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Mechanisms of gut microbiota dysbiosis and colorectal cancer risk: analysis and prospective interventions

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Abstract

This review comprehensively explores the mechanisms linking gut microbiota dysbiosis with the risk of colorectal cancer (CRC). Research indicates that gut microbiota imbalance may promote the occurrence and development of CRC through various pathways, including microbial metabolites, inflammatory responses, and alterations in the immune microenvironment. Specific mechanisms involve reducing short-chain fatty acids (SCFAs), increasing secondary bile acids, enhanced intestinal permeability, and gene-environment interactions. Interventions targeting these mechanisms, such as dietary regulation, prebiotics, probiotics, and fecal microbiota transplantation, show potential in CRC prevention. Future research should focus on personalized treatments and the advancement of precision medicine, emphasizing interdisciplinary collaboration to enhance the comprehensive understanding and clinical application of gut microbiota in relation to CRC.

Key words gut microbiota dysbiosis, colorectal cancer, short-chain fatty acids, secondary bile acids, intestinal permeability, gene-environment interaction, dietary regulation, probiotics

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Introduction

In recent years, the importance of gut microbiota in maintaining human health has gained widespread recognition [1, 2]. The gut, as the core organ of the digestive system, serves as a complex micro-ecosystem, hosting a diverse array of microbial communities [3, 4]. Yoo JY et al. demonstrated that bacteria, viruses, fungi, and other microorganisms play indispensable roles in maintaining gut health, regulating the immune system, and promoting metabolism through interactions with the host [5]. A healthy gut microbiota helps digest food, synthesize vitamins, regulate the host's immune response, and defend against external pathogens [6, 7]. Typically, a dynamic equilibrium between the gut microbiota and the host sustains optimal health. However, changes in lifestyle, environmental factors, and the use of medications disrupt this balance, leading to gut microbiota dysbiosis [8-11]. Dysbiosis involves a reduction in beneficial bacteria, an increase in harmful bacteria, or a decline in microbiota diversity and is strongly linked to the development of various diseases [12, 13]. Arab JP et al. reported that dysbiosis is particularly associated with gastrointestinal conditions such as inflammatory bowel disease, obesity, diabetes, and non-alcoholic fatty liver disease, among others [14]. Recent studies further suggest that gut microbiota dysbiosis may play a significant role in the occurrence and development of colorectal cancer.

Colorectal cancer (CRC) is one of the most common malignant tumors worldwide, with the incidence and mortality rates ranking the highest among malignant tumors [15-17]. According to global cancer statistics, over 1.9 million new CRC cases and more than 930,000 deaths are reported annually [18, 19]. Despite the recent advancements in early detection and survival rates of CRC screening and treatment techniques, its incidence continues to rise, especially in developing countries. The development of CRC is a complex process influenced by multiple factors, including genetic predisposition, dietary habits, lifestyle, and inflammatory responses [20, 21]. Recently, gut microbiota has emerged as a new research focus, garnering significant scholarly interest. Extensive research indicated a significant association between gut microbiota dysbiosis and the development of CRC. Specifically, dysbiosis may affect the course of CRC through mechanisms [22-25], such as the overgrowth of harmful bacteria and the accumulation of their metabolic byproducts, which may lead to the deterioration of the gut environment, inducing chronic inflammation and DNA damage in cells [26, 27]. Additionally, gut microbiota may influence CRC development by modulating the host immune system, altering intestinal permeability, and disrupting cellular signaling pathways. Although these findings offer valuable insights, the specific pathways remain unclear.

Against this backdrop, systematically analyzing the mechanisms linking gut microbiota dysbiosis with CRC risk and exploring potential intervention measures is of significant theoretical and clinical importance [28, 29]. On one hand, such analysis could elucidate CRC mechanisms, providing new perspectives for early diagnosis and prevention. On the other hand, interventions targeting gut microbiota regulation may emerge as novel strategies for CRC treatment. Therefore, this review aims to systematically discuss the potential roles of gut microbiota dysbiosis in CRC and its intervention prospects from multiple aspects, including gut microbiota composition and function, the mechanisms linking dysbiosis and CRC, and potential interventions. We aim to systematically review and analyze existing research findings to establish a robust reference base to inform and guide future research and clinical practice, thereby fostering progress in this field (**Figure 1**).

Overview of gut microbiota imbalance

Composition and function of normal gut microbiota

The normal gut microbiota is a complex microecosystem composed of bacteria, viruses, fungi, and other microorganisms [30-33]. Bacteria, the most abundant microorganism, are primarily divided into four major phyla based on their quantity and distribution in the gut: Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria. Firmicutes and Bacteroidetes account for over 90% of the total gut microbiota, forming the core group that maintains gut microecological balance [34, 35].

