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The Role of Gut Microbiota in Inflammatory Bowel Disease: Mechanisms and Therapeutic Opportunities

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Inflammatory bowel disease (IBD), encompassing *Crohn's disease* and *ulcerative colitis*, is characterized by chronic inflammation within the gastrointestinal tract. Emerging research underscores the pivotal role of alterations in gut microbiota composition and function in driving IBD

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pathogenesis. This paper offers a comprehensive overview of the intricate mechanisms governing the interplay between the gut microbiota and the host immune system, elucidating their contribution to IBD development and progression.
Furthermore, we provide in-depth analysis and synthesis of the therapeutic opportunities presented by targeting the gut microbiota for IBD management. Specifically, we explore the application of probiotics, prebiotics, antibiotics, fecal microbiota transplantation, and microbial-based therapies in the field of IBD studies. Each therapeutic modality is examined for its potential in modulating the gut microbiota and restoring microbial balance, thereby alleviating inflammation and ameliorating IBD symptoms.
By elucidating these therapeutic opportunities and their applications in IBD research, this review not only enhances our understanding of IBD pathophysiology but also informs the development of innovative treatment strategies aimed at improving patient outcomes and enhancing quality of life.

Keywords: Crohn's disease; dysbiosis; gut microbiota; immune dysregulation; inflammatory bowel disease; probiotics; prebiotics; ulcerative colitis.

1. INTRODUCTION

Inflammatory bowel disease (IBD) encompasses a group of chronic inflammatory disorders of the gastrointestinal tract, including Crohn's disease (CD) and ulcerative colitis (UC). The etiology of IBD is multifactorial, involving complex interactions between genetic predisposition, environmental factors, and dysregulated immune responses [1]. Among these factors, emerging evidence suggests that alterations in the composition and function of the gut microbiota play a central role in the pathogenesis of IBD [2].

The gut microbiota comprises trillions of microorganisms, including bacteria, viruses, fungi, and archaea, that inhabit the gastrointestinal tract. These microorganisms form a complex ecosystem that interacts with the host immune system and influences various physiological processes, including metabolism, immune regulation, and barrier function. Dysbiosis, characterized by alterations in the composition and diversity of the gut microbiota, has been consistently observed in patients with IBD, suggesting a causal role in disease pathogenesis [3].

Understanding the mechanisms underlying the interaction between gut microbiota and the host immune system in the development and progression of IBD is essential for identifying novel therapeutic targets and strategies to modulate the gut microbiota for the management of IBD. This paper aims to review the current knowledge on the role of gut microbiota in IBD pathogenesis, mechanisms of immune dysregulation, and therapeutic opportunities targeting the gut microbiota for the treatment of IBD [4].

2. METHODS

A comprehensive literature search was conducted using electronic databases, including PubMed, Google Scholar, and Web of Science, to identify relevant articles, reviews, and clinical studies related to the role of gut microbiota in inflammatory bowel disease. The search terms included "*gut microbiota*," "*inflammatory bowel disease*," "*Crohn's disease*," "*ulcerative colitis*," "*dysbiosis*," "*immune dysregulation*," "*probiotics*," "*prebiotics," "antibiotics*," "*fecal microbiota transplantation*," and "*microbial-based therapies*." Articles published in peer-reviewed journals were selected for inclusion based on their relevance to the topic and quality of evidence.

3. RESULTS AND DISCUSSION

3.1 Role of Gut Microbiota in IBD Pathogenesis

The gut microbiota plays a critical role in maintaining intestinal homeostasis and immune tolerance. Dysbiosis, characterized by alterations in the composition, diversity, and function of the gut microbiota, has been implicated in the pathogenesis of IBD. Patients with IBD exhibit distinct microbial signatures compared to healthy individuals, including reduced microbial diversity, altered microbial composition, and expansion of potentially pathogenic bacteria [5].

