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THE ROLE OF GUT MICROBIOTA IN RHEUMATIC DISEASES: CURRENT EVIDENCE AND FUTURE DIRECTIONS

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ABSTRACT

The gut microbiota plays a fundamental role in sustaining physiological homeostasis, and its disruption–referred to as dysbiosis – has been increasingly associated with the pathogenesis of autoimmune disorders, including rheumatic diseases. Growing evidence underscores the complex bidirectional interactions between the gut microbial community and the host immune system, interactions that may critically influence the initiation and progression of conditions such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and psoriatic arthritis (PsA).

This review synthesizes current knowledge on the relationship between gut microbiota composition and rheumatic disease, with particular emphasis on the underlying immunological mechanisms. It delineates characteristic alterations in microbial profiles reported in patients with selected rheumatic conditions and evaluates how such perturbations may shape immune responses.

Furthermore, the paper examines emerging therapeutic strategies aimed at modulating the gut microbiota, including probiotics, prebiotics, targeted dietary interventions, and the increasingly explored approach of fecal microbiota transplantation (FMT). By critically assessing existing evidence, the review addresses the efficacy and safety of microbiota-centered interventions and outlines prospective avenues for their integration as adjunctive therapies in rheumatic disease management.

KEYWORDS

Gut Microbiota, Rheumatic Diseases, Dysbiosis, Microbiota-Targeted Therapies, Immune System

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Introduction

The human microbiota constitutes a highly complex and dynamic ecosystem composed of bacteria, bacteriophages, viruses, fungi, and protozoa. Its composition varies markedly among individuals and across anatomical niches, including the skin, oral cavity, urogenital tract, and gastrointestinal tract [1]. This microbial community contributes to a broad spectrum of physiological processes, such as inflammation, metabolism, hematopoiesis, and cognitive function. Disruption of its equilibrium – referred to as dysbiosis – may arise from antibiotic exposure, dietary shifts, infections, chronic stress, environmental pollutants, comorbid diseases, aging, or reduced physical activity. Such disturbances have been implicated in the onset and progression of inflammatory and neoplastic disorders [2,3].

Gut microbiota development begins in early life: colonization is initiated at birth, microbial diversity expands during the first five years, and subsequently stabilizes throughout adulthood [3]. This colonization occurs not only in the gastrointestinal tract but also on the skin, and within the respiratory and reproductive systems, shaping multiple physiological pathways, including nutrient assimilation, tumorigenesis, and immune homeostasis [4].

Diet is a major determinant of microbial composition. Fiber-rich dietary patterns favor the expansion of Lachnospiraceae [5], whereas Western-style diets, characterized by high red-meat intake and low fiber content, are associated with the predominance of *Bacteroides spp.* and *Ruminococcus torques* [6]. Through long-term co-evolution with the host, the gut microbiota has become integral to numerous physiological and pathological processes, including nutrient biosynthesis, xenobiotic metabolism, colonization resistance against pathogens, and regulation of immune function [7].

A key metabolic contribution of gut bacteria is the fermentation of otherwise indigestible carbohydrates, yielding short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate. These metabolites serve as signaling molecules and constitute the principal energy source for colonocytes [8]. Increasing attention has been directed toward the interplay between the gut microbiota and innate immunity. Gut-associated lymphoid

tissue (GALT) is central to maintaining mucosal integrity and acts in concert with other mucosa-associated lymphoid tissues (MALT). Innate immune cells residing in these structures recognize pathogens in a non-specific manner, initiate inflammatory responses, and present antigens that prime adaptive immunity. Studies using germ-free (GF) models have demonstrated that the presence of gut microbiota is indispensable for the proper development, maturation, and functional competence of GALT [9].