Normal gut microbiota plays multiple essential roles in host health. It participates in the host's nutritional metabolism. For instance, gut microbiota can ferment undigested carbohydrates, producing short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate [36, 37]. These SCFAs provide energy for the host and regulate the gut's pH balance, inhibiting the growth of harmful microorganisms. Secondly, the gut microbiota is critical in maintaining the host's immune balance. Through interactions with the host's immune system, the normal gut microbiota can stimulate immune cells' development and functional maturation and regulate the host's immune responses, preventing excessive inflammatory reactions. Additionally, the microbiota enhances gut integrity by promoting the regeneration of intestinal epithelial cells, thereby sustaining normal gut permeability.

The figure illustrates how gut microbiota dysbiosis contributes to CRC risk through several interconnected mechanisms. Gut microbiota dysbiosis disrupts the balance of microbial metabolites, altering the short-chain fatty acids and generating toxic compounds that may induce carcinogenesis. Furthermore, this imbalance impacts gut permeability by compromising immune function and micro-movements within the gut barrier, thus fostering an environment prone to inflammation and cancer. Additionally, immune system modulation plays a critical role where immune homeostasis is disturbed, leading to immune activation and escape, particularly through mechanisms involving NF-κB activation. The dysregulated gut microbiome also facilitates immune evasion, permitting nascent cancer cells to avoid detection and enhance their proliferation. Collectively, these processes underscore the complex relationship between gut microbiota dysbiosis and CRC, highlighting multiple pathways through which an imbalanced microbiome can contribute to tumor development.

Definition and causes of gut microbiota imbalance

Gut microbiota imbalance, or dysbiosis, refers to abnormal changes in the composition and function of the gut microbiota. It is characterized by reduced beneficial bacteria, overgrowth of harmful bacteria, and reduced diversity and stability of gut microbiota. Several factors can lead to gut microbiota imbalance, including dietary habits, antibiotic use, infections, stress, lifestyle, and environmental changes [38, 39].

Diet is one of the primary factors influencing the composition and function of the gut microbiota. High-fat, high-sugar, and low-fiber diets can easily lead to gut microbiota imbalance. For instance, a high-fat diet increases bile acid secretion, fostering the growth of harmful sulfate-reducing bacteria in the gut. The metabolic products of these bacteria may damage the gut mucosa, leading to inflammation and disease. The widespread use of antibiotics is another significant factor causing gut microbiota imbalance. Huang K et al. found that antibiotics can kill pathogenic bacteria and severely damage beneficial bacteria in the gut, leading to opportunistic infections and overgrowth of harmful bacteria [40]. Additionally, factors such as acute or chronic intestinal infections, environmental pollution, irregular sleep patterns, and prolonged mental stress may directly or indirectly affect the composition and function of the gut microbiota, inducing dysbiosis.

