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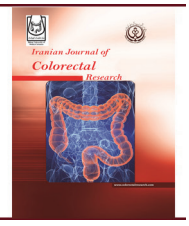

The Role of Gut Microbiome Dysbiosis in Colorectal Cancer: Correlation, Molecular Mechanisms, and Probiotic Potential

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Abstract

The gut microbiome is an extensive and vital community of microbes in the gastrointestinal tract which is crucial for human health as it creates beneficial compounds, aiding fiber digestion, and enhancing the immune system. Colorectal cancer (CRC) is the third most common cancer and second leading cause of cancer-related death worldwide. This review aims to examine the link between gut microbiome imbalance (dysbiosis) and CRC using epidemiological data and molecular mechanisms, emphasizing the significance of probiotic-based therapy as a potential means of prevention and treatment. Probiotics have the ability to intervene by restoring microbial equilibrium, reducing inflammation, and producing anti-tumor compounds. To collect information, we used PubMed, Elsevier, ScienceDirect, Scopus, and Embase, which provided access to a wide range of peer-reviewed articles, case-control studies, and cohort studies essential for a comprehensive analysis of the topic. In this review, key differences in microbiome composition between healthy individuals and patients with CRC have been observed, including a decrease in beneficial butyrate-producing bacteria and an increase in carcinogenic bacteria such as *Fusobacterium nucleatum*. The molecular mechanisms through which dysbiosis accelerates carcinogenic process include the production of harmful metabolites, induction of chronic inflammation, and modulation of the host immune system. Beneficial microorganisms known as probiotics have been proposed as a promising therapeutic option. In conclusion, probiotics can prevent and treat CRC through various mechanisms, such as boosting the immune system, competing with pathogenic bacteria, and producing anticancer compounds including butyrate. However, challenges remain in this field, including high variability across studies, a lack of long-term investigations, and the need to determine optimal dose and strain for each individual. To overcome these obstacles, future research should move towards more comprehensive studies and personalized treatments.

Keywords: Microbiome; Personalized medicine; Dysbiosis; Colorectal cancer; Probiotics

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Introduction

Defining the Gut Microbiome and Its Role in Host Health

The gut microbiome is an collection of microbial genomes from a complex community of microbes such as bacteria, viruses, and fungi, also termed microbiota, that inhabit the human gastrointestinal tract (1). The gut microbiome, consisting of over 100 trillion microbial cells and over a thousand distinct species, is a metabolically active and functioning "metabolic organ" with a 100- to 150-fold larger genome than humans (2, 3). The composition of the microbiome varies among individuals and is influenced by genetics, diet, age, lifestyle, and drug consumption (4). The gut microbiota performs significant physiological and metabolic functions within the body. The microbiota of the intestine ferments non-digestible dietary fiber to yield short-chain fatty acids (SCFAs), mostly butyrate (5). Butyrate possesses strong anti-inflammatory and anti-tumor properties and is a primary source of energy for colon mucosal cells. In addition, symbiotic bacteria in the intestines synthesize important vitamins such as vitamin K and several B vitamins (biotin, folate, and riboflavin), which are used for various important bodily functions (6). The gut microbiome is also involved in maintaining the immune system. These bacteria also interact with gut immune cells to help develop and direct the immune system to mount an appropriate immune response against antigens (7). A balanced gut microbiome also creates a strong defensive barrier that prevent pathogenic bacteria from growing and colonizing (8). Thus, the gut microbiome can be considered an active and powerful environmental unit with a profoundly important role in general health and disease susceptibility in an individual (9).

Colorectal cancer (CRC) is the third most common type of cancer and second leading cause of cancer-related death worldwide (9, 10). According to WHO records, over one million individuals are diagnosed with this condition annually, and hundreds of thousands of them die (11). The established risk factors for CRC are genetic susceptibility, poor diet (high in red and processed meat, low in fiber), obesity, physical inactivity, and alcohol and tobacco consumption (12). However, given the variability in findings across studies on these risk factors, it is necessary to consider the role of other environmental exposures, especially the gut microbiome (4).

Given the increasing evidence of the vital role played by the gut microbiome in disease and health, this paper provides a comprehensive review of the relationship between dysbiosis (imbalance in the composition and function of the microbiome) and pathogenesis of CRC. The overall objective is to identify, differentiate, and compare the main findings from epidemiological and molecular studies that show how changes in the microbiome may initiate or drive carcinogenic processes. Furthermore, this article will particularly highlight the importance of probiotic therapy as a potential strategy for preventing and treating CRC. Subsequent sections will address dysbiosis in CRC patients, the molecular mechanisms underlying CRC pathogenesis, the potential of probiotics as a therapeutic approach, and finally, challenges and future directions in this field, as outlined in the flow diagram above.

Data Acquisition

A systematic literature search was conducted across major electronic databases, including PubMed/MEDLINE, Scopus, Embase, and ScienceDirect, to identify relevant studies published up to 2025. The search strategy employed standardized keywords related to gut microbiota, dysbiosis, and colorectal neoplasms to ensure a comprehensive analysis.

Inclusion criteria were peer-reviewed original research, case-control studies, and cohort studies that investigated the molecular mechanisms of gut dysbiosis in CRC or evaluated the therapeutic efficacy of probiotics. Studies were excluded if they were non-English publications, duplicate reports, or if they provided insufficient data regarding microbial composition and functional analysis.

The study selection and screening process are visually summarized in the PRISMA flow diagram (Figure 1).

