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Targeted Therapy for Colorectal Cancer Using Probiotics as an Advanced Therapy

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Abstract

Colorectal cancer (CRC) is among the most prevalent cancers globally and continues to represent a significant contributor to cancer-related morbidity and mortality. Despite significant advancements in surgical techniques, chemotherapy, targeted treatments, and immunotherapeutic approaches, and variable treatment responses continue to limit clinical outcomes. Accumulating evidence suggests that the intestinal microbiota is closely involved in the development of colorectal cancer and may modulate tumor growth, host immune responses, and the efficacy of anticancer therapies. Probiotics have therefore emerged as promising microbiota-modulating agents with potential applications in CRC prevention and therapy. This review summarizes current evidence regarding the therapeutic potential of probiotics in CRC, focusing on their anticancer mechanisms, probiotic-derived metabolites, advanced targeted delivery systems.

Probiotics may contribute to cancer prevention and control through several interconnected mechanisms, including the re-establishment of gut microbial homeostasis, strengthening of the intestinal barrier, regulation of inflammatory and immune pathways, suppression of cancer-cell growth, promotion of programmed cell death, and generation of biologically active compounds, notably short-chain fatty acids. Recent progress in synthetic biology and advanced encapsulation techniques has facilitated the design of engineered probiotic systems that can serve as vehicles for targeted delivery of therapeutic agents. Although preclinical findings are encouraging, clinical evidence remains heterogeneous and insufficient to establish probiotics as standalone anticancer treatments. Strain specificity, dosage, formulation, safety, and interactions with conventional therapies remain important challenges. Future research should emphasize precision probiotic selection, engineered microbial therapeutics, targeted delivery platforms, and integration with chemotherapy and immunotherapy. Overall, probiotics represent a promising foundation for developing advanced, targeted, and personalized microbiome-based therapeutic strategies for CRC.

Keywords: Colorectal cancer, Probiotics; Gut microbiome, Targeted therapy, Microbial metabolites.

Introduction

Colorectal Cancer: Current Challenges and Therapeutic Limitations

Colorectal cancer (CRC) ranks among the most frequently diagnosed and deadly cancers globally and constitutes a substantial burden on public health. Although substantial advances in early detection, surgical management, chemotherapy, molecularly

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targeted therapy, and immunotherapy have improved clinical outcomes, the treatment of CRC remains challenging, particularly in patients with locally advanced or metastatic disease. The molecular heterogeneity of CRC, including alterations in pathways involving KRAS, NRAS, BRAF, EGFR, HER2, and the mismatch repair (MMR)/ microsatellite instability (MSI) system, contributes to considerable interpatient and intratumoral variability in therapeutic response. Consequently, treatment selection increasingly depends on molecular profiling and predictive biomarkers; however, the clinical benefit of targeted approaches remains restricted to specific molecular subgroups (1-2).

Despite these therapeutic advances, primary and acquired drug resistance remains one of the major limitations in CRC management. Resistance can arise through secondary genetic alterations, activation of alternative signaling pathways, clonal selection, tumor-cell plasticity, and interactions with the tumor microenvironment. Moreover, chemotherapy-associated toxicity and the limited efficacy of immunotherapy in many patients, particularly those with mismatch repair-proficient/microsatellite-stable tumors, further emphasize the need for novel therapeutic strategies.The complexity of these resistance mechanisms highlights the importance of developing approaches that can selectively target tumor-associated pathways while minimizing systemic toxicity. In this context, modulation of the gut microbiota and the use of probiotics have emerged as promising complementary strategies, potentially providing a biological basis for more targeted and advanced therapeutic approaches in CRC (1-3).