Interactions Between the Gut Microbiota and the Immune System

The development and functional training of both innate and adaptive immune responses are profoundly shaped by the host microbiome, while the immune system reciprocally contributes to the preservation of host–microbe symbiosis [10]. Together with mesenteric lymph nodes, specialized intestinal epithelial cells, a diverse array of innate and adaptive immune cells, and microbially derived metabolites, the gut microbiota forms the core architecture of the intestinal immune system [11]. Microbial metabolites play a pivotal role in modulating inflammatory pathways by interacting directly with immune cells or through intermediary signaling mechanisms [12]. Through their interplay with intestinal epithelial cells, the microbiota and its metabolic products influence the maturation, activation, and regulatory capacity of immune networks [13].

The immune system consists of two functionally interconnected branches: innate and adaptive immunity. Innate immunity provides the body's immediate, non-specific response to pathogenic or inflammatory stimuli. Key cellular effectors include granulocytes, natural killer (NK) cells, dendritic cells, and macrophages, which eliminate pathogens through phagocytosis and the secretion of cytokines and chemokines. These mediators promote the activation of adaptive immune cells such as B lymphocytes, which generate pathogen-specific antibodies, and T lymphocytes, comprising helper, cytotoxic, and regulatory T cells (Tregs). While T cells are central to adaptive immunity, they also contribute to the recruitment and modulation of innate immune responses, illustrating the bidirectional nature of the immune system [14].

Gut-associated lymphoid tissues (GALTs), a subset of mucosa-associated lymphoid tissues (MALTs), occupy a crucial interface between the host and the external environment. Immune cells within GALTs constitute the primary immunological barrier of the intestinal mucosa. Their essential functions include nonspecific pathogen detection, initiation of innate immune responses, and antigen presentation that activates adaptive immunity. Importantly, GALTs are also responsible for maintaining immunological tolerance to commensal microorganisms. This dual surveillance – tolerance function is critical to sustaining homeostasis between the gut microbiota and the host immune system [15].

Autoimmune diseases arise from a multifactorial interplay of genetic predisposition and environmental influences. Genetic susceptibility involves both HLA and non-HLA loci, with disease-specific patterns of gene expression. Environmental contributors include tobacco smoking, sedentary or unhealthy lifestyle habits, limited sunlight exposure, and prolonged psychological stress [16]. In recent years, gut dysbiosis – altered composition and function of the gut microbiota – has emerged as a potential risk factor for autoimmunity. However, it remains uncertain whether dysbiosis acts as a causal driver or a consequence of autoimmune pathology [17]. Disturbances in microbial communities have been implicated in several autoimmune diseases, including primary Sjögren's syndrome (SS), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and multiple sclerosis (MS) [18].

Common triggers of dysbiosis include depletion of the intestinal mucus barrier, abrupt dietary changes, antibiotic exposure, infectious insults, chronic inflammation, and gastrointestinal surgical interventions [19]. According to Chen et al., dysbiosis may promote autoimmunity through five major mechanisms: (1) dysregulated Toll-like receptor (TLR) signaling in antigen-presenting cells accompanied by an imbalance between Treg and Th17 cells; (2) generation of neo-autoantigens via microbial enzyme-mediated modification of host proteins; (3) molecular mimicry, wherein microbial peptides resemble host epitopes and activate autoreactive T and B lymphocytes; (4) systemic dissemination of microbial components or metabolites that elicit immunopathological responses; and (5) production of autoantibodies directed against curli – DNA complexes [20].

Microbiota in Rheumatic Diseases: Pathogenic Roles and Therapeutic Opportunities

Rheumatoid Arthritis (RA)

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by persistent synovial inflammation, clinically manifested as joint pain, swelling, and stiffness, with progressive involvement of cartilage and bone. Its development is shaped by genetic susceptibility, environmental exposures, and socioeconomic determinants; however, the complete etiopathogenesis of RA remains incompletely understood [21]. Numerous clinical studies have identified significant alterations in gut microbial diversity among individuals with RA [22].

