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Gut Microbiome Dysbiosis In Autoimmune Diseases: Mechanisms, Biomarkers, And Therapeutic Strategies

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Abstract: The gut microbiome plays an important role in the development and progression of autoimmune diseases(AIDS) like rheumatoid arthritis(RA), systemic lupus erythematosus (SLE), type 1 diabetes (T1D), multiple sclerosis (MS), and inflammatory bowel disease (IBD). This narrative review synthesizes the current evidence on how gut dysbiosis contributes to autoimmunity through different mechanisms. Emerging therapeutic strategies targeting the microbiome, which include probiotics, fecal microbiota transplantation(FMT), dietary interventions, and pharmacological modulators, show a promise in restoring microbial balance. while dysbiosis is told as both a cause and consequence of autoimmunity, its exact role still remains complex. Advances in research could shift AID from management of symptoms to prevention and maybe even cure, revolutionizing autoimmune medicine

I. Introduction

Autoimmune diseases[AID] result from the breakdown of our immune system tolerance, leading the body to attack its own tissues, this includes diseases such as **rheumatoid arthritis [RA]**, **systemic lupus erythematosus [SLE]**, **type 1 diabetes [T1D]**, **multiple sclerosis [MS]**, and **inflammatory bowel disease [IBD]** which develop through interactions between genetic susceptibility and environmental triggers[1]. Growing data suggests that gut bacteria play an important role in these diseases[2].

There are trillions of microorganisms in the human gut[3]. The human gut microbiota is mainly of five phyla of bacteria: Firmicutes, Bacteroidetes, Verrucomicrobia, Actinobacteria, and Euryarchaeota. These microbes help in regulating the intestinal barrier function[4], also influence the development of immune cells[5], and also produce anti-inflammatory compounds[6]. Disruptions in this microbiome, which is known as dysbiosis, contribute to autoimmune disease development[7]

The specific bacteria, like Prevotella copri promote inflammatory responses in rheumatoid arthritis[8]. Systemic lupus erythematosus patients show altered gut bacteria, including reduced lactobacillus and increased Enterococcus gallinarium[4][9], whereas in type 1 diabetes and multiple sclerosis, there is an association with decreased beneficial bacteria that produce short-chain fatty acids[SFCA][10].

The connection between the gut microbiomes and the distant organs occurs through several different mechanisms. An increase in the intestinal permeability allows the bacteria to enter the circulation[11]. Some Microbial proteins resemble human proteins, which is known as molecular mimicry, which triggers the mistaken immune system and attacks its own body [12]. Microbial metabolites affect immune cell function throughout the body [6].

There are potential treatments that target the gut microbiome, which include probiotics[13], fecal microbiota transplantation[6], and dietary changes[13]. These approaches aim to restore the microbial balance in the gut and also reduce the autoimmune symptoms.

This review examines

1. Gut microbiota changes in specific autoimmune diseases
2. Mechanisms linking to immune dysfunction
3. Microbiome-based treatment strategies

II. METHODS

A comprehensive approach was done to gather and analyze relevant studies on the role of the gut microbiome in autoimmune diseases. The methodology included a detailed search strategy, clear inclusion and exclusion criteria for study selection, and its data extraction.

2.1 Search Strategy

The search was conducted across some major databases like PubMed, Scopus, and Google Scholar. These databases were chosen for their broad coverage of multidisciplinary literature. A combination of keywords and Boolean operators was used to find and retrieve the studies. The keywords included “gut microbiome,” “autoimmune diseases,” “dysbiosis,” “immune regulation,” “microbial metabolites,” “probiotics,” and “fecal microbiota transplantation.”

2.2 Inclusion and Exclusion Criteria

To maintain the relevance and quality of the study, inclusion and exclusion criteria were used. Studies were included if they: [1] were published in English, [2] focused on the role of the gut microbiome in autoimmune diseases, [3] provided insights or clinical outcomes related to dysbiosis and autoimmunity. Both the original research articles and also the review articles were considered. Studies were excluded if they: [1] were not related to the gut microbiome or autoimmune diseases, [2] were not available in English, or [3] lacked sufficient methodological detail or clear results.

