) OR (("Gut Microbiome (Camb)"[Journal] OR "gutmicrobiome"[All Fields]) AND ("autoimmune diseases"[MeSH Terms] OR ("autoimmune"[All Fields] AND "diseases"[All Fields]) OR "autoimmune diseases"[All Fields])) AND allergic[All Fields] AND ("disease"[MeSH Terms] OR "disease"[All Fields] OR "diseases"[All Fields]) AND ("probiotics"[MeSH Terms] OR "probiotics"[All Fields]) AND ("prebiotics"[MeSH Terms] OR "prebiotics"[All Fields] OR "prebiotic"[All Fields]) AND "fmt"[All Fields]) OR ("fecal microbiota transplantation"[MeSH Terms] OR ("fecal"[All Fields] AND "microbiota"[All Fields] AND "transplantation"[All Fields]) OR "fecal microbiota transplantation"[All Fields] OR ("fecal"[All Fields] AND "transplant"[All Fields]) OR "fecal transplant"[All Fields]) AND ((medline[sb] AND "open access"[filter] AND "has_associated data"[Filter] AND "author manuscript"[Filter]) AND "2014/12/30"[PDat] : "2024/12/28"[PDat])	Last 10 years, associated data, author manuscripts,open accesses , medline journal	36
Science direct	Autoimmunity and allergy and gut microbiome or dysbiosis and gender and probiotics or prebiotics or fecal transplant	Open access, Open archive	12
Cochrane Library	"Autoimmunity" and "dysbiosis"	Last 10 years ,English	9
	"Allergy" and "dysbiosis"	Last 10 years ,English	6

Table 1 summarizes the comprehensive search strategy used across multiple databases, including PubMed, PMC, Google Scholar, ScienceDirect, and the Cochrane Library. A combination of MeSH terms and keywords related to gut microbiome dysbiosis, immune regulation, autoimmune diseases, allergic conditions, and microbiome-based interventions was employed. Filters were applied to restrict results to human studies published in English within the last 10 years, ensuring relevance and methodological consistency.

Results

A comprehensive search across five databases identified 145 records, of which 28 duplicates were removed, leaving 117 studies for screening. After title and abstract review, 52 records were excluded for not meeting inclusion criteria, and 93 reports were sought for full-text retrieval. Of these, 53 reports could not be retrieved due to restricted full-text availability, limited institutional access, or incomplete publication records, preventing adequate assessment. The remaining 40 articles underwent full-text evaluation and quality assessment using AMSTAR 2, SANRA 2, the Cochrane Collaboration Risk of Bias Tool, and the Jadad scale, with an acceptance threshold of 70%. Twenty-four studies were excluded based on quality criteria, and 16 studies were ultimately included in the final synthesis, comprising six review articles and ten randomized controlled trials. The final data collection date was 22 July 2025, and the study selection process is summarized in Figure 1.

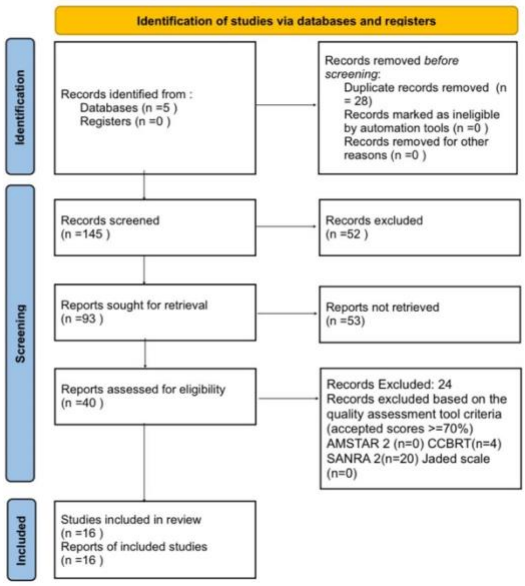

Figure 1: A flowchart demonstrating the selection process of the included articles as per the PRISMA guidelines

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis; SANRA 2: Scale for the Assessment of Narrative Review Articles 2; AMSTAR 2: Assessment of Multiple Systematic Reviews 2; CCRBT: Cochrane Collaboration Risk of Bias Tool

An overview of the quality assessment of the included studies using validated evaluation tools is presented in Table 2.

Quality Assessment tool	Type of study	Items and their characteristics	Total score	Accepted score (>70%)	Accepted studies
SANRA 2	Review Article	Six items: justification of the article's importance to the readership, statement of concrete aims or formulation of questions, description of the literature search, referencing, scientific reason, and appropriate presentation of data. Scored as 0, 1, or 2.	12	9	Wang, X. [1], Campbell, C. [2], Langan, D. [4], Liu, A. [8], Chen, C. [9], De Luca, F. [39].
CCBRT	RCT	Seven items: Random sequence generation and allocation concealment (selection bias), selective outcome reporting (reporting bias), other sources of bias, blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), and incomplete outcome data (attrition bias). The bias was assessed as low-risk, high-risk, or unclear.	7	5	Wang, C. [123], Andresen, V. [124], Zamani, B. [125], Parber, R. S. [126], Ahangari Maleki M [127], Cukrowska B [128], Hou Y [129], Kerla S [130], De Groot P [131], Frethelm H [132].

Table 2 presents an overview of the methodological quality assessment of the included studies using validated evaluation tools. Narrative and systematic review articles were assessed using SANRA 2, while randomized controlled trials were evaluated using the Cochrane Collaboration Risk of Bias Tool. Only studies meeting the predefined quality threshold of at least 70

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percent were included, ensuring reliability and methodological rigor.

The included studies and their quality assessment using validated tools are summarized in Table 3.

