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Gut Microbiota in Rheumatic Diseases: Pathogenic Role and Therapeutic Potential

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Abstract
The gut microbiota plays a vital role in maintaining physiological balance within the body, and its disruption-known as dysbiosis-is increasingly linked to the development of autoimmune diseases, including rheumatic conditions. In recent years, there has been growing interest in the intricate relationship between the gut microbiome and the immune system, which may significantly influence the onset and progression of disorders such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and psoriatic arthritis (PsA).
This paper aims to review the current understanding of the connection between gut microbiota and rheumatic diseases, with a focus on the underlying immunological mechanisms. It highlights observed changes in the gut microbial composition among patients with selected rheumatic disorders and examines the potential impact of these changes on immune system function.
Additionally, the paper explores potential therapeutic approaches aimed at modulating the gut microbiota, including the use of probiotics, prebiotics, dietary modifications, and the innovative technique of fecal microbiota transplantation (FMT). By analyzing existing research, the study assesses the effectiveness and safety of these interventions and suggests future directions for microbiota-focused therapies as supportive treatments for rheumatic diseases.

Keywords: Gut microbiota, Rheumatic diseases, Dysbiosis, Microbiota-targeted therapies, Immune system

Introduction

The human microbiota is a complex community composed of bacteria, bacteriophages, viruses, fungi, and protozoa, which varies significantly between individuals and across different body sites, such as the skin, oral cavity, urogenital tract, and gastrointestinal tract [1]. It plays a crucial role in various physiological processes including inflammation, metabolism, hematopoiesis, and cognitive functions. An imbalance in this microbial community-known as dysbiosis-can be triggered by factors such as antibiotic use, dietary changes, infections, chronic stress, environmental pollutants, chronic diseases, aging, and lack of physical activity, potentially leading to the development of inflammatory and neoplastic diseases [2].

The gut microbiota begins to form in early childhood-colonization starts at birth, microbial diversity increases within the first five years of life, and then stabilizes with age [3]. This colonization takes place not only in the gut but also on the skin, in the respiratory tract, and the reproductive system, influencing numerous physiological processes such as nutrition, tumor development, and immune system balance [4].

Diet also significantly impacts microbiota composition-for instance, a fiber-rich diet supports the growth of bacteria from the Lachnospiraceae family [5], whereas a Western-style diet rich in red meat and low in fiber is associated with the dominance of Bacteroides spp and Ruminococcus torques species [6]. The gut microbiota, which has co-evolved with its host, plays a vital role in numerous physiological and pathological processes, including nutrient production, drug metabolism, protection against pathogens, and immune regulation [7].

Gut bacteria ferment indigestible carbohydrates, producing short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate, which act as biologically active compounds and serve as an energy source for colon epithelial cells [8]. The connection between gut microbiota and innate immunity has become a significant focus of scientific research. Gut-associated lymphoid tissue (GALT) plays a key role in protecting the intestinal mucosa, working in coordination with other mucosa-associated lymphoid tissues (MALT). Innate immune cells located in these tissues recognize pathogens in a non-specific manner, initiate immune responses, and present antigens to activate adaptive immunity. Studies in germ-free (GF) models have shown that the gut microbiota is essential for the physiological function, development, and maturation of GALT [9].

Gut microbiota and the immune system

The development and training of both the innate and adaptive immune systems are significantly influenced by the host's microbiome, while the immune system in turn helps maintain key features of host-microbe symbiosis [10]. The gut microbiota, together with mesenteric lymph nodes, specialized epithelial cells, immune cells from both innate and adaptive branches, and their associated metabolites, make up the core of the intestinal immune system [11]. Metabolites produced by gut microbes play an important role in regulating inflammatory pathways, as they interact with the host’s immune cells either directly or through intermediate mechanisms [12]. Through the action of intestinal epithelial cells, the microbiota and its metabolites can influence the development and functional regulation of the immune system [13].

The immune system is divided into two interconnected components: innate and adaptive immunity, which work together to protect the body from internal and external dangers. The innate immune response acts as the body’s immediate defense mechanism, reacting s wiftly and generally to immunological triggers. Key players in innate immunity include granulocytes, natural killer (NK) cells, dendritic cells, and macrophages, which combat pathogens by engulfing them and releasing signaling molecules such as cytokines and chemokines. These cytokines promote the activation of lymphocytes like B cells, which produce antibodies targeting specific pathogens, and T cells, which include helper T cells, cytotoxic T cells, and regulatory T cells (Tregs). These T cells not only form the core of the adaptive immune system but also help recruit more innate immune cells [14].