Dysbiosis (Microbial Imbalance) in CRC Patients

Growing evidence suggests that gut dysbiosis has a close association with the development and progression of CRC (13). Dysbiosis is a condition in which the natural balance between beneficial and pathogenic bacteria in the gut is altered, microbial diversity is compromised, and the metabolic activities of the microbiome are affected (14). To understand the impact of dysbiosis on CRC, it is essential first to establish the baseline of a healthy microbial ecosystem. In a state of homeostasis, the human gut microbiome is characterized by a high degree of diversity and a stable distribution of specific bacterial taxa. These microbes exist in a symbiotic relationship with the host, contributing to metabolic health, barrier integrity, and immune tolerance. The healthy adult gut is dominated by two major phyla, Firmicutes and Bacteroidetes, which together constitute approximately 90% of the total microbial population. Other essential phyla, including Actinobacteria, Proteobacteria, and Verrucomicrobia, are present in lower proportions but play critical roles in vitamin synthesis and mucosal protection. The typical microbial composition, relative abundance, and key physiological functions of these predominant phyla in healthy individuals are summarized in Table 1 (1, 15-17).

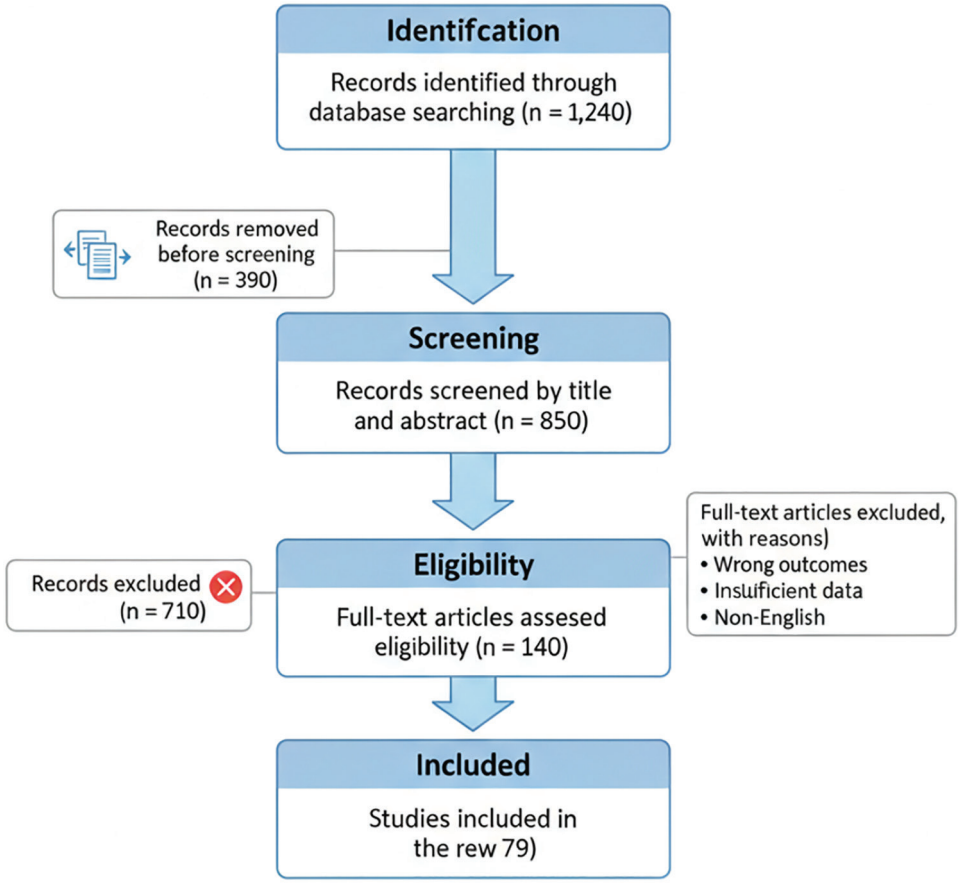

Figure 1: PRISMA Flow Diagram of Study Selection.

Table 1: Microbial profile of healthy individuals

Phylum	Representative Genera	Relative Abundance (%)	Key Functional Roles
Firmicutes	*Faecalibacterium, Clostridium, Lactobacillus*	60% – 65%	Butyrate production, immune regulation, and providing energy for colonocytes.
Bacteroidetes	*Bacteroides, Prevotella*	20% – 30%	Breakdown of complex polysaccharides and assistance in fiber digestion.
Actinobacteria	*Bifidobacterium, Collinsella*	5% – 10%	Synthesis of essential vitamins (B and K) and prevention of pathogen colonization.
Proteobacteria	*Escherichia, Desulfovibrio*	<5%	Maintenance of homeostasis at low levels; overgrowth is a hallmark of dysbiosis.
Verrucomicrobia	*Akkermansia*	<2%	Strengthening of the intestinal mucosal barrier and regulation of glucose metabolism.

Microbiome Differences between Healthy Individuals and Cancer Patients

Numerous studies have found specific differences in gut microbiome composition between healthy and CRC patients. One of the most distinctive findings is a general reduction in microbial diversity (Alpha-diversity) in cancer patients (18). This reduction in diversity indicates a less stable and resistant microbial community. Specific patterns of variation in bacterial species abundance were also found:

Oncomicrobial rise: The presence of certain bacteria, such as *Fusobacterium nucleatum*, *Porphyromonas*, and specific *Escherichia coli* strains (most notably those carrying the *pks* gene and secrete colibactin), is consistently elevated in tumor and fecal samples from CRC patients compared to controls. Bacteria that reside in tumor tissue and thus influence cancer are referred to as oncomicrobes. These bacteria are found to initiate carcinogenic signaling processes in several ways (Figure 2) (19-21).

Decrease in beneficial bacteria: Conversely, the density of butyrate-producing bacteria, particularly from the family Clostridiaceae and *Faecalibacterium prausnitzii* species, is lower in patients with CRC. These bacteria exert a protective effect against cancer, and their decrease is recognized as a key feature of CRC-associated dysbiosis (Figure 2) (21-23).