The Gut Microbiome and Colorectal Cancer

Growing evidence has established the gut microbiota as a key component of the tumor microenvironment in colorectal cancer (CRC), with complex interactions between intestinal microorganisms, epithelial cells, immune responses, and microbial metabolites contributing to colorectal carcinogenesis. Disruption of the normal intestinal microbial ecosystem, commonly referred to as gut dysbiosis, is frequently observed in individuals with colorectal cancer. This condition involves substantial shifts in the abundance, diversity, and relative distribution of bacterial populations, resulting in an imbalance between potentially harmful microorganisms and health-promoting commensal species. Several bacterial taxa have been implicated in colorectal tumorigenesis, with *Fusobacterium nucleatum*, enterotoxigenic *Bacteroides fragilis*, and genotoxic strains of *Escherichia coli* receiving particular attention. These microorganisms may contribute to colorectal carcinogenesis by promoting a persistent inflammatory state and altering the local intestinal environment in ways that favor tumor initiation and progression (2-4).

The contribution of the intestinal microbiota to colorectal cancer extends beyond changes in the composition of bacterial communities. A major part of its biological activity is mediated through metabolites generated during microbial metabolism. Compounds such as short-chain fatty acids (SCFAs), modified bile acids, indole-derived molecules, polyamines, and other signaling metabolites can interact with intestinal epithelial cells and immune populations, thereby affecting multiple processes involved in intestinal homeostasis and tumor biology. Through these interactions, microbial metabolites may regulate epithelial barrier function, inflammatory responses, immune activity, cellular proliferation, and programmed cell death. Depending on the microbial environment and metabolic profile, these effects may either promote malignant transformation or contribute to the maintenance of antitumor conditions (4-5).

The microbiota can also modify how patients respond to anticancer therapies by influencing both treatment effectiveness and therapy-associated adverse effects. These interactions are particularly relevant to chemotherapy and immune-based treatments, in which the intestinal microbial environment may affect drug activity, host immune responses, and treatment tolerance. Therefore, strategies aimed at reshaping or controlling the gut microbiota have emerged as a potential component of CRC management. In this context, probiotics and other microbiome-directed approaches (4-5).

Probiotics and Their Therapeutic Potential in CRC

Probiotics have gained considerable attention as potential microbiome-based interventions in colorectal cancer because of their capacity to influence the intestinal ecosystem and host–microbe interactions. Their biological activity is not limited to a single pathway; rather, different probiotic strains may exert beneficial effects through multiple mechanisms. These include reshaping an imbalanced microbial community, strengthening epithelial barrier function, and regulating local inflammatory processes and host immune activity. Probiotic microorganisms can also generate metabolites with biological activity, particularly short-chain fatty acids, which may contribute to maintaining intestinal homeostasis. Furthermore, by competing with harmful bacteria and reducing the abundance or activity of microorganisms associated with carcinogenesis, probiotics may create a less favorable environment for tumor development. Experimental findings have additionally indicated that some probiotic strains can directly affect malignant cells by reducing their proliferative capacity, promoting programmed cell

death, and altering molecular pathways involved in colorectal tumor growth. Taken together, these diverse interactions with the intestinal microbiota, epithelial tissue, immune system, and tumor cells provide a biological basis for considering probiotics as potential agents for both CRC prevention and therapeutic management (4- 6).

Beyond their direct antitumor effects, probiotics may have potential as adjunctive therapeutic agents alongside conventional CRC treatments. Evidence from clinical and preclinical studies indicates that probiotic supplementation may help alleviate treatment-associated gastrointestinal complications, improve intestinal microbiota composition, and potentially enhance the therapeutic efficacy of chemotherapy and other anticancer interventions. However, the effects of probiotics are highly dependent on bacterial strain, dose, formulation, treatment duration, and host-specific factors. Therefore, despite promising findings, further well-designed clinical studies are required to establish strain-specific efficacy, optimal dosing regimens, safety profiles, and potential interactions with anticancer therapies. These considerations are particularly relevant to the development of probiotics as advanced and targeted therapeutic strategies for CRC (6- 7).