Index	First Author, Year	Report type	The Quality assessment tool used	Score
1.	Wang, X., 2024 [1]	Review Article	SANRA	11
2.	Campbell. C., 2023 [2]	Review Article	SANRA	11
3.	Langan.D., 2020 [4]	Review Article	SANRA	10
4.	Liu.A, 2021 [8]	Review Article	SANRA	11
5.	Chen.C.,2019 [9]	Review Article	SANRA	10
6.	De Luca .F., 2019 [39]	Review Article	SANRA	11
7.	Wang .C., 2022 [123]	RCT	CCBRT	5
8.	Andresen. V., 2020 [124]	RCT	CCBRT	6
9.	Zamani.B., 2016 [125]	RCT	CCBRT	6
10.	Farber.R.S., 2024 [126]	RCT	CCBRT	5
11.	Ahangari Maleki.M., 2023 [127]	RCT	CCBRT	6
12.	Cukrowska B, 2021 [128]	RCT	CCBRT	6
13.	Hou .Y., 2024 [129]	RCT	CCBRT	6
14.	Kedia S, 2022 [130]	RCT	CCBRT	5
15.	De Groot P, 2021 [131]	RCT	CCBRT	6
16.	Fretheim H, 2020 [132]	RCT	CCBRT	6

Table 3 summarizes the key characteristics of the studies included in this review, including publication year, study design, quality assessment tool used, and final quality scores. The included literature consisted of six review articles and ten randomized controlled trials, all of which met the accepted quality criteria and contributed to the final qualitative synthesis. SANRA checklist accepted score (>=70%): Minimum score 9 out of 12. CCBRT accepted score (>=70%) Minimum score 5 out of 7, RCT= Randomized Control Trial

Discussion

Microbiome and its functions

The human gut is home to a diverse range of microbiota, including bacteria, fungi, viruses, and other microorganisms. Recent advancements in sequencing methods, such as 16S rRNA and metagenomics, have allowed the identification of key microbiota linked to human health, including phyla like Firmicutes, Bacteroidetes, Pseudomonadota, and Actinomycetota. In contrast, less attention has been given to others, such as Fusobacteria [1]. The diverse functions of the gut microbiome and their impact on human health are summarized in Figure 2.

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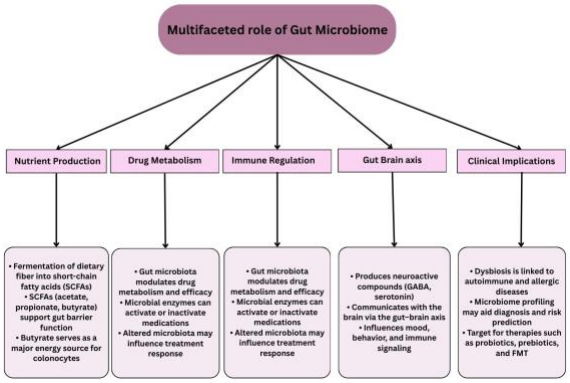
Figure 2. Multifaceted roles of the gut microbiome in human health.



This original figure, designed by the first author, illustrates the diverse roles of the gut microbiota in human health, including metabolism, immune regulation, neurochemical signaling, and clinical implications. The figure provides a conceptual overview of how gut microbiota and host interactions influence physiological processes and disease outcomes.

Role of gut microbiome in maintaining immune stability

The relationship between gut microbiota and innate immunity-

The gut-associated lymphoid tissues (GALTs) play a pivotal role in safeguarding the intestinal mucosa, functioning in coordination with the mucosa-associated lymphoid tissues (MALTs). Innate immune cells within these tissues perform key functions such as non-specific pathogen recognition, initiating innate immune responses, and presenting antigens to activate the adaptive immune system [1,2]. Studies using germ-free (GF) models have demonstrated that gut microbiota are essential for regulating the physiological functions of GALTs, contributing to their development and maturation. Additionally, metabolic by-products like short-chain fatty acids (SCFAs), produced by commensal microbiota, modulate the immune response of GALTs through epigenetic mechanisms, enhancing both their defensive capabilities and immune tolerance [2].
Innate lymphoid cells (ILCs) are crucial components of GALTs. Although ILC development occurs independently of the gut microbiota, their specific functions are heavily influenced by commensal microbiota. For example, ILC3, a prominent subset of ILCs, supports epithelial cell survival, stimulates antimicrobial peptide production, and facilitates IL-22 secretion. IL-22 is a critical cytokine for the host immune response to *Citrobacter* infections. SCFAs have been shown to enhance IL-22 production in ILC3 by activating the aromatic hydrocarbon receptor (AHR) through the AKT-STAT3 and ERK-STAT3 signaling pathways. Moreover, SCFAs promote the proliferation of intestinal ILCs by modulating G protein-coupled receptor (GPCR) activity. The gut microbiota also facilitates interactions between ILC3 and other cell types, increasing the expression of protective proteins such as fucosyltransferase 2 (FUT2), which fortifies the intestinal mucosal barrier. As the gut microbiota matures, ILC1 levels rise, suggesting that their development depends on commensal microbiota [1,2].
The relationship between gut microbiota and adaptive immunity-

The adaptive immune system in the gut mucosa primarily comprises intraepithelial lymphocytes (IELs) and lamina propria lymphocytes (LPLs), with γδ T cells being a notable subset of IELs due to their expression of the Helios transcription factor. These cells play a critical role in preventing bacterial dissemination by secreting pro-inflammatory cytokines and antimicrobial proteins, such as IL-22 and calprotectin, and are influenced by gut bacteria and their metabolites. Deficiency in γδ T cells can lead to increased bacterial translocation, as observed in conditions like sepsis and inflammatory bowel disease. The gut microbiota interacts with the adaptive immune system to prevent bacterial translocation and promote the development of mucosal lymphocytes, including CD4+ and CD8+ T cells. CD8+ T cells are essential for eliminating intracellular pathogens, aided by antigen-presenting cells, while tissue-resident memory CD8+ T cells offer protection against reinfections. Th17 cells, influenced by specific microbes like segmented filamentous bacteria (SFB), contribute to both host defense and pathological inflammation, with Th17 inflammation regulated by factors such as α2,6-sialyl ligands. Regulatory T cells (Tregs), induced by gut microbiota and dietary exposure, maintain immune tolerance and balance Th17 activity. Additionally, gut microbiota regulates secretory IgA production, crucial for maintaining gut homeostasis and preventing bacterial translocation, with maternal IgA transfer during breastfeeding further supporting immune development in offspring [2].

