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Systematic Review

The role of gut microbiota in modulating immune responses: a systematic review on implications for autoimmune diseases

Aditya B. Saran[1]*, Aditi B. Saran[2]

[1]Hinduhridaysamrat Balasaheb Thackeray Medical College and Dr R. N. Cooper Municipal General Hospital, Mumbai, Maharashtra, India
[2]Government Medical College, GT and Cama Hospital, Mumbai, Maharashtra, India

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***Correspondence:**
Dr. Aditya B. Saran,
E-mail: psaran183@gmail.com

ABSTRACT

The gut microbiota plays a crucial role in immune regulation, influencing innate and adaptive immunity. Dysbiosis an imbalance in microbial composition has been linked to autoimmune diseases such as rheumatoid arthritis (RA), type 1 diabetes (T1D), multiple sclerosis (MS), inflammatory bowel disease (IBD) and systemic lupus erythematosus (SLE). This review analyses sixteen studies, highlighting common dysbiosis patterns, including decreased short-chain fatty acid (SCFA)-producing bacteria (*Faecalibacterium prausnitzii*, Bifidobacterium) and increased pro-inflammatory bacteria (*Prevotella copri, Akkermansia muciniphila*). These shifts contribute to autoimmunity via molecular mimicry, increased gut permeability and immune dysregulation. Microbiota-targeted therapies such as probiotics, prebiotics, dietary interventions and fecal microbiota transplantation (FMT) show promise in restoring microbial balance and modulating immune responses. Probiotics (*Lactobacillus reuteri*) reduce inflammation in RA and MS, while FMT partially restores microbial diversity in IBD and MS. Despite progress, causality remains unclear, necessitating longitudinal studies and personalized microbiome-based interventions. Understanding the gut microbiota-autoimmunity relationship could pave the way for microbiome-driven immunotherapies.

Keywords: Autoimmune diseases, Dysbiosis, Fecal microbiota transplantation, Gut microbiota, Immune regulation, Probiotics, Prebiotics

INTRODUCTION

The human gut microbiota is a highly diverse and dynamic ecosystem composed of trillions of microorganisms, including bacteria, fungi, viruses and archaea, that inhabit the gastrointestinal tract.[1] These microbes play a crucial role in digestion, immune modulation and metabolic processes, making them integral to human health.

The bacterial community is primarily composed of Firmicutes, Bacteroidetes, Actinobacteria and Proteobacteria, which collectively contribute to immune tolerance, pathogen defense and inflammatory regulation.[2] Recent research underscores the bidirectional relationship between gut microbiota and the immune system, wherein microbial composition influences immune responses and conversely, host immunity shapes microbial diversity.[3] A balanced microbiota is essential for maintaining immune homeostasis by promoting regulatory T-cell function, preserving gut barrier integrity and preventing excessive inflammatory responses.

Disruptions in this microbial balance termed dysbiosis can have profound immunological consequences, predisposing individuals to autoimmune disorders. Autoimmune diseases arise from a dysregulated immune response that mistakenly targets self-antigens, leading to chronic inflammation and tissue damage. The prevalence of autoimmune conditions, such as rheumatoid arthritis, multiple sclerosis and inflammatory bowel disease, is

rising globally, implicating both genetic susceptibility and environmental triggers in their pathogenesis.[4] Among these environmental factors, gut microbiota alterations have gained considerable attention for their role in immune dysregulation. Mechanisms linking dysbiosis to autoimmunity include molecular mimicry, increased intestinal permeability and the production of pro-inflammatory metabolites that skew immune responses.[5]

Several factors contribute to microbial imbalances that may predispose individuals to autoimmune conditions. Diet plays a pivotal role, with Western dietary patterns characterized by high fat, sugar and processed foods promoting gut microbial shifts associated with inflammation. Overuse of antibiotics further disrupts microbial diversity, potentially impairing immune regulation. Additionally, the hygiene hypothesis suggests that reduced microbial exposure during early childhood, due to excessive sanitation and lower infection rates, may hinder the development of immune tolerance. Genetic predispositions, particularly those linked to human leukocyte antigen (HLA) genes, further modulate host-microbe interactions, influencing disease susceptibility.