2.3 Study Selection Process

The study selection procedure was divided into many stages to guarantee that only the high-quality and relevant studies were included. Firstly, the titles and abstracts of all retrieved articles were evaluated for relevancy using the inclusion and exclusion criteria. Secondly, after the evaluation full text reviews were done of the articles. During the full-text review, papers were assessed for methodological rigor, relevance to the study issue, and contribution to our understanding of the gut microbiome-autoimmunity relationship.

2.4 Data Extraction and Analysis

Data extraction was performed in which key information was collected from each study, including: [1] study design, [2] sample characteristics , [3] key findings related to the gut microbiome and autoimmune diseases, [4] mechanisms [e.g., gut barrier dysfunction, molecular mimicry, microbial metabolites], and [5] therapeutic interventions investigated [e.g., probiotics, fecal microbiota transplantation, dietary modifications]. The extracted data was then analyzed to identify common patterns, mechanisms, and gaps in the literature.

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2.5 Synthesis of Findings

The findings from the selected studies were synthesized to provide a comprehensive overview of the role of the gut microbiome in autoimmune diseases.

III. Results

3.1: Microbiota Alterations in Autoimmune Diseases

The Research reveals different gut microbiome modifications in autoimmune diseases, summarized in Table 3.1. In **rheumatoid arthritis[RA]**, the bacteria Prevotella copri dominates in the early-stage patients and correlates with the Th-17 mediated inflammation[1]and also there is increase in Bacteroides sartorii, Eggerthella, Prevotella, lactobacillus, Streptococcaceae and Streptococcus[4], and also there is reduction in Ruminococcaceae, and Bacteriodes fragilis impair the anti-inflammatory SCFA production and also the gut barrier integrity[5][14][4]. In **Systemic Lupus Erythematosus[SLE]**, there is a increase in Alistipes, Bacilli, Bacteroides, Clostridium, Eggerthella, Escherichia, Klebsiella, Lactobacillus, Prevotella, Ruminococcus, and Streptococcus[4], Bacteroides, Dialister, Faecalibacterium, Odoribacter, Roseburia, and Ruminococcus are depleted[4] which can have an overall impact of decreased ability to produce anti-inflammatory SCFA like butyrate, leading to chronic gut inflammation and immune system dysregulation. For **Type 1 Diabetes[T1D]**, clostridium clusters IV/XIVa decrease precedes the onset of the disease, and there is also a rise in bacteroides, which alters the immunity[15]. Multiple sclerosis[MS] has an increase in Actinomyces, Akkermansia, Clostridium, Eggerthella, and Streptococcus and decrease in Bacteroides, Butyricimonas, Clostridium, Eubacterium, Faecalibacterium, Lachnospira, Lactobacillus, Megamonas, Parabacteroides, Prevotella, and Sutterella[4][16]. in **Inflammatory bowel disease[IBD]** there is decrease Faecalibacterium prausnitzii and increase in E. Coli[13] which can cause Pro-inflammatory responses. In **Psoriasis** ,there can be an increase in Phascolarctobacterium, Dialister, and also Escherichia[17], and a decrease in Eubacterium rectale[1]

Table 3.1 **Gut Microbiota Alterations in Autoimmune Diseases**

Autoimmune disease	Increased microorganisms	Decreased microorganisms	Citations
Rheumatoid arthritis[RA]	*Prevotella copri*[species of prevotella], *Bacteroides sartorii, Eggerthella, Prevotella, Lactobacillus, Streptococcaceae, Streptococcus*	*Ruminococcaceae, Bacteroides fragelis*	[1][4][5][14]
Systemic Lupus Erythematosus[SLE]	*Alistipes, Bacilli, Bacteroides, Clostridium, Eggerthella, Escherichia, Klebsiella, Lactobacillus, Prevotella, Ruminococcus, Streptococcus*	*Bacteroides, Dialister, Faecalibaterium, Odoribacterium, Roseburia, Ruminococcus*	[4]
Type 1 Diabetes[T1D]	*Bacteroides*	*Clostridium Clusters IV/XIVa*	[15]
Multiple Sclerosis[MS]	*Actinomyces, Akkermansia, Clostridium, eggerthella, Streptococcus*	*Bacteriodes, Butyricimonas, Clostridium,*	[4][16]