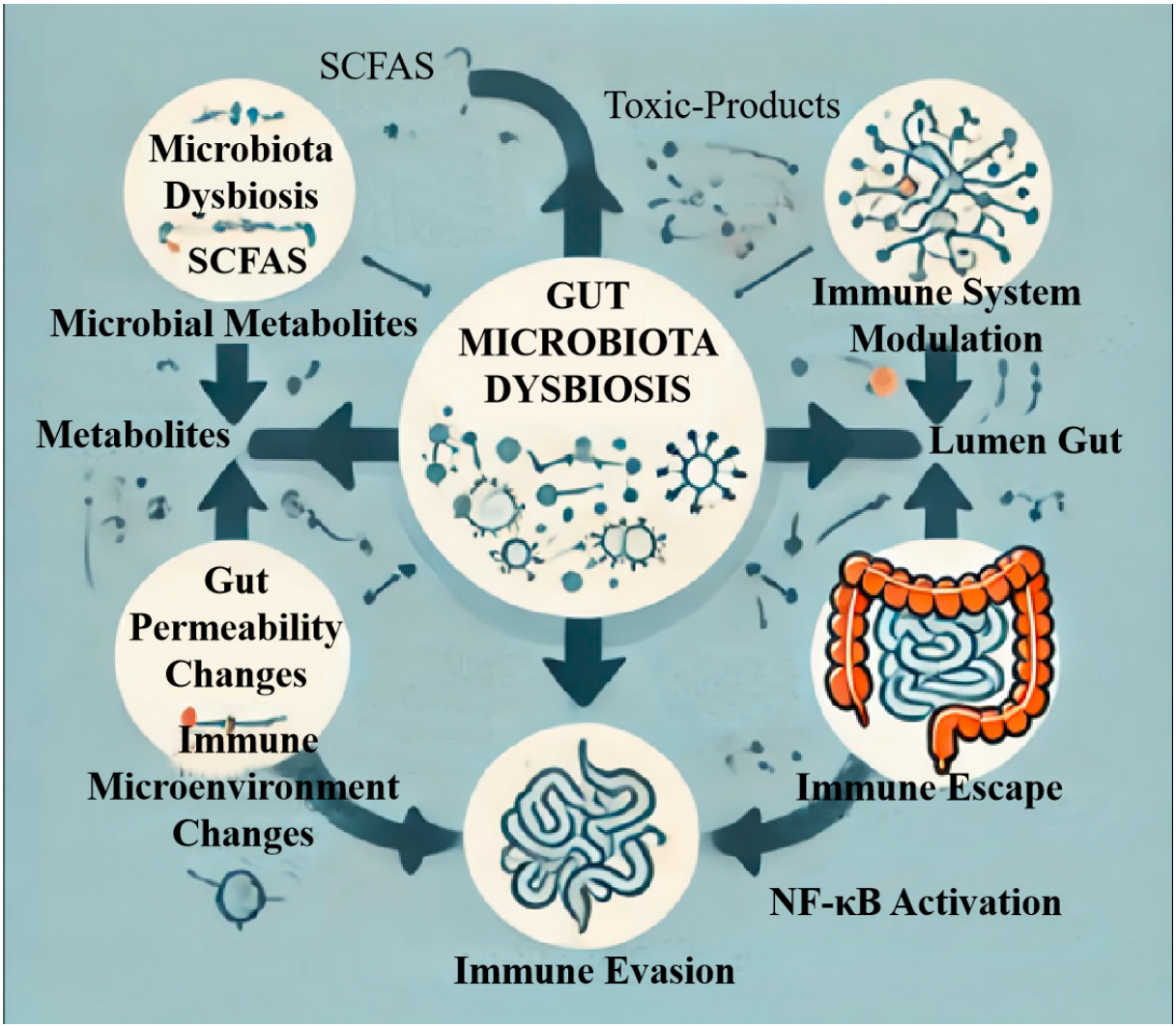

Figure 1. Mechanisms linking gut microbiota dysbiosis to CRC risk.

Physiological and pathological impacts of gut microbiota imbalance

Gut microbiota dysbiosis profoundly affects the host's physiological and pathological states [41-45]. Firstly, it disrupts the host's metabolic balance, leading to the development of metabolic diseases. Studies, including the findings of Rutsch A et al., indicate a strong correlation between dysbiosis and conditions such as obesity, type 2 diabetes, and non-alcoholic fatty liver disease. Dysbiosis alters the host's energy metabolism, increases fat deposition, and affects insulin sensitivity, promoting these diseases [42]. Secondly, gut microbiota imbalance is closely related to various digestive system diseases. Inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis, are closely associated with gut microbiota imbalance. Dysbiosis may contribute to the development and progression of chronic intestinal inflammation by disrupting the gut mucosal barrier and activating excessive immune responses.

Moreover, gut microbiota imbalance may increase the risk of CRC. The overgrowth of specific harmful bacteria, such as Escherichia coli and Clostridium, along with their toxic metabolic byproducts, can damage the DNA of intestinal epithelial cells, potentially inducing cancer. Gut microbiota imbalance also significantly affects the host's immune system. Moreover, dysbiosis significantly influences the immune system by abnormal activation or suppression, increasing susceptibility to infections and immune-mediated conditions such as allergies, rheumatoid arthritis, and systemic lupus erythematosus. Doroszkiewicz J et al. reported that dysbiosis affects the host's nervous system function through the gut-brain axis, leading to the development of mental and neurological disorders such as depression, autism, and Parkinson's disease [46].

The association between gut microbiota imbalance and colorectal cancer

Microbial metabolites and carcinogenesis mechanisms

The gut microbiota influences host health by metabolizing ingested food into various metabolites, including short-chain fatty acids (SCFAs), secondary bile acids, amines, indoles, and others. These metabolites can impact the occurrence and development of CRC through various mechanisms. For instance, harmful bacteria, such as sulfate-reducing bacteria and Enterococcus faecalis, can produce carcinogenic metabolites like hydrogen sulfide and nitrosamines, which can damage DNA and induce mutations [47, 48]. Moreover, microbial metabolites contribute to CRC risk by regulating the gut's redox balance and eliciting oxidative stress

responses, thereby exacerbating the risk of carcinogenesis in intestinal epithelial cells.