Review of Case-Control and Cohort Studies

The evidence on dysbiosis in CRC has largely been obtained from two types of epidemiological studies:

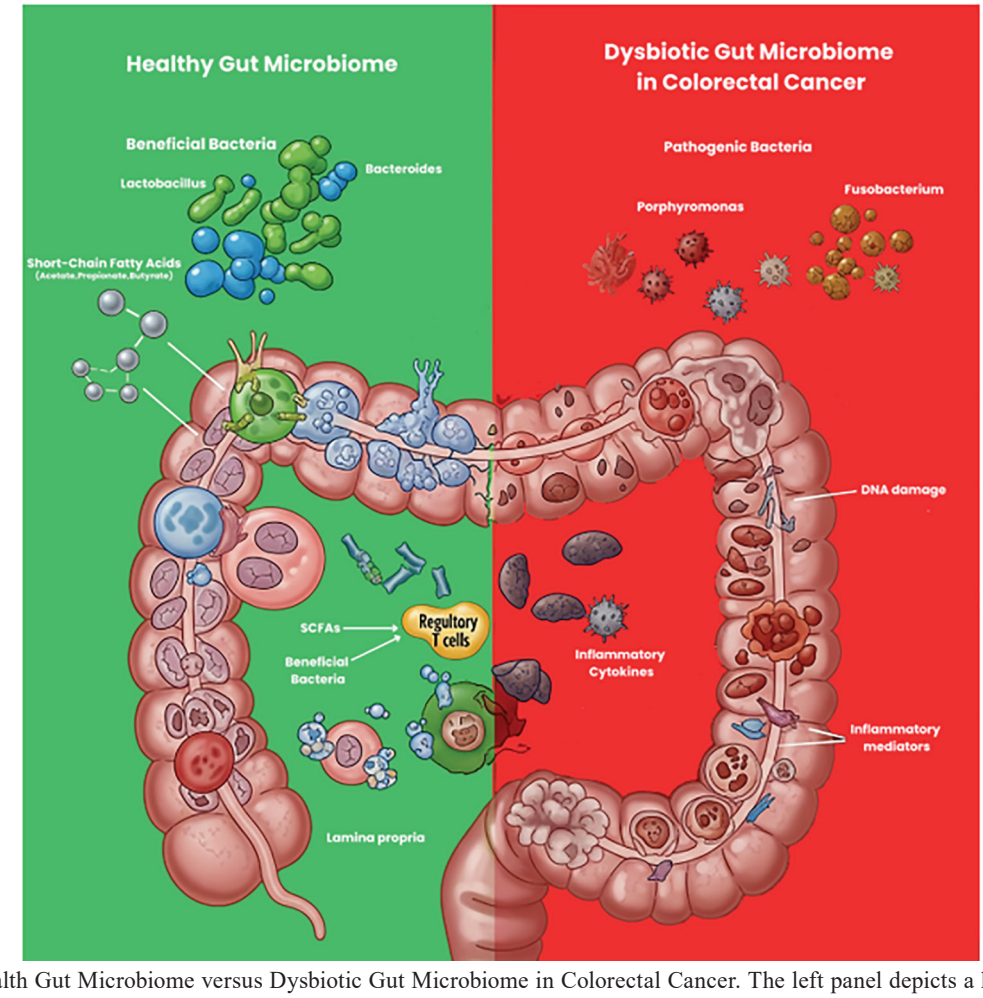

Figure 2: Health Gut Microbiome versus Dysbiotic Gut Microbiome in Colorectal Cancer. The left panel depicts a healthy gut with balanced microbiome dominated by beneficial bacteria, e.g., Bacteroides. Beneficial bacteria generate short-chain fatty acids such as butyrate that nourish colonocytes, shape the immune system by expanding regulatory T-cells, and suppress inflammation. The right panel illustrates a dysbiotic gut, where the microbial balance is disrupted. This condition is marked by overgrowth of pathogenic bacteria such as Fusobacterium and certain subtypes of Bacteroides fragilis. Microbial imbalance leads to a pro-inflammatory environment through the release of inflammatory mediators and cytokines, as well as the induction of DNA damage and colorectal carcinogenesis.

Case-Control Studies: In these studies, the microbiome composition of patients with CRC (case group) is compared with that of matched controls (control group). The results from such studies have consistently demonstrated the presence of specific microbial signatures in cancer patients. For example, studies have reported that the presence of *Fusobacterium nucleatum* in tumor tissue is associated with poor prognosis and metastasis (24-27).

Cohort Studies: In these studies, healthy individuals are followed over a long period to determine who develops CRC. Although such studies are stronger for establishing causality, they are less common because they are more expensive and time-consuming. Nevertheless, preliminary results suggest that certain microbial patterns may serve as biomarkers for anticipating the development of CRC (28, 29).

Molecular Mechanisms and Signaling Pathways Linked to Dysbiosis and Carcinogenesis

The role of dysbiosis in CRC is a complex, multi-stage biological process that involves multiple molecular mechanisms. An unbalanced microbiome may enhance the carcinogenic process by producing some metabolites, inducing chronic inflammation, and directly modulating the host immune system (13, 30, 31). Microbial metabolism can play a seemingly contradictory role in gut health, as it produces both beneficial and carcinogenic metabolites (32).