Autoimmune Diseases and Allergies

Autoimmune diseases can be systemic, such as systemic lupus erythematosus, affecting multiple organs like the skin, joints, kidneys, and CNS, or organ-specific, like type 1 diabetes, which targets the pancreas. These conditions often involve a loss of B cell or T cell tolerance, with the human leukocyte antigen (HLA) locus being a common genetic risk factor. Despite advances in understanding the molecular, immunological, genetic, and clinical mechanisms of some autoimmune diseases, the exact drivers, including environmental triggers and the resulting pathogenesis, remain poorly understood [3]. Innate immune pathways play a key role in autoimmune disorders, requiring deeper investigation into their mechanisms. Advanced technologies like intravital imaging and Qdot systems can help refine old concepts and uncover new approaches for better prevention and treatment [4].

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Allergic diseases arise from complex interactions between genetic and environmental factors, leading to immune dysfunction. Advances in genetics and epigenetics, including GWAS, SNP analysis, and EWAS, have enhanced our understanding of these disorders, focusing on DNA methylation, histone modifications, and non-coding RNAs. These studies offer insights into immune response mechanisms and potential diagnostic and therapeutic targets [5] . Also, studies showed the interplay between gut microbiota, immune regulation, and environmental factors is critical in shaping immune responses and influencing the development of conditions like allergic asthma [6-8].

Advances in understanding the Gut Microbiome and epigenetic mechanisms have opened avenues for targeted prevention and treatment strategies, such as microbiota modulation through probiotics [9,10], cutting-edge techniques like CAR T-cell therapy [11], and dapirolizumab pegol plus standard of care in people living with moderate-to-severe lupus[12] and dietary interventions like keto diet [13] and many more. Further research is essential to harness these insights for effective, personalized approaches including Fecal Microbiota Transplantation [14] as a re-emerging therapy to manage allergic and autoimmune diseases [6,7].

Dysbiosis- Mediators and effects

Historically, the microbiome was primarily linked to infectious diseases, as evidenced by Koch's postulates and the germ theory of disease; however, it is now recognized as a key player in the pathogenesis of autoimmune and allergic diseases through immune dysregulation [9]. Gut microbiota and their metabolites significantly influence the immune system by targeting various immune cells and modulating their functions. For instance, Lactobacillus sakei K040706 enhances the activity of NK cells in the spleen and supports the maturation of germinal centers [15], Listeria monocytogenes drives the proliferation of yolk sac-derived macrophages, aids in the development of stable bone marrow macrophages, and regulates CCR2, which facilitates macrophage migration to the gut [16,17], Segmented filamentous bacteria induce Th17 cell differentiation in gut-associated lymphoid tissue [18] and Bacteroides fragilis stimulates anti-inflammatory IL-10 production in Treg cells through polysaccharide-A secretion [19]. Other bacteria like Lactobacillus, Sutterella, and Klebsiella influence B cell functions by promoting the differentiation of naïve B cells into regulatory B cells in mesenteric lymph nodes. They also contribute to energy production through ATP synthesis, which plays a critical role in activating P2X and P2Y receptors on dendritic cells. This activation leads to the production of key cytokines, including IL-6 and TGF-β, which are essential for immune regulation. Additionally, these bacteria support the type arrangement and secretion of immunoglobulin A (IgA), a vital component of the mucosal immune response, enhancing gut immunity and maintaining homeostasis [20]. Bacillus polyfermenticus activates dendritic and NK cells, increasing their cytotoxicity and promoting IFN-γ secretion [21,22] and Lactobacillus and Bifidobacterium induce CD4+CD25+FoxP3+ Treg cells, promoting immune tolerance and balance [23].

Short-chain fatty acids (SCFAs) produced by gut bacteria regulate immune responses in the following ways. Short-chain fatty acids (SCFAs) increase the number of ILC1 cells [24] and they also regulate CD4+ T cell differentiation, induce Treg cell generation, promote IL-10 production by Th1 cells, enhance FOXP3 expression, inhibit Th9 cell differentiation and IL-9 secretion, reduce IL-17a secretion, and act as histone deacetylase inhibitors [23,25-29]. SCFAs enhance CD8+ T cell memory, metabolism, cytotoxicity, and Tc17-to-CTL transition[30][31] and also activate epithelial cells via GPR41/43, induce IgA production regulate B cell differentiation, and inhibit autoantibodies[32][33].SCFAs inhibit DC maturation, suppress CD80, CD83, and MHC II expression, enhance endocytosis, modulate cytokine production, and reduce chemokine release [34-36] and stimulate macrophage secretion of NO(nitric oxide), IL-6, IL-12p40, enhance histone H3 acetylation, and promote IL-10 production [37,38].

Gut Microbiota: A Key Player in Autoimmune Diseases

The connection between gut microbiota and autoimmune diseases is increasingly evident, as highlighted by Rinaldi [39,40]. Their study revealed that autoantibodies targeting the cell wall mannan of *Saccharomyces cerevisiae*(phosphopeptide mannan), a common commensal microorganism, are present in several autoimmune conditions, including rheumatoid arthritis, systemic lupus erythematosus, and antiphospholipid syndrome. Notably, anti-*S. Cerevisiae* antibodies (ASCAs) are a specific serological marker for Crohn’s disease (CD), appearing before disease onset in 32% of cases. Furthermore, *S. cerevisiae*, commonly used as an adjuvant in vaccines, has raised concerns about its potential role in triggering abnormal immune activation associated with autoimmune/inflammatory syndrome induced by adjuvants (ASIA) [40,41]. For example, Gut microbiome alterations, including reduced microbial diversity and dysbiosis with overgrowth of *Proteobacteria* and families like *Enterobacteriaceae* and *Fusobacteriaceae*, contribute to inflammatory bowel diseases (IBD) like Crohn's disease and ulcerative colitis [42-44], as well as type 1 diabetes mellitus (T1DM), where decreased *Intestinimonas* and increased *Blautia* levels are observed [45]. The key clinical features, diagnostic factors, and gut microbiota alterations associated with major autoimmune diseases are summarized in Table 4.