The role of short-chain fatty acids (SCFAs)

SCFAs are metabolic byproducts produced by the gut microbiota through the fermentation of undigested carbohydrates, such as dietary fiber. The main SCFAs include acetate, propionate, and butyrate, which are important in maintaining gut health and regulating host metabolism [49, 50]. Butyrate, in particular, is extensively studied SCFAs in CRC prevention. It serves as a vital energy source for intestinal epithelial cells and exhibits anti-inflammatory, antioxidant, and anticancer properties. Butyrate can inhibit the occurrence and progression of CRC through various mechanisms. Firstly, it can inhibit the proliferation of CRC cells and promote their apoptosis. By inhibiting the activity of histone deacetylases (HDACs), butyrate increases the expression of specific tumor suppressor genes, thereby inhibiting cancer cell growth. Secondly, butyrate's anti-inflammatory actions are mediated through the activation of G-protein-coupled receptors (e.g., GPR43 and GPR109A), inhibiting the activation of the NF-κB signaling pathway, reducing the release of inflammatory mediators, and decreasing chronic inflammation [51, 52]. Additionally, butyrate enhances the gut mucosal barrier function, reducing gut permeability, preventing the entry of harmful substances into the body, and lowering the risk of inflammation and cancer.

However, gut microbiota imbalance reduces SCFA production, especially butyrate levels, which could be essential in developing CRC. Studies have shown that the relative abundance of Firmicutes and Bacteroidetes, the primary producers of SCFAs, is significantly reduced in CRC patients. Therefore, increasing dietary fiber intake to promote SCFA production may be a crucial strategy for preventing CRC.

Secondary bile acids and carcinogenic risk

Bile acids, synthesized by the liver and secreted into the intestine through bile, facilitate fat digestion. Primary bile acids are converted into secondary bile acids, such as deoxycholic acid (DCA) and lithocholic acid (LCA), by the gut microbiota [53-55]. Excessive accumulation of secondary bile acids in the gut may have carcinogenic effects. Research indicates a strong correlation between elevated levels of secondary bile acids and CRC development.

Secondary bile acids promote CRC through various pathways. Firstly, they induce oxidative stress responses in intestinal epithelial cells, leading to DNA damage and gene mutations, thereby increasing the risk of carcinogenesis. Secondly, secondary bile acids can activate the Wnt/β-catenin signaling pathway, a common carcinogenic pathway in CRC. Activation of this pathway can promote tumor cell proliferation and metastasis. Moreover, secondary bile acids can induce chronic inflammation by activating inflammatory signaling pathways such as the NF-κB pathway, further promoting cancer development. Therefore, reducing the accumulation of secondary bile acids or blocking their carcinogenic signaling pathways may be an important strategy for preventing and treating CRC.

Gut permeability and inflammatory response

Gut permeability refers to the intestinal barrier's ability to selectively regulate the passage of substances. Under normal conditions, the intestinal barrier can selectively absorb nutrients while preventing harmful substances, such as pathogens and toxins, from entering the body. However, Yu S et al. reported that gut microbiota imbalance may increase gut permeability, known as "leaky gut". This condition impairs the intestinal barrier, allowing harmful substances to infiltrate the body, provoking excessive immune responses and chronic inflammation [56]. Chronic inflammation is considered an important mechanism in the development of CRC.

Increased gut permeability can trigger a series of inflammatory responses, including the activation of macrophages and other immune cells, the release of pro-inflammatory factors, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP) [57]. Bardelčíková AT et al. found that these inflammatory factors promote cancer cell proliferation, inhibit their apoptosis, and promote tumor angiogenesis and metastasis through various mechanisms. Additionally, chronic inflammation induces oxidative stress, further exacerbating DNA damage and gene mutations, increasing the risk of CRC [58]. Therefore, maintaining intestinal barrier integrity and reducing gut permeability is pivotal in preventing CRC. Interventions such as probiotics, prebiotics, and dietary fiber can regulate gut microbiota composition, enhance intestinal barrier function, reduce inflammatory responses, and lower the risk of CRC.

Alterations in the immune microenvironment

The gut microbiota influences the immune microenvironment within the tumor by interacting with the host's immune system, thereby affecting the occurrence and progression of CRC. The gut microbiota plays a role in immune surveillance by maintaining the balance of immune cells, including regulatory T cells (Tregs), Th17 cells, and cytotoxic T lymphocytes (CTLs) in the intestinal mucosa [59]. However, gut microbiota imbalance can disrupt this balance, leading to immune escape and promoting tumor development.

