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Review Article

Microbiota and Cancer: Unraveling the Pathways of Microorganism–Tumor Interaction

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Abstract

Cancer is one of the leading causes of death worldwide, with high incidence and a significant impact on public health. In Brazil, it is estimated that approximately 704,000 new cases will occur annually between 2023 and 2025, with breast, prostate, colorectal, and rectal tumors being the most prevalent. Various behavioral, environmental, and biological factors influence carcinogenesis, including the microbiota, which plays a key role in maintaining homeostasis, immune modulation, and inflammatory responses. Alterations in its composition known as dysbiosis are associated with the development of several types of cancer, especially those affecting the gastrointestinal tract, such as colorectal, gastric, and esophageal cancers. Pathogenic microorganisms can promote chronic inflammation, production of reactive species, and immunosuppression, whereas commensal or probiotic species exert protective effects. The complexity of these interactions underscores the relevance of the microbiota in tumor pathophysiology and suggests its potential as a therapeutic target for cancer prevention and treatment. This narrative review summarizes current evidence on the interface between the microbiota and carcinogenesis, highlighting the molecular mechanisms involved and their possible clinical applications.

Keywords: *Dysbiosis, Carcinogenesis, Gut Microbiota, H. pylori*

1. Introduction

Among the leading causes of death worldwide, cancer remains the second most common cause of mortality globally and one of the greatest challenges to modern public health. It is estimated that in many countries, cancer is responsible for premature deaths before the age of 70, significantly impacting life expectancy [1, 2]. In the United States, more than 3.3 million deaths were recorded in 2020, with a significant increase compared to 2019. However, cancer mortality has been steadily declining since 1991.

This 33% reduction is attributed to decreased tobacco use, more effective screening strategies (such as mammography and colonoscopy), and advances in treatment, particularly the use of targeted therapies and immunotherapies for tumors such as lung, melanoma, and kidney cancers [3].

Between 2023 and 2025, approximately 704,000 new cancer cases per year are expected in Brazil. The most prevalent projected tumors include those of the breast (in women), prostate, colon and rectum, lung, stomach, and cervix. The geographical distribution of these cases is not uniform, with a predominance in the Southeast and South regions, which account for about 65.5% of the total projected cases. This reflects socioeconomic disparities and differences in access to diagnostic services [1]. Several factors have been associated with cancer development, including behavioral and environmental elements. Among the most relevant are poor dietary patterns, alcohol consumption, ultraviolet radiation exposure, and lifestyle-related aspects, which may act independently or synergistically in carcinogenesis [4,5].

The microbiota has emerged as a key factor in the context of cancer, playing roles in both the promotion and suppression of tumor development [6]. It is defined as the collection of microorganisms in the body, performing digestive, immune, and protective functions, and is influenced by environmental and physiological factors. Among the various types, the gastrointestinal microbiota has been widely studied due to its central role in regulating immune responses and maintaining intestinal homeostasis. Alterations in its composition have been linked to the development of gastrointestinal tract neoplasms, including esophageal, gastric, and colorectal cancers [7]. Colorectal cancer (CRC) is one of the leading causes of cancer-related deaths worldwide. In addition to genetic predispositions, chronic inflammation of the colon stands out as a major risk factor, influenced by an integrated network involving the innate and adaptive immune systems, cytokine signaling, and the composition of the intestinal microbiota [8,9].

Beyond the intestine, the microbiota also affects systemic health through the gut-brain axis, influencing immune and metabolic responses with potential implications for the development of brain tumors. Microorganism-derived substances, such as metabolites and inflammatory mediators like cytokines (IL-4, IL-6, IL-13, IL-17A, IFN-γ) and reactive oxygen (ROS) and nitrogen species (RNS), modulate the activity of immunosuppressive cells in the bone marrow, thereby interfering with the antitumor response [10]. The oral microbiota has also been associated with an increased risk of cancer in different tissues, with evidence suggesting that pathogenic oral bacteria can interfere with immune pathways and cellular processes involved in carcinogenesis. However, the complexity of these mechanisms makes it difficult to establish a direct causal relationship [11].