SCFA Production: SCFAs, especially butyrate, are the major end product of dietary fiber fermentation by beneficial bacteria, such as members of the Lachnospiraceae and Ruminococcaceae families (33). Butyrate exerts a potent anti-cancer protective effect through several key mechanisms. It is the principal fuel of colonocytes, thereby contributing to epithelial barrier health. Its anti-proliferation effect is central: it inhibits histone deacetylase (HDAC), which increases the expression of genes involved in apoptosis (programmed cell death) and induces cell cycle arrest, specifically in cancer cells and not in normal cells. Furthermore, butyrate's anti-inflammatory action results from the inhibition of the transcription factor NF-κB, which blocks the synthesis of pro-inflammatory cytokines, a process often implicated in cancer initiation. In the absence

of butyrate-producing bacteria, which are induced by dysbiosis, these protective functions are lost, and the host is vulnerable to carcinogenic toxins such as colibactin and other toxic metabolites (22, 34-36).

Chronic inflammation is a recognized risk factor for CRC, and dysbiosis is the main driver of the initiation and perpetuation of this inflammation (37). In a healthy microbiome, the intestinal epithelial barrier protects the submucosa from bacterial penetration and bacterial products. However, dysbiosis may lead to the generation of compounds that damage the barrier, increase its permeability, and allow the passage of bacterial products such as lipopolysaccharides (LPS) into the blood and underlying intestine layers (38, 39). The translocation of LPS into submucosa triggers the innate immune response and leads to activation of the transcription factor NF-κB. Persistent activation of NF-κB directly increases the expression of genes involved in cell growth, proliferation, and survival in cancer cells. This cycle of inflammatory and cell injury creates an ideal microenvironment for tumor growth and proliferation (40-43).

The microbiome's role in modulating colorectal carcinogenesis extends beyond inflammation to include the regulation of anti-tumor immune responses (37). Dysbiosis may lead to a reduction in the population and effectiveness of regulatory T cells, which play a key role in controlling inflammatory reactions. Furthermore, the microbial imbalance can polarize helper T cell responses, specifically by decreasing the activity of cytotoxic CD8+ T cells and Natural Killer (NK) cells, the primary effectors of anti-tumor immunity, while promoting a pro-tumorigenic Th17 environment. This shift allows cancer cells to evade detection by the host's cellular defense mechanisms (44-47). In parallel, dysbiosis significantly impacts the humoral immune response by disrupting the production of secretory Immunoglobulin A (sIgA), which is the first line of defense at the mucosal surface. A decrease in sIgA levels or its coating efficiency allows pathobionts to adhere more effectively to the epithelial wall, maintaining a state of chronic antigenic stimulation. Moreover, the gut microbiota influences systemic humoral immunity, affecting the maturation of B cells and the production of specific antibodies that can either inhibit or facilitate tumor progression (48-51). In addition to its role in development, a series of recent reports has shown that the composition of the gut microbiome can significantly influence patient responses to immunotherapy. Specific bacteria, such as *Bifidobacterium* and *Akkermansia*, are associated with improved responses to immune checkpoint inhibitors in the treatment of various cancers. This finding suggests that the gut microbiome influences not only cancer development but also the effectiveness of modern treatments (52, 53).

Probiotics and Their Potential in the Prevention and Treatment of CRC

Since dysbiosis plays an important role in the development of CRC, strategies to restore microbiome homeostasis, with the use of probiotics among them, have increasingly been viewed as preventive and therapeutic strategies for the disease (54). Probiotics are live microorganisms that, when ingested in adequate quantities, confer a health benefit to the host. Their anti-tumor effects are multimodal and extend beyond the mere normalization of microbial equilibrium (55-57). Figure 3 compares a healthy gut, a dysbiotic gut that leads to carcinogenesis, and the effects of subsequent probiotic intervention. Probiotic treatment ultimately helps restore microbial balance and reduce inflammation, thereby inhibiting tumor growth.

Anti-Cancer Mechanisms of Probiotics

Probiotics suppress carcinogenic processes through several direct and indirect mechanisms (Table 2) (58):

Modulation of Immune System: Probiotics can modulate the immune system of the gut towards an anti-tumor effect. Probiotics modulate immune cells, i.e., dendritic cells and macrophages, to secrete more anti-inflammatory cytokines and activate cytotoxic T cells. These cells are essential for identifying and destroying cancer cells. Probiotics also modulate immune responses to prevent chronic inflammation, a precancerous state (59-61).

Pathogenic Bacterial Competition: By occupying gut mucosa ecological niches, probiotics compete against carcinogenic bacteria, such as *Fusobacterium nucleatum* and *Escherichia coli*. Competition occurs through the use of food substrates and intestinal epithelial cell attachment sites, thereby preventing pathogenic bacterial growth and colonization (62-64).

Production of Anti-Tumor Compounds: Probiotics exert anti-cancer effects by producing specific metabolites and compounds. The most prominent among these is increased production of SCFAs, particularly butyrate. As noted previously, butyrate directly inhibits tumor growth by suppressing HDAC activity and inducing cancer cell apoptosis. In addition to SCFAs, specific probiotic strains can produce other anti-cancer metabolites, such as conjugated linoleic acid (CLA) and antimicrobial peptides (36, 65-67).