For example, the reduction in beneficial bacteria such as Bifidobacterium and Lactobacillus and the overgrowth of harmful bacteria can inhibit the activity of CTLs. Li Y e tal. reported that it reduces the immune system's ability to kill tumor cells and promote tumor immune escape [60]. On the other hand, gut microbiota imbalance can increase the proportion of immunosuppressive cells such as Tregs, inhibit the host's anti-tumor immune responses, and further promote tumor development. Additionally, gut microbiota imbalance can regulate immune responses by modulating the levels of immune-related signaling molecules, such as cytokines and chemokines, within the tumor microenvironment. Some harmful bacteria can secrete specific cytokines and chemokines, promoting the recruitment and activation of immune cells that suppress anti-tumor immunity and enhance tumor cell proliferation, invasion, and metastasis [61, 62]. Therefore, regulating gut microbiota composition and function may provide new therapeutic strategies for CRC. Interventions targeting gut microbiota, such as probiotics, prebiotics, and fecal microbiota transplantation, can potentially restore immune microenvironment balance, enhance anti-tumor immune responses, and improve CRC treatment outcomes.

The impact of antibiotics and the gut microbiota on CRC

The widespread use of antibiotics significantly impacts the composition and function of the gut microbiota, potentially influencing the risk of CRC. Antibiotics disrupt the balance by destroying the beneficial and harmful bacteria. Studies have shown that long-term or high-dose antibiotic use is associated with an increased risk of CRC [63-65].

Firstly, antibiotics reduce the gut microbiota diversity, leading to the overgrowth of specific harmful bacteria. These bacteria contribute to carcinogenesis by producing toxins, metabolites, and other toxic factors. Secondly, antibiotics can inhibit the production of beneficial metabolites, such as SCFAs, and weaken the