The gastrointestinal tract houses the majority of the body's immune cells, and its continuous interaction with the gut microbiota is critical for shaping immune cell phenotype and function. This microbial community engages in dynamic, bidirectional communication with the host immune system to maintain a finely tuned balance between tolerance and activation, depending on whether microbes are recognized as commensals or pathogens [23]. Within gut-associated lymphoid tissue (GALT), innate immune cells form the first immunological barrier against luminal antigens. Disturbance of the gut microbial ecosystem can lead to aberrant activation of these cells, resulting in elevated production of proinflammatory cytokines – including interleukin-12 (IL-12), IL-23, and type I interferons – and diminished secretion of anti-inflammatory mediators such as transforming growth factor-β (TGF-β) and IL-10 [24].

Adaptive immune cells, particularly T and B lymphocytes, also play central roles in the initiation and propagation of RA. Proinflammatory gut microbes can skew immune homeostasis by driving exaggerated innate immune activation, thereby disrupting adaptive immune regulation. Antigen-presenting cells, such as dendritic cells and macrophages, can process microbial antigens and present them to $CD4^+$ T cells, promoting differentiation into inflammatory effector subsets. Among these, Th17 cells – a proinflammatory lineage of $CD4^+$ T cells – are defined by their secretion of interleukin-17 (IL-17) and have been strongly implicated in RA pathogenesis [25]. By contrast, regulatory T cells (Tregs), which also differentiate from $CD4^+$ precursors, suppress excessive immune activation and counterbalance Th17-mediated inflammation [26]. An elevated Th17/Treg ratio is a hallmark of RA and is strongly influenced by gut microbiota and their metabolic derivatives [27].

Microbial dysbiosis also affects humoral immunity. Microbial antigens can induce exaggerated B-cell activation, supported by T follicular helper cells, driving differentiation into plasma cells that produce pathogenic autoantibodies – an essential feature of RA immunopathology [28]. Thus, gut dysbiosis, inflammatory signaling, and immune dysregulation form an interconnected network that contributes to RA development [29].

Integrity of the intestinal epithelial barrier is essential for preventing translocation of luminal microbes and toxins. In RA, this barrier is often compromised, facilitating microbial leakage into gut tissues and, potentially, the systemic circulation. Such translocation promotes excessive local and systemic immune activation [30]. Dysbiosis-driven immune imbalance may also facilitate the migration of autoreactive immune cells to synovial tissues, where they initiate and sustain joint inflammation [31]. Within the joint microenvironment, activated immune cells stimulate macrophages to release proinflammatory cytokines such as tumor necrosis factor-α (TNF-α), IL-6, and IL-1. These cytokines induce fibroblasts to produce matrix metalloproteinases and receptor activator of nuclear factor κB ligand (RANKL), accelerating cartilage degradation and bone resorption – key processes in RA progression [32].

Mechanistic links between microbial dysbiosis and intestinal barrier dysfunction have been highlighted in recent studies. *Collinsella aerofaciens*, found in increased abundance in patients with RA, has been shown to reduce tight junction protein expression in intestinal epithelial cells, thereby weakening barrier integrity. In HLA-DQ8 transgenic mice with collagen-induced arthritis (CIA), elevated *C. aerofaciens* levels intensified disease severity [33]. Conversely, *Faecalibacterium prausnitzii* – a beneficial commensal reduced in RA – supports epithelial barrier function, maintains Th17/Treg equilibrium, and exerts potent anti-inflammatory effects [34]. Collectively, these findings suggest that shifts in gut microbial composition can compromise intestinal permeability and contribute to both the onset and progression of RA [35].

Systemic Lupus Erythematosus (SLE)

Systemic lupus erythematosus (SLE) is one of the most common systemic autoimmune diseases, predominantly affecting women of reproductive age and involving multiple organ systems, including the skin, joints, kidneys, lungs, heart, and gastrointestinal tract. Nearly all individuals diagnosed with SLE develop a broad spectrum of autoantibodies directed against nucleic acid – associated proteins, most notably antinuclear antibodies (ANAs), anti-double-stranded DNA (anti-dsDNA), anti-Smith (Sm), and autoantibodies against SSA/Ro and SSB/La antigens, the latter also associated with Sjögren's syndrome [36].