The interaction between gut microbiota and the host immune system is bidirectional, with the gut microbiota shaping immune responses and the immune system regulating the composition and function of the gut microbiota.

Dysregulated immune responses to commensal microorganisms can lead to chronic inflammation and tissue damage in susceptible individuals, contributing to the development and progression of IBD [6].

3.2 Mechanisms of Immune Dysregulation

Several mechanisms have been proposed to explain how alterations in the gut microbiota contribute to immune dysregulation and intestinal inflammation in IBD. These mechanisms include:

Disruption of epithelial barrier function: *Dysbiosis* can compromise the integrity of the intestinal epithelial barrier, leading to increased intestinal permeability and translocation of luminal bacteria and microbial products into the mucosa. This breach in barrier function triggers immune responses and promotes inflammation in the gut [7].

Activation of innate immune pathways: *Dysbiotic microbiota* can activate innate immune pathways, such as *Toll-like receptors (TLRs*) and nucleotide-binding oligomerization domain-like receptors (NLRs), leading to the production of pro-inflammatory cytokines and chemokines. Chronic activation of innate immune pathways contributes to sustained inflammation and tissue damage in IBD [8].

I**mbalance in *T-cell* responses:** Dysbiosis can skew *T-cell* differentiation towards pro-inflammatory phenotypes, such as Th1 and Th17 cells, while inhibiting regulatory T-cell (Treg) responses. This imbalance in T-cell responses promotes the production of *inflammatory cytokines* and perpetuates intestinal inflammation in IBD [9].

3.3 Therapeutic Opportunities Targeting Gut Microbiota

Modulating the gut microbiota represents a promising therapeutic approach for the management of IBD. Several strategies have been investigated to restore microbial homeostasis and promote intestinal health in patients with IBD. These therapeutic opportunities include:

Probiotics: Probiotics are live microorganisms that confer health benefits to the host when administered in adequate amounts. Several probiotic strains, such as Lactobacillus and Bifidobacterium species, have been studied for their potential immunomodulatory effects and efficacy in IBD. Probiotics may help restore microbial balance, strengthen the intestinal barrier, and regulate immune responses in IBD [10].

Prebiotics: Prebiotics are non-digestible dietary fibers that selectively stimulate the growth and activity of beneficial microorganisms in the gut. By promoting the growth of beneficial bacteria, prebiotics may enhance microbial diversity, improve intestinal barrier function, and modulate immune responses in IBD. Common prebiotics include inulin, *fructooligosaccharides (FOS)*, and galactooligosaccharides (GOS) [11].

Antibiotics: Antibiotics have been used empirically to induce remission in patients with IBD, particularly in cases of active luminal inflammation or perianal disease. Antibiotics may exert their therapeutic effects by reducing microbial load, suppressing pathogenic bacteria, and modulating immune responses in the gut. However, long-term antibiotic use may lead to dysbiosis and antibiotic resistance, highlighting the need for judicious antibiotic stewardship in IBD management [12].

Fecal Microbiota Transplantation (FMT): FMT involves the transfer of fecal microbiota from healthy donors to patients with dysbiosis-associated diseases, such as recurrent Clostridioides difficile infection (CDI) and IBD. FMT aims to restore microbial diversity, rebalance dysbiotic communities, and modulate immune responses in the gut. Clinical trials evaluating the efficacy and safety of FMT in IBD are ongoing, with promising preliminary results [13].

Microbial-Based Therapies: Emerging microbial-based therapies, such as microbial consortia, engineered bacteria, and microbial metabolites, hold promise for modulating the gut microbiota and improving outcomes in patients with IBD. These therapies aim to deliver specific microbial strains or metabolites with immunomodulatory properties to restore microbial homeostasis and promote intestinal health [14].