Targeted Anticancer Mechanisms of Probiotics

Probiotics exert anticancer effects against colorectal cancer (CRC) through multiple, interconnected molecular and cellular mechanisms. At the cellular level, probiotics may exert anticancer activity by directly altering molecular processes that control the survival and growth of colorectal tumor cells. Certain probiotic strains and the metabolites they produce have been reported to interfere with mechanisms responsible for uncontrolled cell division and to activate pathways associated with apoptosis. This activity may involve enhancement of apoptotic mediators, including BAX and caspase proteins, together with a reduction in the expression or activity of anti-apoptotic factors such as BCL-2. Probiotic-associated effects have also been linked to changes in major intracellular signaling networks, including the PI3K/AKT, MAPK, and NF-κB pathways, which play important roles in tumor-cell proliferation, survival, and inflammatory responses. Among microbiota-derived compounds, short-chain fatty acids (SCFAs) have attracted particular interest because of their ability to interact with colorectal epithelial and tumor cells. Butyrate, one of the principal SCFAs generated by intestinal bacteria, may alter cellular metabolism and gene regulation and thereby contribute to the suppression of malignant-cell growth and induction of apoptotic responses (6- 7).

Beyond direct effects on tumor cells, probiotics can modify the tumor-associated inflammatory and immune microenvironment, providing an additional mechanism for targeted anticancer activity. Probiotic strains and their metabolites may suppress pro-inflammatory signaling, including the TLR4/MyD88/NF-κB and NLRP3 pathways, while promoting intestinal barrier integrity and regulating cytokine production. Furthermore, modulation of host immunity can enhance antitumor responses through increased activity of cytotoxic immune cells and improved immune surveillance. These combined effects, direct inhibition of tumor growth, induction of apoptosis, attenuation of chronic inflammation, and enhancement of antitumor immunity, support the potential of probiotics and probiotic-derived molecules as microbiota-based therapeutic tools for CRC (8- 9).

Probiotic-Derived Metabolites as Therapeutic Targets

Probiotic-derived metabolites have emerged as important mediators of the anticancer effects associated with beneficial microorganisms and represent promising therapeutic targets in colorectal cancer (CRC). Among these metabolites, short-chain fatty acids (SCFAs), particularly butyrate, acetate, and propionate, have received considerable attention because of their ability to regulate intestinal epithelial homeostasis, inflammatory responses, and tumor-cell behavior. Butyrate can function as an energy substrate for normal colonocytes while exerting antitumor effects suppression of proliferative signaling, and induction of apoptosis in colorectal cancer cells. Importantly, supplementation with SCFA-producing probiotics may increase the local availability of these metabolites and consequently contribute to restoration of a metabolically favorable intestinal environment.

Beyond SCFAs, probiotic-associated metabolites and bioactive compounds, including bacteriocins, exopolysaccharides, lactate, indole derivatives, and other microbial products, may influence CRC through modulation of inflammation, intestinal barrier integrity, immune responses, and tumor-associated signaling pathways. In contrast, dysbiosis can increase the production of potentially tumor-promoting metabolites, highlighting the importance of restoring a favorable microbial metabolic profile rather than simply increasing bacterial abundance. Therefore, targeting probiotic-derived metabolites represents a potentially more precise therapeutic strategy, in which specific microbial metabolic pathways could be manipulated through probiotics, prebiotics, dietary substrates, postbiotics, or engineered microbial systems to enhance beneficial metabolites and suppress pro-tumorigenic metabolic

signals (10- 11).

Advanced and Targeted Probiotic-Based Therapies

Recent advances in synthetic biology, nanotechnology, and drug-delivery systems have expanded the therapeutic potential of probiotics beyond their conventional role in microbiota modulation. Engineered probiotics can be genetically modified to express therapeutic proteins, peptides, enzymes, or immunomodulatory molecules and may be designed to preferentially localize within the tumor microenvironment. For example, engineered Escherichia coli Nissle 1917 has been investigated as a tumor-targeting probiotic platform capable of delivering anticancer molecules directly to colorectal tumors. Such approaches can potentially increase local therapeutic concentrations while reducing systemic exposure and off-target toxicity. In addition, inducible genetic circuits may allow therapeutic payloads to be expressed in response to specific characteristics of the tumor microenvironment, providing an additional level of spatial and functional control.