Gut-associated lymphoid tissues (GALTs), part of the broader group of mucosa-associated lymphoid tissues (MALTs), are situated at the interface between the body and its external environment. Immune cells within GALTs act as the first line of defense for the intestinal mucosa. Their main tasks include the nonspecific detection of pathogens, initiation of innate immune responses, and antigen presentation to activate the adaptive immune system. GALTs are essential for maintaining immune tolerance to commensal microorganisms. The dual function of GALTs is central to sustaining the balance between the immune system and gut microbiota [15].

The origins of autoimmune diseases are multifactorial, involving both genetic predispositions and environmental influences. Genetic susceptibility involves both HLA and non-HLA genes, with their expression patterns varying depending on the specific autoimmune disorder. In contrast, environmental triggers include factors such as tobacco use, unhealthy lifestyle habits, limited sunlight exposure, and long-term stress [16]. Recently, alterations in gut microbiota-referred to as gut dysbiosis-have gained recognition as a potential risk factor for autoimmunity. However, it remains unclear whether dysbiosis is a cause or a consequence of autoimmune diseases [17]. Conditions like primary Sjögren's syndrome (SS), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and multiple sclerosis (MS) have all been associated with disruptions in gut microbial composition [18].

Common contributors to dysbiosis include thinning of the mucus barrier, abrupt dietary shifts, antibiotic usage, infections, inflammation, and surgical procedures involving the gastrointestinal tract [19]. According to Chen et al., there are five main mechanisms through which dysbiosis may promote autoimmune diseases: 1) dysregulated Toll-like receptor (TLR) signaling in antigen-presenting cells and an imbalance between Treg and Th17 cells; 2) creation of novel autoantigens due to microbial enzyme-induced alterations of host proteins; 3) molecular mimicry, where microbial molecules resemble host peptides, leading to activation of autoreactive T and B cells; 4) spread of microbial components or metabolites throughout the body, causing immunopathological effects; and 5) generation of autoantibodies targeting curli-DNA complexes [20].

Microbiota and rheumatic diseases

Rheumatoid Arthritis (RA)

Rheumatoid arthritis (RA) is a chronic autoimmune condition marked by persistent inflammation of synovial tissues, which clinically manifests as joint pain, swelling, and stiffness, and may also affect bones and cartilage. The development of RA is believed to be influenced by genetic predispositions, environmental exposures, and socioeconomic conditions. While these elements contribute significantly to the disease process, the complete etiopathogenesis of RA is still not fully understood [21]. Numerous clinical investigations have documented alterations in microbial diversity in individuals with RA [22].

The gastrointestinal tract is home to the majority of the body's immune cells, and its continuous interaction with the gut microbiota plays a crucial role in shaping immune cell function and characteristics. This gut microbiota engages in ongoing, bidirectional communication with the host's immune system, maintaining a delicate balance between tolerance and immune activation, depending on whether microbes behave as pathogens or harmless commensals [23]. Within gut-associated lymphoid tissue (GALT), innate immune cells serve as the body's initial defense against foreign substances from the gut. Disruption of the gut microbial community can lead to abnormal activation of these innate immune cells, resulting in increased production of proinflammatory cytokines—such as interleukin-12 (IL-12), IL-23, and type I interferons-and decreased production of anti-inflammatory mediators like transforming growth factor-β and IL-10 [24].

Moreover, adaptive immune cells, particularly T and B lymphocytes, are critical contributors to autoimmune processes. Abnormal activation of these cells plays a central role in the onset and progression of RA. Proinflammatory gut microbes can alter immune balance by overstimulating innate immunity, which in turn leads to dysfunctional adaptive immune responses. Dendritic cells and macrophages can present microbial antigens to CD4+ T cells, promoting the development of inflammatory T cell subsets. Among these, Th17 cells-a proinflammatory subset of CD4+ T cells-are characterized by their secretion of interleukin-17 (IL-17) [25]. In contrast, regulatory T cells (Tregs), which also originate from CD4+ T cells, suppress immune responses and counterbalance Th17 activity [26]. An increased Th17/Treg ratio has been closely associated with RA, and this balance is strongly influenced by gut microbiota and their metabolic products [27].