The clinical heterogeneity of SLE reflects its multifaceted and polygenic nature. Although numerous susceptibility loci have been identified, these genetic variants account for only approximately 28% of the heritable risk [37]. The molecular pathways driving the broad clinical spectrum of SLE remain insufficiently understood, and a variety of environmental triggers are thought to significantly influence both disease onset and progression [38].

Alterations in gut microbiota composition have been consistently documented in SLE patients, revealing distinct differences in microbial structure and abundance relative to healthy individuals. These include an increased prevalence of Proteobacteria, Bacteroidetes, and Actinobacteria, along with a reduction in Firmicutes [39]. Among the taxa of growing interest is the genus *Prevotella*, which has been implicated in autoimmune pathogenic mechanisms and appears to be influenced by both diet and host genetic background. Other genera – *Rhodococcus, Eggerthella, Klebsiella, Prevotella, Eubacterium, Flavonifractor*, and members of *Incertae sedis* – are enriched in SLE patients, whereas *Dialister* and *Pseudobutyrivibrio* are significantly reduced [39].

At the species level, *Ruminococcus gnavus* (RG), a Firmicutes member, has been strongly associated with impaired gut barrier function, particularly in SLE patients with renal involvement. Microbial richness has been positively correlated with disease activity, as assessed by the SLE Disease Activity Index (SLEDAI). Moreover, anti-RG antibody levels show a positive correlation with both SLEDAI scores and anti – native DNA titers, and an inverse relationship with complement proteins C3 and C4 [40].

Short-chain fatty acids (SCFAs), produced through microbial fermentation, are essential for appropriate differentiation of T and B lymphocytes and for maintaining immune tolerance by modulating regulatory T cells (Tregs) [41]. Members of the Firmicutes phylum are the primary producers of butyrate, a metabolite crucial for Treg induction, stability, and function – particularly within the gut mucosa [42]. Butyrate also inhibits differentiation of T cells into proinflammatory Th17 and Th1 subsets, thereby helping sustain a balance between anti-inflammatory and inflammatory cytokine responses.

In SLE, compromised gut epithelial integrity – often referred to as "leaky gut" – has been well documented. Increased abundance of bacteria such as *R. gnavus* and *Enterococcus gallinarum* has been linked to enhanced release of inflammatory mediators that aggravate systemic inflammation [43]. Microbial translocation into the lamina propria, accompanied by recruitment of autoreactive T and B cells, results in activation of Toll-like receptor pathways and subsequent production of inflammatory cytokines, type I interferons, and autoantibodies. Once disseminated systemically, these immune components contribute to the breakdown of self-tolerance and drive multisystem tissue injury characteristic of SLE [44].

Psoriatic Arthritis (PsA)

Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized by both dermatological and musculoskeletal manifestations. Clinically, it presents with psoriasis-like skin lesions, nail dystrophy, and dactylitis, alongside joint-related inflammation such as peripheral arthritis, enthesitis, and axial involvement [45]. A large meta-analysis [46] estimates that PsA – defined according to the Classification Criteria for Psoriatic Arthritis (CASPAR) – affects approximately 23.8% of individuals with psoriasis. This high prevalence contributes substantially to disability, impairing daily functioning, work capacity, and overall productivity [47]. Moreover, comorbid conditions, notably cardiovascular disease and metabolic syndrome, critically influence life expectancy, general health status, and quality of life in patients with PsA [48].

A recent study by Yihong Gan and colleagues employed summary-level data from the MiBioGen consortium's large-scale GWAS meta-analysis of the gut microbiome, together with PsA-related data from the FinnGen R9 dataset. Using bidirectional two-sample Mendelian randomization (MR) to minimize confounding, the researchers evaluated potential causal relationships between specific microbial taxa and PsA. Their findings indicate that certain gut microbes – including *Methanobacteria, Methanobacteriales, Methanobacteriaceae*, the *Eubacterium fissicatena* group, and *Methanobrevibacter* – may exert protective effects. Conversely, taxa such as *Rikenellaceae* and *Ruminococcaceae UCG011* emerged as potential

microbial risk factors. Notably, reverse MR analyses revealed that PsA itself may influence gut microbiota composition, with *Ruminococcaceae UCG011* demonstrating a bidirectional association.