In the case of colorectal cancer, the interaction among intestinal microbiota, inflammatory agents, and the immune system is a central aspect of disease pathophysiology. Experimental studies indicate that certain microbial profiles may either promote or prevent tumor formation through the regulation of inflammatory pathways such as NF-κB and interferons, as well as modulation of both innate and adaptive immune responses [9, 12]. The diversity of the microbiota, combined with factors such as diet, highlights the potential for therapeutic strategies involving microbiota modulation as preventive or therapeutic approaches. Nevertheless, many microorganisms remain as commensals without inducing tumor effects, underscoring the complexity of host-microbiota interactions in carcinogenesis [13].

The composition and diversity of the intestinal microbiome vary among individuals, conferring resilience to external disturbances. However, when this balance is disrupted, dysbiosis occurs a condition characterized by changes in the structure and function of the microbiota [14]. Several factors can trigger this imbalance, with antibiotic use being one of the main contributors. These drugs may affect the microbiota in various ways, depending on factors such as the route of administration, excretion mechanism, bioavailability in the intestinal mucosa, and the host's pre-existing microbial profile. Such alterations may contribute to carcinogenic processes by influencing distinct stages of cancer development [15]. Given the growing relevance of this topic and the need for a better understanding of host-microbiota-carcinogenesis interactions, this narrative review aims to compile and discuss the most recent evidence on this complex relationship.

2. Host–Microbiota Interaction

The human gut microbiota comprises a vast and complex community of microorganisms, playing a fundamental role in maintaining physiological balance. Among these microorganisms, bacteria and fungi are especially prominent, exhibiting remarkable taxonomic and functional diversity throughout the gastrointestinal tract and in various body regions [16, 17]. These microorganisms form a complex biofilm along the gut, interacting with each other and with epithelial and immune host cells, thereby playing a key role in sustaining both local and systemic homeostasis [18].

The interaction between the bacterial microbiome and the host is critical to maintaining homeostatic regulation, modulating various physiological responses. This relationship contributes to the regulation of nutrient absorption and the synthesis of essential metabolites such as vitamins, short-chain fatty acids, and neurotransmitters. These metabolites directly influence intestinal barrier cells and participate in regulating inflammatory responses and mechanisms of immune tolerance [18]. On a systemic level, these compounds also affect the host's overall metabolism, modulating both innate and adaptive immunity, as well as chronic inflammatory processes that can impact tissues beyond the gut [18].

The gut microbiota is strongly influenced by lifestyle, which can either contribute to or inhibit cancer progression, as observed in colorectal cancer (CRC). Diet, in particular, plays a decisive role in modulating the gut microbiota, potentially promoting the growth of microorganisms that produce or degrade compounds with pro-inflammatory and genotoxic potential, such as nitrosamines and secondary bile acids [12]. However, dietary responses vary among individuals, as microbiota composition is highly individualized. Thus, the same dietary pattern may yield beneficial effects for some individuals while increasing risk for others [13].

Moreover, specific bacterial species, such as Bacteroides fragilis, produce factors that modulate pro-tumoral signaling pathways including NF-κB, STAT3, and β-catenin, thereby enhancing local inflammation and promoting colonic tumorigenesis. This type of interaction is not confined to the gut; there is evidence that the intestinal microbiota also influences the endocrine homeostasis of the thyroid gland. Its dysregulation may contribute to thyroid cancer development and progression, through the action of microbial metabolites on the hormonal environment [19].

2.1 Microbiota Imbalance: Dysbiosis

Intestinal dysbiosis, defined as the imbalance in the composition and function of the resident microbiota, has been widely associated with the initiation and progression of various types of cancer, particularly those of the gastrointestinal tract. From an immunological perspective, dysbiosis directly affects intestinal mucosal homeostasis by impairing innate immunity mechanisms and promoting the activation of chronic inflammatory pathways that facilitate neoplastic transformation [14]. This condition is primarily characterized by reduced microbial diversity and altered relative abundance of commensal and pathogenic species.

