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Gut Microbiota in Chronic Inflammatory Diseases - Literature Review

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ABSTRACT

Introduction

The gut microbiota, a complex community of microorganisms residing in the human gastrointestinal tract, is integral to various bodily functions.

Understanding the role of gut microbiota is essential due to its significant influence on human health and disease. Current research indicates that gut microbiota can modulate immune responses and maintain homeostasis.

Despite extensive studies, the specific mechanisms by which gut microbiota influences chronic inflammatory diseases remain unclear.

Investigating the interaction between gut microbiota and the immune system can provide new insights into potential therapeutic strategies for chronic inflammatory diseases.

Aim of the study

This study aims to elucidate the mechanisms by which gut microbiota affects immune responses, particularly in chronic inflammatory conditions. We hypothesize that alterations in gut microbiota composition can significantly modulate immune responses, thereby influencing the progression of chronic inflammatory diseases.

Conclusions

We discuss potential therapeutic interventions targeting the gut microbiota for chronic inflammatory diseases that encompass several approaches. These include the administration of probiotics and prebiotics, fecal microbiota transplantation (FMT), diverse dietary modifications. Personalized microbiome-based therapies offer tailored interventions that combine various methodologies. Further scientific investigation is necessary to comprehensively elucidate and optimize these therapeutic strategies.

Keywords: Gut microbiota, chronic inflammation, inflammatory bowel diseases, microbial dysregulation, therapeutic strategies

I. Introduction

The gut microbiota plays a crucial role in modulating innate and acquired immune responses, significantly impacting the delicate balance between inflammation and tolerance (Diamanti et al., 2016). This complex microbial community in the human gastrointestinal tract is essential

for the development and function of the gut immune barrier, with the crosstalk between microbiota-gut epithelium and the gut immune system determining an individual's health status (Gasaly et al., 2021). Dysregulation of this intricate relationship can lead to dysbiosis, which has been associated with various chronic inflammatory diseases, including inflammatory bowel diseases (IBD), celiac disease, and even neurodegenerative disorders (Hörmannsperger & Haller, 2009; Serra et al., 2019). Recent studies have revealed that alterations in gut microbiota composition are correlated with the severity of inflammation in various conditions, such as spondyloarthritis and rheumatoid arthritis (Diamanti et al., 2016). The gut microbiota interacts with the host through multiple mechanisms, including the production of metabolites like short-chain fatty acids (SCFAs), secondary bile acids, and tryptophan catabolites, which play crucial roles in regulating immune responses and maintaining intestinal homeostasis (Gasaly et al., 2021). In conclusion, the intricate relationship between the gut microbiota and the immune system has far-reaching implications for human health. Understanding these interactions is crucial for developing novel therapeutic approaches to manage chronic inflammatory diseases and promote healthy aging (Rehman, 2012). Further research into the microbiota-gut-brain axis and the potential of probiotic and prebiotic interventions may offer promising strategies for ameliorating both intestinal and systemic disorders (Serra et al., 2019; Shabbir et al., 2021).

II. Methods

This literature review employed a comprehensive and structured approach to examine the role of gut microbiota in modulating immune responses and its implications for chronic inflammatory diseases.

We utilized a methodology to synthesize existing research on the gut microbiota and its impact on immune responses in chronic inflammatory conditions.

A thorough literature review was conducted using databases such as PubMed, Scopus, and Web of Science to identify relevant studies published between 2000 and 2025.

The studies included in this review involved human participants diagnosed with chronic inflammatory diseases such as Crohn's disease, ulcerative colitis, and rheumatoid arthritis.

Studies were included if they investigated the relationship between gut microbiota and immune responses in patients with chronic inflammatory diseases and were published in peer-reviewed journals. Data from the selected studies were extracted using a standardized data extraction form to ensure consistency and accuracy. The extracted data were analyzed to identify common themes, patterns, and significant findings related to the gut microbiota's role in immune

response modulation. As this study is a review of previously published research, ethical approval was not required.

Informed consent was not applicable to this study as it did not involve direct interaction with human participants.