Short-chain fatty acids (SCFAs) – including acetate, propionate, and butyrate – are microbial metabolites produced through fermentation of dietary fiber. They play essential roles in regulating immune, metabolic, and neurophysiological pathways [49] and have been implicated in both bone homeostasis and immune cell differentiation [50]. The butyrate-producing *Eubacterium fissicatena* group may confer protection against PsA by maintaining microbial equilibrium and gut barrier integrity, consistent with prior observations of reduced butyrate levels in psoriasis patients at heightened PsA risk [51]. SCFAs such as butyrate mediate anti-inflammatory effects through activation of receptors including GPR109a on macrophages and dendritic cells, promoting the expansion of regulatory T cells (Tregs) and IL-10 – secreting T cells [52].

Methanogens – including members of *Methanobacteria* – are anaerobic archaea that generate methane and carbon dioxide through metabolism of diverse substrates [53]. These organisms inhabit several body sites, with particularly high abundance in the gut. Reduced methanogen levels have been observed in individuals with inflammatory bowel disease (IBD), a well-established risk factor for PsA [54]. One proposed explanation is that frequent diarrhea characteristic of IBD may facilitate the removal of methanogens from the gastrointestinal tract, potentially linking their reduced abundance to PsA pathogenesis [55].

In contrast, microbial taxa such as *Rikenellaceae* and *Ruminococcaceae UCG011* have been associated with increased PsA susceptibility. *Rikenellaceae* – a Gram-negative bacterial family – can be enriched by high-fat diets and has been linked to obesity and systemic inflammation [56]. Interestingly, studies in HLA-B27 transgenic rats demonstrated reduced *Rikenellaceae* abundance compared with wild-type animals [57], suggesting that host genetics, dietary patterns, or additional regulatory factors may influence microbial dynamics in a disease-specific manner. Further research is required to elucidate the complex interactions between these microbial communities and the risk of developing PsA.

Microbiota-Targeted Therapies: Mechanisms, Efficacy, and Clinical Potential

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 contribute to host health through several mechanisms, including stabilization of gut microbial communities, restoration of homeostasis following dysbiosis, production of bioactive metabolites, and modulation of innate and adaptive immune responses.

Both preclinical and clinical studies have investigated the therapeutic potential of probiotics in the prevention and management of rheumatoid arthritis (RA). Among the most extensively studied are strains belonging to the *Lactobacillus* and *Bifidobacterium* genera. In a collagen-induced arthritis (CIA) rat model, multiple *Lactobacillus* strains were evaluated for their immunomodulatory and clinical effects. *L. reuteri, L. casei, L. rhamnosus,* and *L. fermentum* significantly attenuated disease severity by suppressing strain-specific proinflammatory cytokines and altering gut microbiota composition and its metabolites, particularly short-chain fatty acids (SCFAs) [59]. For example, *L. reuteri and L. casei* predominantly downregulated Th1-mediated immune responses, whereas *L. rhamnosus* and *L. fermentum* effectively suppressed Th17-driven inflammation. Although *L. plantarum* influenced both pathways, it failed to yield clinical improvement, and *L. salivarius* merely delayed disease onset without meaningful immune modulation [59].

Clinical evidence supports these findings. In a randomized, double-blind trial, 8-week supplementation with *L. casei* 01 in RA patients resulted in significant reductions in proinflammatory cytokines (TNF-α, IL-6, IL-12), elevations in the anti-inflammatory cytokine IL-10, and improvement in clinical disease activity [60]. Additional studies revealed that *L. rhamnosus* GR-1 and *L. reuteri* RC-14 enhanced functional outcomes, as reflected by improved Health Assessment Questionnaire (HAQ) scores and achievement of an ACR20 response [61].