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Qiu P, Ishimoto T, Fu L, Zhang J, Zhang Z, Liu Y. The Gut Microbiota in Inflammatory Bowel Disease. Front Cell Infect Microbiol. 2022;12:733992.
   DOI: 10.3389/fcimb.2022.733992
2. Allen-Vercoe, E, Coburn B. A microbiota-derived metabolite augments cancer immunotherapy responses in mice. Cancer Cell. 2020;38(4):452–453.
   DOI: 10.1016/j.ccell.2020.09.005
3. Anderson CJ, Medina CB, Barron BJ, Karvelyte L, Aaes TL, Lambertz I. Microbes exploit death-induced nutrient release by gut epithelial cells. Nature. 2021;596 (7871):262–267.
   DOI: 10.1038/s41586-02103785-9
4. Britton GJ, Contijoch EJ, Spindler MP, Aggarwala V, Dogan B, Bongers G. Defined microbiota transplant restores Th17/RORgammat (+) Regulatory T Cell Balance in Mice Colonized With Inflammatory Bowel Disease Microbiotas. Proc. Natl. Acad. Sci. U. S. A. 2020;117 (35):21536–21545.
   DOI: 10.1073/pnas.1922189117
5. Campbell C, McKenney PT, Konstantinovsky D, Isaeva OI, Schizas M, Verter J. Bacterial metabolism of bile acids promotes generation of peripheral regulatory T cells. Nature. 2020;581 (7809):475–479.
   DOI: 10.1038/s41586-020-2193-0
6. Caruso R, Lo BC, Nunez G. Host-microbiota interactions in inflammatory bowel disease. Nat. Rev. Immunol. 2020;20(7):411–426.
   DOI: 10.1038/s41577-019-0268-7
7. Chen Y, Chen Y, Cao P, Su W, Zhan N, Dong W. Fusobacterium nucleatum facilitates ulcerative colitis through activating IL-17F signaling to NF-kappaB via the upregulation of CARD3 Expression. J. Pathol. 2020;250(2):170–182.
   DOI: 10.1002/path.5358
8. Deleu S, Machiels K, Raes J, Verbeke K, Vermeire S. Short chain fatty acids and its producing organisms: An overlooked therapy for IBD? EBioMedicine. 2021;66: 103293.
   DOI: 10.1016/j.ebiom.2021.103293
9. Dore MP, Rocchi C, Longo NP, Scanu AM., Vidili G, Padedda F. Effect of probiotic use on adverse events in adult patients with inflammatory bowel disease: A Retrospective cohort study. Probiotics Antimicrob. Proteins. 2020;12(1):152–159.
   DOI: 10.1007/s12602-019-9517-0
10. Kayama H, Okumura R, Takeda K. Interaction between the microbiota, epithelia, and immune cells in the intestine. Annu. Rev. Immunol. 2020;38: 23–48.
    DOI: 10.1146/annurev-immunol-070119-115104.
11. Kudelka MR, Stowell SR., Cummings RD, Neish AS. Intestinal epithelial glycosylation in homeostasis and gut microbiota interactions in IBD. Nat. Rev. Gastroenterol. Hepatol. 2020;17(10);597–617.
    DOI: 10.1038/s41575020-0331-7
12. Langan D, Perkins DJ, Vogel SN, Moudgil KD. MicrobiotaDerived Metabolites, Indole-3-Aldehyde and Indole-3-Acetic Acid, Differentially Modulate Innate Cytokines and Stromal Remodeling Processes Associated With Autoimmune Arthritis. Int. J. Mol. Sci. 2021;22(4).
    DOI: 10.3390/ ijms22042017
13. Michaudel C, Sokol H. The Gut Microbiota at the Service of Immunometabolism. Cell Metab. 2020;32(4);514–523.
    DOI: 10.1016/j.cmet. 2020.09.004
14. Read E, Curtis MA, Neves JF. The Role of Oral Bacteria in Inflammatory Bowel Disease. Nat. Rev. Gastroenterol. Hepatol. 2021;18(10):731742.
    DOI: 10.1038/s41575-021-00488-4

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