Accumulated evidence indicates that intestinal microbial dysbiosis is a central component in the etiology of several cancers, especially colorectal cancer [20]. One of the main external triggers of dysbiosis is the use of broad-spectrum antibiotics, which significantly alter the structure and function of the microbiota. Studies have reported that different classes of antibiotics induce specific effects on microbial density and diversity, beyond their antimicrobial properties [15, 21].

Several factors have been associated with microbiota alteration leading to dysbiosis (Figure 1). Obesity, for example, is an established risk factor for colorectal cancer, promoting changes in the intestinal microenvironment such as increased mucosal permeability and the selection of bacterial communities with a pro-inflammatory profile. It is estimated that obesity is linked to approximately 5% of incident cases of the disease [12]. Similarly, chronic alcohol consumption and smoking contribute to the production of toxic and genotoxic metabolites, compromising colonic mucosal integrity and enhancing metastatic processes in colorectal cancer patients. Smoking, in particular, exposes the body to various carcinogenic agents (such as nicotine, aldehydes, polycyclic aromatic hydrocarbons, and heavy metals), which promote both inflammation and genomic instability in the intestinal epithelium [12].

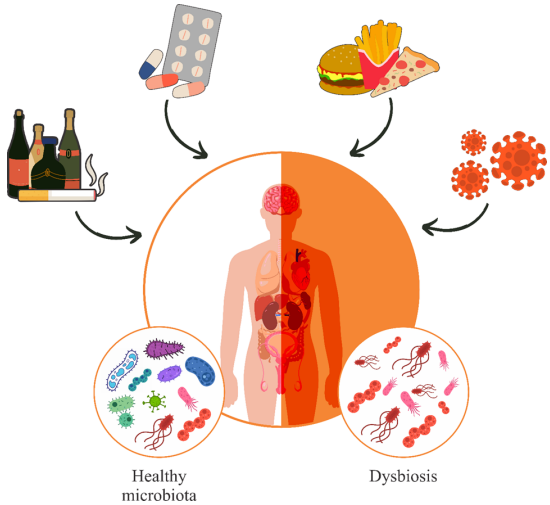

Figure 1. *Factors associated with intestinal microbiota dysbiosis, including smoking, alcoholism, excessive antibiotic use, inadequate diet, and pathogen infections.*

3. Gut Microbiota as a Tumor Suppressor: Mechanisms and Therapeutic Implications

A healthy gut microbiota establishes a beneficial relationship with the host, playing an essential role in maintaining organismal homeostasis. This microbial community contributes to the protection of the intestinal epithelium, modulates the immune system, and regulates inflammatory responses, acting as a protective agent against pathologies, including cancer [22]. The complexity of this interaction between the host and its resident microbial communities has been extensively explored in the context of carcinogenesis not only for its potential oncogenic effects but also for its ability to exert antitumor functions [23].

At the molecular level, the microbiota's protective effects against cancer primarily involve two mechanisms: the induction of tumor cell death and the favorable modulation of immune responses [6]. Metabolites produced by microorganisms, with genotoxic or anti-inflammatory properties, can either promote or inhibit DNA damage, influencing the risk of mutations, genomic instability, and malignant transformation [23].

Much of the microbiota's antitumor activity is related to its effects on the epithelial barrier and immune cells. Species such as Lactobacillus rhamnosus GG (LrGG) have demonstrated significant protective effects against tumorigenesis, widely recognized for their anti-inflammatory action and positive modulation of the immune system. LrGG can directly inhibit the proliferation of neoplastic cells while exerting indirect effects through immune response regulation and microbiota restoration in patients undergoing antineoplastic therapies, such as chemotherapy and radiotherapy [22].

These microbial interactions also directly impact the efficacy of cancer therapies. Recent studies suggest that the presence of certain commensal species may enhance responses to immunotherapy, positioning the microbiota as a functional link between the gut, immune system, central nervous system, and spleen. This communication influences the formation or regression of the tumor microenvironment, demonstrating the systemic role of these microbial communities [24].