Another emerging strategy involves targeted delivery and encapsulation of probiotics to improve their survival during gastrointestinal transit and enhance their accumulation at the colorectal tumor site. Advanced micro- and nano-encapsulation systems can protect probiotic cells from gastric acidity, bile salts, and other adverse gastrointestinal conditions while improving mucosal adhesion, colon-specific release, and bacterial viability.[2] Single-cell encapsulation and responsive nanocoatings represent particularly promising approaches because they can provide controlled release in response to specific physicochemical or biological characteristics of the intestinal and tumor microenvironment.[2] Collectively, these technologies may transform probiotics from conventional microbiome-modulating agents into precision therapeutic platforms capable of targeted delivery, controlled release, and localized anticancer activity in CRC. However, their clinical translation still requires rigorous evaluation of safety, stability, targeting specificity, dosing, and long-term effects (12- 13).

Preclinical and Clinical Evidence Supporting the Therapeutic Potential

Preclinical evidence provides substantial support for the potential anticancer activity of probiotics in colorectal cancer (CRC). Findings obtained from in vitro experiments and preclinical animal models suggest that probiotic microorganisms, especially species belonging to the *Lactobacillus* and *Bifidobacterium* groups, may interfere with the development of colorectal tumors. Their proposed anticancer activity appears to involve several interconnected processes, such as limiting the growth of malignant cells, activating apoptotic mechanisms, reducing intestinal and systemic inflammatory activity, and improving epithelial barrier integrity. In addition, these microorganisms may influence host immune regulation and modify microbial metabolic processes, which can collectively contribute to creating an intestinal environment less favorable to colorectal carcinogenesis.

A systematic assessment of preclinical animal research indicated that most of the studies analyzed reported beneficial effects associated with probiotic interventions in colorectal lesions or tumor development following probiotic administration, although considerable heterogeneity in probiotic strains, doses, experimental models, and study quality limits direct comparison between studies.

Clinical evidence is encouraging but remains less conclusive than the preclinical literature. Randomized controlled trials in patients with CRC have suggested that probiotic supplementation can improve gut microbial composition, reduce postoperative complications and treatment-associated gastrointestinal toxicity, and modulate inflammatory responses. However, clinical outcomes are highly dependent on the probiotic strain, formulation, dose, treatment duration, disease stage, and concomitant anticancer therapy. Importantly, current evidence does not yet establish probiotics as a stand-alone anticancer treatment, and larger, well-designed, strain-specific clinical trials are required to determine their therapeutic efficacy and optimal integration with chemotherapy, immunotherapy, and other targeted treatments (14- 15).

Challenges and Safety Considerations

Despite the promising therapeutic potential of probiotics in colorectal cancer (CRC), several challenges limit their translation into standardized clinical applications. One of the major concerns is the strain-specific nature of probiotic effects, as different strains within the same species may exhibit substantially different biological activities, mechanisms of action, and safety profiles. In addition, variability in dosage, formulation, viability, treatment duration, and host-specific factors can contribute to inconsistent outcomes among clinical studies. Safety assessment is particularly important when probiotics are considered as adjunctive therapies in cancer patients, who may have altered intestinal barriers or compromised immune function. Potential risks include opportunistic infections, gastrointestinal adverse effects, metabolic disturbances.