Disease	Clinical and diagnostic factors	Bacteria involved

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RA	1. Inflammation and pain of the joints 2. Systemic involvement Antibodies- 1. Rheumatoid factor (RF) 2. Anti-citrullinated peptide antibodies (ACPA) [39].	1. *Porphyromonas gingivalis*, a bacterium linked to the pathogenesis of the periodontitis [46,47] 2. *P.intermedia*/*Tannerella forsythia* were found and high titers of antibodies against these microorganisms have been detected in the serum and synovial fluids of patients with RA [48] 3. Decrease of *Bacteroidaceae* and an increase of *Firmicutes* and *Proteobacteria* (i.e. *Ruminococcaceae*, *Lachnospiraceae*) and *Desulfovibrionaceae* during the immune-priming phase of arthritis in the collagen-induced arthritis (CIA) [49] 4. Increase of *P. copri* and lower numbers of *Bifidobacteria*, the *Bacteroides–Porphyromonas* group, the *B. fragilis* subgroup , and *Eubacterium rectal–Clostridium coccoides* [50-52]
(SLE)	Heterogeneous autoimmune disease [53].	1. The *Firmicutes*/*Bacteroidetes* ratio was lower and the abundance of several genera has been reported: *Rhodococcus*, *Eggerthella*, *Klebsiella*, *Prevotella*, *Eubacterium*, and *Flavonifractor* were enriched significantly, while *Dialister* and *Pseudobutyrivibrio* were decreased in SLE patients [53,54]. 2. Lower levels of *Synergistetes* (a microorganism associated positively with the *Firmicutes* to *Bacteroidetes* ratio) were found [55]. 3. Reduction in the abundance of *Lactobacillaceae* and an increase of *Lachnospiraceae*were observed in patients with SLE [56,57]. 4. By other findings, Bankole *et al*. highlighted an increase of *Proteobacteria phyla* and the family of *Lachnospiraceae* and a decrease *of Rikenellaceae*, *Odoribacteraceae*, *Christensenellaceae*, and *Peptococcaceae*families in samples from 21 patients with SLE [58].
Type 1 Diabetes	There is the destruction of i β-cells in the pancreatic islets of Langerhans by self-reactive T cells [45,59]	1. Patients exhibited an increased abundance of Bacteroidetes, along with a reduced presence of Firmicutes [60-62]. 2. Qi et al. reported an overall reduction in bacterial richness among T1D patients, characterized by an increased abundance of the genus Blautia and a decreased presence of genera such as Haemophilus, Lachnospira, and Dialister [63].
Multiple Sclerosis	Multiple sclerosis (MS) is a central nervous system disease involving immune-mediated demyelination and neurodegeneration symptoms and recovery [64].	1. Patients showed a lower abundance of Firmicutes and higher levels of Bacteroidetes and Proteobacteria compared to their household relatives, with no significant difference in Actinobacteria between the groups [65]. 2. In the study of Italian patients, five families, including Christensenellaceae, Desulfovibrionaceae, and Clostridiales, were significantly more abundant, while four families, such as Bacteroidaceae, Tannerellaceae, Veillonellaceae, and Burkholderiaceae, were more prevalent in the control group [65]. 3. Numerous studies have shown that the gut microbiota of relapsing-remitting type of MS (RRMS) patients differs from healthy controls in the relative abundance of the families Lachnospiraceae and Ruminococcaceae [65-67]. 4. The species Clostridium bolteae, Ruthenibacterium lactatiformans, and the genus Akkermansia were found to be more abundant in both RRMS and progressive MS, with certain Clostridium species correlating with higher disability and fatigue scores [68].
Psoriatic arthritis (PsA)	An autoimmune disease with multiple clinical features, e.g., joint pain, stiffness, and swelling that many times occur in adult people with a several-year psoriasis history [69].	1. A study found that the relative abundance of Clostridium, Akkermansia, and Ruminococcus was reduced in PsA compared to other groups [70]. 2. At the phylum level, PsA was most prevalent with Bacteroidetes, followed by Firmicutes, Proteobacteria, and Actinobacteria. The gut microbiota of the PsA group resembled the no-PsA group, except for a significantly higher abundance of Actinobacteria in PsA. Significant differences were also observed across various taxonomic levels [71].
Hashimoto's disease (HD)	In HD pathogenesis, intrathyroidal mononuclear cells infiltrate the thyroid, leading to the production of autoantibodies against thyroglobulin and thyroid peroxidase. This process causes organ enlargement, gland fibrosis, reduced thyroid hormone levels, and ultimately decreased metabolic activity in multiple tissues [72].	1. In the fecal matter of HD individuals, the bacterial phyla *Firmicutes* and *Actinobacteria* were increased, while *Bacteroidetes* and *Proteobacteria* were decreased [73]. In a study of 27 HD patients, *Proteobacteria* were most prevalent in HD patients, followed by Graves' disease patients and the control group, respectively [74]. 2. Multiple studies have shown that the gut microbiota of the HD group had a high abundance of families such as Lachnospiraceae, Bacteroidaceae, Enterobacteriaceae, Alcaligenaceae, Coriobacteriaceae, Erysipelotrichia, and Bacillobacteriaceae, while Prevotellaceae, Ruminococcaceae, and Veillonellaceae were reduced [73-75].
Graves' disease (GD)	A thyroid gland-specific autoimmune disorder characterized by hyperthyroidism caused by autoantibodies activating the thyrotropin receptor, leading to symptoms such as weight loss, fatigue, tachycardia, heat intolerance, and exophthalmos [76,77].	1. In Chinese adult GD patient samples, *Proteobacteria* and *Erysipelotrichia* were elevated. Additionally, the relative abundances of *Erysipelotrichaceae*, *Lachnospiraceae*, *Alcaligenaceae*, and *Christensenellaceae* were higher compared to the control and HD groups. At the genus level, *Prevotella_9*, *Ruminococcus_2*, and *Lachnospiraceae_NK4A136_group*were enriched in the fecal matter of GD patients [74]. 2. A clinical study of 37 GD patients revealed an upregulation of *Bacilli*, *Lactobacillales*, *Prevotella*, *Megamonas*, and *Veillonella* compared to healthy individuals [78]. 3. In severe GD, the relative abundances of *Akkermansia muciniphila*, *Bifidobacterium adolescentis*, *Butyricimonas faecalis*, and *Faecalibacterium prausnitzii* were decreased, while *Eggerthella lenta*, *Fusobacterium mortiferum*, *Veillonella parvula*, *Streptococcus parasanguinis*, and *Streptococcus salivarius* were more prevalent compared to controls [79]. 4. The bacterial genera *Bacillus*, *Blautia*, *Bacteroides*, *Ornithinimicrobium*, *Alistipes*, and *Prevotella* have been identified as potential markers for distinguishing GD from healthy individuals [74,80].
Sjögren's syndrome (SS)	An inflammatory autoimmune disorder, primary or secondary to RA, SLE, or other rheumatic diseases, affecting lacrimal and salivary glands, with symptoms like dry eyes, reduced salivary flow, and positive anti-Ro antibodies or rheumatoid factor [81].	1. *Firmicutes* were identified as the most abundant phylum, followed by *Bacteroidetes*, *Proteobacteria*, and *Actinobacteria* [82,83]. 2. Family-level sequence analysis revealed that the relative abundances of *Actinomycetaceae*, *Eggerthellaceae*, *Lactobacillaceae*, *Akkermansiaceae*, *Coriobacteriaceae*, and *Eubacteriaceae* were significantly higher compared to healthy individuals [82]. 3. Some studies found increased *Clostridiaceae*, *Prevotellaceae*, *Rikenellaceae*, *Odoribacteraceae*, and *Veillonellaceae* but decreased *Porphyromonadaceae* and *Bifidobacteriaceae* in SS patients. Other studies reported lower *Ruminococcaceae*, *Lachnospiraceae*, and *Bacteroidaceae* compared to healthy controls [82,83]. 4. Cano-Ortiz reported increased *Prevotella*, *Megasphaera*, and *Veillonella*, and decreased *Bacteroides* and *Faecalibacterium*, while Mendez noted opposite trends for *Veillonella* and *Parabacteroides* [82,83].