Beyond LrGG, other species with anti-tumor properties have been identified. *Faecalibacterium prausnitzii*, known for producing butyrate, is negatively correlated with the incidence of colon cancer and contributes to intestinal barrier integrity. Species such as *Clostridium butyricum, Holdemanella biformis*, and *Bifidobacterium* spp. also produce short-chain fatty acids (SCFAs), particularly butyrate, which promote epigenetic modifications in tumor cells, inducing apoptosis and inhibiting cell proliferation. Meanwhile, *Akkermansia muciniphila* is involved in maintaining the intestinal mucus layer, aiding in epithelial barrier preservation and the regulation of local inflammatory processes [14, 12].

Dietary compounds, such as polyphenols, significantly influence the composition and activity of the gut microbiota. These bioactive compounds favor the growth of beneficial probiotic strains like *Lactobacillus* and *Bifidobacterium* while reducing populations of opportunistic and pro-inflammatory microorganisms. This microbial modulation is particularly relevant in inflammatory conditions, such as colitis and inflammation-associated colorectal cancer (CAC), where polyphenols demonstrate protective effects on intestinal barrier integrity, promote dysbiosis reversal, and stimulate the production of SCFAs especially butyrate, known for its anti-inflammatory and antitumor properties [22, 25].

SCFAs, in turn, exert relevant immunomodulatory effects by interacting with immune cells, particularly macrophages. Metabolites like butyrate, propionate, and acetate can activate hypoxia-inducible factor 1 (HIF-1), primarily through histone deacetylase (HDAC) inhibition, resulting in increased antimicrobial molecule production and a more effective response against pathogens. These effects are associated with GPR43 receptor activation and the modulation of inflammatory pathways, contributing to an antitumor microenvironment [26]. These mechanisms act synergistically with the direct effects of probiotics like LrGG, which exhibit proven antineoplastic and immunomodulatory activity *in vitro* and *in vivo* models [22].

4. Gut Microbiota as a Cancer Promoter

The gut microbiota does not merely act as an accessory element in the host's physiological homeostasis but plays a central role in modulating inflammation, immune responses, and the process of carcinogenesis. Growing evidence shows that under conditions of microbial imbalance—dysbiosis—certain microorganisms can act as promoters of chronic inflammation, capable of causing DNA damage and facilitating immune surveillance evasion, key factors in tumor transformation [23, 25].

Preclinical models provide causal support for the association between colonization by specific bacterial strains and increased susceptibility to colorectal cancer (CRC), primarily through the induction of persistent colonic inflammation. Beyond inflammation, other observed alterations include loss of microbial diversity and the presence of pathogenic mucosal biofilms, features commonly reported in CRC patients [25,23]. These findings align with clinical observations in patients with inflammatory bowel diseases, such as ulcerative colitis, who exhibit an elevated risk of colitis-associated colorectal cancer, often accompanied by altered gut microbiota profiles compared to healthy individuals [14].

In addition to inflammatory mediation, the gut microbiota contributes to carcinogenesis through distinct molecular mechanisms (Figure 2), including:

(I) Genotoxic effects, such as those exerted by colibactin, a toxin produced by *Escherichia coli*, which induces DNA damage, promotes reactive oxygen species (ROS) generation, and interferes with repair pathways, fostering mutations and genomic instability [6, 14];

(II) Direct interference with DNA damage response, as seen in *Helicobacter pylori*, which induces double-strand DNA breaks and impairs cellular repair mechanisms [6];

(III) Activation of abnormal signaling pathways linked to cell proliferation and differentiation [6];

(IV) Immune suppression, which compromises the detection and elimination of transformed cells [6].