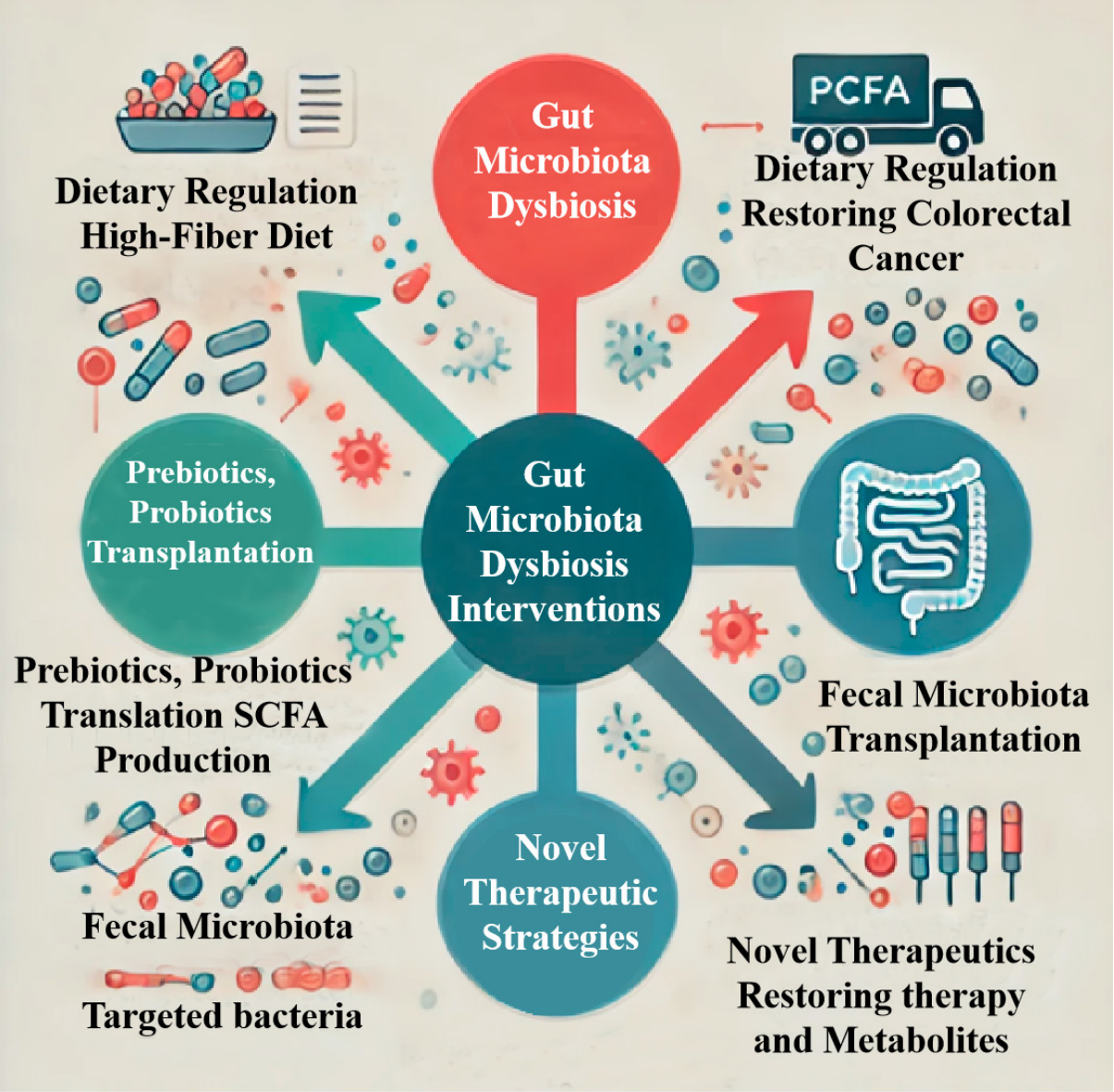

Figure 2. Potential interventions for gut microbiota dysbiosis.

protective effects of the gut microbiota on the intestinal barrier and immune system, thereby increasing the risk of cancer. Moreover, antibiotics induce gut microbiota imbalance, promoting chronic inflammation and immune dysregulation, further contributing to CRC development. Therefore, careful and appropriate use of antibiotics is essential for preventing gut microbiota imbalance and reducing CRC risk. Additionally, probiotics, prebiotics, and dietary adjustments may help restore gut microbiota balance and reduce the adverse effects of antibiotics on CRC risk.

Interventions and their potential roles (Figure 2)

The figure highlights various interventions targeting gut microbiota dysbiosis to prevent and manage CRC. Dietary regulation, including high-fiber diets and specific dietary interventions, is emphasized as a foundational approach to restoring gut balance. Prebiotics, probiotics, and synbiotics are critical in promoting beneficial microbial communities and enhancing the production of short-chain fatty acids (SCFAs), essential for maintaining gut health. Fecal microbiota transplantation and targeted bacterial therapies represent more direct methods of modulating gut microbiota composition. Novel therapeutic strategies, including emerging interventions to restore microbial diversity and enhance immune responses, are also featured. These interventions collectively provide a comprehensive approach to addressing gut microbiota dysbiosis and its role in CRC prevention and treatment.

Dietary regulation and improvement of gut microbiota

Diet is a key factor influencing the composition and function of gut microbiota. Proper dietary management can effectively improve the balance of gut microbiota and reduce the risk of CRC. Healthy nutritional components such as dietary fiber, plant polyphenols, and ω-3 fatty acids increase the abundance of beneficial bacteria, reduce the number of pathogenic bacteria, and restore the balance of the gut micro-ecosystem. For instance, a high-fibre diet promotes the production of short-chain fatty acids (SCFAs) like butyrate, enhances intestinal mucosal barrier function, reduces

intestinal inflammation, and lowers the risk of CRC development [66]. Conversely, Mohseni AH et al. reported that a diet high in fat and sugar disrupts gut microbiota, increases the production of harmful metabolites such as secondary bile acids, and raises the likelihood of developing CRC [67]. Therefore, optimizing gut microbiota composition through dietary regulation is crucial for preventing CRC.

Application of prebiotics, probiotics, and synbiotics

The application of prebiotics, probiotics, and synbiotics significantly contributes to restoring the balance of gut microbiota and improves host health. Prebiotics, such as fructooligosaccharides and inulin, selectively foster beneficial bacteria like Bifidobacterium and Lactobacillus, enhancing gut microbiota composition. Probiotics, identified by Ashaolu TJ et al. as beneficial microorganisms like Bifidobacterium and Lactobacillus, improve gut microbiota balance and boost immune function [68]. Synbiotics, a combination of prebiotics and probiotics, further enhance the stability and diversity of gut microbiota through dual action. Research indicates that prebiotics and probiotics can significantly increase beneficial bacteria, reduce the growth of harmful bacteria, improve the gut microenvironment, and reduce the risk of CRC. Aindelis G. et al. found that probiotics offer anticancer benefits through pathogen exclusion, carcinogen production inhibition, intestinal barrier enhancement, and immune response regulation [69]. The application of synbiotics further enhances these benefits, offering new options for preventing and treating CRC.