Table 4 provides a comparative overview of major autoimmune diseases, highlighting their key clinical features, diagnostic markers, and associated patterns of gut microbiota dysbiosis. Across conditions such as rheumatoid arthritis, systemic lupus erythematosus, type 1 diabetes, multiple sclerosis, and autoimmune thyroid diseases, consistent alterations in microbial diversity and composition were observed, supporting a strong association between gut dysbiosis and autoimmune pathogenesis.

Gut Microbiota: A Key Player in Allergic Diseases

Dysbiosis, an imbalance in the microbiota, is increasingly recognized as a key factor in childhood allergy development [84]. Healthy gut microbiota plays a vital role in digestion [85], metabolism [86], and immune regulation [87], with its connection to allergic diseases gaining significant scientific attention

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Asthma

Asthma-related microbiome studies indicate increased *Moraxella*, *Haemophilus*, and *Proteobacteria* in nasal and bronchial samples of asthmatic individuals, linked to epithelial damage, inflammatory cytokines (IL-8, IL-33), and Th17-related genes [88-90]. Reduced bacterial diversity correlates with high Th2 inflammation [91]. Gut microbiome studies show lower abundances of *Lachnospira*, *Faecalibacterium*, *Roseburia*, and *Rothia* in children at risk or with asthma [92], while *Clostridium difficile* and *Clostridium neonatale* are associated with increased asthma risk [93].

Food Allergy

In children with food allergy, decreased levels of the phylum Bacteroidetes and increased levels of the phylum Firmicutes, increased levels of the families Bacteroidaceae, Clos- tridiaceae, Lachnospiraceae, Leuconostocaceae, Ruminococca- ceae, and Streptococcaceae as well as decreased levels of the genera Citrobacter, Clostridium, Dialister, Dorea, Haemophilus, Lactococcus, and Oscillospira have been reported [94].

Atopic dermatitis

Children with atopic dermatitis show reduced levels of the genera *Akkermansia*, *Bacteroides*, *Bifidobacterium*, *Faecalibacterium*, and *Lactobacillus*, along with increased levels of *Gemella* and *Rhodotorula* [95,96].

Chronic urticaria

Song et al. conducted a study comparing the intestinal flora of chronic spontaneous urticaria (CSU) patients with and without resistance to non-sedating antihistamines (nsAH). The results revealed that CSU patients with nsAH resistance exhibited higher levels of the genera *Prevotella*, *Megamonas*, *Escherichia*, *Succinivibrio*, *Klebsiella*, and *Colidextribacter*. In contrast, those without nsAH resistance showed lower levels of the genera *Blautia*, *Alistipes*, and *Anaerostipes[98]*. Additionally, a study by Liu et al. identified *Lachnospira* as a biomarker for nsAH-related characteristics. However, further research is necessary to elucidate the underlying mechanisms [97,99].

Harnessing Gut Power: Prebiotics, Probiotics, and Fecal Microbiota transplantation (FMT) in Disease Management

Several microbiota-based interventions have been explored for their therapeutic potential in modulating gut health and immune function. Probiotics, which are live microorganisms—most commonly *Lactobacillus* and *Bifidobacterium*species—have demonstrated potential in supporting gut microbiota, improving brain function and mood, and managing metabolic disorders such as diabetes by reducing oxidative stress, inflammation, and enhancing antioxidant absorption [100]. Prebiotics, in contrast, are non-digestible food ingredients such as inulin-type fructans (ITF) and short-chain fructo-oligosaccharides (scFOS) that selectively stimulate the growth and activity of beneficial gut bacteria. Their fermentation in the colon supports energy production, reduces intestinal endotoxins, and contributes to improved glucose metabolism and reduced inflammation [100].