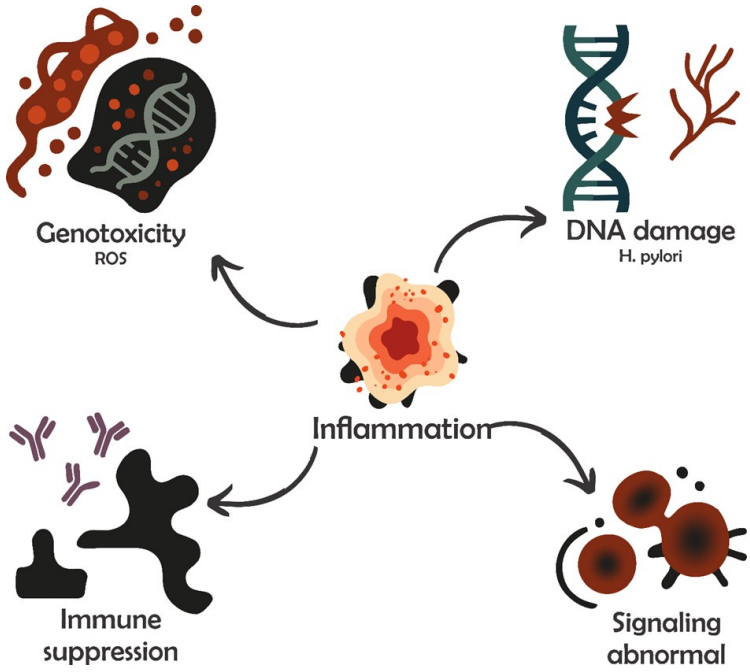

Figure 2. *Molecular mechanisms of action contributing to inflammation-mediated carcinogenesis in the gut microbiota.*

Given this evidence, the gut microbiota has been proposed as a promising biomarker for detecting and monitoring disease progression, including cancer, while also representing a potential target for therapeutic strategies based on its modulation [27]. Another emerging axis of tumor regulation involves the interaction between microRNAs (miRNAs), diet, and microbiota. Intestinal miRNAs modulate gene expression in commensal bacteria, while microbial metabolites can alter host miRNA expression profiles. This bidirectional pathway regulates cellular processes such as proliferation, cell fate, and immune response, establishing a critical link between host and microbiota in maintaining intestinal health [28, 29].

4. Intratumoral Microbiota Influences Cancer Development

Similar to the gut microbiota, microorganisms residing within tumor tissues termed the intratumoral microbiota have emerged as central players in modulating carcinogenesis. These microbes are not merely passive bystanders but actively influence tumor development through multifactorial mechanisms, including: Inducing host genetic mutations, Remodeling the immune microenvironment, and Interfering with metabolic and signaling pathways linked to tumor progression [30, 31].

The composition of intratumoral microbiota varies significantly across cancer types, with distinct microbial signatures identified in brain, breast, lung, and pancreatic tumors. Notably, species like Fusobacterium nucleatum are recurrently found in colorectal, breast, and pancreatic tumors and are associated with chronic inflammation, immune evasion, and increased tumor aggressiveness, particularly through interactions with macrophages [30, 31].

Beyond passive colonization, these microorganisms actively shape the host immune response. The intratumoral microbiota can modulate the activity of immune cells such as macrophages, neutrophils, T lymphocytes, and NK cells tipping the balance between pro- and anti-tumor responses [30]. Another key mechanism involves epigenetic interactions, particularly with miRNAs. Evidence suggests that differential miRNA expression in colorectal tumors correlates with specific bacterial species, indicating that these regulatory RNAs may mediate tumor glycan expression, fostering pathogenic microbial colonization [29].

Despite advances in characterizing tumor-associated microbiota, the causal mechanisms underlying intratumoral dysbiosis remain incompletely understood. However, disruptions in these microbial communities both in the gut and tumor microenvironment are linked to therapy resistance, immunosuppression, and cancer progression [32]. For example, indiscriminate antibiotic use can deplete resident microbiota, reducing diversity and impairing natural defenses against pathogens and tumorigenesis [15].

In colorectal cancer (CRC), the microbiota directly influences tumor-infiltrating immune cells, particularly tumor-associated macrophages (TAMs). Under physiological conditions, TAMs support homeostasis, but dysbiotic microbiota can reprogram them into a pro-tumor M2 phenotype, which secretes cytokines, chemokines, and exosomes that promote tumor survival, invasiveness, and metastasis [33]. Interactions between TAMs, IL-17, and regulatory T cells further reinforce an immunosuppressive microenvironment, enabling tumor immune evasion [34].