The development of probiotics as advanced therapeutic platforms also requires rigorous evaluation of genetic stability, virulence-associated

factors, antibiotic-resistance determinants, and product quality. These considerations become even more critical for engineered or next-generation probiotics designed to deliver therapeutic molecules directly to the tumor microenvironment. Current evidence emphasizes the importance of strain-level identification, whole-genome sequencing, standardized manufacturing, and systematic monitoring of adverse events before clinical translation. Furthermore, the heterogeneity of CRC and the complex interactions between probiotics, the resident microbiome, host immunity, and anticancer drugs make it difficult to predict therapeutic responses on an individual basis (16- 17).

Future Perspectives

The future development of probiotic-based therapies for colorectal cancer (CRC) is likely to move from conventional, non-specific supplementation toward precision microbiome medicine. Advances in genomics, metabolomics, and microbiome profiling may enable the selection of specific probiotic strains according to the individual patient's microbial composition, tumor characteristics, and therapeutic response. In parallel, engineered probiotics and next-generation live biotherapeutics could be designed to sense tumor-associated signals and selectively deliver therapeutic molecules within the colorectal tumor microenvironment. Such programmable systems may provide greater targeting specificity and allow controlled production of anticancer proteins, immune-modulating factors, or therapeutic metabolites directly at the site of disease.

Another promising direction is the integration of probiotics with nanotechnology, targeted delivery systems, chemotherapy, and immunotherapy. Advanced encapsulation strategies may improve probiotic survival during gastrointestinal transit, enhance colon-specific delivery, and facilitate controlled release at the tumor site. Furthermore, combining microbiome modulation with immune checkpoint inhibitors or other targeted therapies could potentially overcome treatment resistance by reshaping the tumor-associated microbial and immune environment. Future research should therefore focus on strain-specific mechanisms, patient stratification using multi-omics approaches, standardized clinical protocols, and long-term safety evaluation. Ultimately, the development of personalized and engineered probiotic platforms may transform probiotics from conventional dietary supplements into precision living therapeutics for CRC (18- 19).

Conclusion

Colorectal cancer (CRC) arises from a complex interplay of genetic, environmental, microbial, and host-related factors, with the intestinal microbiota increasingly recognized as an important regulator of disease development and progression. Changes in the gut microbial ecosystem may affect tumorigenesis, immune-system activity, and the response of patients to anticancer interventions. Within this context, probiotics have attracted attention as potential microbiome-directed agents. Their proposed protective and therapeutic activities include rebalancing intestinal microbial communities, strengthening the epithelial barrier, regulating immune and inflammatory processes, generating biologically active metabolites, and restricting the proliferation and survival of colorectal cancer cells. Nevertheless, current evidence supports probiotics primarily as a complementary or adjunctive therapeutic strategy, rather than an established standalone treatment for CRC. The heterogeneity of probiotic strains, treatment protocols, patient populations, and clinical endpoints remains a major obstacle to translating promising experimental findings into standardized clinical applications.

Future development of probiotic-based CRC therapy should therefore focus on precision and targeted approaches, including strain-specific selection, engineered probiotics, targeted delivery systems, and integration with chemotherapy and immunotherapy. Recent advances in encapsulation technologies and live bacterial therapeutics provide opportunities to improve probiotic survival, colon-specific delivery, and localized release of therapeutic molecules within the tumor microenvironment. Large-scale, well-controlled clinical trials combined with multi-omics and microbiome profiling will be essential for identifying responsive patient populations and establishing optimal dosage, safety, and therapeutic combinations. Ultimately, the transition from conventional probiotic supplementation toward precision microbiome-based and engineered probiotic therapeutics may provide a promising avenue for improving the prevention and treatment of CRC (20- 21).

Overall, the available evidence supports a biologically plausible role for probiotics in CRC, particularly through modulation of the gut microbiome, intestinal barrier, inflammation, and microbial metabolites. However, the clinical evidence remains heterogeneous. Notably, the phase III trial by Mego et al. did not demonstrate a significant reduction in severe irinotecan-induced diarrhea in the overall population, highlighting the importance of strain specificity, patient selection, and personalized probiotic interventions (22- 25).