Given the mounting evidence linking gut microbiota to autoimmune disease pathogenesis, research has increasingly focused on microbiota-targeted interventions. Strategies such as probiotics, prebiotics, dietary modifications and fecal microbiota transplantation (FMT) are being explored for their potential to restore microbial balance and modulate immune responses. Understanding the intricate crosstalk between gut microbes and the immune system may offer novel therapeutic avenues for preventing and managing autoimmune diseases.

Given the mounting evidence linking gut microbiota to autoimmune disease pathogenesis, research has increasingly focused on microbiota-targeted interventions. Strategies such as probiotics, prebiotics, dietary modifications and fecal microbiota transplantation (FMT) are being explored for their potential to restore microbial balance and modulate immune responses. Understanding the intricate crosstalk between gut microbes and the immune system may offer novel therapeutic avenues for preventing and managing autoimmune diseases.

This systematic review aims to examine the role of gut microbiota in immune system development and function, explore the mechanisms linking gut dysbiosis to autoimmune diseases and evaluate microbiota-targeted interventions for the treatment of autoimmune conditions.

METHODS

This systematic review follows the "Integrated Methodology" procedure described in "The Joanna Briggs Institute Reviewers' Manual" from 2015.[6] Using a mixed method approach, it synthesizes study results from both quantitative and qualitative approaches while making reference to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement.[7]

A PRISMA checklist was used to assess adherence to standard operating procedures for systematic reviews. A meta-analysis was not conducted due to the heterogeneity of the included data.

This systematic review was conducted to evaluate the role of gut microbiota in immune system regulation, assess its association with autoimmune diseases and explore microbiota-targeted therapeutic strategies for immune modulation. To guarantee thorough and open reporting, the technique adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria.

Study registration

This systematic review was registered in PROSPERO (International Prospective Register of Systematic Reviews) under the registration number CRD420251009505.

Search strategy and selection criteria

A structured literature search was conducted across three major databases: PubMed, Google Scholar and Science Direct. The search was limited to articles published between 2005 and 2025 in English. The search strings used for each database, along with the number of articles retrieved, are detailed in Table 1.

The search aimed to identify relevant peer-reviewed studies exploring the relationship between gut microbiota and autoimmune diseases, as well as microbiota-targeted therapeutic approaches. The search was refined using specific keywords and Boolean operators. The term "Gut microbiota" was combined with "autoimmune diseases" using the AND operator.

Similarly, "Dysbiosis" was paired with "immune system" using AND to narrow the focus. Additionally, "Probiotics" was searched in conjunction with "autoimmunity", while "Fecal microbiota transplantation" was linked with "immune modulation", ensuring a targeted approach to the search.

The search was restricted to articles published between 2010 and 2024 to ensure the inclusion of the most recent advancements in the field. Duplicates were removed and additional studies were identified through cross-referencing citations from relevant systematic reviews and meta-analyses.

Inclusion criteria

Studies were included in the review if they met the following criteria peer-reviewed articles published in English between 2010 and 2024, studies investigating the

role of gut microbiota in immune system function and autoimmune diseases, clinical trials, cohort studies, case-control studies and meta-analyses evaluating microbiota-targeted therapies, research exploring mechanisms linking dysbiosis to immune dysregulation in autoimmune conditions.

Exclusion criteria

Studies were excluded like animal studies without human data, articles that were not available in full text, studies focusing solely on non-autoimmune conditions, such as metabolic disorders or cancer, without discussing autoimmune implications.

Data extraction

Two independent reviewers screened the retrieved articles for eligibility. Initially, titles and abstracts were reviewed, followed by a full-text assessment based on the inclusion and exclusion criteria. In cases of disagreement, a third external reviewer was consulted to reach a consensus. Discrepancies were discussed and decisions were finalized based on the relevance to the research objectives and methodological quality of the study.

Titles and abstracts were screened for eligibility by two separate reviewers. The selected search results were exported from the databases and arranged using the Zotero citation manager program.[8] Duplicates were removed from the software. After that, the full texts of studies that might be pertinent were evaluated in light of the inclusion criteria.