The combination of probiotics and prebiotics, termed synbiotics, has also shown promising outcomes in regulating intestinal flora. For example, studies in elderly individuals receiving synbiotic formulations reported increased counts of *Bifidobacterium* and *Lactobacillus*, indicating enhanced gut microbial balance [101]. Another evolving therapeutic strategy is fecal microbiota transplantation (FMT)—the transfer of stool from a healthy donor to a patient's gastrointestinal tract to restore microbial diversity and balance. Originally documented in 4th-century China by Ge Hong for treating severe diarrhea and food poisoning, FMT is now an evidence-based treatment with cure rates exceeding 85% for recurrent *Clostridioides difficile* infections (CDI) [102,103]. Current research continues to explore its potential applications in autoimmune, allergic, and metabolic diseases [102,103].

Mechanism of Probiotics, Prebiotics, and FMT in Immunity Flare-Ups

Probiotics, prebiotics, and fecal microbiota transplantation modulate immune flare ups through multiple interconnected mechanisms. Short chain fatty acids such as butyrate, acetate, and propionate are produced by bacterial fermentation of prebiotics and contribute to immune homeostasis by strengthening the intestinal barrier, promoting regulatory T cell differentiation, and suppressing proinflammatory cytokines [104]. Butyrate in particular exhibits strong anti-inflammatory effects that are essential for maintaining gut immune balance [105].

Tryptophan metabolism by gut microbes generates bioactive metabolites including indoles that activate the aryl hydrocarbon receptor. This activation enhances interleukin 22 production, supports intestinal barrier integrity, and regulates innate and adaptive immune responses [106 to 108]. Probiotic derived indole metabolites further promote immune tolerance by increasing interleukin 10 and reducing tumor necrosis factor alpha [109].

Transforming growth factor beta signaling plays a central role in regulatory T cell induction and immunoglobulin A production. Several probiotic strains enhance this pathway, leading to increased Foxp3 positive regulatory T cells and reduced intestinal inflammation [104,110 to 117]. In addition, specific probiotics regulate immune responses through adenosine signaling pathways, suppressing proinflammatory T helper cell activity, and reducing systemic inflammation [118-121]. Together, these mechanisms highlight the therapeutic potential of

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microbiota-based interventions in preventing immune dysregulation and controlling inflammatory flare ups. An overview of selected studies examining the effects of probiotics and prebiotics on immune modulation and disease outcomes is presented in Table 5.

Multiple Sclerosis [126].	Rheumatoid Arthritis [125].	Irritable Bowel Syndrome(IBS) [124].	Type 1 Diabetes Mellitus [123].	Diseases
Rebecca	Batol	Viola Andresen	Chung-H-sing	First Author
A randomized, open-label trial	Randomized,double-blind,placebo-controlled trial	Double-blind, placebo-controlled trial in which patients with IBS	A randomized, double-blind,placebo-controlled trial	Type of study
July 2024	May 2016	July 2020	March 2022	Study year
This trial investigated the effects of probiotics (*Vebiome*, containing *Lactobacillus*, *Bifidobacterium*, and *Streptococcus* species) and prebiotics (*Prebiotin*, containing oligofructose-enriched inulin) in participants with relapsing-remitting multiple sclerosis (MS) on B-cell depletion therapy	In This study 60 rheumatoid arthritis (RA) patients aged 25–70 were assigned to receive either daily probiotic capsules (*Lactobacillus acidophilus*, *Lactobacillus casei*, and *Bifidobacterium bifidum*, 2 × 10^9 CFU/g each) or placebo capsules containing cellulose for 8 weeks.	A trial in Germany randomized IBS patients (Rome III criteria) to receive either placebo or non-viable *B. bifidum* HI-MIMBb75 capsules daily for 8 weeks. The primary endpoint was at least 30% improvement in abdominal pain and relief of IBS symptoms for 4 of 8 weeks. Exclusions included chronic systemic or inflammatory diseases and recent corticosteroid or antibiotic use. Safety and efficacy were assessed in all patients receiving at least one dose.	The study included patients aged 6 to 18 years diagnosed with Type 1 Diabetes Mellitus (T1DM), defined by meeting at least two of the following criteria: 1) ketoacidemia, 2) presence of insulin-related autoantibodies, and 3) insufficient insulin-secreting capacity.	Method used
Prebiotics and probiotics had similar adherence rates and were well tolerated in people with MS (pwMS), with minor, mild, and self-limited adverse events reported for both. Participants showed a subjective preference for prebiotics over probiotics. While significant differences were observed between prebiotics and probiotics in patient-reported global symptom burden (MSRS-R Total) and bowel control (BWCS), only probiotics significantly improved bowel control from baseline to post-supplementation.	The results of this study showed that an 8-week probiotic supplementation significantly improved Disease Activity Score of 28 joints (DAS-28), reduced insulin levels, decreased HOMA-B, and lowered hs-CRP levels in patients with rheumatoid arthritis (RA), indicating its beneficial effects.	This study demonstrated that *Bifidobacterium bifidum* HI-MIMBb75 significantly alleviates IBS symptoms, with 34% of treated patients meeting the primary endpoint compared to 19% in the placebo group (p=0.0007). Adverse events were rare and similar between groups, with abdominal pain being the most common. Tolerability was rated as very good or good by 91% of the *B. bifidum* group versus 86% of the placebo group, highlighting its safety and efficacy in a real-life setting, independent of bacterial cell viability.	A 6-month probiotic intervention in T1DM patients improved glycemic control (reduced Glucose AC and HbA1c), lowered inflammatory cytokines (IL-8, TNF-α, IL-17, MIP-1β, RANTES), increased the anti-inflammatory cytokine TGF-β1, and increased microbiota diversity by increasing *B. animalis*, *L. salivarius*, and *Akkermansia* , with sustained benefits observed three months post-intervention.	Result