In addition to affecting T cells, microbial antigens can also drive excessive activation of B cells with assistance from T follicular helper cells. These B cells can differentiate into plasma cells that produce pathogenic autoantibodies, further contributing to RA pathogenesis [28]. Therefore, gut dysbiosis, inflammatory signaling, and immune dysregulation are interconnected and collectively influence the development of RA [29].

The intestinal epithelial barrier, maintained by the gut lining, acts as a defense system by blocking harmful substances in the intestinal lumen. In individuals with RA, this barrier is compromised, allowing microbes to pass into gut tissues and potentially enter the bloodstream. Such translocation can lead to excessive immune activation in local tissues and result in systemic immune imbalances [30]. Disrupted gut microbial communities may also drive the migration of autoreactive immune cells to the joints, leading to localized inflammation [31]. Once there, these cells activate macrophages, which produce inflammatory cytokines. Cytokines like tumor necrosis factor-alpha (TNF-α), IL-6, and IL-1 stimulate fibroblasts to release matrix metalloproteinases and receptor activator of nuclear factor κB ligand (RANKL), both of which are involved in the breakdown of bone and cartilage, contributing to RA progression [32].

One study found that *Collinsella aerofaciens*, a gut microbe present in elevated levels in RA patients, reduces the expression of tight junction proteins in intestinal epithelial cells. This weakening of the gut barrier was shown to increase disease severity in HLA-DQ8 transgenic mice with collagen-induced arthritis (CIA) [33]. Conversely, *Faecalibacterium prausnitzii*, a beneficial gut bacterium whose levels are decreased in RA patients, supports intestinal barrier integrity, helps maintain the Th17/Treg balance, and exerts strong anti-inflammatory effects [34]. These findings suggest that shifts in gut microbial diversity may disrupt intestinal permeability and contribute to the onset and progression of RA [35].

Systemic Lupus Erythematosus (SLE)

Systemic lupus erythematosus (SLE) is among the most prevalent systemic autoimmune disorders. It primarily affects women during their reproductive years and can impact multiple organ systems, including the skin, joints, kidneys, lungs, heart, and the gastrointestinal tract. Nearly all individuals with SLE produce a wide range of autoantibodies targeting proteins associated with nucleic acids—namely DNA and RNA. Particularly notable are antinuclear antibodies (ANAs), anti-double-stranded DNA (anti-dsDNA), anti-Smith (Sm), and antibodies targeting SSA/Ro and SSB/La antigens, which are linked to Sjögren's syndrome [36].

The wide variety of clinical symptoms seen in SLE reflects its complex and multifactorial origin. Although genetic studies have uncovered numerous susceptibility loci, these variants explain only around 28% or less of the disease's heritable component [37]. The exact molecular mechanisms underlying the diverse clinical spectrum of SLE remain largely unresolved. Additionally, various environmental triggers are believed to contribute significantly to the onset and progression of SLE-related autoimmune responses [38].

Changes in the gut microbiota composition have also been observed in SLE patients, with notable differences in bacterial abundance and structure compared to healthy individuals. These alterations include an overrepresentation of Proteobacteria, Bacteroidetes, and Actinobacteria, and a relative reduction in Firmicutes [39]. One genus of growing interest in autoimmune pathogenesis is *Prevotella*. Diet and genetic predisposition may influence gut microbial imbalances differently across populations with autoimmune conditions. Moreover, microbial genera such as *Rhodococcus*, *Eggerthella*, *Klebsiella*, *Prevotella*, *Eubacterium*, *Flavonifractor*, and *Incertae sedis* appear significantly more common in SLE patients, whereas *Dialister* and *Pseudobutyrivibrio* are markedly less abundant [39].

At the species level, *Ruminococcus gnavus* (RG), a member of the Firmicutes phylum, has been implicated in weakening the gut barrier-particularly in SLE patients with kidney involvement. The richness of microbial species has also been found to positively correlate with SLE disease activity, as measured by the SLEDAI index. Furthermore, anti-RG antibodies show a positive correlation with both SLEDAI scores and levels of anti-native DNA, and a negative correlation with complement proteins C3 and C4 [40].

Short-chain fatty acids (SCFAs), produced by gut bacteria, are essential for the proper differentiation of T and B cells and the preservation of immune tolerance through the modulation of regulatory T cells (Tregs) [41]. Bacteria from the Firmicutes phylum are the primary producers of butyrate, a metabolite that plays a key role in the generation and stability of Tregs within various body tissues, particularly the gastrointestinal tract [42]. Butyrate also inhibits the transformation of T cells into proinflammatory Th17 and Th1 subtypes, helping to maintain equilibrium between anti-inflammatory and inflammatory cytokine responses.