Role of a high-fiber diet

A high-fiber diet is important in regulating gut microbiota and preventing CRC. Langfeld LQ et al. reported that dietary fiber, as a primary source of prebiotics, promotes the growth of beneficial bacterial communities like Bacteroidetes and Firmicutes in the gut and generates SCFAs (such as butyrate) through fermentation. The SCFAs are crucial in maintaining gut health, regulating inflammation, and immune responses [70]. A high-fiber diet increases stool bulk, shortens intestinal transit time, and reduces the contact time of harmful substances with the intestinal lining, lowering the risk of CRC. Additionally, dietary fiber can lower intestinal pH, inhibit the growth of pathogenic bacteria, and reduce the formation of carcinogenic substances, further decreasing cancer incidence. Nucci D et al. have shown that populations with high dietary fiber intake have a significantly lower incidence of CRC than those with low fiber intake [71]. Therefore, increasing dietary fiber prevents CRC effectively [71, 72].

Recovery of gut microbiota after antibiotic use

Antibiotics are crucial in treating infectious diseases, yet their impact on gut microbiota cannot be overlooked. The widespread use of antibiotics can alter gut microbiota imbalance, increase harmful bacteria proliferation, decrease beneficial bacteria, and subsequently increase the risk of CRC. Broad-spectrum antibiotics disrupt the microecological balance, increasing antibiotic-resistant strains and opportunistic pathogen infections. Therefore, restoring the balance of gut microbiota after antibiotic treatment is vital for preventing and treating CRC. Probiotics, prebiotics, and their combined use (synbiotics) effectively restore gut microbiota balance after antibiotic use. These substances effectively address the gut microbiota imbalance caused by antibiotics by promoting beneficial bacteria, suppressing harmful ones, and enhancing the intestinal barrier [73]. The rational use of antibiotics, including selecting appropriate antibiotics based on infection type and limiting unnecessary usage, is key to reducing gut microbiota imbalance and lowering the risk of CRC.

Application of fecal microbiota transplantation (FMT) in CRC prevention

Fecal microbiota transplantation (FMT) involves transplanting the gut microbiota from a healthy donor into a patient's intestine to restore balance. FMT has proven effective in treating refractory Clostridium difficile infections and is now being explored for CRC prevention. Restoring gut microbiota reduces the risk of CRC through various mechanisms [74]. Previous FMT has effectively restored the abundance of beneficial bacteria in the gut, reduced the number of pathogenic bacteria, and improved the gut microenvironment [75]. Additionally, FMT reduces the risk of inflammation and carcinogenesis by increasing SCFA production, enhancing intestinal mucosal barrier function, and regulating immune responses [76]. However, FMT efficacy in CRC prevention is still in the research stage, and further clinical studies are needed to verify its safety and efficacy.

Precision interventions targeting specific bacterial populations

As research on gut microbiota progresses, precision interventions targeting specific bacterial populations have become a new direction for CRC prevention. Sędzikowska A et al. found that gut microbiota composition varies significantly among individuals, and the overgrowth of specific carcinogenic bacteria may be an important cause of CRC [77]. Therefore, precision interventions aimed at specific bacterial populations offer the potential for more effective prevention and treatment. Based on metagenomics and microbiome analysis techniques, researchers can identify carcinogenic bacterial populations closely associated with CRC, such as specific strains of Escherichia coli and Clostridia. Precision intervention strategies may include selective use of antibiotics, targeted supplementation of probiotics, and regulation of specific metabolites. Additionally, personalized treatment plans based on the individual gut microbiota characteristics of patients may improve the prevention and treatment of CRC.

Prospects of novel therapeutic strategies

New therapeutic strategies deepen understanding of the relationship between gut microbiota and CRC. The combination of metabolic regulation and immunotherapy is at the forefront of CRC treatment. Modulating gut microbiota metabolites, such as increasing SCFA production and reducing secondary bile acid accumulation, alters the gut microenvironment and potentially decreases the incidence and progression of CRC [78]. Furthermore, the interaction between gut microbiota and the host immune system provides new insights for immunotherapy. The role of gut microbiota in immunotherapy has been preliminarily confirmed. Certain gut microbiota can enhance the host immune system's anti-tumor response, improving the efficacy of immunotherapeutic drugs like immune checkpoint inhibitors. Therefore, future research may enhance immunotherapy's effectiveness by modulating gut microbiota and developing more precise and personalized treatment plans. Overall, targeting gut microbiota presents substantial opportunities for preventing and treating CRC. Through strategies such as dietary regulation, application of prebiotics, probiotics, FMT, precision interventions, and exploration of novel therapeutic strategies, more comprehensive and effective solutions approaches are anticipated. Future research will further reveal the mechanisms and effects of these interventions, bringing new hope for the prevention and treatment

of CRC.