III. Gut Microbiota Composition and Development

The gut microbiota is a complex community of bacteria residing in the intestine, with its composition and diversity playing crucial roles in human health. Alpha diversity in the gut microbiome is associated with better health outcomes, as patients with low α diversity are more prone to obesity, insulin resistance, fatty liver disease, and low-grade peripheral inflammation compared to those with high α diversity (Wen & Duffy, 2017). The gut microbiota undergoes significant changes during early life, with a notable decrease in diversity and an increase in the relative abundance of Firmicutes between 8 and 15 days of age in some bird species (Teyssier et al., 2018). Multiple factors influence the composition and development of the gut microbiota, including genetics, mode of delivery at birth, infant feeding method, medication use (especially antibiotics), and diet (Wen & Duffy, 2017). Environmental factors also play a significant role, with the nesting environment shaping the gut microbiota during later stages of nestling development in birds (Teyssier et al., 2018). In humans, gestational age, cesarean section delivery, human milk consumption, living with siblings, and attending daycare centers have been associated with specific microbiota characteristics at 3.5 years of age (Toubon et al., 2023). The development of gut microbiota from infancy is a critical process that sets the foundation for long-term health. The infant gut microbiome begins to develop at birth and undergoes major transitions during breastfeeding and the introduction of solid foods (Catassi et al., 2024). The first three years of life represent a crucial window for establishing a diverse and stable gut microbiome (Parkin et al., 2021). Over time, beneficial microbes such as Bifidobacterium, Lactobacillus, and Blautia increase in the infant's gut, while pathological bacteria like Escherichia-Shigella, Enterobacter, Staphylococcus, and Klebsiella decrease (Yang et al., 2019). Understanding these developmental patterns and influencing factors is essential for promoting optimal gut health and preventing dysbiosis-related diseases in later life.

IV. Dysbiosis and Chronic Inflammatory Diseases

A. Definition of dysbiosis

Dysbiosis, particularly gut dysbiosis, plays a significant role in the pathogenesis of chronic inflammatory diseases. Gut dysbiosis is characterized by reduced bacterial diversity, decreased abundance of beneficial bacteria like Firmicutes and Bacteroidetes, and increased presence of proinflammatory microbes such as Proteobacteria (Eom et al., 2018; Matsuoka & Kanai, 2014; Sultan et al., 2021).

B. Link between gut microbiota dysbiosis and inflammatory bowel diseases (IBD)

This imbalance in the gut microbiota can lead to alterations in host metabolic and immune functions, contributing to the development of inflammatory bowel disease, rheumatoid arthritis (RA), and other chronic inflammatory conditions (Kim et al., 2017). In IBD, gut dysbiosis is associated with depleted diversity, reduced abundance of short-chain fatty acid (SCFA) producers, and enriched proinflammatory microbes (Sultan et al., 2021). The dysbiosis can affect the immune system and metabolic pathways, leading to functional perturbations in host-microbiota interactions (Sultan et al., 2021). Interestingly, oral microbiota dysbiosis has also been linked to IBD development, with ectopic colonization of oral bacteria potentially leading to intestinal epithelial barrier destruction and excessive inflammatory cytokine secretion (Qi et al., 2021).

C. Role of gut microbiota in rheumatoid arthritis

Regarding rheumatoid arthritis, gut dysbiosis is believed to contribute to its pathogenesis through multiple mechanisms, including alterations in gut barrier function, molecular mimicry, and influences on innate and acquired immune cell activation and differentiation (Romero-Figueroa et al., 2023). Recent studies have highlighted the substantial role of gut microbiota-derived metabolites, especially butyrate, in RA pathogenesis (Romero-Figueroa et al., 2023). While the review does not provide specific information on microbiota alterations in multiple sclerosis, it is mentioned as one of the chronic inflammatory diseases affected by gut dysbiosis (Kim et al., 2017).

D. Gut microbiota alterations in multiple sclerosis

In conclusion, dysbiosis, particularly in the gut microbiota, plays a crucial role in the development and progression of chronic inflammatory diseases such as IBD and RA. Understanding these microbial alterations and their impact on host metabolism and immune function may lead to novel therapeutic approaches, including microbiota-targeted interventions, for managing these conditions (Eom et al., 2018; Kim et al., 2017; Matsuoka & Kanai, 2014).

V. Therapeutic Approaches Targeting Gut Microbiota

Therapeutic approaches targeting gut microbiota include probiotics, prebiotics, fecal microbiota transplantation (FMT), and dietary interventions, all aimed at restoring microbial balance and promoting beneficial strains in the gut (Alswat, 2024).