Bifidobacterium species have shown similarly promising results. In CIA rat models, five strains of *B. adolescentis* mitigated arthritic symptoms, restored immune equilibrium, and corrected intestinal dysbiosis [62]. Preclinical research on *B. longum* RAPO demonstrated its capacity to decrease RA incidence, reduce inflammation, and prevent joint destruction – effects attributed to suppression of IL-17 and other proinflammatory mediators [63]. Clinically, a combined formulation of *L. acidophilus, L. casei,* and *B. bifidum* improved DAS28 scores and decreased C-reactive protein (CRP) levels. Notably, *B. bifidum* ATT has been patented for its potential utility in RA prevention and therapy [64].

Another emerging probiotic, *Prevotella histicola*, has shown considerable efficacy in HLA-DQ8 transgenic mouse models of RA. It reduced disease severity by suppressing Th17-mediated inflammation,

enhancing IL-10 transcription, and promoting antimicrobial peptide production and tight junction protein expression – suggesting a supportive role in maintaining gut barrier integrity and modulating butyrate production [65].

Probiotic strains of the *Bacillus* genus, particularly *Bacillus coagulans* (GBI-30, 6086), have also demonstrated clinical benefit. In a 60-day clinical trial in RA patients, *B. coagulans* supplementation improved pain and mobility. This strain produces SCFAs, including butyrate, which supports mucosal immunity and gastrointestinal health [66]. Furthermore, combined administration of *B. coagulans* and inulin in arthritic rats reduced inflammatory markers such as serum amyloid A and fibrinogen, and decreased paw edema and proinflammatory cytokine levels, including TNF-α [67].

Fecal Microbiota Transplantation (FMT) in Autoimmune Conditions

Fecal microbiota transplantation (FMT) consists of transferring a community of gut microorganisms from a healthy donor to the gastrointestinal tract of a recipient with the aim of restoring microbial homeostasis (eubiosis). This procedure may be administered through several routes, including nasogastric or nasojejunal tubes, colonoscopy, or orally ingested capsules containing processed donor material [68]. FMT is widely regarded as a safe therapeutic modality [69] and is now well established as the most effective treatment for recurrent *Clostridioides difficile* infection [70]. Nevertheless, its applicability to extraintestinal disorders – including autoimmune and systemic inflammatory diseases–remains an active and controversial area of investigation [71].

An expanding body of evidence underscores the contribution of the gut microbiome and its metabolites to the pathogenesis of autoimmune conditions [72]. Both oral and intestinal microbial communities exert substantial influence on immune homeostasis, shaping innate and adaptive immune responses, and may participate in the initiation or amplification of autoimmune processes [73].

FMT in Rheumatoid Arthritis (RA)

One illustrative case report described a 20-year-old woman with rheumatoid arthritis (RA) who underwent FMT by colonoscopy using donor material from a healthy 8-year-old child. The intervention resulted in marked clinical improvement without adverse effects [74]. Although such findings are encouraging, the therapeutic application of FMT in rheumatic diseases remains controversial.

Animal studies have produced heterogeneous and sometimes contradictory results. In germ-free mice colonized with microbiota from TNFΔARE$^{+/-}$ donors – a model of spontaneous arthritis – researchers observed joint deformation, heightened inflammatory responses, increased CD4^{+}/CD8^{+} T-cell activity, behavioral abnormalities, and impaired gut barrier integrity. These data underscore the complex interplay between gut microbial communities, immune activation, and the gut–brain axis [75].

In a separate collagen-induced arthritis (CIA) model, mice treated with broad-spectrum antibiotics followed by FMT from RA patients developed depression-like behaviors. Immunologically, these mice exhibited elevated percentages of CD3e^{+} and CD4^{+} T cells in Peyer's patches and the spleen, an increased Th1/Th2 ratio, and reduced regulatory T cells (CD25^{+}, FOXP3^{+}). Genera such as *Bacteroides* and *Phascolarctobacterium* were associated with these immunologic perturbations [76].