Future research directions and challenges

Challenges in studying the mechanisms of gut microbiota and CRC

Despite recent advances in the study of gut microbiota and CRC, this field still faces numerous challenges. First, the diversity and complexity of the gut microbiota complicate understanding its role in CRC development. The gut microbiota is a complex ecosystem composed of hundreds of different microorganisms. Its function is influenced by the individual's genetic background and various external factors such as diet, environment, and medication use. Therefore, accurately deciphering the causal relationship between gut microbiota and CRC remains a key challenge for future research. Secondly, most current studies are cross-sectional or based on animal models, lacking long-term follow-up studies to verify the direct causal relationship. Additionally, inconsistencies across studies may stem from variations in study population, experimental design, and sample processing methods. Therefore, Standardizing research methodologies and conducting large-scale prospective studies are crucial to generating consistent, reliable results. Finally, the carcinogenic mechanisms of the gut microbiota in CRC are complex, involving microbial metabolism, inflammatory response, and immune regulation. Thus, comprehensively revealing the specific mechanisms by which gut microbiota contributes to the development of CRC through multi-level and multi-dimensional research approaches is also an important direction for future research.

The development prospects of personalized treatment and precision medicine

As research on the relationship between gut microbiota and CRC deepens, personalized treatment and precision medicine emerged as promising areas. The individualized nature of gut microbiota composition underlines the need to develop tailored prevention and treatment strategies. Future research is increasingly focused on personalizing approaches based on unique microbiota profiles. For example, by analyzing an individual's gut microbiota composition, identifying high-risk microbial groups, and then taking targeted intervention measures such as dietary adjustments, probiotics, or fecal microbiota transplantation, it is expected to significantly reduce the risk of CRC. Moreover, the development of precision medicine also relies on in-depth studies of the interaction between gut microbiota and host gene-environment interactions. Leveraging high-throughput techniques such as metagenomics, metabolomics, and immunomics allows researchers to delineate the mechanisms by which gut microbiota plays a role in personalized cancer prevention and treatment. This helps develop new biomarkers for early diagnosis and risk prediction and may promote the development of novel therapeutic strategies, such as precision immunotherapy and metabolic product regulation based on gut microbiota characteristics.

The importance of interdisciplinary research

Research on gut microbiota and CRC involves multiple disciplines, including microbiology, oncology, immunology, and metabolism, underscoring interdisciplinary research crucial for an in-depth understanding of its complex mechanisms. By integrating diverse knowledge and technical approaches, researchers can explore the role of gut microbiota in CRC from various angles. For instance, microbiological research helps identify carcinogenic microbial groups closely related to CRC. In contrast, oncological research can explore how these microbial groups influence tumor development through metabolic products, inflammatory responses, and other pathways. Immunology and metabolism studies also play important roles in the mechanistic links between gut microbiota and CRC. Researchers can develop more precise and effective intervention strategies by investigating how gut microbiota regulates the host immune response, influences the tumor microenvironment, and affects the growth and differentiation of tumor cells through metabolic products. Therefore, future research should emphasize collaborative efforts across disciplines. By promoting interdisciplinary research, we can advance the comprehensive understanding of the mechanisms linking gut microbiota and CRC and its clinical applications.

Conclusion

This review has discussed in detail the mechanisms linking gut microbiota dysbiosis and CRC risk. Research indicates that gut microbiota dysbiosis plays a significant role in the development and progression of CRC through various pathways, including metabolic products, inflammatory responses, and immune regulation. Specifically, mechanisms such as short-chain fatty acids, secondary bile acids, gut permeability, and changes in the immune microenvironment have been confirmed to be closely related to CRC risk. Moreover, research into gene-environment interactions highlights the potential role of gut microbiota in individual cancer susceptibility. Future research should explore these mechanisms, particularly their potential applications in personalized treatment and precision medicine. By developing targeted interventions for specific microbial groups, such as dietary regulation, probiotics, and fecal microbiota transplantation, it is expected that effective prevention and treatment of CRC can be achieved. Additionally, leveraging interdisciplinary research strengths will deepen our understanding of the complex associations between gut microbiota and CRC, opening up new opportunities for clinical applications in this field. In summary, the continued research on gut microbiota will provide new ideas and methods for preventing, diagnosing, and treating CRC. Advances in technology and interdisciplinary approaches are expected to yield more precise and personalized interventions, significantly improving clinical outcomes and reducing CRC risk.

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Availability of data and materials

Data and materials are available on request from the authors.

Ethical policy

Not applicable.

Author contributions

DKQ conceptualized, designed, conducted research, and wrote the manuscript; NH contributed to the revision and figure production.

Competing interests

I declare that there is no conflict of interest regarding the publication of this document. I confirm that neither I nor my collaborators have any financial or personal relationships that could inappropriately influence or bias the content of this work.

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