Taken together, the available evidence suggests that probiotics may serve as a valuable adjunct in the management of colorectal cancer by acting at multiple levels of the gut–tumor axis. Their

Table 1. Selected preclinical and clinical studies investigating probiotic-based approaches in colorectal cancer.

Study	Study type / Model	Probiotic intervention	Main objective	Key findings
Peluzio et al., 2020 (1)	Systematic review of preclinical and clinical studies	Probiotics and synbiotics	To evaluate the potential of probiotics/synbiotics in CRC prevention and identify their underlying mechanisms	Probiotics and synbiotics were associated with reduced inflammation, inhibition of tumor growth, induction of apoptosis, modulation of immune responses, improvement of intestinal barrier function, and production of potentially anticarcinogenic metabolites.
Wierzbicka et al., 2021 (2)	Systematic review of 6 clinical trials; 457 patients with CRC	Probiotics/synbiotics	To determine whether probiotic administration could modulate the gut microbiota in patients with CRC	Probiotic/synbiotic supplementation increased beneficial bacteria, including Lactobacillus and Bifidobacterium, while reducing potentially harmful bacteria. Improvements in intestinal permeability, tight-junction function, and inflammatory parameters were also reported.
Dikeocha et al., 2021 (3)	Systematic review of 23 randomized controlled trials To evaluate the clinical effects of probiotics in patients with CRC	Various Lactobacillus and Bifidobacterium-based preparations	To evaluate the clinical effects of probiotics in patients with CRC	Probiotic supplementation was associated with improved gut microbiota diversity, reduced postoperative infectious complications, decreased chemotherapy-related adverse effects, improved quality of life, and shorter hospital stays.
Mego et al., 2023 (4)	Phase III randomized, double-blind, placebo-controlled trial; 242 metastatic CRC patients	Bifidobacterium animalis BB-12 + Lacticaseibacillus rhamnosus GG To determine whether probiotics could prevent irinotecan-induced diarrhea	To determine whether probiotics could prevent irinotecan-induced diarrhea	The primary endpoint was not met: grade 3/4 diarrhea was 7.9% with probiotics vs 11.8% with placebo (P=0.38). However, a subgroup of patients with colostomy showed a potential benefit, including better diarrhea-free survival and reduced loperamide use. No probiotic-related infections were observed.
Yang et al., 2024 (5)	Preclinical study; AOM/DSS-induced CRC mouse model	Limosilactobacillus fermentum GR-3	To investigate whether a probiotic strain could prevent or attenuate colorectal tumorigenesis through microbiome modulation	GR-3 reduced tumor incidence by 51.2%, attenuated intestinal barrier disruption and inflammation, increased beneficial SCFA-associated bacteria and metabolites, and reduced potentially harmful secondary bile acids.

potential benefits include reshaping the intestinal microbial community, reinforcing epithelial barrier function, influencing host inflammatory and immune pathways, generating metabolites with potentially protective properties, and limiting the growth and viability of malignant cells. Nevertheless, substantial variation among probiotic strains, study designs, treatment protocols, and patient populations makes the existing clinical findings difficult to generalize. Therefore, although probiotics represent a promising complementary approach, current evidence does not support their use as an independent replacement for established anticancer therapies. Further well-designed clinical trials are required to determine

the most effective strains, doses, formulations, and treatment combinations for CRC (25- 27). Differences in probiotic strains, dosage, formulation, treatment duration, patient characteristics, and concomitant anticancer therapies represent major barriers to clinical translation. Future research should therefore move toward precision probiotic therapy, with strain-specific selection based on patient microbiome profiles and tumor characteristics. Advances in next-generation probiotics, engineered microorganisms, targeted encapsulation, and controlled delivery systems may enable localized delivery of therapeutic molecules to colorectal tumors and improve treatment efficacy while minimizing systemic effects. Large-scale randomized clinical trials combined with multi-omics approaches will be essential to establish optimal strains, doses, treatment combinations, and safety profiles, potentially transforming probiotics from conventional supplements into precision microbiome-based therapeutics for CRC.