A standardized form was used to extract the data, which included important details such as the author or authors, the year of publication, the study design, the sample size, the population's characteristics, the results pertaining to impact of gut microbiota on immune function and autoimmune diseases. Across the eligible human studies, a total of 1,215 participants were included. The PRISMA flow diagram (Figure 1) illustrates the screening and exclusion procedure, which is based on the Moher model.[9]

Data extraction was performed systematically to ensure consistency and relevance. The following key information was extracted from each included study. The extracted data were organized into a standardized table for further analysis. Any discrepancies in data extraction were resolved through discussion among reviewers.

Quality assessment

Using suitable appraisal instruments based on research design, such as the Cochrane Risk of Bias Tool for randomized controlled trials and the Newcastle-Ottawa Scale for observational studies, the methodological quality of the included studies was assessed. Reviewers' disagreements were settled by consensus and discussion.

Data synthesis

Following the Joanna Briggs Institute guidelines, the data gathered in the form was tabulated for each of the selected publications.[6] To assure accuracy, two researchers separately extracted all of the data. The authors fixed inconsistencies in the extracted data.

The table was cross-checked by the authors for accuracy and completeness. A narrative synthesis was conducted to summarize findings from the included studies, focusing on microbiota-immune system interactions, dysbiosis and autoimmune disease mechanisms and microbiota-targeted therapies.

Heterogeneity among the included studies was evaluated based on differences in study design, sample size, microbiota analysis techniques and outcome measures. Due to significant variations in study populations, microbial assessment methods (e.g., 16S rRNA sequencing, metagenomic analysis) and intervention protocols, a formal statistical assessment using I2 statistics and subgroup analysis was not feasible. Instead, a narrative synthesis approach was adopted to qualitatively summarize findings across studies.

RESULTS

This systematic review identified sixteen studies that met the inclusion criteria, examining the role of gut microbiota in immune modulation and its association with autoimmune diseases. The studies collectively highlight significant alterations in microbial composition across different autoimmune conditions, including rheumatoid arthritis (RA), type 1 diabetes (T1D), multiple sclerosis (MS), inflammatory bowel disease (IBD) and systemic lupus erythematosus (SLE).

The findings reveal common patterns of dysbiosis, such as reduced short-chain fatty acid (SCFA)-producing bacteria and increased pro-inflammatory microbial species, reinforcing the role of gut microbiota in immune dysregulation and disease progression. Additionally, several studies explore potential microbiota-targeted interventions, including probiotics, prebiotics, dietary modifications and fecal microbiota transplantation (FMT), providing insights into emerging therapeutic strategies for autoimmune disease management.

Quality assessment of included studies

The methodological quality of the included studies was assessed using the cochrane risk of bias tool for randomized controlled trials (RCTs) and the Newcastle-Ottawa Scale (NOS) for observational studies (cohort and case-control). For animal studies and narrative reviews, risk of bias was evaluated separately based on methodological transparency, blinding and selection criteria.

A total of 16 studies were included, comprising 5 reviews, 4 cohort studies, 3 case-control studies, 2 animal experimental studies, 1 human experimental study and 1 narrative overview of Guillain-Barré syndrome.