In SLE, compromised gut barrier integrity—commonly referred to as "leaky gut"-has been documented. Increased levels of bacteria such as *R. gnavus* and *Enterococcus gallinarum* have been linked to the release of inflammatory mediators that exacerbate systemic inflammation [43]. The translocation of bacteria into the lamina propria, along with autoreactive T and B cells, activates toll-like receptor pathways and promotes the production of inflammatory cytokines, type I interferons, and autoantibodies. These immune components, once in circulation, contribute to the breakdown of immune tolerance and drive tissue and organ damage in SLE [44].

Psoriatic Arthritis (PsA)

Psoriatic arthritis (PsA) is a chronic inflammatory condition that involves both dermatological and musculoskeletal symptoms. It presents with psoriasis-like skin lesions, changes in the nails, and dactylitis, along with joint-related inflammation such as peripheral arthritis, enthesitis, and axial disease manifestations [45]. According to a comprehensive analysis [46], PsA-defined by the Classification Criteria for Psoriatic Arthritis (CASPAR)-affects about 23.8% of individuals with psoriasis. This high prevalence significantly contributes to disability, negatively affecting patients' ability to carry out daily tasks, maintain employment, and perform productively [47]. Moreover, the presence of comorbid conditions like cardiovascular diseases and metabolic syndrome has a profound impact on life expectancy, general health status, and quality of life in PsA patients [48].

A study conducted by Yihong Gan and colleagues utilized summary data from the MiBioGen consortium's large-scale GWAS meta-analysis on the gut microbiome, as well as PsA-related data from the FinnGen R9 dataset. A bidirectional two-sample Mendelian randomization (MR) analysis was performed to reduce confounding and explore potential causal relationships between specific gut microbes and PsA. Their findings revealed that certain taxa-such as *Methanobacteria*, *Methanobacteriales*, *Methanobacteriaceae*, *Eubacterium fissicatena* group, and *Methanobrevibacter*-may have protective roles. In contrast, *Rikenellaceae* and *Ruminococcaceae UCG011* were identified as potential microbial risk factors. Notably, reverse MR analyses indicated that PsA itself might influence gut microbiota composition, with *Ruminococcaceae UCG011* showing a clear bidirectional link.

Short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate, are organic compounds generated by gut microbes through fermentation of dietary fibers. They play essential roles in regulating the immune, nervous, and metabolic systems [49], and have been shown to affect both bone homeostasis and immune cell behavior [50]. The butyrate-producing *Eubacterium fissicatena* group may help prevent the development of PsA by supporting gut microbial balance and intestinal health. This aligns with previous findings indicating reduced butyrate levels in psoriasis patients predisposed to PsA [51]. SCFAs like butyrate exert their effects by activating receptors such as GPR109a on immune cells like macrophages and dendritic cells, which promotes the expansion of anti-inflammatory regulatory T cells (Tregs) and IL-10-producing T cells [52].

Methanogens, including *Methanobacteria*, are anaerobic archaea that produce methane and carbon dioxide by metabolizing various substrates [53]. These microorganisms inhabit various areas of the human body, especially the gut. Decreased methanogen levels have been reported in individuals with inflammatory bowel disease (IBD), which is recognized as a risk factor for PsA [54]. One theory proposes that frequent diarrhea in IBD may lead to the elimination of methanogens from the gut, potentially linking their reduced presence to PsA pathogenesis [55]. Conversely, taxa such as *Rikenellaceae* and *Ruminococcaceae UCG011* have been associated with increased PsA susceptibility. *Rikenellaceae*-a Gram-negative bacterium-can be enriched by high-fat diets and has connections to both obesity and inflammation [56]. Interestingly, studies in HLA-B27 transgenic rats reported a reduction of *Rikenellaceae* compared to wild-type animals [57], suggesting that species-specific differences or additional regulatory mechanisms may be at play. Further research is needed to better understand the complex interactions between these microbial communities and PsA risk.

Microbiota-targeted therapies

Probiotics and Their Role in Rheumatoid Arthritis (RA)

Probiotics are defined as "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host" [58]. These beneficial microbes support health through multiple mechanisms, including maintaining gut microbiota balance, restoring homeostasis after dysbiosis, producing bioactive compounds, and modulating immune responses.