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Data Availability

The data underlying the findings of this study can be obtained from the corresponding author upon reasonable request.

Declarations

Competing Interests

The authors confirm that they have no financial or non-financial conflicts of interest, nor any personal relationships that could be perceived as having influenced the research or its findings.

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

References

1.Mármol I, Sánchez-de-Diego C, Pradilla Dieste A, Cerrada E, Rodriguez Yoldi MJ. Colorectal carcinoma: a general overview and future perspectives in colorectal cancer. Int J Mol Sci. 2021;22(1):127. doi:10.3390/ijms22010127.

2.Tirendi S, Marengo A, Domenicotti C, Bassi AM, Almonti T, Vernazza C. Colorectal cancer and therapy response: a focus on the main mechanisms involved. Int J Mol Sci. 2023;24(15):12125. doi:10.3390/ijms241512125.

3.Dazio G, Epistolio S, Frattini M, Saletti P. Recent and future strategies to overcome resistance to targeted therapies and immunotherapies in metastatic colorectal cancer. J Clin Med. 2022;11(24):7523. doi:10.3390/jcm11247523.

4.Janney A, Powrie F, Mann EH. Host-microbiota maladaptation in colorectal cancer. Nature. 2023;615(7953):131-141. doi:10.1038/s41586-023-05796-0.

5. Wong SH, Yu J. Gut microbiota in colorectal cancer: mechanisms of action and clinical applications. Nat Rev Gastroenterol Hepatol. 2023;20(7):429-452. doi:10.1038/s41575-023-00766-x.

6.Rahmani N, Pourali G, Hosseini N, Fiuji H, Maftooh M, Hassanian SM, et al. Probiotics as a therapeutic approach in colorectal cancer. Curr Cancer Drug Targets. 2023;23(10):764-777. doi:10.2174/1568009623666230413081513

7.Ha S, Zhang X, Yu J. Probiotics intervention in colorectal cancer: from traditional approaches to novel strategies. Chin Med J (Engl). 2024;137(1):8-20. doi:10.1097/CM9.0000000000002955.

8.Huang Y, Wu S, Li Y, et al. Mechanism of probiotics in the intervention of colorectal cancer: a review. Appl Microbiol Biotechnol. 2024;108:528. doi:10.1007/s00253-024-13324-9.

9.Al-Waeli A, et al. Effects of probiotics at the interface of metabolism and immunity to prevent colorectal cancer-associated gut inflammation: a systematic network and meta-analysis with molecular docking studies. Front Microbiol. 2022;13:878297. doi:10.3389/fmicb.2022.878297.

10.Wong CC, Yu J. Gut microbiota in colorectal cancer development and therapy. Nat Rev Clin Oncol. 2023;20(7):429-452. doi:10.1038/s41571-023-00766-x.

11.Amara A, et al. Probiotic-derived bioactive compounds in colorectal cancer treatment. Biomed Pharmacother. 2023;164:114919. doi:10.1016/j.biopha.2023.114919.

12.Han H, Zhang Y, Tang H, Zhou T, Khan A. A review of the use of native and engineered probiotics for colorectal cancer therapy. Int J Mol Sci. 2024;25(7):3896. doi:10.3390/ijms25073896.

13.Zhong H, Jiang J, Chen L, Guan R. The encapsulation strategies for targeted delivery of probiotics in preventing and treating colorectal cancer: a review. Adv Sci (Weinh). 2025;12:e2500304. doi:10.1002/advs.202500304.