Asthma [8].	Seasonal allergic rhinitis [129].	Atopic Dermatitis [128].	Axial spondyloarthritis (axSpA) [127].
Ailing	Yangfan	Bozena	Masoud
Randomizedand double-blind human trial	A prospective,randomized,double-blind,placebo-controlled clinical trial	A Multicenter randomized placebo-controlled trial	A Randomized, double-blin placebo controlled trial
October 2021	November 2024	April 2021	August 2022
A 3-month randomized, double-blind, and placebo-controlled human trial was performed to investigate the adjunctive efficacy of probiotics in managing asthma	The test group was given probiotics combined with prebiotics, whereas the placebo group was administered simulated preparation for 90 days	The Effectiveness of Probiotic Lactobacillus rhamnosus and Lactobacillus reuteri Strains in Children with Atopic Dermatitis and Cow's Milk Protein Allergy: A Multicenter, Randomized, Double Blind, Placebo Controlled Study	Forty-eight axSpA patients were randomized to receive A synbiotic or placebo daily for 12 weeks. Primary outcomes included BASDAI and ASDAS-CRP scores, while secondary outcomes assessed IL-17/IL-23 levels, gene expression, and IL17+ CD4+ T cells at baseline and trial end.
Probiotic adjuvant therapy, particularly with Probio-M8, demonstrates significant clinical efficacy in alleviating asthma by modulating gut microbiota and the gut-lung axis. Probio-M8 maintained gut microbiota diversity, enhanced anti-inflammatory pathways, increased beneficial microbial species, and supported immune homeostasis. Co-administration with conventional treatments improved clinical outcomes, reduced inflammation, and stabilized gut virome diversity, offering a promising approach for managing asthma and related disorders.	This study demonstrates that probiotics combined with prebiotics significantly alleviate seasonal allergic rhinitis (AR) symptoms by modulating gut microbiota, increasing beneficial bacteria, and altering metabolic functions such as acetate production. Improvements in clinical and immune indicators, including elevated Th1 cytokines and reduced IL-17, suggest a role of the gut-lung axis in symptom relief. While further research is needed, this study highlights the potential of probiotics and prebiotics as an alternative therapy for AR.	Supplementing the children's diet with this probiotic preparation for three months led to a significant reduction in AD symptom severity, as measured by the SCORAD index.	Synbiotic supplementation in axSpA patients reduced IL-17/IL-23 pathway activity by lowering IL-17-expressing CD4+ T cells and gene expression of IL-17 and IL-23 but did not improve disease activity scores.

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Table 5 summarizes selected clinical studies evaluating the effects of probiotics and prebiotics in autoimmune and allergic diseases. The studies demonstrate that these interventions are generally well tolerated and are associated with improvements in immune markers, inflammatory profiles, and disease-specific clinical outcomes, supporting their potential role as adjunctive therapies.

An overview of selected clinical and experimental studies examining fecal microbiota transplantation is presented in Table 6.

Disease	Ulcerative colitis [130].	Type 1 diabetes (T1D) [131].
First author	Saurabh	Pieter
Type of study	An open-label randomized controlled trial (RCT)	A randomized controlled trial
Year of publication	December 2022	January 2021
Methods	This study investigated treatments for patients with mild-to-moderate ulcerative colitis (UC), defined by a Simple Clinical Colitis Activity Index (SCCAI) score of 3–9 and endoscopic evidence of active disease (Ulcerative Colitis Endoscopic Index of Severity [UCEIS] > 1). Participants on stable baseline medications were randomly assigned in a 1:1 ratio to either fecal microbiota transplantation combined with an anti-inflammatory diet (FMT-AID) or optimized standard medical therapy (SMT).	Patients aged 18–30 years with recent-onset type 1 diabetes (T1D) (within <6 weeks) were randomized into two groups to receive either three autologous or allogeneic (from healthy donors) fecal microbiota transplants (FMTs) over 4 months. The primary endpoint was the preservation of stimulated C-peptide release, measured through mixed-meal tolerance tests over 12 months. Secondary outcomes included changes in glycemic control, fasting plasma metabolites, T-cell autoimmunity, small intestinal gene expression profiles, and intestinal microbiota composition.
Results	The combination of fecal microbiota transplantation (FMT) and an anti-inflammatory diet proved to be effective in inducing both clinical and endoscopic remission in patients with mild-to-moderate ulcerative colitis (UC). Additionally, the antidiet group showed greater success in sustaining remission over time, highlighting its potential as a long-term, low-cost, and patient-friendly strategy. This approach not only offers a practical alternative to repeated FMT sessions but also emphasizes the importance of diet in maintaining gut health and disease remission. These findings suggest that combining microbiome-based therapies with dietary modifications could be a promising avenue for managing UC, particularly in resource-limited settings.	FMT preserved endogenous insulin production in recently diagnosed T1D patients within 12 months of onset, with gut microbiota-derived metabolites and specific bacterial strains linked to beta cell function, highlighting the microbiome's role in T1D.

Disease	Systemic sclerosis (SSc) [132].	Food allergy [133].
First author	Havard	Emily Henderson
Type of study	A double-blind, placebo-controlled randomized pilot trial	A Clinical Trial
Year of publication	May 2020	February 2022
Methods	A 16-week pilot study randomized 10 SSc patients with GI symptoms to commercially available anaerobic cultivated human intestinal microbiota (ACHIM) or placebo, assessing safety, GI symptom improvement, and changes in fecal microbiota.	A first-of-its-kind clinical trial at Boston Children's Hospital which enrolled 15 peanut-allergic participants who received FMT via capsules, with or without antibiotic pretreatment, and assessed peanut tolerance, immune changes, and microbiota composition at 1 and 4 months post-treatment.
Results	ACHIM FMT was effective in reducing bloating, diarrhea, and/or fecal incontinence in 4 out of 5 patients, compared to 2 out of 4 in the placebo group. It caused mild and transient side effects, while serious gastroduodenoscopy-related complications occurred in the placebo group, including one laryngospasm and one duodenal perforation. FMT also led to greater fluctuations in the abundance, richness, and diversity of total, IgA-coated, and IgM-coated bacteria, suggesting gut microbiota modulation as a potential mechanism of action.	FMT increased peanut tolerance in 30% of participants receiving FMT alone and 60% of those pretreated with antibiotics. Responders showed increased regulatory T cells, reduced T helper cells, and altered gut microbiota. Transplanted microbiota protected allergy-prone mice from anaphylaxis, confirming the microbiome's role in reducing peanut allergy.