4.2 Microorganisms of Significance in Cancer

Numerous microbial species have been implicated in carcinogenesis, particularly in CRC, highlighting the microbiota's dual role in both promoting and suppressing tumors. Many of these species are commensals that naturally inhabit the human body but, under certain conditions, can adopt pathogenic functions that drive genomic instability, chronic inflammation, and tumor progression (Figure 3).

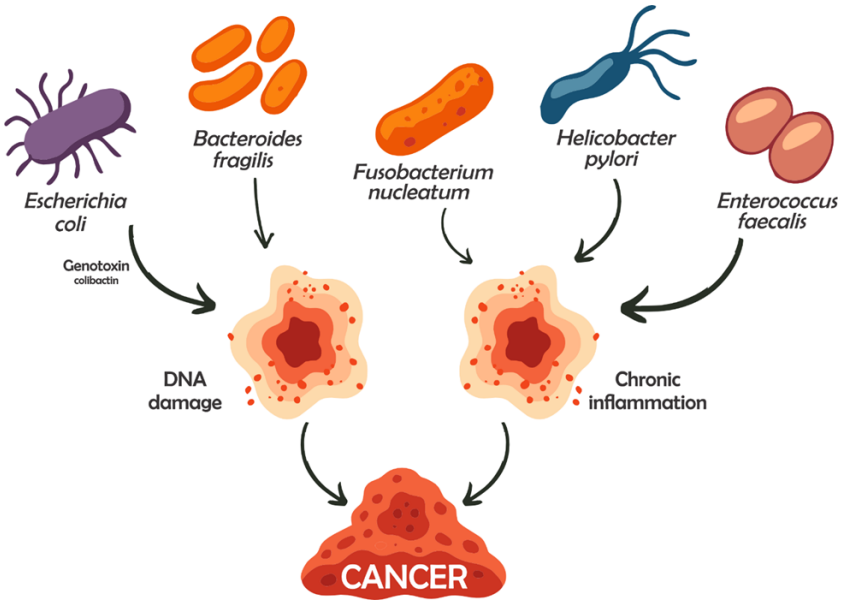

Figure 3. *Bacterial microorganisms of significance in the development of cancer and tumors.*

Fusobacterium nucleatum, an oral cavity commensal anaerobe, shows elevated abundance in colorectal, breast, and pancreatic tumors, as well as in human colitis cases. This species exerts pro-inflammatory effects that promote cancer progression and correlates with poorer prognosis and reduced treatment response, as demonstrated by metagenomic studies [6, 12, 30, 31].

Escherichia coli, an invasive *Enterobacteriaceae* strain, produces colibactin - a genotoxin inducing DNA double-strand breaks. Murine models demonstrate its association with increased intestinal tumor incidence. Its adherent and invasive capabilities exacerbate intestinal tissue inflammation, directly contributing to carcinogenesis [12, 14, 20, 31].

Enterotoxigenic Bacteroides fragilis generates reactive oxygen and nitrogen species (ROS/RNS), causing epithelial DNA damage and genomic instability. Chronic B. fragilis infection correlates with pre-neoplastic lesions and colonic adenomas [6, 20], while additionally upregulating E-cadherin, β-catenin, NF-κB, and STAT3 pathways [19].

Helicobacter pylori, while classically linked to gastric cancer, also associates with colorectal cancer through systemic immune modulation and pro-inflammatory cytokine release. Its eradication correlates with reduced inflammatory markers and lower colorectal lesion risk [6, 12, 23]. Like B. fragilis, *H. pylori* activates β-catenin signaling - crucially involved in proliferation/differentiation control - thereby promoting epithelial changes favoring carcinogenesis [14, 31].

Enterococcus faecalis, a common gut commensal, becomes pathogenic upon tissue translocation. Its hydrogen peroxide production damages intestinal epithelium and creates a chronic inflammatory microenvironment conducive to tumor development [12].

