

DISBIOSE INTESTINAL NA DOENÇA DE CROHN: MECANISMOS DE INTERAÇÃO ENTRE MICROBIOTA E RESPOSTA IMUNE

INTESTINAL DYSBIOSIS IN CROHN'S DISEASE: MECHANISMS OF INTERACTION BETWEEN THE GUT MICROBIOTA AND THE IMMUNE RESPONSE

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Eixo Temático: 1

RESUMO

A Doença de Crohn é uma doença inflamatória intestinal crônica e multifatorial, cuja fisiopatologia envolve fatores genéticos, ambientais, imunológicos e alterações da microbiota intestinal. Nesse contexto, a disbiose tem sido associada à perda da homeostase intestinal e à perpetuação da resposta inflamatória. O presente estudo teve como objetivo analisar os mecanismos de interação entre a microbiota intestinal e a resposta imune na Doença de Crohn, com ênfase no papel da disbiose, dos metabólitos microbianos, da barreira intestinal e das interações entre bacterioma e viroma. Trata-se de uma revisão narrativa de literatura, realizada por meio de buscas na base de dados PubMed, utilizando os termos “Crohn’s disease”, “gut microbiota”, “mechanisms” e “immune response”, combinados pelo operador booleano AND. Foram considerados estudos publicados entre 2024 e agosto de 2026, além do Protocolo Clínico e Diretrizes Terapêuticas da Doença de Crohn para contextualização clínica e terapêutica. Os estudos analisados evidenciaram alterações na composição e diversidade da microbiota, com redução de microrganismos associados à homeostase intestinal e aumento de grupos potencialmente pró-inflamatórios. A redução de metabólitos imunorreguladores, especialmente ácidos graxos de cadeia curta, foi relacionada à alteração da barreira intestinal e à modulação de células imunes. Também foram identificadas alterações do viroma e das interações entre bacteriófagos e bactérias. Conclui-se

que a disbiose participa de uma interação bidirecional com o sistema imunológico, contribuindo para a manutenção da inflamação intestinal, destacando-se como possível alvo para futuras estratégias terapêuticas.

Palavras-chave: Doença de Crohn. Disbiose. Microbiota Gastrointestinal. Resposta Imune.

ABSTRACT

Crohn's disease is a chronic, multifactorial inflammatory bowel disease; its pathophysiology involves genetic, environmental, and immunological factors, as well as alterations in the gut microbiota. In this context, dysbiosis has been linked to the loss of intestinal homeostasis and the perpetuation of the inflammatory response. This study aimed to analyze the mechanisms of interaction between the gut microbiota and the immune response in Crohn's disease, focusing on the roles of dysbiosis, microbial metabolites, the intestinal barrier, and interactions between the bacteriome and the virome. This is a narrative literature review conducted via searches in the PubMed database using the terms "Crohn's disease," "gut microbiota," "mechanisms," and "immune response," combined with the Boolean operator AND. Studies published between 2024 and August 2026 were considered, alongside the Clinical Protocol and Therapeutic Guidelines for Crohn's Disease for clinical and therapeutic context. The analyzed studies revealed alterations in microbiota composition and diversity, characterized by a reduction in microorganisms associated with intestinal homeostasis and an increase in potentially pro-inflammatory groups. A reduction in immunoregulatory metabolites—particularly short-chain fatty acids—was linked to intestinal barrier alterations and immune cell modulation. Alterations in the virome and in interactions between bacteriophages and bacteria were also identified. The study concludes that dysbiosis engages in a bidirectional interaction with the immune system, contributing to the maintenance of intestinal inflammation and emerging as a potential target for future therapeutic strategies.

Keywords: Crohn's disease. Dysbiosis. Gastrointestinal microbiota. Immune response.

INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory bowel disease of multifactorial nature, with a pathogenesis resulting from genetic, environmental, and immunological factors, as well as components of the gut microbiota. Its clinical heterogeneity and the absence of universal diagnostic criteria stem from its complexity and the difficulty in understanding its pathophysiological mechanisms. In this context, alterations in the composition and function of the gut microbiota have been linked to the pathogenesis of CD, with dysbiosis playing a significant role in disrupting intestinal homeostasis.^{1, 2}

The gut microbiota plays fundamental roles in maintaining epithelial barrier integrity and regulating the immune response. In Crohn's disease, alterations in this ecosystem may be associated with a reduction in potentially beneficial microorganisms, the expansion of inflammatory groups, and changes in the interaction between microorganisms and the human host. These alterations can compromise the intestinal barrier and promote increased exposure

of the immune system to microbial components, contributing to the maintenance of the inflammatory response.^{2,3}

Beyond bacterial composition, recent evidence demonstrates that the interaction between the microbiota and the immune system involves metabolites produced by microorganisms, innate immune cells, and various signaling pathways. Dysbiosis can alter the production of metabolites—such as short-chain fatty acids—and influence immune cell activity, thereby contributing to a pro-inflammatory environment. Thus, the relationship between the microbiota and immunity should not be viewed as a unidirectional association, but rather as a dynamic interaction in which microbial changes can trigger inflammatory responses while, simultaneously, inflammation can modify the intestinal environment and microbiota composition.³

In addition to the bacteriome, the gut virome also appears to play a role in this process. Recent studies have demonstrated alterations in the ileal mucosal virome of patients with Crohn's disease (CD), accompanied by changes in the interactions between bacteriophages and bacteria, suggesting that transformations within this ecosystem may contribute to intestinal inflammation.⁴