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		Eubacterium, Faecalibacterium, Lachnospira, Lactobacillus, Megamonas, Parabacteroides, Prevotella, Sutterella	
Inflammatory bowel Disease[IBD]	*Escheriria coli*	*Faecalibaterium prausnitzii*	[13]
Psoriasis	*Phascolarctobecterium, Dialister, Escherichia*	*Eubacterium rectale*	[1][17]

3.2:Mechanisms linking gut microbiota to Autoimmunity

Research shows that the gut microbiota contributes to autoimmunity through several mechanisms. Impaired intestinal barrier function, characterized by tight junction protein disruption [occludin/claudin], increases permeability to microbial products, This is clinically indicated by higher lactulose/mannitol ratios in individuals with RA, T1D, and MS[2] , allowing the translocation of microorganisms like Enterococcus gallinarum to extraintestinal sites in sle[10][18]. **Molecular mimicry,** in which immune responses directed against bacterial components cross-react with self-tissues, is made possible by structural similarities between microbial and host antigens[7][13][12][10][19][18], This type of activity is exhibited by Prevotella copri in rheumatoid arthritis, whose antigens mirror synovial proteins and Bacteroides thetaiotaomicron in SLE, which shares epitopes with the Ro60 autoantigen[10]. The compromised intestinal barrier with increased gut permeability is a mechanism called "**leaky gut**"[20][21], permitting translocation of the microbial products into the systemic circulation and distant organs.

Dysbiosis alters the immune cell balance by promoting Th17 responses through segmented filamentous bacteria[22], while decreasing the regulatory T cells due to decreased SCFA production due to depleted SFCA-producing bacteria. Microbial metabolites directly modulate immunity, since SCFAs increase Treg levels and reduce inflammatory responses through histone acetylation[12]. The gut microbiota has a substantial impact on the **balance of Treg and Th17** cells. Gut species can boost Treg and Th17 helper T cell responses, which are associated with autoimmune immunopathogenesis.[6]

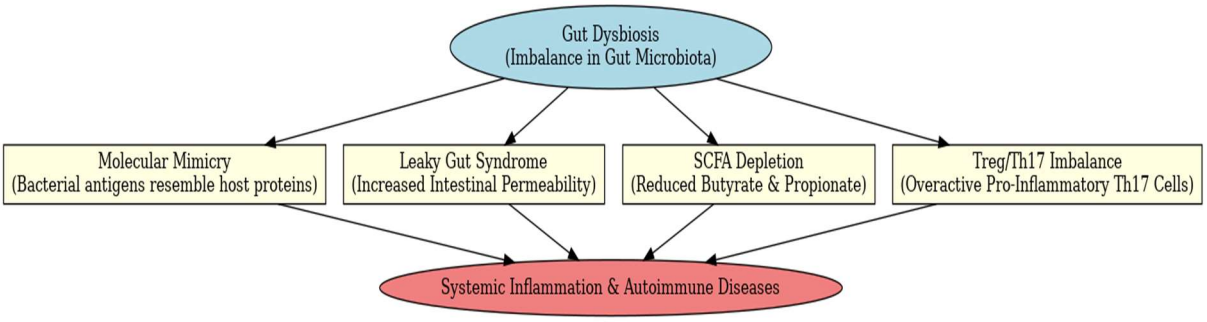

Figure 3.2 **Mechanisms Linking Gut Dysbiosis to Autoimmune Diseases**

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3.3 : Microbiome-based treatment strategies

Antibiotics: Because they increase anti-inflammatory IL-10 and decrease inflammatory cytokines, antibiotics can also have a role in the pathophysiology of ADs. Immunosuppressive drugs that change the composition of the gut microbiota and non-specifically weaken the immune system have been the traditional standard therapies for autoimmunity [23].