Establishing the Efficacy of Single Probiotic Strains

Probiotic trials have established that their potency is strain-dependent and that the activity of one strain should not be extrapolated to another. Numerous studies have focused on the genera *Lactobacillus* and *Bifidobacterium*:

Positive Results: Research has shown that supplementation with strains such as *Lactobacillus rhamnosus* and *Bifidobacterium longum* reduces the number and size of precancerous polyps. In human clinical trials, although the evidence is not yet

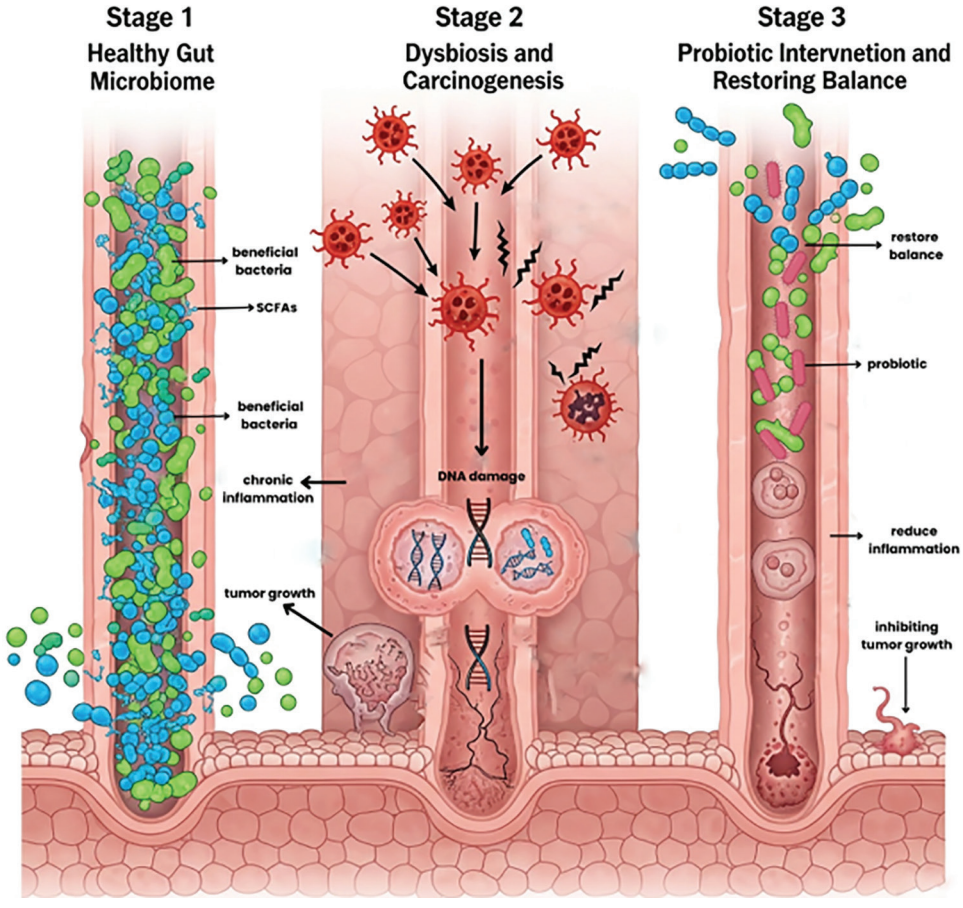

Figure 3: Comparison of a Healthy Gut with a Dysbiotic Gut that Leads to Carcinogenesis, and Subsequent Probiotic Intervention. Stage 1 shows a healthy gut microbiome with beneficial bacteria (green and blue) and short-chain fatty acid production, which strengthens the intestinal barrier. Stage 2 shows a state of dysbiosis where harmful bacteria (red and orange) cause DNA damage and chronic inflammation, leading to tumor growth. In Stage 3, probiotic interventions help restore balance and reduce inflammation, inhibiting tumor growth.

Table 2: Anti-Cancer Mechanisms of Probiotics

Probiotics' Anti-Cancer Mechanisms	Description	Key Points
1. Modulation of the Immune System	Modulates immune cells (e.g., dendritic cells and macrophages) to secrete higher amounts of anti-inflammatory cytokines. Stimulates cytotoxic T cells, which identify and destroy cancer cells. Prevents chronic inflammation, a known precancerous state.	Modulates the host's immune system to mount an anti-tumor response.
2. Pathogenic Bacterial Competition	Competes with carcinogenic bacteria such as *Fusobacterium nucleatum* and *Escherichia coli* for ecological niches on the gut mucosa. Outcompetes pathogens for food substrates and intestinal epithelial cell attachment sites, thus inhibiting their growth and colonization.	Competes with pathogenic bacteria to prevent their colonization of the gut.
3. Production of Anti-Tumor Compounds	Produces short-chain fatty acids (SCFAs), particularly butyrate, which directly counteracts tumor growth by inhibiting HDAC and inducing apoptosis. Produces other anti-cancer metabolites, such as conjugated linoleic acid (CLA) and antimicrobial peptides.	Produces butyrate and other beneficial compounds to suppress the growth of cancer cells.

definitive, probiotic supplementation has been shown to reduce inflammation and regulate the expression of cancer-related genes in patients with CRC (68, 69).

Current Challenges: These include determining the optimal dose, ideal strain, and treatment duration. Additionally, inter-individual variability in microbiome composition and diet may hamper probiotic efficacy. Large-scale, standardized clinical trials will be needed to confirm these findings and to integrate probiotics into treatment recommendations (70-72).

Challenges, Limitations, and Future Perspectives

Although evidence for the role of the gut microbiome in CRC is promising, critical barriers to clinical translation remain, primarily involving methodological challenges and therapeutic constraints. A major methodological hurdle is the diversity and lack of standardization of data, as studies vary in sample types and sequencing protocols, making it difficult to compare results (20, 73). Additionally,

there is a shortage of longitudinal research, which is necessary to fully understand the causal association between cancer and dysbiosis. Probiotic interventions also face operational challenges, including the lack of proven protocols for dose and duration, as well as the high strain-dependence and individual microbiome heterogeneity that influence effectiveness (74, 75). Safety remains a concern for immunocompromised patients, alongside the technological challenge of ensuring probiotic stability during transit to the large intestine (64, 76). Future research should move toward advanced methods such as Whole-Genome Metagenomics to analyze functional potential and personalized medicine (77). By tailoring treatments to an individual's microbiome profile – for example, using specific combinations of prebiotics or probiotics – the efficacy of both conventional and microbial-based treatments can be significantly improved (78, 79).