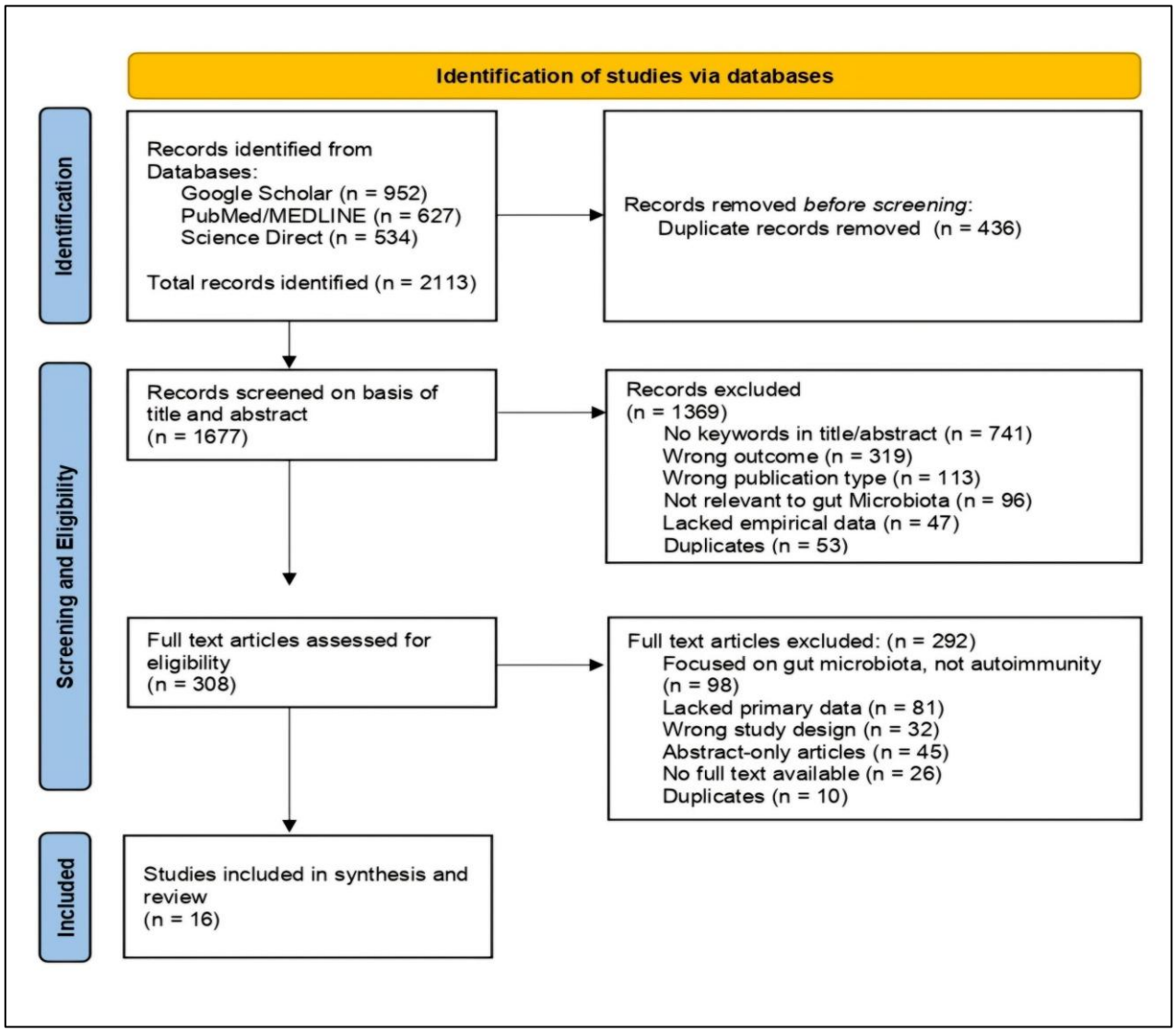

Figure 1: PRISMA Flowchart.

Key findings from the quality assessment

Reviews (n=5) were considered low risk of bias as they synthesized previously published research. However, the comprehensiveness of included data varied. Cohort studies (n=4) had moderate to low risk of bias, but some studies lacked blinding in microbiome sequencing analysis. Case-control studies (n=4) had moderate to high risk of bias, particularly in patient selection and blinding issues. Animal experimental studies (n=3) were moderate to high risk of bias due to lack of randomization and blinding in outcome assessments. The human experimental study (David et al, 2014) had moderate to high risk of bias due to potential confounding factors and lack of dietary blinding. The detailed Risk of Bias Assessment Table is presented in table 5.

Common limitations across studies included small sample sizes, heterogeneity in microbiota assessment methods and lack of long-term follow-up. Despite these limitations, the overall quality of the included studies was sufficient to draw meaningful conclusions regarding the relationship between gut microbiota and autoimmune diseases. To provide a clearer overview of the included studies, table 2 presents the study characteristics, including study design, sample size, autoimmune diseases studied and key findings. The studies encompass a mix of review articles, cohort studies, case-control studies, experimental human studies and animal models, covering various autoimmune conditions such as rheumatoid arthritis (RA), type 1 diabetes (T1D), multiple sclerosis (MS), inflammatory bowel disease (IBD) and Guillain-Barré syndrome (GBS).