Probiotics: Research has demonstrated that immune-regulatory probiotics lower autoantibodies, the Th1-Th17 cell population, IFN-γ, and IL-17, indicating their potential utility in the treatment of SLE. To ascertain whether probiotics work as immunosuppressive agents or by controlling or reestablishing the composition of the gut microbiota, more research is required [23]. One of the most popular probiotics for treating IBD is VSL#3. The eight bacteria in VSL#3, a probiotic blend, are Bifidobacterium breve, Bifidobacterium longum, Bifidobacterium infantis, Lactobacillus acidophilus, Lactobacillus plantarum, Lifidobacterium paracasei, Lifidobacterium delbrueckii subsp. Bulgaricus, and Streptococcus thermophilus.By improving the intestinal environment, boosting microbial diversity, and adjusting the concentration of particular bacteria—for example, increasing that of Bifidobacterium and decreasing that of Turicibacter in animal models—VSL#3 alleviates the symptoms of IBD [24]. They also generate antibiotics and improve the intestinal barrier, influencing immunological function [5]. Probiotics and commensal bacteria, e.g., Faecalibacterium prausnitzii, Eubacterium rectale, Eubacterium hallii, Ruminococcus bromii—create SCFAs in the colon.SCFAs block the NF-κB pathway, they reduce inflammation as they interact with intestinal receptors FFAR2, FFAR3, GPR109a , its production increases if given in combination of probiotics and prebiotics. SCFAs maintains gut health, reduces colorectal cancer risk, and influences CNS -mediated energy expenditure via binding to FFAR2/FFAR3 receptors on colonocytes, which triggers the release of GLP-1 and PYY, not only this it has additional benefits, reducing neutrophilocyte synthesis and hence halting macrophage NF-κB activation, exhibiting strong anti-inflammatory properties [25].

Prebiotic treatment has a well-established effect on improving the gut environment in both humans and animal models. Prebiotics like inulin and Bacillus coagulans encourage good bacteria, improve RA. Synbiotics combine prebiotics and probiotics for amplified benefits, enhancing them even more.[23][13] Bifidobacterium decreases CD4+ T cell overstimulation, while Lactobacillus casei and L. reuteri decrease nephritis, autoantibody levels, and increase regulatory T cells.[18]

FMT: It can restore intestinal mucosal immunological homeostasis in patients with IBD, which is a current research hotspot, given the important role that gut microbiota plays in the pathophysiology of IBD. Moderate to severe IBD that is exacerbated by recurrent or refractory Clostridium difficile infection can be treated with FMT. By reducing colon damage and restoring colon length, FMT improved intestinal barrier functioning, reduced colon inflammation, and alleviated colitis in mice with DSS-induced colitis. Certain gut microbiota that cause inflammation, like Bacteroides acidifaciens, Escherichia-Shigella, and Blautia, were less common in mice given FMT [24] .Over 12 weeks in a short, safe human trial, oral FMT capsules reduced SLEDAI scores, anti-dsDNA levels, and pro-inflammatory signs like IL-6. [18]

Diet Therapy: The host immune system may be significantly impacted by diet, hence it is crucial to find strategies for both preventing and treating autoimmune illnesses through diet therapy. For instance, food emulsifiers, which are often found in processed foods in Western diets, promote early inflammatory lesions in IBD and increase bacterial intestinal permeability in vitro. In contrast, dietary fiber, which is in short supply in Western diets, inhibits these responses. [24].V**itamin C** improves cardiovascular risk, while **Omega-3** lowers cytokines, CRP, and anti-dsDNA.Retinoic acid enhances renal function and gut barrier integrity.[18]It decreases inflammation and leukocyte chemotaxis, and studies show PUFAs enhance RA outcomes. According to a controlled study, Anti-inflammatory foods significantly improved disease activity. Primary Sjögren's syndrome [pSS] and systemic lupus erythematosus [SLE] are also impacted by diet and microbiome, with microbial alterations impacting the course of the disease. Dietary therapy helps to control RA symptoms. Foods like red meat, salt, and high caloric intake worsen RA, while polyunsaturated fats [PUFAs] offer anti-inflammatory and antioxidant effects. There are different kinds of diets, such as the Mediterranean diet, vegetarianism, fasting, and elimination diets show varying effects on RA symptoms. RA is associated with dysbiotic interactions between the mucosal immune system and synovial joints. [26] **Lipid peroxidation** is decreased by consuming traditional Indian fermented milk that has been enhanced with Lactobacillus acidophilus and Lactobacillus casei [23.] Bifidobacterium decreases CD4+ T cell overstimulation, while Lactobacillus casei and L. reuteri decrease nephritis, autoantibody