5. Gastrointestinal Cancers and Microbiome

5.1 Esophageal Cancer

Esophageal cancer ranks among the most lethal gastrointestinal malignancies, presenting a growing global public health challenge. While its incidence remains lower than other cancers, the high mortality rate underscores limitations in early diagnosis and therapeutic efficacy, reflecting the disease's aggressive nature. In Brazil, this neoplasm shows high incidence rates, particularly in the Southeast and South regions - paradoxically areas with better healthcare access - suggesting environmental and lifestyle factors significantly influence its geographic distribution [1].

The etiopathogenesis of esophageal cancer involves complex, multifactorial interactions between genetic predisposition, environmental exposures, and microbial alterations. Key environmental risk factors include chronic alcohol consumption, tobacco use, and diets rich in processed foods but poor in fiber and antioxidants. These factors contribute to cumulative esophageal mucosal damage, promoting chronic inflammation that facilitates somatic mutations, genomic instability, and epigenetic changes favoring carcinogenesis [4, 5].

Recent research has established the gastrointestinal microbiota as a modulator of oncological risk, including in esophageal cancer. Microbial dysbiosis - characterized by imbalance between commensal and pathogenic species - has been implicated in inflammatory pathway activation and immune dysfunction, creating a tumorigenic microenvironment. Notably, bacteria like *Fusobacterium nucleatum*, traditionally associated with colorectal cancer, have been detected in esophageal tumors, suggesting these microorganisms may contribute to tumor progression through pro-inflammatory cytokine induction, immune surveillance evasion, and enhanced cell survival [11, 31].

Escherichia coli has been implicated in carcinogenesis through production of colibactin, a genotoxin inducing DNA double-strand breaks that promote genomic instability and epithelial mutations. In esophageal cancer, increased presence of these pathogenic strains associates with chronic inflammatory responses that favor cellular transformation and tumor progression. Furthermore, *E. coli* colonization may disrupt local immune responses, compromising immune surveillance and promoting neoplastic cell survival, particularly in individuals exposed to risk factors like smoking and excessive alcohol consumption [4, 6, 31].

Current studies emphasize the microbiota's role, including *E. coli*, in modulating the esophageal tumor microenvironment, suggesting these bacteria participate not only in cancer initiation but also influence progression and treatment resistance. The identification of microbial biomarkers and intestinal microbiota modulation are emerging as promising strategies for esophageal cancer prevention and adjuvant therapies. Therefore, understanding the molecular and immunological mechanisms mediated by *E. coli* could facilitate development of innovative therapeutic approaches to mitigate this bacterium's impact on esophageal carcinogenesis [5, 11].

5.2 Gastric Cancer

Helicobacter pylori has been recognized as a significant risk factor for the development of gastrointestinal neoplasms, particularly gastric cancer [23]. Consistent epidemiological studies demonstrate that eradication of this bacterium is associated with a substantial reduction in gastric tumor incidence. A meta-analysis revealed that among 12,899 patients who successfully underwent eradication therapy, 119 (0.9%) developed gastric cancer, compared to 208 cases (1.1%) in 18,654 untreated patients, with a combined relative risk of 0.46, indicating a significant protective effect of bacterial eradication [35].

From a mechanistic perspective, *H. pylori* contributes to a pro-tumor microenvironment by inducing chronic inflammation and activating various cellular signaling pathways. The infection can lead to hypochlorhydria, epithelial atrophy, and morphofunctional changes in gastric tissue, all factors that promote carcinogenesis [35]. One proposed molecular mechanism involves activation of the β-catenin pathway, a key regulator of cell proliferation and differentiation whose activity is modulated through interactions with adhesion proteins such as E-cadherin [31]. This pathway has been identified as one of the primary molecular targets through which H. pylori may contribute to tumor progression, both in gastric and potentially colonic tissues [12, 14].

Beyond the stomach, *H. pylori's* influence may extend to other segments of the gastrointestinal tract. Reports have associated this bacterium with worsening lesions in the gallbladder mucosa, accompanied by increased cellular proliferation in this tissue, suggesting a potential role in biliary carcinogenesis [14]. Although the mechanisms remain under investigation, a positive correlation has also been observed between *H. pylori* and colorectal cancer, expanding the scope of research into its extra-gastric effects [12].