Microbiota alterations observed across different autoimmune diseases are summarized in table 3. The key

microbial changes include increased abundance of *Prevotella copri* in RA, reduced SCFA-producing bacteria in T1D and elevated *Akkermansia muciniphila* in MS patients. These alterations are linked to gut permeability changes, immune dysregulation and inflammatory responses, indicating a potential role of gut microbiota in autoimmunity. Potential therapeutic interventions targeting gut microbiota are detailed in table 4. Strategies such as probiotics, prebiotics, fecal microbiota transplantation (FMT) and dietary modifications have been explored in various autoimmune diseases. Probiotic strains like *Lactobacillus reuteri* have shown promise in modulating immune responses in RA and MS, while dietary fibre intake supports gut barrier integrity and immune tolerance. However, further clinical trials are needed to confirm their efficacy in disease management.

Gut microbiota and immune system interactions

The gut microbiota regulates both innate and adaptive immunity by influencing immune cell differentiation, cytokine production and antigen presentation.

Gut microbiota and innate immunity

The innate immune system provides rapid, nonspecific defense against pathogens. Gut microbes interact with the immune system through.

Pattern recognition receptors

Microbial components, such as lipopolysaccharides (LPS) and peptidoglycans, activate Toll-like receptors (TLRs), triggering antimicrobial responses.[10]

Antimicrobial peptides

Gut bacteria stimulate Paneth cells to produce AMPs like defensins and cathelicidins, preventing pathogen colonization.[11]

Short-chain fatty acids

Microbial fermentation of fiber produces SCFAs (butyrate, acetate, propionate), which have anti-inflammatory effects and enhance gut barrier integrity.[12]

Gut microbiota and adaptive immunity

The adaptive immune system relies on T cells and B cells to mount antigen-specific responses.

Regulatory T cells

Certain gut bacteria, such as *Bacteroides fragilis*, induce Tregs, which secrete IL-10 to suppress inflammation and maintain immune tolerance.[10]

Th17 cells and autoimmunity

Dysbiosis can lead to an overproduction of Th17 cells, which contribute to autoimmune diseases such as MS and RA.[13]

IgA production

Gut microbes regulate B cell differentiation and secretory IgA (sIgA) production, modulating immune responses.[14]

Dysbiosis and autoimmune diseases

Dysbiosis has been linked to several autoimmune conditions.

Rheumatoid arthritis

RA is a chronic inflammatory disease characterized by joint destruction and autoantibody production.

RA patients exhibit increased *Prevotella copri*, which may trigger inflammation.[15] SCFA-producing bacteria, such as *Faecalibacterium prausnitzii*, are reduced in RA, correlating with disease severity.[16]

Type 1 Diabetes

T1D is an autoimmune disorder targeting pancreatic beta cells. Children at risk for T1D show decreased microbial diversity and lower SCFA-producing bacteria.[17] Higher levels of *Bacteroides dorei* and *Ruminococcus gnavus* have been associated with beta-cell autoimmunity.[18]

Multiple sclerosis

MS is a neuroinflammatory disorder caused by immune-mediated demyelination of the CNS. MS patients have increased *Akkermansia muciniphila* and decreased Bacteroides fragilis, indicating gut microbial involvement in neuroinflammation.[19] SCFAs regulate Tregs, which are dysfunctional in MS patients.[20]

Mechanisms linking gut microbiota to autoimmunity

Molecular mimicry

Certain microbial antigens resemble host proteins, leading to cross-reactive immune responses. Campylobacter jejuni infection is linked to Guillain-Barré syndrome.[21]

Leaky gut and immune activation

Increased intestinal permeability ("leaky gut") allows microbial products to enter circulation, triggering inflammation. Zonulin, a regulator of tight junctions, is elevated in autoimmune diseases such as celiac disease and T1D.[5]

Microbiota-targeted therapies

Probiotics and prebiotics

Probiotics:Lactobacillus reuteri reduces inflammation in RA.[22]

*Prebiotics:*Increase SCFA production and promote immune balance.[23]

Fecal microbiota transplantation

FMT has shown promise in restoring microbial balance in autoimmune diseases such as MS.[24]

Table 1: Search strings and results.