A. Probiotics and their immunomodulatory effects

Probiotics, particularly Bifidobacterium and Lactobacillus strains, have indeed shown improvement in irritable bowel syndrome (IBS) symptoms. Multiple studies have demonstrated the efficacy of these probiotic strains in alleviating IBS symptoms. For instance, a comprehensive meta-analysis found moderate certainty evidence for the benefit of Lactobacillus strains and low certainty evidence for Bifidobacterium strains in reducing abdominal pain (Goodoory et al., 2023). Another study specifically highlighted the effectiveness of a probiotic product containing Lactobacillus casei, Lactobacillus plantarum P-8, and Bifidobacterium animalis subsp. lactis V9 in reducing IBS symptom severity scores and inflammatory markers (Xu et al., 2020). Interestingly, while many studies support the use of probiotics, some research has shown contradictory results. For example, one study found that Bifidobacterium spp. decreased in the probiotic group compared to the placebo group (Kajander et al., 2007). This highlights the complexity of the gut microbiome and the need for further research to understand the specific mechanisms of action for different probiotic strains. In conclusion, while probiotics, especially Bifidobacterium and Lactobacillus strains, show promise in managing IBS symptoms, the efficacy appears to be strain-specific and dose-dependent. A network meta-analysis ranked Lactobacillus acidophilus DDS-1 as the most effective strain for improving IBS Symptom Severity Scale (Xie et al., 2023). However, the optimal probiotic combination or strain remains unclear, and more research is needed to determine the most effective probiotic therapies for IBS management (Wu et al., 2024; Zhang et al., 2023).

B. Prebiotics and their role in promoting beneficial bacteria

According to the available information, prebiotics have not shown significant improvement in IBS symptoms, and there is limited evidence to support their clinical use for this condition. Ooi et al. (2019) specifically states that "Despite preclinical studies of some prebiotics demonstrated the potential use in improving gut microbiome and intestinal inflammatory response, the beneficial effect of prebiotics for IBS remains theoretical. Two systematic reviews found no

evidence to support the clinical use of prebiotics for IBS." This contradicts the claim that prebiotics can nourish beneficial microorganisms and enhance microbial diversity in IBS patients. While probiotics and dietary modifications have shown some promise in managing IBS symptoms and altering gut microbiota composition (Dale & Lied, 2020; Mazzawi, 2022; Spiller, 2008), the efficacy of prebiotics remains unproven. The focus of current research appears to be more on probiotics, low FODMAP diets, and fecal microbiota transplantation as potential therapeutic approaches for IBS (Dale & Lied, 2020; Mazzawi, 2022; Ooi et al., 2019). In conclusion, based on the provided context, there is insufficient evidence to support the claim that prebiotics can significantly improve gut microbial diversity and activity in IBS patients. More research is needed to establish the potential benefits of prebiotics in IBS management.

C. Fecal microbiota transplantation (FMT) as a potential therapy

FMT has emerged as a promising treatment for various conditions, including Clostridium difficile infection, inflammatory bowel disease, and potentially autoimmune diseases (Bakker & Nieuwdorp, 2017; Yang et al., 2023). It has shown effectiveness in restoring altered gut microbiota composition and mediating immune responses (Yang et al., 2023). However, the exact mixture of beneficial bacteria for each individual remains to be identified, and more data is needed before FMT can be regarded as a standard treatment for conditions like IBS (Mazzawi, 2022). In conclusion, while these therapeutic approaches show promise, considerable efforts are still needed to increase our knowledge in the field of gut microbiota modulation for therapeutic purposes (Cammarota et al., 2014). Future research should focus on understanding the complex interactions between the gut microbiota and the host to develop personalized medicine approaches and microbiota-based therapies for various conditions (Alswat, 2024; Zhou et al., 2024).

Tab. 1. Therapeutic Approach Summary Key Findings References

Therapeutic Approach	Summary	Key Findings	References
Probiotics	Probiotics, especially Bifidobacterium and Lactobacillus strains, show potential in improving IBS	- **Effective Strains**: Lactobacillus casei, Lactobacillus plantarum P-8, Bifidobacterium	Goodoory et al., 2023; Xu et al., 2020; Kajander et al., 2007; Wu