Table 6 outlines key clinical and experimental studies investigating fecal microbiota transplantation in autoimmune and allergic conditions. The findings indicate that FMT can restore microbial diversity and improve clinical outcomes in selected diseases such as ulcerative colitis and type 1 diabetes. However, variability in study design and limited long-term data highlights the need for further large-scale trials.

Interpretation and Analysis

This systematic review underscores the pivotal role of the gut microbiome in autoimmune and allergic diseases, revealing key patterns of dysbiosis characterized by reduced microbial diversity and increased pro-inflammatory bacteria. In autoimmune conditions such as rheumatoid arthritis, lupus, type 1 diabetes, and multiple sclerosis, specific microbial imbalances, including the presence of Porphyromonas gingivalis and a Firmicutes-Bacteroidetes shift, drive immune activation, inflammation, and autoimmunity. Similarly, allergic diseases like asthma, food allergies, atopic dermatitis, and chronic urticaria share disrupted microbiota profiles, with reduced beneficial bacteria such as Lachnospira and Faecalibacterium contributing to weakened gut barrier integrity, pro-inflammatory pathways, and heightened disease susceptibility. Mechanistically, the gut microbiome regulates immune responses through metabolite production (e.g., SCFAs), interactions with gut-associated lymphoid tissue (GALT), and systemic effects via the gut-lung and gut-skin axes, linking gut health to distant organs.

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Therapeutically, interventions such as probiotics, prebiotics, and fecal microbiota transplantation (FMT) offer promising potential to restore microbial balance, enhance immune tolerance, and reduce inflammation. The integration of these microbiome-based strategies with conventional treatments presents opportunities to improve clinical outcomes in autoimmune and allergic diseases, though further research is essential to optimize their application.

Challenges and Limitations

Research on the gut microbiome presents significant challenges due to variability across published studies. The studies included in this review differed in design, patient populations, disease definitions, microbiome assessment techniques, and intervention protocols, which limited direct comparison and prevented quantitative synthesis. While strong evidence supports the role of gut microbiota and microbial metabolites such as short-chain fatty acids in immune regulation and maintenance of intestinal barrier integrity, the clinical application of microbiome-based therapies remains evolving. In particular, interventions such as probiotics, prebiotics, and fecal microbiota transplantation are still considered investigational in many autoimmune and allergic conditions.

Many included studies involved small sample sizes and short follow-up durations, which may limit the generalizability of their findings and the assessment of long-term safety. Considerable heterogeneity was observed in microbial strains, dosing regimens, treatment duration, and outcome measures. Additional challenges include the lack of standardized protocols and regulatory constraints, especially fecal microbiota transplantation and donor screening. Furthermore, a proportion of studies could not be retrieved during full-text screening due to restricted access, which may have reduced the overall scope of evidence included in this review.

Future Directions

The analysis highlights the need for personalized approaches, where microbiome profiling identifies disease-specific dysbiosis patterns to enable tailored interventions that optimize therapeutic outcomes. Standardized protocols are essential, as uniform methodologies for microbiota analysis and therapy implementation improve reproducibility and comparability across studies. Further research is required to elucidate the precise mechanisms through which the microbiome influences immune responses and disease progression. Additionally, integrating microbiome modulation with dietary, pharmacological, and lifestyle interventions as combination therapies holds promise for enhancing therapeutic efficacy and improving patient adherence.

Conclusion

This review underscores the pivotal role of the gut microbiome in autoimmune and allergic diseases, where dysbiosis disrupts immune regulation, driving inflammation and disease progression. Autoimmune conditions such as rheumatoid arthritis, systemic lupus erythematosus, type 1 diabetes, and multiple sclerosis exhibit microbial imbalances, including increased pro-inflammatory bacteria like Porphyromonas gingivalis and altered Firmicutes-Bacteroidetes ratios, which exacerbate immune activation. Similarly, allergic diseases such as asthma and atopic dermatitis are associated with reduced beneficial microbes, including Lachnospira and Faecalibacterium, leading to impaired gut barriers, heightened inflammatory pathways, and increased disease susceptibility. Mechanistically, the microbiome influences disease progression through metabolite production (e.g., short-chain fatty acids or SCFAs), modulation of gut-associated lymphoid tissue (GALT), and systemic interactions such as the gut-lung and gut-skin axes.

Probiotics, prebiotics, and fecal microbiota transplantation (FMT) emerge as promising therapeutic strategies to address dysbiosis and restore immune homeostasis. Probiotics enhance microbial diversity, promote regulatory T-cell activity, stabilize the gut barrier, and reduce inflammatory cytokine production. Prebiotics serve as substrates for beneficial bacteria, supporting SCFA production and fostering an anti-inflammatory environment. FMT directly restores a diverse and balanced microbiota, showing potential in conditions such as ulcerative colitis and type 1 diabetes by reducing immune activation and preserving organ function. Despite their promise, challenges such as methodological variability, accessibility, and long-term safety require further exploration.

Future research should prioritize personalized and disease-specific approaches to microbiota-based therapies. Integrating probiotics, prebiotics, and FMT with dietary, lifestyle, and pharmacological interventions offers a transformative pathway for managing autoimmune and allergic diseases, delivering more effective, sustainable, and patient-centered solutions.

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