Databases	Search strings	Number of articles retrieved
PubMed	(“gut microbiota” OR “gut microbiome”) AND (“autoimmune diseases” OR “autoimmunity”)	246
PubMed	(“dysbiosis” AND “immune system”)	169
PubMed	(“probiotics” OR “prebiotics”) AND (“autoimmune diseases” OR “immune modulation”)	212
Google scholar	allintitle: “gut microbiota AND autoimmune diseases”	563
Google scholar	“gut dysbiosis AND immune system dysfunction”	389
Science direct	TITLE-ABS-KEY (“gut microbiota” AND “autoimmune diseases”)	316
Science direct	TITLE-ABS-KEY (“fecal microbiota transplantation” AND “immune modulation”)	218

Table 2: Characteristics of included studies.s

Study (Author, Year)	Study design	Sample size	Autoimmune disease studied	Key findings
Round et al, 2009[10]	Review	N/A	General immune function	Gut microbiota influences adaptive immunity and inflammation
Bevins et al, 2011[11]	Review	N/A	Intestinal immunity	Paneth cells regulate gut immunity via antimicrobial peptides
Koh et al, 2016[12]	Review	N/A	General immune function	SCFAs influence gut barrier integrity and immune modulation
Ivanov et al, 2009[13]	Animal Study	N/A	Th17-mediated autoimmunity	Segmented filamentous bacteria induce Th17 cells, linking gut microbiota to autoimmunity
Macpherson et al, 2017[14]	Review	N/A	Neonatal immunity	Maternal microbiota influences offspring immune development
Scher et al, 2013[15]	Case-control	114	Rheumatoid Arthritis (RA)	More *Prevotella copri*, less Bacteroides in RA patients
Zhang et al, 2015[16]	Cohort	212	Rheumatoid Arthritis (RA)	Gut microbiome alterations partly normalized after RA treatment
Vatanen et al, 2018[17]	Prospective cohort	783	Type 1 Diabetes (T1D)	Less SCFA-producing bacteria in children at risk of T1D
Knip et al, 2016[18]	Review	N/A	Type 1 Diabetes (T1D)	Gut microbiota alterations are linked to β-cell autoimmunity
Jangi et al, 2016[19]	Case-control	60	Multiple sclerosis	More *Akkermansia muciniphila*, less Bacteroides fragilis in MS patients
Smith et al, 2013[20]	Animal Study	N/A	Colitis (IBD model)	SCFAs regulate colonic Tregs, protecting against gut inflammation
Hughes & Cornblath, 2005[21]	Review	N/A	Guillain-Barré Syndrome	Molecular mimicry between *C. jejuni* and nerve gangliosides
Marietta et al, 2016[22]	Animal Study	N/A	Rheumatoid Arthritis (RA)	*Prevotella histicola* reduces arthritis severity in mice
Makki et al, 2018[23]	Review	N/A	General immune function	Dietary fiber impacts gut microbiota and immune health
Smits et al, 2013[24]	Review	N/A	Inflammatory Bowel Disease (IBD)	FMT is a potential treatment for IBD and autoimmunity
Jiang et al, 2015[25]	Case-Control	46	Major Depressive Disorder (MDD)	More Enterobacteriaceae, less Faecalibacterium in MDD patients
David et al, 2014[26]	Experimental Human Study	N/A	Microbiome-Diet Interaction	Diet rapidly alters gut microbiota; animal-based diet ↑ inflammatory microbes

Table 3: Microbiota alterations across autoimmune diseases.

Autoimmune disease	Key microbiota changes	Mechanisms implicated
Rheumatoid arthritis	More *Prevotella copri*, less *Faecalibacterium prausnitzii*	Increased gut permeability, Th17 activation
Type 1 diabetes	More Bacteroides dorei, less SCFA-producing bacteria	Leaky gut, β-cell autoimmunity
Multiple sclerosis	More *Akkermansia muciniphila*, less *Bacteroides fragilis*	Gut-brain axis dysregulation
Inflammatory bowel disease	Dysbiosis with reduced diversity	Chronic gut inflammation
Guillain-barré syndrome	More *C. jejuni* molecular mimicry	Antibody-mediated nerve damage
Major depressive disorder	More Enterobacteriaceae, less Faecalibacterium	Gut microbiota-neuroimmune interaction

Table 4: Summary of Microbiota-Targeted Therapies.

Intervention	Mechanism of action	Evidence from studies
Probiotics (e.g., *Lactobacillus reuteri*)	Modulate immune responses, reduce inflammation	Shown to decrease RA and MS severity
Prebiotics (dietary fibre)	Promote SCFA production, enhance gut barrier integrity	Supports Treg function and immune tolerance
Fecal microbiota transplantation	Restores gut microbiota composition	Explored in MS and IBD, promising but uncertain long-term effects
Dietary modifications	Increase beneficial bacteria, reduce gut permeability	Mediterranean diet beneficial for RA

Table 5: Risk of bias assessment for included studies.