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levels, and increase regulatory T cells. [18] **Vitamin D** plays a significant role in immune defense in the gut. It classically acts through the vitamin D receptor [VDR] to regulate gene transcription, inhibiting Th17 and Th1 responses, promoting Tregs, impairing B cell development and function, and stimulating antimicrobial peptides from immune cells. Vitamin D status/exposure can alter the composition of the gut microbiome, with rodent studies showing that vitamin D deficiency promotes increases in the Bacteriodetes and Proteobacteria phyla. Vitamin D supplementation has been shown to reduce bacterial taxa and changes in bacterial abundance in autoimmune disease patients. In a 4-week intervention for vitamin D deficient CD patients in remission, megasphaera and Lactobacillus were enriched at week 4, but still comprised a relatively low abundance overall. [22]

DMARDs may indirectly alter and modify the composition and activity of the gut flora. Research has shown that microbial variations in RA patients' gastrointestinal tracts may influence methotrexate's bioavailability and subsequent clinical results. In turn, it has been demonstrated that methotrexate treatment helps RA patients regain the normal structure of their gut flora. Bacterial azoreductases in the large intestine break down another DMARD, sulfasalazine, producing mesalazine and sulfapyridine. By controlling gut microbiota, sulfapyridine appears to normalize lymphocyte activity and has an impact on the immune system. Sulfasalazine treatment significantly reduced the fecal levels of Escherichia coli and Clostridium perfringens in a trial of patients with active RA. However, there is still a dearth of comprehensive characterization of how sulfasalazine medication affects the gut flora in RA. [5]

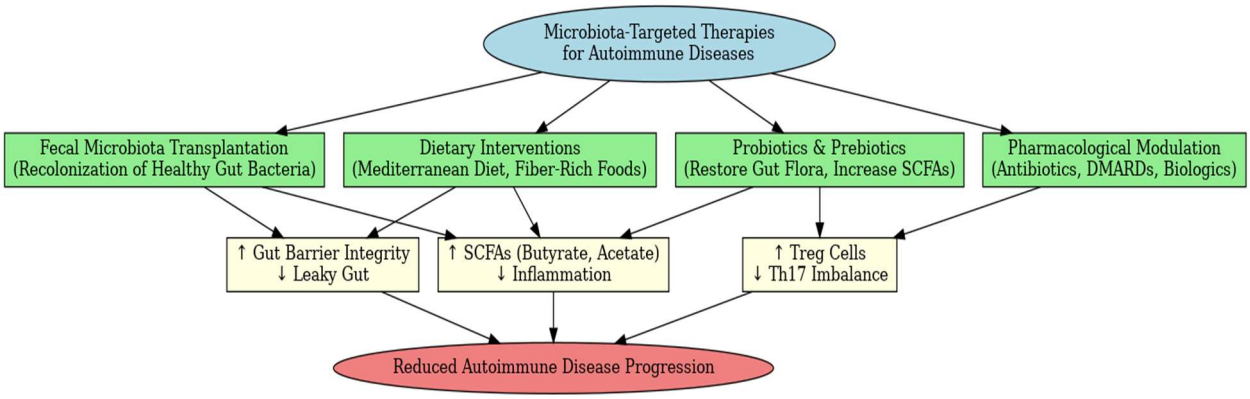

Figure 3.3 **Microbiome-Targeted Therapies for Autoimmune Diseases**

IV. Discussion

4.1 Interplay between genetics, environment, and microbiota in autoimmune diseases.

Autoimmune Diseases arise mainly due to an intricate interaction between genetics, environmental factors, and gut microbiota. Recent studies suggest how these interact to shape immune responses, thereby causing autoimmune pathologies.