Conclusion

The interaction between dysbiosis (intestinal microbiota imbalance) and CRC is highly complex and multifaceted. As the body of literature suggests, the gut microbiota, rather than being a passive observer, plays an active role in carcinogenesis. This interaction occurs via detailed molecular mechanisms, such as production of carcinogenic metabolites and modulation of host inflammatory and immune responses. The reduction of butyrate-producing beneficial bacteria and the increased abundance of oncogenic pathogens such as *Fusobacterium nucleatum* are the most significant features of this microbiological dysbiosis and play a direct role in tumor initiation and growth.

Given the central role of dysbiosis in the etiopathogenesis of CRC, therapies targeting the gut microbiota, specifically the application of probiotics, hold promise as preventive and therapeutic strategies. Probiotics are effective anticancer tools because they reconstitute microbial balance, suppress inflammation, produce anti-tumor metabolites, and modulate immune mechanisms.

Nevertheless, for these discoveries to be translated into clinical practice, methodological challenges remain. Foremost among these is the need to establish the optimal strain and dose, which has yet to be achieved. Innovative studies are increasingly focusing on whole-genome metagenomics and, more importantly, on personalized medicine, in which therapies are tailored to each individual's microbial signature, which holds enormous promise for more effective treatments. Indeed, in the near future, knowledge of the gut microbial ecosystem will enrich not only the management of CRC but also open up novel microbial therapies for other human pathologies.

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Authors' Contribution

R. N. and P. S. have read and approved the final version of the manuscript. R. N. and P. S. were involved in conceptualization; R. N. was involved in literature search and drafting and writing of the manuscript. R. N. and P. S. were involved in writing and reviewing of the manuscript. P. S. was involved in supervision and project management.

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References

1. Gomaa EZ. Human gut microbiota/microbiome in health and diseases: a review. Antonie Van Leeuwenhoek. 2020;113(12):2019–40.
2. Çakırlar FK. Microbiota and Metabolic Syndrome. Metabolic Syndrome: A Comprehensive Update with New Insights: Bentham Science Publishers; 2025. p. 295–327.
3. de Almeida JIS. Generation and large-scale expansion of highly functional hpsc-derived hepatocytes for cellular therapies and bioengineered livers: the unknown role of human microbiome: Universidad de Zaragoza; 2022.
4. Parizadeh M, Arrieta M-C. The global human gut microbiome: genes, lifestyles, and diet. Trends in Molecular Medicine. 2023;29(10):789–801.
5. Portincasa P, Bonfrate L, Vacca M, et al. Gut microbiota and short chain fatty acids: implications in glucose homeostasis. International journal of molecular sciences. 2022;23(3):1105.
6. Ahamad R, Parveen S. Gut Microbiota and Nutrient Enrichment: Mechanism and Production of Vitamins. Probiotics: CRC Press; 2024. p. 56–75.
7. Wiertsema SP, van Bergenhenegouwen J, Garssen J, et al. The interplay between the gut microbiome and the immune system in the context of infectious diseases throughout life and the role of nutrition in optimizing treatment strategies. Nutrients. 2021;13(3):886.
8. Khan I, Bai Y, Zha L, et al. Mechanism of the gut microbiota colonization resistance and enteric pathogen infection. Frontiers in Cellular and Infection Microbiology. 2021;11:716299.
9. Kim B, Song A, Son A, et al. Gut microbiota and epigenetic choreography: Implications for human health: A review. Medicine. 2024;103(29):e39051.
10. Xi Y, Xu P. Global colorectal cancer burden in 2020 and projections to 2040. Translational oncology. 2021;14(10):101174.
11. Klimeck L, Heisser T, Hoffmeister M, et al. Colorectal cancer: A health