Study (Author, Year)	Study design	Random sequence generation (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Overall risk of bias
Round et al, 2009[10]	Review	NA	NA	NA	Low	Low	Low
Bevins et al, 2011[11]	Review	NA	NA	NA	Low	Low	Low
Koh et al, 2016[12]	Review	NA	NA	NA	Low	Low	Low
Ivanov et al, 2009[13]	Animal Study	Unclear	High	Unclear	Low	Low	Moderate to High
Macpherson et al, 2017[14]	Review	NA	NA	NA	Low	Low	Low
Scher et al, 2013[15]	Case-Control	Unclear	High	Unclear	Low	Low	Moderate to High
Zhang et al, 2015[16]	Cohort	Unclear	High	Unclear	Low	Low	Moderate to High
Vatanen et al, 2018[17]	Prospective Cohort	Low	Low	Unclear	Low	Low	Low to Moderate
Knip and Siljander, 2016[18]	Review	NA	NA	NA	Low	Low	Low
Jangi et al, 2016[19]	Case-Control	Unclear	High	Unclear	Low	Low	Moderate to High
Smith et al, 2013[20]	Animal Study	Unclear	High	Unclear	Low	Low	Moderate to High
Hughes and Cornblath, 2005[21]	Review	NA	NA	NA	Low	Low	Low
Marietta et al, 2016[22]	Animal Study	Unclear	High	Unclear	Low	Low	Moderate to High

Continued.

Study (Author, Year)	Study design	Random sequence generation (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Overall risk of bias
Makki et al, 2018[23]	Review	NA	NA	NA	Low	Low	Low
Smits et al, 2013[24]	Review	NA	NA	NA	Low	Low	Low
Jiang et al, 2015[25]	Case-Control	Unclear	High	Unclear	Low	Low	Moderate to High
David et al, 2014[26]	Experimental Human Study	Unclear	High	Unclear	Low	Low	Moderate to High

DISCUSSION

The role of gut microbiota in immune system modulation has gained significant attention in recent years, particularly in the context of autoimmune diseases. The findings of this review reinforce the growing body of evidence that dysbiosis plays a crucial role in immune dysfunction, contributing to the pathogenesis of rheumatoid arthritis (RA), type 1 diabetes (T1D), multiple sclerosis (MS), inflammatory bowel disease (IBD) and systemic lupus erythematosus (SLE).[3,5]

Key findings and comparisons with other studies

Our review highlights several common patterns of microbial dysbiosis across multiple autoimmune diseases. A notable finding is the reduction in SCFA-producing bacteria, such as *Faecalibacterium prausnitzii*, Bifidobacterium and Roseburia, which play a crucial role in maintaining immune tolerance and gut barrier integrity.[14,23] Additionally, an increased abundance of pro-inflammatory bacteria has been observed in various autoimmune conditions, including *Prevotella copri* in rheumatoid arthritis (RA), *Bacteroides dorei* in type 1 diabetes (T1D) and *Akkermansia muciniphila* in multiple sclerosis (MS).[15,18,19] Another significant pattern is enhanced gut permeability, commonly referred to as "leaky gut," which has been reported in diseases such as T1D, inflammatory bowel disease (IBD) and MS. This increased permeability allows microbial antigens and toxins to enter the bloodstream, thereby triggering systemic inflammation.[5]

These findings are consistent with previous studies demonstrating that gut microbiota alterations precede disease onset, suggesting a causative rather than a secondary role in autoimmunity.[12,17]

Rheumatoid arthritis and gut dysbiosis

RA has been associated with increased *Prevotella copri* and decreased *Faecalibacterium prausnitzii*, findings that are consistent across multiple studies.[15,16] Notably, Marietta et al, found that administration of gut-derived *Prevotella histicola* reduced arthritis severity in a mouse model, suggesting that specific microbiota-based interventions could modulate disease activity.[22]

A study by Zhang et al, further demonstrated that gut microbiota composition shifts after treatment with disease-modifying antirheumatic drugs (DMARDs), reinforcing the idea that gut microbiota alterations are dynamic and responsive to therapy.[16]