14.Brasiel PGA, et al. Preclinical evidence of probiotics in colorectal carcinogenesis: a systematic review. Dig Dis Sci. 2020;65(11):3197-

3210. doi:10.1007/s10620-020-06062-3.
15.Zawadzki PJ, et al. Probiotics supplementation in patients with colorectal cancer: a systematic review of randomized controlled trials. Am J Clin Nutr. 2021;113(6):1498-1510. doi:10.1093/ajcn/nqaa393.
16. Ranjbar S, Ghotaslou R, Ganbarov K, Köse Ş, Abbasi A, Samadi Kafil H. Safety assessment of probiotics and postbiotics: a critical review. Curr Drug Saf. 2026. doi:10.2174/0113892010419857251208064650.
17. Sanders ME, Merenstein DJ, Reid G, Gibson GR, Rastall RA. Probiotics and prebiotics in intestinal health and disease: from biology to the clinic. Nat Rev Gastroenterol Hepatol. 2023;20:1-16.
18.Zhong H, Jiang J, Chen L, Guan R. The encapsulation strategies for targeted delivery of probiotics in preventing and treating colorectal cancer: a review. Adv Sci (Weinh). 2025;12(15):e2500304. doi:10.1002/advs.202500304.
19.Li N, Yin L, Wang J, Zhang J, Tong Y. Programmable probiotics as next-generation living therapeutics: bridging synthetic biology and precision medicine. Curr Opin Biotechnol. 2025;96:103375. doi:10.1016/j.copbio.2025.103375.
20.Wong CC, Yu J. Gut microbiota in colorectal cancer development and therapy. Nat Rev Clin Oncol. 2023;20(7):429-452. doi:10.1038/s41571-023-00766-x.
21.Zhong H, Jiang J, Hussain M, Zhang H, Chen L, Guan R. The encapsulation strategies for targeted delivery of probiotics in preventing and treating colorectal cancer: a review. Adv Sci (Weinh). 2025;12(18):e2500304. doi:10.1002/advs.202500304.
22.Zhou T, Wu J, Khan A, Hu T, Wang Y, Salama ES, Su S, Han H, Jin W, Li X. A probiotic Limosilactobacillus fermentum GR-3 mitigates colitis-associated tumorigenesis in mice via modulating gut microbiome. npj Science of Food. 2024 Sep 6;8(1):61.
23.Ekhteraei-Tousi S, Mohammad-Soltani B, Sadeghizadeh M, Mowla SJ, Parsi S, Soleimani M. Inhibitory effect of hsa-miR-590-5p on cardiosphere-derived stem cells differentiation through downregulation of TGFB signaling. Journal of cellular biochemistry. 2015 Jan;116(1):179-91.
24.Tajer-Mohammad-Ghazvini P, Kasra-Kermanshahi R, Nozad-Golikand A, Sadeghizadeh M, Ghorbanzadeh-Mashkani S, Dabbagh R. Cobalt separation by Alphaproteobacterium MTB-KTN90: magnetotactic bacteria in bioremediation. Bioprocess and biosystems engineering. 2016 Dec;39(12):1899-911.
25.Noormohammadi Z, Hosseini-Mazinani M, Trujillo I, Rallo L, Belaj A, Sadeghizadeh M. Identification and classification of main Iranian olive cultivars using microsatellite markers. Hortscience. 2007 Dec 1;42(7):1545-50.
26.Arzi L, Riazi G, Sadeghizadeh M, Hoshyar R, Jafarzadeh N. A comparative study on anti-invasion, antimigration, and antiadhesion effects of the bioactive carotenoids of saffron on 4T1 breast cancer cells through their effects on Wnt/β-catenin pathway genes. DNA and cell biology. 2018 Aug;37(8):697-707.
27.Safari S, Malekvandfard F, Babashah S, Alizadehasl A, Sadeghizadeh M, Motavaf M. Mesenchymal stem cell-derived exosomes: A novel potential therapeutic avenue for cardiac regeneration. Cellular and Molecular Biology. 2016 Jun 30;62(7):66-73.