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Commentary

Microbial Diversity and Immune Outcomes in Helminth-Associated Diseases

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DESCRIPTION

The interconnection between the gut microbiome, parasitic helminths and the human immune system has garnered considerable attention in recent years. This tripartite relationship is particularly relevant in the context of autoimmune diseases, where the immune system mistakenly targets the body's own tissues. Understanding the gut microbiome–helminth–immune axis offers insights into mechanisms that could inform the development of novel therapeutic strategies.

The gut microbiome: A dynamic ecosystem

The gut microbiome comprises trillions of microorganisms, including bacteria, fungi, viruses and archaea, that coexist in the gastrointestinal tract. These microorganisms play a fundamental role in maintaining host homeostasis by contributing to nutrient metabolism, modulating immune responses and protecting against pathogens.

In autoimmune diseases such as Multiple Sclerosis (MS), Rheumatoid Arthritis (RA) and Inflammatory Bowel Diseases (IBD), disruptions in the gut microbiome referred to as dysbiosis have been consistently observed. Dysbiosis is characterized by reduced microbial diversity, an overgrowth of potentially harmful bacteria and a loss of beneficial microbes. Such imbalances can contribute to the breakdown of immune tolerance, leading to exaggerated inflammatory responses.

Helminths: Parasites with immunomodulatory potential

Helminths are parasitic worms that infect billions of individuals worldwide, particularly in tropical and subtropical regions. While often associated with negative health outcomes, helminths have been shown to modulate host immune responses in ways that can suppress inflammation and promote tissue repair.

The immunomodulatory effects of helminths are largely attributed to their ability to induce regulatory immune pathways. They stimulate the production of regulatory T cells (Tregs) and anti-inflammatory cytokines, such as Interleukin-10 (IL-10) and Transforming Growth Factor-beta (TGF-β). These responses can counteract the pro-inflammatory mechanisms that drive autoimmune diseases.

Interactions between the gut microbiome and helminths

Helminths interact with the gut microbiome in complex ways, often reshaping the microbial community composition. These interactions can have profound effects on immune regulation and disease outcomes.

Effects on microbial diversity: Helminth infections are associated with increased microbial diversity in the gut, a feature often lacking in individuals with autoimmune diseases. The presence of helminths has been shown to enrich populations of beneficial bacteria, such as those belonging to the genera Bacteroides and Lactobacillus. This enrichment can restore microbial balance and enhance the production of Short-Chain Fatty Acids (SCFAs), which have anti-inflammatory properties.

Influence on metabolites: Helminths can alter the metabolic activity of the gut microbiome, leading to changes in the production of bioactive molecules. For example, helminths may enhance the synthesis of SCFAs, which promote gut barrier integrity and regulate immune responses. Additionally, helminths can influence the production of bile acids and tryptophan metabolites, both of which play roles in immune modulation.

Shared immune pathways: Both the gut microbiome and helminths engage the host's immune system through shared pathways, such as Pattern Recognition Receptors (PRRs) and the Aryl Hydrocarbon Receptor (AHR). These pathways mediate the recognition of microbial and helminth-derived molecules, shaping immune responses that can mitigate autoimmune disease progression.

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The immune system as a mediator: The immune system acts as a mediator of the interactions between the gut microbiome and helminths. These interactions influence the balance between pro-inflammatory and anti-inflammatory immune responses, which is critical in the context of autoimmune diseases.

Regulatory T cells and cytokines: Both the gut microbiome and helminths promote the expansion of Tregs and the secretion of anti-inflammatory cytokines. This immunoregulatory environment helps suppress the aberrant immune activation observed in autoimmune diseases.

Evidence from autoimmune disease studies

Rheumatoid arthritis: RA is characterized by chronic joint inflammation driven by an overactive immune response. Both gut microbiome dysbiosis and helminth infections have been linked to changes in systemic inflammation. Helminth therapy has shown potential in reducing joint inflammation and autoantibody production in preclinical models.

Inflammatory Bowel Diseases (IBD): In Crohn's disease and ulcerative colitis, two major types of IBD, dysbiosis and gut barrier dysfunction play central roles in disease pathogenesis. Helminth infections can restore gut barrier integrity and reduce inflammation by modulating microbial composition and enhancing Treg activity. Clinical trials with helminth therapy have shown promising results, including symptom reduction and improved mucosal healing.

Therapeutic implications: The gut microbiome–helminth–immune axis offers a unique perspective on the treatment of autoimmune diseases. While direct helminth infections pose practical and ethical challenges, helminth-derived molecules and microbiome-based therapies hold potential for clinical application.

Helminth-derived molecules: Helminth-secreted proteins and metabolites can mimic the immunomodulatory effects of live infections without the associated risks. For instance, helminth-derived proteins such as ES-62 and helminthic glycoproteins are being explored for their ability to modulate immune responses in autoimmune diseases.

Probiotics and prebiotics: Probiotics containing beneficial bacterial strains and prebiotics that promote the growth of these bacteria can help restore microbial balance. These interventions, when combined with insights from helminth–microbiome interactions, could enhance therapeutic efficacy.

Fecal Microbiota Transplantation (FMT): FMT has emerged as a promising approach to correct dysbiosis in autoimmune diseases. By introducing a diverse microbial community, FMT can restore microbial balance and improve immune regulation.

CONCLUSION

The intricate relationship between the gut microbiome, helminths, and the immune system offers valuable insights into managing autoimmune diseases. By enhancing microbial diversity and promoting anti-inflammatory immune responses, helminths and microbiome-based interventions present promising therapeutic avenues. Future therapies could harness helminth-derived molecules and microbiome modulation to restore immune balance and mitigate the progression of autoimmune conditions.