and economic problem. Best practice & research clinical gastroenterology. 2023;66:101839.
12. Hossain MS, Karuniawati H, Jairoun AA, et al. Colorectal cancer: a review of carcinogenesis, global epidemiology, current challenges, risk factors, preventive and treatment strategies. Cancers. 2022;14(7):1732.
13. Fan X, Jin Y, Chen G, et al. Gut microbiota dysbiosis drives the development of colorectal cancer. Digestion. 2021;102(4):508–15.
14. Hrncir T. Gut microbiota dysbiosis: triggers, consequences, diagnostic and therapeutic options. MDPI; 2022. p. 578.
15. Jandhyala SM, Talukdar R, Subramanyam C, et al. Role of the normal gut microbiota. World journal of gastroenterology: WJG. 2015;21(29):8787.
16. Hossain KS, Amarasena S, Mayengbam S. B vitamins and their roles in gut health. Microorganisms. 2022;10(6):1168.
17. Tarracchini C, Lordan C, Milani C, et al. Vitamin biosynthesis in the gut: interplay between mammalian host and its resident microbiota. Microbiology and Molecular Biology Reviews. 2025;89(2):e00184–23.
18. Role of the Gut Microbiome in Colorectal Cancer: 서울대학교 대학원; 2025.
19. Joo JE, Chu YL, Georgeson P, et al. Intratumoral presence of the genotoxic gut bacteria pks+ E. coli, Enterotoxigenic Bacteroides fragilis, and Fusobacterium nucleatum and their association with clinicopathological and molecular features of colorectal cancer. British Journal of Cancer. 2024;130(5):728–40.
20. Kamel F, Eltarhoni K, Nisar P, et al. Colorectal cancer diagnosis: the obstacles we face in determining a non-invasive test and current advances in biomarker detection. Cancers. 2022;14(8):1889.
21. Li S, Liu J, Zheng X, et al. Tumorigenic bacteria in colorectal cancer: mechanisms and treatments. Cancer biology & medicine. 2022;19(2):147–62.
22. Ionescu VA, Diaconu CC, Gheorghe G, et al. Gut Microbiota and Colorectal Cancer: A Balance Between Risk and Protection. International Journal of Molecular Sciences. 2025;26(8):3733.
23. Gasaly N, Hermoso MA, Gotteland M. Butyrate and the fine-tuning of colonic homeostasis: implication for inflammatory bowel diseases. International journal of molecular sciences. 2021;22(6):3061.
24. Carson TL, Byrd DA, Smith KS, et al. A case–control study of the association between the gut microbiota and colorectal cancer: exploring the roles of diet, stress, and race. Gut Pathogens. 2024;16(1):13.
25. Nagata N, Nishijima S, Kojima Y, et al. Metagenomic identification of microbial signatures predicting pancreatic cancer from a multinational study. Gastroenterology. 2022;163(1):222–38.
26. Lee JB, Kim K-A, Cho HY, et al. Association between Fusobacterium nucleatum and patient prognosis in metastatic colon cancer. Scientific reports. 2021;11(1):20263.
27. Ye C, Liu X, Liu Z, et al. Fusobacterium nucleatum in tumors: from tumorigenesis to tumor metastasis and tumor resistance. Cancer biology & therapy. 2024;25(1):2306676.
28. Saraiva MR, Rosa I, Claro I. Early-onset colorectal cancer: A review of current knowledge. World journal of gastroenterology. 2023;29(8):1289.
29. Beniwal SS, Lamo P, Kaushik A, et al. Current status and emerging trends in colorectal cancer screening and diagnostics. Biosensors. 2023;13(10):926.
30. Zhang H, Shi Y, Lin C, et al. Overcoming cancer risk in inflammatory bowel disease: new insights into preventive strategies and pathogenesis mechanisms including interactions of immune cells, cancer signaling pathways, and gut microbiota. Frontiers in immunology. 2024;14:1338918.
31. Burgos-Molina AM, Téllez Santana T, Redondo M, et al. The crucial role of inflammation and the immune system in colorectal cancer carcinogenesis: a comprehensive perspective. International Journal of Molecular Sciences. 2024;25(11):6188.
32. Sun H, Zhai Q, Liu J, et al. Interplay between the gut microbiota, its metabolites and carcinogens. Clinical and Translational Oncology. 2025:1–14.
33. Vinelli V, Biscotti P, Martini D, et al. Effects of dietary fibers on short-chain fatty acids and gut microbiota composition in healthy adults: a systematic review. Nutrients. 2022;14(13):2559.
34. Salvi PS, Cowles RA. Butyrate and the intestinal epithelium: modulation of proliferation and inflammation in homeostasis and disease. Cells. 2021;10(7):1775.
35. Mederle AL, Semenescu A, Drăghici GA, et al. Sodium Butyrate: A Multifaceted Modulator in Colorectal Cancer Therapy. Medicina. 2025;61(1):136.
36. Mohamed Elfadil O, Mundi MS, Abdelmagid MG, et al. Butyrate: more than a short chain fatty acid. Current nutrition reports. 2023;12(2):255–62.
37. Schmitt M, Greten FR. The inflammatory pathogenesis of colorectal cancer. Nature Reviews Immunology. 2021;21(10):653–67.
38. Gieryńska M, Szulc-Dąbrowska L, Struzik J, et al. Integrity of the intestinal barrier: the involvement of epithelial cells and microbiota—a mutual relationship. Animals. 2022;12(2):145.
39. Di Vincenzo F, Del Gaudio A, Petito V, et al. Gut microbiota, intestinal permeability, and systemic inflammation: a narrative review. Internal and emergency medicine. 2024;19(2):275–93.
40. Kaur H, Ali SA. Probiotics and gut microbiota: Mechanistic insights into gut immune homeostasis through TLR pathway regulation. Food & Function. 2022;13(14):7423–47.
41. Candelli M, Franza L, Pignataro G, et al. Interaction between lipopolysaccharide and gut microbiota in inflammatory bowel diseases. International journal of molecular sciences. 2021;22(12):6242.
42. Sadati S, Khalaji A, Bonyad A, et al. NF-κB and apoptosis: colorectal cancer progression and novel strategies for treatment. European Journal of Medical Research. 2025;30(1):616.
43. Zhao H, Wu L, Yan G, et al. Inflammation and tumor progression: signaling pathways and targeted intervention. Signal transduction and targeted therapy. 2021;6(1):263.
44. Augustine T, Kumar M, Al Khodor S, et al. Microbial dysbiosis tunes the immune response towards allergic disease outcomes. Clinical Reviews in Allergy & Immunology. 2023;65(1):43–71.
45. Cremonesi E, Governa V, Garzon JFG, et al. Gut microbiota modulate T cell trafficking into human colorectal cancer. Gut. 2018;67(11):1984–94.
46. Aghamajidi A, Maleki Vareki S. The effect of the gut microbiota on systemic and anti-tumor immunity and response to systemic therapy against cancer. Cancers. 2022;14(15):3563.
47. Pinco P, Facciotti F. Unconventional T Cells' Role in Cancer: Unlocking Their Hidden Potential to Guide Tumor Immunity and Therapy. Cells. 2025;14(10):720.
48. Li Y, Jin L, Chen T. The effects of secretory IgA in the mucosal immune system. BioMed research international. 2020;2020(1):2032057.