4.1.1 Eubiosis to Dysbiosis of the Microbiota

A disturbed gut microbiota is a significant environmental factor contributing to the pathogenesis of autoimmune disorders [2].

The five mechanisms through which gut dysbiosis causes autoimmune disorders are: TLR dysregulation in APCs and an imbalance in the Treg/Th17 ratio; microbial components that resemble self-peptides and activate autoreactive B and T cells; the spread of microbial components or metabolites throughout the host; the production of autoantibodies against curli-DNA composites; and the production of new autoantigens as a result of microbial enzymes altering host proteins[4]

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There also exists a Mutual Influence between Gut Microbiota and Host Immunity. In order to stop luminal bacteria from interacting directly with the host and to assist create a physical barrier that is consistent with the tight connection of the epithelium, mucosal IgA of the gut lumen may attach itself to them. By influencing the colonization and pro-inflammatory potential of gut microbiota, secretory IgA controls their composition. On the other hand, certain gut microorganisms trigger and regulate the IgA response [14]. Dysbiosis of the microbiome can induce pro-inflammatory and immune deregulatory effects, leading to pathogenic autoimmune responses [7].

4.1.2 Gut dysbiosis: A Modifiable factor or not.

Changes in gut microbiota profiles in individuals with a genetic predisposition can lead to compromised gut ecology and pathogenic autoimmune pro-inflammatory responses, such as Th17 activation[7]. Gut dysbiosis is connected to autoimmune diseases like Multiple Sclerosis ,which includes different compositions of bacteria such as elevated Methanobrevibacter and Akkermansia and low butyricimonas levels [10]. Microbes like B. fragilis, P. histicola, Bifidobacterium, Lactobacillus, and E. coli Nissle 1917 strain activate Tregs and suppress Th1/Th17 responses, hence reducing inflammation. [10].

Microbial dysbiosis and autoimmunity are associated with gut microbiome composition.[22] Factors such as genetics, diet, lifestyle, and geographic distribution can alter the microbial structure, leading to compromised immunological structures in germ-free [GF] and antibiotic-treated mice [2]. Oral Lactobacillus and Bifidobacterium spp. Clinical trials have shown symptom alleviation, suggesting the therapeutic value of altering the gut flora in MS [10]. Therefore, addressing and changing the variables may assist in modifying the disruption to the gut microbiota, potentially undoing the consequences of gut dysbiosis.

4.2 The Bidirectional Relationship: Gut Dysbiosis as Cause and Consequence of Autoimmunity

There is a reciprocal link between autoimmune illnesses and intestinal dysbiosis. Several research suggest that autoimmune disorders can be brought on by gut dysbiosis, but autoimmune diseases can also cause dysbiosis through changes in the immune system, persistent inflammation, and gut permeability.

4.2.1 Gut Dysbiosis as a Driver of Autoimmune Pathogenesis

I. Bacterial Translocation & Leaky Gut:

- Gut dysbiosis could trigger autoimmune disease through two potential pathways: after promoting a leaky gut, bacterial antigens could stimulate intestinal immune cells, generating autoreactive cells that subsequently migrate systemically to their target peripheral organs and initiate an attack[16].
- Patients with SLE have Enterococcus gallinarum, which moves from the stomach to the liver and lymph nodes during bacterial translocation, exposing immune cells to autoantigens such as dsDNA, β2GPI, and RNA and hence causing systemic inflammation and the production of autoantibodies [2] [18] [8].
- Prevotella copri causes Th17-driven inflammation in patients with early-stage rheumatoid arthritis [RA], which may be related to the onset of the disease [7].