Both animal models and human clinical studies have explored the potential of probiotics in the prevention and treatment of RA. Among the most extensively studied are strains from the *Lactobacillus* and *Bifidobacterium* genera. In an experimental model of collagen-induced arthritis (CIA) in rats, various *Lactobacillus* strains were tested for their therapeutic impact. *L. reuteri*, *L. casei*, *L. rhamnosus*, and *L. fermentum* significantly alleviated disease symptoms by suppressing strain-specific proinflammatory cytokines and influencing gut microbial composition and metabolites like short-chain fatty acids (SCFAs) [59]. For instance, *L. reuteri* and *L. casei* reduced Th1 immune responses, while *L. rhamnosus* and *L. fermentum* were effective in suppressing Th17-related inflammation. However, *L. plantarum* affected both pathways without producing clinical improvements, and *L. salivarius* merely delayed disease onset without notable immune modulation [59].

In a randomized, double-blind clinical trial, daily supplementation with *L. casei* 01 over 8 weeks in RA patients led to reduced levels of proinflammatory cytokines (TNF-α, IL-6, IL-12), elevated levels of the anti-inflammatory cytokine IL-10, and overall improvement in disease activity [60]. Additional studies showed that *L. rhamnosus* GR-1 and *L. reuteri* RC-14 enhanced functional outcomes, reflected in improved HAQ scores and achievement of an ACR 20 response [61].

Bifidobacterium species have shown promising results as well. In CIA rat models, five strains of *B. adolescentis* alleviated arthritic symptoms, helped rebalance the immune system, and corrected intestinal dysbiosis [62]. Similarly, *B. longum* RAPO was shown in preclinical studies to lower the incidence of RA, reduce inflammation, and prevent joint damage, likely by suppressing IL-17 and other proinflammatory mediators [63]. A clinical combination of *L. acidophilus*, *L. casei*, and *B. bifidum* was found to improve DAS-28 scores and reduce C-reactive protein (CRP) levels in patients. Notably, a novel strain-*B. bifidum* ATT-has been patented for its potential use in RA prevention and treatment [64].

Another promising probiotic, *Prevotella histicola*, demonstrated effectiveness in reducing RA severity in HLA-DQ8 transgenic mice. It suppressed Th17-mediated inflammation, enhanced IL-10 transcription, and promoted the expression of antimicrobial peptides and tight junction proteins, suggesting its potential to support gut barrier integrity and enhance butyrate production [65].

Probiotic strains from the *Bacillus* genus, particularly *Bacillus coagulans* (GBI-30, 6086), have also yielded positive outcomes. In a 60-day clinical trial involving RA patients, *B. coagulans* supplementation resulted in improved pain management and mobility. This strain produces SCFAs, including butyrate, which supports mucosal immunity and gut health [66]. Furthermore, a combination of *B. coagulans* and inulin, tested in arthritic rats, led to reduced levels of inflammatory markers such as serum amyloid A and fibrinogen, alongside decreased paw swelling and proinflammatory cytokines like TNF-α [67].

Fecal Microbiota Transplantation (FMT) in Autoimmune Conditions

Fecal microbiota transplantation (FMT) involves transferring gut microbiota from a healthy donor into the gastrointestinal tract of a recipient, with the goal of restoring microbial balance (eubiosis). This is typically achieved through delivery methods such as nasogastric tubes, colonoscopy, or capsules [68]. FMT is generally considered a safe intervention [69] and has gained widespread acceptance as an effective treatment for recurrent *Clostridioides difficile* infections [70]. However, its potential as a therapy for extraintestinal conditions, including autoimmune diseases, remains a subject of ongoing debate [71].

A growing body of research highlights the role of the gut microbiome and its metabolites in the pathogenesis of autoimmune diseases [72]. Both oral and intestinal microbiota have been shown to significantly influence immune regulation and may contribute to the development of autoimmunity [73].

FMT in Rheumatoid Arthritis (RA)

One notable case report involved a 20-year-old woman with RA who received FMT via colonoscopy using fecal material from a healthy 8-year-old donor, resulting in clinical improvement without adverse effects [74]. Despite such promising cases, the use of FMT in anti-rheumatic therapy remains controversial.