49. Abokor AA, McDaniel GH, Golonka RM, et al. Immunoglobulin A, an active liaison for host-microbiota homeostasis. Microorganisms. 2021;9(10):2117.
50. Botía-Sánchez M, Alarcón-Riquelme ME, Galicia G. B cells and microbiota in autoimmunity. International Journal of Molecular Sciences. 2021;22(9):4846.
51. Ge Y, Wang X, Guo Y, et al. Gut microbiota influence tumor development and Alter interactions with the human immune system. Journal of Experimental & Clinical Cancer Research. 2021;40(1):42.
52. Kiousi DE, Kouroutzidou AZ, Neanidis K, et al. The role of the gut microbiome in cancer immunotherapy: current knowledge and future directions. Cancers. 2023;15(7):2101.
53. Li X, Zhang S, Guo G, et al. Gut microbiome in modulating immune checkpoint inhibitors. EBioMedicine. 2022;82.
54. Fong W, Li Q, Yu J. Gut microbiota modulation: a novel strategy for prevention and treatment of colorectal cancer. Oncogene. 2020;39(26):4925–43.
55. Gupta V, Garg R. Probiotics. Indian journal of medical microbiology. 2009;27(3):202–9.
56. Parichat P, Pongsak R. Probiotics: Sources, selection and health benefits. Res J Biotechnol. 2023;18:5.
57. Barone M, Tavella T, Rampelli S, et al. Host microbiomes in tumor precision medicine: how far are we? Current Medicinal Chemistry. 2022;29(18):3202–30.
58. Mazziotta C, Tognon M, Martini F, et al. Probiotics mechanism of action on immune cells and beneficial effects on human health. Cells. 2023;12(1):184.
59. Ye Z, Liang L, Xu Y, et al. Probiotics influence gut microbiota and tumor immune microenvironment to enhance anti-tumor efficacy of doxorubicin. Probiotics and Antimicrobial Proteins. 2024;16(2):606–22.
60. Yeşilyurt N, Yılmaz B, Ağagündüz D, et al. Involvement of probiotics and postbiotics in the immune system modulation. Biologics. 2021;1(2):89–110.
61. Naeem H, Hassan HU, Shahbaz M, et al. Role of probiotics against human cancers, inflammatory diseases, and other complex malignancies. Journal of Food Biochemistry. 2024;2024(1):6632209.
62. Gong D, Adomako-Bonsu AG, Wang M, et al. Three specific gut bacteria in the occurrence and development of colorectal cancer: a concerted effort. PeerJ. 2023;11:e15777.
63. Wong CC, Yu J. Gut microbiota in colorectal cancer development and therapy. Nature reviews Clinical oncology. 2023;20(7):429–52.
64. Han S, Lu Y, Xie J, et al. Probiotic gastrointestinal transit and colonization after oral administration: a long journey. Frontiers in cellular and infection microbiology. 2021;11:609722.
65. Thoda C, Touraki M. Molecular Mechanisms of Probiotic Action Against Gastrointestinal Cancers. International Journal of Molecular Sciences. 2025;26(16):7857.
66. Peng F, Li S, Wang L, et al. Combination of Hdac Inhibitor Sodium Butyrate and Immunotherapy in Glioma: Regulation of Immunologically Hot and Cold Tumors Via Gut Microbiota and Metabolites. Available at SSRN 4942877.
67. George J, Ghosh AR. Conjugated Linoleic Acid in Cancer Therapy. Current Drug Delivery. 2025;22(4):450–64.
68. Kazmierczak-Siedlecka K, Roviello G, Catalano M, et al. Gut microbiota modulation in the context of immune-related aspects of Lactobacillus spp. and Bifidobacterium spp. in gastrointestinal cancers. Nutrients. 2021;13(8):2674.
69. Dikeocha IJ, Al-Kabsi AM, Eid EE, et al. Probiotics supplementation in patients with colorectal cancer: a systematic review of randomized controlled trials. Nutrition Reviews. 2022;80(1):22–49.
70. Maftei N-M, Raileanu CR, Balta AA, et al. The potential impact of probiotics on human health: an update on their health-promoting properties. Microorganisms. 2024;12(2):234.
71. Wolter M, Grant ET, Boudaud M, et al. Leveraging diet to engineer the gut microbiome. Nature reviews Gastroenterology & hepatology. 2021;18(12):885–902.
72. Fassarella M, Blaak EE, Penders J, et al. Gut microbiome stability and resilience: elucidating the response to perturbations in order to modulate gut health. Gut. 2021;70(3):595–605.
73. Khannous-Lleiffe O, Willis JR, Saus E, et al. Microbiome profiling from fecal immunochemical test reveals microbial signatures with potential for colorectal cancer screening. Cancers. 2022;15(1):120.
74. Budu O, Banciu C, Pinzaru I, et al. A combination of two probiotics, Lactobacillus sporogenes and Clostridium butyricum, inhibits Colon Cancer Development: an in Vitro Study. Microorganisms. 2022;10(9):1692.
75. Meroni G, Panelli S, Zuccotti G, et al. Probiotics as therapeutic tools against pathogenic biofilms: have we found the perfect weapon? Microbiology Research. 2021;12(4):916–37.
76. Yang Z, Zhang S, Ying L, et al. The effect of probiotics supplementation on cancer-treatment complications: A critical umbrella review of interventional meta-analyses. Critical Reviews in Food Science and Nutrition. 2025;65(19):3702–27.
77. Purushothaman S, Meola M, Egli A. Combination of whole genome sequencing and metagenomics for microbiological diagnostics. International journal of molecular sciences. 2022;23(17):9834.
78. Shukla V, Singh S, Verma S,et al. Targeting the microbiome to improve human health with the approach of personalized medicine: Latest aspects and current updates. Clinical Nutrition ESPEN. 2024;63:813–20.
79. Singh TP, Natraj BH. Next-generation probiotics: a promising approach towards designing personalized medicine. Critical Reviews in Microbiology. 2021;47(4):479–98.