Conversely, in an adjuvant-induced arthritis model, oral administration of tuna elastin peptides reduced proinflammatory cytokine production and increased anti-inflammatory mediators. These beneficial effects were transmissible to naïve recipient mice via FMT, suggesting that favorable immunomodulation can be conveyed through gut microbial transfer [77]. Interestingly, RA-related dysbiosis was not transmitted from TNFΔARE$^{+/-}$ donors to conventional mice, implying that a resilient, healthy microbiota may resist colonization or influence from pathogenic microbial communities [75].

Adding further complexity, Pu et al. identified 12 microbial biomarkers potentially associated with RA, seven of which were enriched in mice receiving FMT from RA patients [76]. Another case report described symptom improvement in a patient with refractory RA following FMT, including reductions in rheumatoid factor levels and improvement in overall disease activity [11]. In contrast, FMT conducted after *Porphyromonas gingivalis* exposure exacerbated arthritis severity, emphasizing the critical importance of donor microbial composition [78]. Unexpectedly, infection with *Clostridioides difficile* strain VPI 10463 attenuated arthritis manifestations independently of FMT, while FMT alone conferred no therapeutic benefit in this model [79].

Beyond RA, FMT is being explored as a potential therapeutic strategy for additional musculoskeletal disorders, including juvenile idiopathic arthritis and osteoarthritis [80].

FMT in Psoriatic Arthritis (PsA)

FMT has been investigated in a limited number of clinical studies for psoriatic arthritis (PsA). In a double-blind, parallel-group trial evaluating the safety of a single duodenal FMT dose in patients with active peripheral PsA, the intervention was generally well tolerated. Reported adverse effects – including abdominal discomfort, nausea, and vomiting – were mild, transient, and without serious clinical consequences [81].

Unexpectedly, follow-up analysis by the same research group revealed that the placebo arm demonstrated superior clinical outcomes: 81% of placebo-treated patients achieved a clinical response compared with only 40% of those receiving FMT. Additionally, participants in the placebo group exhibited more pronounced improvements in the Health Assessment Questionnaire Disability Index (HAQ-DI) [82]. These findings suggest that FMT may not consistently confer therapeutic benefits in PsA and highlight the importance of rigorous trial design and adequately powered studies.

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

Overall, current evidence does not support the routine use of FMT in PsA management. Nevertheless, the safety profile and preliminary mechanistic insights warrant further investigation. Additional well-designed clinical trials are needed to elucidate the therapeutic potential and underlying biological pathways through which FMT may modulate autoimmune processes.

Conclusions and Summary

The gut microbiota is a fundamental determinant of immunological homeostasis and plays a pivotal role in the pathogenesis of autoimmune conditions, including rheumatic diseases. Accumulating evidence indicates that disturbances in microbial composition – collectively referred to as dysbiosis – may contribute to the initiation and amplification of inflammatory pathways involved in rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and psoriatic arthritis (PsA). The bidirectional communication between the gut microbiota and the immune system, encompassing effects on T-cell differentiation, cytokine networks, and intestinal barrier integrity, offers novel therapeutic avenues.

Emerging strategies aimed at modulating the gut microbiome – such as probiotics, prebiotics, targeted dietary interventions, and fecal microbiota transplantation (FMT) – show considerable promise. However, despite encouraging preliminary findings, current evidence remains insufficient to support their widespread clinical application. Heterogeneity in study design, limited cohort sizes, and short follow-up durations hinder robust conclusions regarding the efficacy and long-term impact of these interventions in rheumatic disease management.

Consequently, there is a pressing need for rigorously designed clinical trials and mechanistic studies to elucidate the causal pathways linking gut microbial dysregulation to rheumatic disease onset and progression. Future research should prioritize the identification of specific microbial taxa and metabolites with anti-inflammatory or immunoregulatory properties, and systematically evaluate the safety, durability, and therapeutic potential of microbiota-targeted interventions. Advancing our understanding of these complex host – microbe interactions may ultimately enable the development of personalized, microbiome-informed treatment strategies, thereby enhancing therapeutic precision and improving patient outcomes in rheumatology.

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