Animal studies have provided mixed insights. In germ-free mice colonized with microbiota from TNFΔARE+/− donors (a model for spontaneous arthritis), researchers observed joint deformities, elevated inflammatory markers, increased CD4+/CD8+ T-cell activity, behavioral changes, and disrupted gut integrity-suggesting complex interactions between gut microbes, immunity, and the gut-brain axis [75].

In a separate study using a collagen-induced arthritis (CIA) model, mice treated with antibiotics followed by FMT from RA patients exhibited depression-like behaviors. Immunologically, these mice showed increased percentages of CD3e+ and CD4+ T cells in Peyer's patches and the spleen, an elevated Th1/Th2 ratio, and a reduction in regulatory T cells (CD25+, FOXP3+). Certain bacterial genera, including *Bacteroides* and *Phascolarctobacterium*, were associated with these immune alterations [76].

In another model of adjuvant-induced arthritis, oral administration of tuna elastin peptides reduced inflammatory cytokines and increased anti-inflammatory cytokines. These beneficial effects were transferable to recipient mice through FMT, suggesting that positive immunomodulation can be conveyed via gut microbiota [77]. Interestingly, RA-associated dysbiosis was not transmitted from TNFΔARE+/− donors to conventional mice, suggesting that a healthy microbiota might resist the influence of pathogenic microbial communities [75].

Further supporting this complexity, Pu et al. identified 12 microbial biomarkers potentially linked to RA, seven of which were enriched in mice receiving FMT from RA patients [76]. A case report also described symptom improvement in a patient with refractory RA following FMT, including reduced rheumatoid factor and improved disease activity [11]. Conversely, FMT following *Porphyromonas gingivalis* exposure worsened arthritis, highlighting the importance of donor microbial profiles [78]. Surprisingly, infection with *C. difficile* strain VPI 10463 independently attenuated arthritis symptoms, whereas FMT alone had no therapeutic effect in this model [79].

FMT is also under investigation for other musculoskeletal conditions, including juvenile idiopathic arthritis and osteoarthritis [80].

FMT in Psoriatic Arthritis (PsA)

FMT has been evaluated in limited clinical settings for psoriatic arthritis. A double-blind, parallel-group study assessing the safety of a single duodenal FMT dose in patients with active peripheral PsA found the procedure to be generally well tolerated. Reported side effects-such as abdominal discomfort, nausea, and vomiting-were mild and transient, with no serious adverse events [81].

Interestingly, follow-up analysis by the same research team revealed unexpected results: the placebo group had a higher clinical response rate (81%) compared to the FMT group (40%), and showed greater improvements in the Health Assessment Questionnaire Disability Index (HAQ-DI) [82]. These findings suggest that FMT may not be consistently effective in treating PsA and underline the need for more robust, controlled trials.

In another randomized, placebo-controlled trial involving patients with methotrexate-refractory PsA, FMT did not outperform placebo in terms of efficacy, although it remained safe and well tolerated [82].

Overall, while current evidence does not definitively support the routine use of FMT in PsA, preliminary results indicate potential for future exploration. Continued research is necessary to fully understand the therapeutic value and underlying mechanisms of FMT in autoimmune disorders.

Conclusions and Summary

The gut microbiota is a key component in maintaining immunological balance and plays a significant role in the pathogenesis of autoimmune diseases, including rheumatic disorders. A growing body of research suggests that disruptions in gut microbial composition-known as dysbiosis-may contribute to the activation of inflammatory processes underlying conditions such as RA SLE and PsA. The bidirectional interaction between the gut microbiota and the immune system, including its influence on T cells, cytokine production, and the integrity of the intestinal barrier, presents new therapeutic opportunities.

Promising strategies include the modulation of the gut microbiome through probiotics, prebiotics, tailored dietary interventions, and FMT. While preliminary results are encouraging, current evidence remains inconclusive. Variability in study designs, small sample sizes, and short follow-up periods limit the ability to draw definitive conclusions about the efficacy of these approaches in treating rheumatic diseases.

Therefore, there is a clear need for further well-designed clinical and experimental studies to better understand the underlying mechanisms linking gut microbiota to rheumatic disease pathogenesis and progression. Future research should focus particularly on identifying specific microbial strains with anti-inflammatory properties, as well as evaluating the long-term safety and effectiveness of microbiota-targeted therapies. A deeper understanding of these relationships could pave the way for the development of personalized therapeutic approaches in rheumatology, offering more effective and patient-centered care.

Disclosure

Author Contributions

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