5.3 Colorectal Cancer (CRC)

Colorectal Cancer (CRC) represents one of the leading causes of cancer mortality worldwide. In Brazil, it is among the neoplasms with the highest estimated number of new cases for the 2023-2025 triennium, reflecting lifestyle changes, population aging, and greater access to diagnostic methods [1]. The etiopathogenesis of CRC involves a complex interaction between genetic factors, chronic inflammation, diet, obesity, smoking, and alcohol consumption, which contribute to an environment favorable for tumor development [12].

In this context, the gut microbiota plays a crucial role from tumor initiation to progression. Intestinal dysbiosis, characterized by an imbalance in the composition and function of the microbiota, has been associated with CRC by promoting chronic inflammation, loss of epithelial barrier integrity, and immune response evasion [14, 20]. Prolonged antibiotic use can compromise microbial diversity, triggering functional imbalances that impair intestinal homeostasis [15].

Specific bacterial species have been directly implicated in carcinogenesis. Colibactin-producing *Escherichia coli* induces DNA double-strand breaks, increasing genomic instability. Enterotoxigenic Bacteroides fragilis activates inflammatory pathways such as NF-κB and STAT3, in addition to causing oxidative damage to the intestinal epithelium. *Fusobacterium nucleatum* is associated with immune evasion, stimulation of tumor proliferation, and treatment resistance [6, 12, 19].

Conversely, protective microorganisms are also found in the gut microbiota, such as *Faecalibacterium prausnitzii, Clostridium butyricum*, and *Lactobacillus rhamnosus* GG, which produce short-chain fatty acids (SCFAs), particularly butyrate, capable of inducing apoptosis in tumor cells, restoring the epithelial barrier, and modulating the immune response [22, 23].

In addition to the gut microbiota, CRC presents a distinct intratumoral microbiota, predominantly composed of pathogenic bacteria that interact with the local immune microenvironment. These bacteria modulate the phenotype of tumor-associated macrophages (TAMs), promoting the secretion of pro-tumor cytokines and chemokines, favoring invasiveness, metastasis, and immune evasion [30, 33].

Given this scenario, modulation of the gut microbiota has been proposed as a promising therapeutic strategy for CRC treatment, using probiotics, prebiotics, and polyphenol-rich diets, compounds that help reverse dysbiosis and promote the growth of beneficial bacteria [25]. Thus, the microbiota emerges as a potential biomarker for diagnosis, prognosis, and monitoring of therapeutic response in colorectal cancer patients [27].

6. Conclusion

Understanding the complex relationship between microbiota and cancer has advanced significantly in recent decades, revealing the role of these microbial communities in both promoting and suppressing tumors. Accumulated evidence demonstrates that the gut microbiota profoundly influences the host's immunological, metabolic, and inflammatory processes, directly interfering with epithelial homeostasis and the tumor microenvironment. Dysbiosis, characterized by imbalances in the composition and function of the microbiota, has emerged as a determining factor in carcinogenesis, especially in gastrointestinal tumors such as colorectal, gastric, and esophageal cancers.

The data presented in this review indicate that certain bacterial species, such as *F. nucleatum*, *E. coli*, and *B. fragilis*, exhibit pro-tumor potential through genotoxic, inflammatory, and immunosuppressive mechanisms. On the other hand, commensal and probiotic microorganisms, such as *F. prausnitzii*, *L. rhamnosus*, and *A. muciniphila*, exert protective functions by positively modulating the immune response, preserving intestinal barrier integrity, and promoting tumor cell apoptosis.

Thus, microbiota modulation through dietary strategies, use of prebiotics and probiotics, and personalized therapeutic interventions presents itself as a promising approach for cancer prevention, diagnosis, and adjuvant treatment. However, the individuality of microbial composition and the complexity of interactions between microorganisms, host cells, and environmental factors require further investigation, with robust clinical studies that can translate these discoveries into effective and safe interventions. The recognition of microbiota as a functional axis integrated with the immune, metabolic, and endocrine systems represents a paradigm shift in oncological approaches, reinforcing the need for more personalized and integrative medicine.

Conflict of Interest

The authors declare no conflict of interest.

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