Therapeutic Approach	Summary	Key Findings	References
	symptoms through their immunomodulatory effects.	animalis subsp. lactis V9 reduced IBS symptoms and inflammation (Xu et al., 2020). - **Variability**: Lactobacillus acidophilus DDS-1 ranked most effective for IBS symptom severity (Xie et al., 2023). - **Contradictory Findings**: Some studies showed decreased Bifidobacterium spp. in the probiotic group (Kajander et al., 2007). - **Conclusion**: Strain-specific and dose-dependent efficacy. More research needed.	et al., 2024; Zhang et al., 2023
Prebiotics	Prebiotics theoretically promote beneficial bacteria and microbial diversity but have not shown significant clinical benefits for IBS.	- **Limited Evidence**: Systematic reviews found no significant benefit in IBS patients. - **Contradictions**: Preclinical studies suggest potential improvements in gut microbiota, but clinical evidence remains lacking.	Ooi et al., 2019; Dale & Lied, 2020; Mazzawi, 2022; Spiller, 2008

Therapeutic Approach	Summary	Key Findings	References
Fecal Microbiota Transplantation (FMT)	FMT aims to restore altered gut microbiota composition and regulate immune responses, showing promise for conditions like Clostridium difficile infection and potentially IBS.	-**Focus**: More attention is directed towards probiotics, low FODMAP diets, and FMT as therapeutic options for IBS. - **Effectiveness**: Successfully restores gut microbiota in certain conditions (Bakker & Nieuwdorp, 2017; Yang et al., 2023). - **Challenges**: Optimal bacterial composition for IBS patients is unclear. -**Conclusion**: Promising but requires more research before becoming a standard treatment for IBS.	Bakker & Nieuwdorp, 2017; Yang et al., 2023; Mazzawi, 2022

VI. Future Directions and Challenges

A. Personalized microbiome-based therapies

Personalized microbiome-based therapies are emerging as a promising avenue for addressing various health conditions. Strategies such as fecal microbiota transplantation (FMT), probiotics, prebiotics, and synbiotics are being explored to restore microbiome balance and improve health outcomes (Shukla et al., 2024). These approaches, combined with advances in metagenomics

and sequencing technologies, enable tailored interventions based on individual microbiome profiles (Shukla et al., 2024; Zmora et al., 2016).

B. Developing novel diagnostic tools based on gut microbiota profiles

Developing novel diagnostic tools is crucial for advancing microbiome research and its clinical applications. Nanotechnology-based approaches show potential for creating point-of-care devices that meet REASSURED guidelines, enabling real-time, affordable, and user-friendly microbiome diagnostics (Fuentes-Chust et al., 2021). Additionally, deep learning provides a novel approach for transforming large, multi-modal data into decision support tools, bridging the translational gap to the clinical setting (Papadakis et al., 2019).

C. Overcoming limitations in current research methodologies

Overcoming limitations in microbiome research remains a significant challenge. Key issues include the susceptibility of low-biomass samples to exogenous contamination and undetermined microbial viability from NGS-based microbial profiling (Cheng et al., 2023). Standardization of research approaches, improved analytical tools, and a focus on host-microbe interactions are necessary to address these challenges (Cheng et al., 2023; Fountain-Jones et al., 2023). Furthermore, ethical, legal, and societal issues related to microbiome R&D and innovation must be carefully considered as the field advances (Fuentes-Chust et al., 2021). In conclusion, the future of microbiome research lies in developing personalized therapies, creating innovative diagnostic tools, and addressing current limitations. By focusing on these areas, researchers can harness the potential of the microbiome to revolutionize precision medicine and improve patient outcomes across various health conditions.

VII. Conclusions

Our review encapsulates significant findings in gut microbiota research and their implications for human health. It underscores the critical role of gut microbiota in immune regulation and disease pathogenesis, elucidates the factors influencing microbial composition, and explores potential therapeutic interventions. Furthermore, the work delineates future research trajectories, encompassing personalized therapeutic approaches and enhanced diagnostic methodologies, while emphasizing the necessity for standardized research protocols and ethical considerations. The intricate interplay between gut microbiota, the immune system, and various health conditions is accentuated, highlighting the potential for developing innovative therapeutic strategies for chronic inflammatory disorders and promoting healthy aging processes.

Disclosure

Author's contribution

Conceptualization: J. Zygadło, P. Bakuła; methodology: P. Bakuła; software: K. Jałocha; check: K. Jałocha, J. Zygadło; formal analysis: P. Bakuła; investigation: K. Jałocha; resources: J. Zygadło; data curation: P. Bakuła, K. Jałocha; writing-rough preparation: J. Zygadło; writing – review and editing: P. Bakuła; visualization: K. Jałocha; supervision: J. Zygadło; project administration: P. Bakuła, J. Zygadło

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Conflict of interest

The authors deny any conflict of interest.

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