II. Molecular Mimicry & Autoimmune Activation

- Dysbiosis and gut barrier breakdown cause inflammation and AID through antigenic mimicry. The colonization of gut microbiota starts at birth and by the age of 3, it get stability develops.SCFAs and retinoic acid promotes RORγ[+] Treg cells, and contribute to long-term protection against inflammatory diseases like colitis[10].
- By imitating bacterial Ro60 protein, Bacteroides thetaiotaomicron induces lupus-like autoimmunity, hence activating Ro60-specific T cells to react with both bacterial and human Ro60[10].
- Streptococcus contributes to autoimmunity by producing antigens that promote the formation of autoantibodies[4].

III. Dysbiosis Alters Immune Balance

- Pro-inflammatory cytokines like interleukin-12 [IL-12], IL-23, and type I interferons, among others, can be upregulated, and anti-inflammatory cytokines like transforming growth factor β and IL-10 can be downregulated due to inadequate innate immune cell activation caused by disturbed gut microbiota. [5]
- Tregs, which are also derived from CD4+ T cells, have the ability to block Th17 responses and instead display immunosuppressive characteristics. The gut microbiota and its metabolites have an active impact on the Th17/Treg balance, and autoimmune diseases like Rheumatoid Arthritis is intimately linked to an elevated Th17/Treg ratio [5].
- Segmented filamentous bacteria [SFB] have a well-documented ability to promote a Th17 response. Coinfection with SFB and Listeria monocytogenes generate Th17 and Th1 cells, respectively, demonstrating that individual bacteria can elicit specific immune cell responses [22].
- Inflammation also results from the loss of bacteria that produce SCFA, such as Faecalibacterium prausnitzii, and is observed in T1D, SLE, and MS [15] [11] [27].

4.2.2 Autoimmune-Mediated Disruption of the Gut Microbiome

I. Inflammatory Cytokines Disrupt Gut Microbiota:

Increased levels of type I IFN, IL-6, and IL-17 in SLE change the makeup of gut microbes, favoring harmful species including Enterococcus and Eggerthella [18]. Patients with RA exhibit more inflammatory microorganisms and less helpful Lactobacillus [28] [13].

II. Autoantibodies & Gut Permeability

Autoantibodies in T1D cause increased intestinal permeability in addition to attacking pancreatic beta cells [10].

III. Immune-Mediated Microbiota Shifts

By changing IgA responses and impacting gut microbial balance, chronic B-cell activation in lupus contributes to gut dysbiosis [8].

Therefore, it is clear that there is a vicious loop of reinforcement between autoimmune disorders and intestinal dysbiosis. This cycle implies that autoimmune disorders may be prevented or lessened by adjusting the gut flora.

4.3 Challenges and Limitations to Control of Dysbiosis

4.3.1 Genetic predisposition

Genetic predisposition affects immune system tolerance and modulation, which is a major factor in raising the risk for autoimmune illnesses.

- Mutations in T cell receptor [TCR] signaling affect gut dysbiosis and self-reactive T cell selection. [2] [16]
- HLA genes are linked to a higher incidence of conditions, including Systemic Lupus Erythematosus [SLE] and Type 1 Diabetes [T1D]. [15]

4.3.2 Diet

The host immune system may be significantly impacted by diet. Foods like red meat, salt, and high caloric intake worsen RA, while polyunsaturated fats [PUFAs] offer anti-inflammatory and antioxidant effects[26]

- Westernization of diets: immune-related illnesses like IBD, hay fever, and celiac disease, as well as non-communicable diseases, have been brought on by factors like the rising incidence of high-fat and high-sugar diets.

- Food emulsifiers, which are often found in processed foods in Western diets, promote early inflammatory lesions in IBD and increase bacterial intestinal permeability in vitro. In contrast, dietary fiber, which is in short supply in Western diets, inhibits these responses.[24]
- Reduced autoimmune symptoms and enhanced gut microbial diversity have been associated with omega-3 fatty acids and polyphenols [17].

4.3.3 Sex

Because males and females have different hormonal profiles and immunological responses, sex is a key risk factor for autoimmune disorders.

