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THE RELATIONSHIP BETWEEN THE GUT MICROBIOTA AND THE HUMAN IMMUNE SYSTEM: MODERN MICROBIOLOGICAL APPROACHES

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Abstract

The gut microbiota is a complex community of microorganisms inhabiting the human body and plays an important biological role in the development and functioning of the immune system. The relationship between the gut microbiota and the immune system is bidirectional: microorganisms shape immune responses, while the immune system regulates the composition and activity of the microbiota [1]. Short-chain fatty acids produced by the microbiota, particularly acetate, propionate, and butyrate, influence the intestinal epithelial barrier and the activity of immune cells [2]. In addition, the microbiota participates in bile acid metabolism and affects the formation of metabolic signals that regulate immune responses [3]. Alterations in the composition of the microbiota, known as dysbiosis, may be associated with disruption of immunological homeostasis [1,4]. This article analyzes the main mechanisms underlying the interaction between the gut



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microbiota and the immune system, as well as modern microbiological methods used to investigate these interactions.

Keywords: gut microbiota, immune system, microbiome, dysbiosis, IgA, T lymphocytes, B lymphocytes, short-chain fatty acids (SCFAs), metagenomics, 16S rRNA, metabolomics.

Introduction

The intestine is one of the anatomical environments in the human body where interaction with microorganisms is most active. In addition to bacteria, the gut microbiota includes viruses, fungi and other microorganisms [1]. The microbiota is of great importance for the development and functional maturation of the human immune system. Experimental studies have shown that in animals raised in a germ free environment, the development of intestinal lymphoid structures and of certain T lymphocyte subpopulations is impaired [4]. These data indicate that the normal microbiota acts as a biological stimulus in the formation of the immune system. The relationship between the gut microbiota and the immune system is bidirectional. The microbiota stimulates the immune system and modulates its activity, while the immune system ensures that microorganisms are kept under control within the intestinal lumen [1,5].

Aim of the study

To analyze the mechanisms of interaction between the gut microbiota and the human immune system on the basis of modern microbiological data, and to describe the effects of microbial metabolites on the immune system, the immunological consequences of dysbiosis, and the modern molecular methods used to study the microbiota.



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Materials and methods

This work was carried out as a literature review. Scientific articles devoted to the gut microbiota, the immune system, microbial metabolites and modern microbiological technologies were selected for the study. The main methods of analysis were: analysis of the scientific literature; comparison of the mechanisms linking the microbiota and the immune system; analysis of data on 16S rRNA sequencing; review of metagenomic studies; and analysis of the immunological effects of microbial metabolites. The development of culture independent genomic technologies in microbiome research has made it possible to study the composition and functions of microorganisms in greater depth [1].

Results and discussion

Interaction between the gut microbiota and the immune system
The gut microbiota influences both the innate and the adaptive branches of the immune system. Microbial antigens and metabolites are recognized by immune cells and activate various immunological signaling pathways [1]. The immune system, in turn, does not remain passive. The intestinal epithelium, the mucus layer, antimicrobial substances and immunoglobulins limit the approach of microorganisms to the intestinal wall and their uncontrolled entry into tissues [5]. The gut microbiota can influence the differentiation and function of T lymphocytes. In particular, Treg and Th17 cells occupy an important place in the immunological balance associated with the gut microbiota [4]. Treg cells participate in maintaining immunological tolerance and limiting excessive inflammation, whereas Th17 cells take part in certain protective mechanisms of the intestinal mucosa [4]. Therefore, the gut microbiota affects not only the “activation” of the immune system but also the balance of the immune response. One of the key protective mechanisms of the intestinal mucosa is secretory immunoglobulin A (IgA). IgA helps to limit the



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adhesion of microorganisms to the intestinal epithelium and their passage across the intestinal barrier. At the same time, IgA is also involved in regulating the composition of the microbiota [5]. By fermenting dietary fiber, gut bacteria produce short chain fatty acids (SCFAs) such as acetate, propionate and butyrate [2]. SCFAs influence the function of the intestinal epithelial barrier, mucosal immunity and the function of certain immune cells [2]. A 2024 article in Nature Reviews Immunology identified signaling through G protein coupled receptors and the regulation of histone deacetylase activity as important mechanisms of SCFA action [2]. Gut microorganisms are involved in altering the chemical structure of bile acids. The resulting microbially modified bile acids can act as signaling molecules for the immune system [3]. A 2024 review in Nature Reviews Immunology highlighted the relationship between the microbiota and bile acids as an important direction for understanding immune homeostasis and disease processes [3]. Dysbiosis is a disturbance of the balance in the composition or functional activity of the gut microbiota. Dysbiosis can affect immune related processes. Disrupted interactions between the microbiota and the immune system have been studied in inflammatory bowel diseases, certain autoimmune diseases and other immune mediated disorders [1]. At the same time, the detection of an association between changes in the microbiota and a disease does not always imply a cause and effect relationship. This issue remains one of the major challenges of modern microbiome research [1]. 16S rRNA sequencing is a molecular genetic method used to determine the taxonomic composition of bacteria. It makes it possible to identify bacterial groups within the microbiota and to compare microbial diversity between different samples. Shotgun metagenomics allows large scale analysis of the total DNA of the microbiota. With this method, it is possible to study not only the presence of microorganisms but also the genes encoding their potential functions [6]. Metabolomics studies the small molecules produced by the



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microbiota and the host organism. Among the metabolites associated with the gut microbiota, SCFAs and microbially modified bile acids are of particular importance [2,3].

Conclusion

The relationship between the gut microbiota and the human immune system is complex, dynamic and bidirectional [1]. The microbiota influences the development and function of the immune system, while the immune system controls the balance of microorganisms in the intestinal environment [1,5]. Short chain fatty acids are important metabolites through which the gut microbiota affects the immune system, modulating the epithelial barrier and the activity of immune cells [2]. The microbial modification of bile acids is also an important metabolic mechanism in the regulation of the immune response [3]. A disturbance of the balance in the composition of the microbiota, known as dysbiosis, may be associated with changes in immunological homeostasis [1]. Modern methods such as 16S rRNA sequencing, shotgun metagenomics and metabolomics are making it possible to study the composition and functions of the gut microbiota in greater depth.

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