Given this, understanding the mechanisms by which gut dysbiosis interferes with the immune response—and how that response, in turn, contributes to the perpetuation of dysbiosis—is crucial for broadening our understanding of the pathophysiology of Crohn's disease. Thus, this review aims to analyze the mechanisms of interaction between the gut microbiota and the immune response in Crohn's disease, with an emphasis on the roles of dysbiosis, microbial metabolites, the intestinal barrier, and the interactions between the bacteriome and the virome.²⁻⁴

METHOD

This is a narrative literature review based on searches conducted in the PubMed database. The terms “Crohn’s disease,” “gut microbiota,” “mechanisms,” and “immune response” were used, combined with the Boolean operator AND. Studies published between 2024 and August 2026 were considered. Articles deemed relevant to understanding the mechanisms involved in the interaction between gut microbiota and the immune system in Crohn’s disease were selected. Articles lacking a direct relationship to the proposed topic, duplicate studies, and publications whose content did not contribute to the review's objective were excluded. Additionally, the Clinical Protocol and Therapeutic Guidelines (PCDT) for Crohn’s disease were used to provide clinical and therapeutic context.

RESULTS

Analysis of the selected studies revealed a consistent relationship between the pathophysiology of Crohn's disease and intestinal dysbiosis, involving alterations in the composition and function of the gut microbiota that compromise immunomodulation and the intestinal mucosal barrier. Changes in gut microbiota composition are characterized notably by reduced microbial diversity and a decrease in groups associated with intestinal homeostasis. Microorganisms reported to be reduced include *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, and members of the Firmicutes and Bacteroidetes phyla, whereas potentially pro-inflammatory groups—such as Proteobacteria and Actinobacteria—show an increase. Consequently, the reduced production of immunoregulatory metabolites by bacteria, particularly short-chain fatty acids, contributes to the failure of intestinal barrier mechanisms and the control of the inflammatory response.^{2,3}

The alteration in microbial composition observed in Crohn's disease is linked to the production of metabolites involved in maintaining intestinal homeostasis. A reduction in short-chain fatty acid-producing bacteria—particularly those associated with butyrate production—can compromise mechanisms responsible for epithelial barrier integrity and the regulation of the inflammatory response. Butyrate exerts immunomodulatory effects on various cell groups, including neutrophils, macrophages, and dendritic cells, and is associated with a reduction in pro-inflammatory mediators, reactive oxygen species production, and NETosis.³

The findings indicate that the relationship between the gut microbiota and the immune system is bidirectional. Dysbiosis promotes the exposure of immune cells to microbial stimuli and alters the availability of metabolites capable of modulating their activity. In dendritic cells, changes in this environment can favor pro-inflammatory responses, including increased IL-23 production and consequent stimulation of the Th17 axis. In macrophages, a reduction in microbiota-derived metabolites can contribute to a predominance of pro-inflammatory phenotypes, whereas metabolites such as butyrate and tryptophan derivatives exhibit effects associated with the regulation of inflammation and mucosal repair.³

The interaction between the microbiota and the immune system is mutual. While dysbiosis can promote the activation of inflammatory pathways, the inflammatory process also modifies the intestinal environment and influences microbial composition. Thus, a feedback loop is established in which the loss of microbial homeostasis favors immune activation, while inflammation contributes to the maintenance or intensification of dysbiosis.^{2,3}

Recent evidence also identifies the involvement of the virome in the dysbiosis associated with Crohn's disease. Alterations in virome composition were observed in the ileal mucosa of patients with the disease, including a lower representation of bacteriophages and a reduction in specific phage-bacteria interactions. These changes were more pronounced in individuals with intestinal inflammation, suggesting that the inflammatory state influences virome structure. Furthermore, experiments using murine models demonstrated that viral particles derived from the ileal mucosa of Crohn's disease patients could modify bacterial ecology and subsequently exacerbate intestinal inflammation, providing experimental evidence that alterations in the viral ecosystem may play a role in the disease's pathophysiology.⁴

CONCLUSION

This review highlights that intestinal dysbiosis in Crohn's disease is associated not only with alterations in the composition and diversity of the microbiota but also with functional changes capable of directly interfering with the immune response. A reduction in microorganisms associated with the production of immunoregulatory metabolites, such as butyrate, can compromise intestinal barrier integrity and promote the activation of neutrophils, macrophages, and dendritic cells, while alterations in pathways such as IL-23/Th17 and AHR contribute to the persistence of inflammation. Thus, these findings reinforce the existence of a reciprocal relationship between the microbiota and the immune system, wherein dysbiosis promotes inflammation and the inflammatory process, in turn, contributes to the perpetuation of microbial imbalance.^{2,3}

These findings contribute to a broader understanding of Crohn's disease by demonstrating that the microbiota should be considered an integral part of the mechanisms involved in maintaining intestinal inflammation, rather than merely a consequence of the disease. In practice, this knowledge supports the investigation of therapeutic strategies that link the control of the inflammatory response to the restoration of microbial homeostasis, including interventions targeting metabolites, immune pathways, and microbiota modulation. However, evidence for approaches such as fecal microbiota transplantation remains insufficient and inconsistent specifically for Crohn's disease. Future research must, therefore, elucidate the molecular mechanisms of this interaction, determine which microbial alterations are causally linked to the disease, and establish safer, more durable, and personalized microbiota modulation strategies that take into account each patient's microbiological and immunological profile.²

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