- Women are more prone to Autoimmune Diseases, due to their greater immune responses and hormonal effects [estrogen, progesterone, testosterone] on immune cell activity. Female-biased autoimmunity may also be influenced by gut microbiome. [29]
- Male-associated bacteria [such as greater abundances of beneficial species like Akkermansia muciniphila] may reduce autoimmune risk, while female-associated microbial profiles may promote inflammation. [29]

4.3.4 C- section births

C-section births increase the risk of autoimmune conditions like T1D and MS as they inhibit the natural transfer of maternal microorganisms, which results in a change in the makeup of the gut microbiota and consequent dysregulation of the immune system [12].

4.3.5 Medications & their Effects

- Antibiotics such as minocycline have been used as second-line treatments for mild RA, while others indicate that broad-spectrum antibiotic use raises the risk of autoimmune diseases by suppressing beneficial gut microbes [2].
- Immunosuppressive medications, including methotrexate, sulfasalazine, and hydroxychloroquine, can alter gut microbial populations either directly or indirectly, which enhances their therapeutic effects [28] [14].
- As a result, it is evident that many factors influence gut microbiota, and since every individual has a different microbiome, it is difficult to create a single treatment.

4.4 Future Directions

4.4.1 Standardization and Thorough Clinical Trials

- FMT and EGFR or stem cell-based epithelium regeneration may be used in future therapies[6]. FMT trials are increasingly promising regarding the health benefits of inflammatory diseases. [17]
- FMT increases gut microbial diversity and alters microbial composition by enhancing Eubacterium hallii and Roseburia inulivorans species in active UC patients, leading to disease remission. However, more clinical trials are needed to demonstrate its in psoriasis patients and investigate whether modulation of the intestinal microbiota plays a crucial role in this process.[17]

4.4.2 Advanced Multi-Omics Approaches

The use of metagenomics, metabolomics, and proteomics to map the interactions between gut microbiome and host interactions is very promising. This will enable focused therapies by assisting in the discovery of new biomarkers and mechanistic insights. [13]

4.4.3 Customized Interventions and Personalized Medicine

- This focuses on creating customized treatment plans based on a patient's exposures to the environment, microbial profile, and genetic background.
- These include using specific prebiotics, probiotics, and FMT as crucial steps. [13]
- When compared to the placebo group, probiotic-based therapy for T1D patients has demonstrated a substantial decrease in HbA1c and insulin bolus dosages[15].
- Gut microbiome-targeted therapies for psoriasis: suggest that modulation of the gut microbiota, both through dietary approaches and supplementation with probiotics and prebiotics, could represent a new therapeutic target in autoimmune pathologies, such as multiple sclerosis, celiac disease, and psoriasis[17].
- Combination therapy of probiotics, dietary intervention, natural compounds, and vitamin D therapy in regulating the microbiota to prevent RA progression would be a fruitful area for further work. [27]

4.4.4 Emphasis on Microbial Metabolites and Their Potential for Treatment

- Short-chain fatty acids [SCFAs] and other microbial metabolites have immune-regulatory properties through their inhibition of inflammatory cytokines and NF-kB activation. [23]
- The integrity of the intestinal barrier and immunological equilibrium may be restored by targeting these metabolites therapeutically.

V. CONCLUSION

The gut microbiome plays a key role in the autoimmune disease pathogenesis. It has a role in immune regulation, intestinal permeability, and systemic inflammation. This research has shown us that there is a strong association between conditions like dysbiosis and autoimmunity. The exact relationship remains unclear. Future research should address topics like microbial imbalances being a primary cause of autoimmune diseases or a secondary consequence of chronic inflammation.

There is an urgent requirement for large-scale human trials to validate microbiota-based interventions, including custom tailored probiotics, dietary interventions, fecal microbiota transplantation[FMT]. Advancements in metagenomics, metabolomics, and artificial intelligence-based microbial analysis can enable precise medicine and personalized interventions based on the individual's gut microbiota.

In the coming years, microbiome-targeted therapies could shift the present autoimmune disease management from the symptom-control approach to a disease-modification approach or maybe even prevention. If utilized correctly, gut microbiota research has tremendous potential to revolutionize not just autoimmune medicine but the entire field of immunology.

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