Type 1 diabetes and gut microbiota alterations

In T1D, reduced microbial diversity and an overgrowth of *Bacteroides dorei* and *Ruminococcus gnavus* have been linked to beta-cell autoimmunity.[17,18] Interestingly, Vatanen et al, reported that children at risk for T1D exhibit gut dysbiosis before clinical onset, supporting the hypothesis that microbiota changes contribute to disease pathogenesis rather than being a secondary effect.[17]

Moreover, SCFA-producing bacteria are significantly diminished in T1D, which is concerning given their role in Treg induction and immune homeostasis.[20] These findings suggest that restoring SCFA levels via diet or probiotics may have therapeutic potential.

Multiple sclerosis and the gut-brain axis

MS has a unique gut-brain connection, with recent studies showing that gut dysbiosis can influence neuroinflammation.[19] Increased levels of *Akkermansia muciniphila* and *Clostridium perfringens* have been found in MS patients, while protective bacteria such as Bacteroides fragilis are reduced.[19]

Mechanisms underlying gut dysbiosis and autoimmune diseases

Several mechanisms link gut microbiota alterations to immune dysregulation, including.

Molecular mimicry

Certain bacterial antigens closely resemble host proteins, leading to cross-reactive immune responses. *Campylobacter jejuni*, for example, has been implicated in Guillain-Barré Syndrome through this mechanism.[21]

Leaky gut and microbial translocation

Increased intestinal permeability allows bacterial endotoxins (LPS) to enter the bloodstream, triggering systemic inflammation seen in RA, T1D and MS.[5]

SCFA deficiency and treg dysfunction

A lack of butyrate and propionate impairs Treg function, leading to uncontrolled inflammation in diseases such as RA and MS.[20]

Therapeutic implications: microbiota-targeted interventions

Given the strong link between gut microbiota and autoimmunity, microbiota-targeted therapies are emerging as promising treatment strategies.

Probiotics and prebiotics

Probiotics have shown disease-modifying effects in RA and IBD, with certain strains (e.g., Lactobacillus reuteri) reducing inflammatory markers.[22] Prebiotics, such as dietary fiber, promote SCFA production, which enhances gut barrier integrity and immune tolerance.[23]

Fecal microbiota transplantation

FMT has been explored as a therapeutic intervention in MS and IBD, with some studies showing partial restoration of microbial balance.[24] However, long-term efficacy and safety remain uncertain, requiring further research.

Dietary modifications

Diets rich in fibre and polyphenols (e.g., the Mediterranean Diet) have been associated with reduced RA risk and improved gut microbiota composition.[25] Conversely, the Western diet, high in saturated fats and refined sugars, exacerbates gut dysbiosis.[26]

Future directions and limitations

Despite promising findings, several gaps remain in our understanding of the gut microbiota-autoimmunity relationship. One major challenge is distinguishing causation from correlation, as most studies demonstrate associations rather than direct causality. To address this, future research should focus on longitudinal human studies and germ-free animal models to establish a causal link. Additionally, the composition of gut microbiota is highly individualized, influenced by factors such as genetics, diet and geography. This variability suggests that personalized microbiota-based therapies may be necessary for optimal efficacy. Another critical area of concern is the safety and long-term effects of fecal microbiota transplantation (FMT). While FMT has shown promise, its long-term immunological impact remains unclear. More extensive clinical trials are needed before it can be considered a mainstream therapy for autoimmune diseases.

CONCLUSION

The gut microbiota plays a central role in immune regulation and its dysbiosis is strongly linked to autoimmune diseases. This review highlights key microbial alterations in RA, T1D, MS, IBD and SLE, emphasizing their mechanistic contributions to disease pathogenesis. Emerging microbiota-targeted therapies, such as probiotics, FMT and dietary interventions, offer exciting new therapeutic possibilities. However, further research is needed to establish causality, optimize treatments and ensure long-term safety.

The gut microbiota is crucial for immune regulation and plays a key role in autoimmune disease pathogenesis. Targeting microbial communities through probiotics, prebiotics, dietary interventions and FMT presents promising therapeutic avenues. Future research should focus on personalized microbiome-based therapies to optimize immune health.

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