World Journal of Clinical Oncology

Submit a Manuscript: https://www.f6publishing.com

World J Clin Oncol 2025 October 24; 16(10): 107877

DOI: 10.5306/wjco.v16.i10.107877

ISSN 2218-4333 (online)

REVIEW

Gut microbiome and nutritional strategies in gastrointestinal cancers: Clinical implications and therapeutic perspectives

Vilma Pacheco-Barcia, Axel Mariño-Mendez, Enrique Hernandez-Jimenez, Paula Jimenez-Fonseca, Andrés Jesús Muñoz Martín, Sara Custodio-Cabello, Magda Palka-Kotlowska, Ivan Gonzalez-Diaz, Luis Cabezon-Gutierrez

Specialty type: Oncology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B, Grade B, Grade C, Grade C

Novelty: Grade B, Grade C, Grade C, Grade C

Creativity or Innovation: Grade B, Grade C, Grade C, Grade C

Scientific Significance: Grade A, Grade B, Grade C, Grade C

P-Reviewer: Le KLK, MD, Lecturer, Viet Nam; Liu TF, PhD, China; Xu HY, PhD, China

Received: April 2, 2025

Revised: May 29, 2025

Accepted: September 22, 2025

Published online: October 24, 2025

Processing time: 208 Days and 8.5 Hours

Vilma Pacheco-Barcia, Sara Custodio-Cabello, Magda Palka-Kotlowska, Luis Cabezon-Gutierrez, Department of Medical Oncology, Hospital Universitario de Torrejon, Madrid 28850, Spain

Vilma Pacheco-Barcia, Faculty of Medicine, Francisco de Vitoria University, Madrid 28223, Spain

Axel Mariño-Mendez, Paula Jimenez-Fonseca, Department of Medical Oncology, Hospital Universitario Central de Asturias, Oviedo 33011, Spain

Enrique Hernandez-Jimenez, Department of Research and Development, Loop Diagnostics, Barcelona 08005, Catalonia, Spain

Andrés Jesús Muñoz Martín, Department of Medical Oncology, Hospital General Universitario Gregorio Marañón, Universidad Complutense Madrid, Madrid 28007, Spain

Ivan Gonzalez-Diaz, Department of Gynecology, Hospital Universitario Severo Ochoa, Leganes 28914, Madrid, Spain

Corresponding author: Vilma Pacheco-Barcia, MD, PhD, Professor, Department of Medical Oncology, Hospital Universitario de Torrejon, C/Mateo Inurria S/N, Madrid 28850, Spain. vepacheco@torrejonsalud.com

Abstract

Gastrointestinal malignancies, particularly pancreatobiliary and gastroesophageal cancers, are associated with poor prognosis due to their frequent late-stage diagnosis. Many of these tumors contribute to anorexia-cachexia syndrome and malnutrition, further exacerbating disease progression. Inflammation plays a crucial role in tumor proliferation, and growing evidence suggests that gut microbiome significantly influence inflammatory responses and clinical outcomes in these patients. Additionally, the gut microbiome contributes to carcinogenesis through multiple mechanisms, including DNA damage, activation of oncogenic pathways, and modulation of immune responses. The emerging field of nutritional interventions highlight the microbiome's impact on anticancer drug responses, affecting both chemotherapy and molecular-targeted treatments. Given its pivotal role, microbiome modulation through probiotics, fecal microbiome transplantation, and antibiotics represents a promising approach for cancer pre-vention and treatment. In this review, we explore the intricate interplay between gut micro-

biome, inflammation, and nutritional status in gastrointestinal cancers, emphasizing potential therapeutic strategies to improve patient outcomes.

Key Words: Gut microbiome; Nutritional interventions; Gastrointestinal cancer; Therapeutic approach; Carcinogenesis; Probiotics

Core Tip: Gastrointestinal malignancies, more specifically pancreatobiliary and gastroesophageal cancers, harbor a bad prognosis mainly because tumors are frequently diagnosed in an advanced stage. Most of the tumors of the digestive tract associate anorexia-cachexia syndrome as well as malnutrition. Inflammation is a key feature of neoplasic proliferation and gut microbiome may have an interplay in inflammation and outcomes of these patients. In this article, we want to address this association and the impact of nutritional strategies in patients with gastrointestinal malignancies.

Citation: Pacheco-Barcia V, Mariño-Mendez A, Hernandez-Jimenez E, Jimenez-Fonseca P, Muñoz Martín AJ, Custodio-Cabello S, Palka-Kotlowska M, Gonzalez-Diaz I, Cabezon-Gutierrez L. Gut microbiome and nutritional strategies in gastrointestinal cancers: Clinical implications and therapeutic perspectives. *World J Clin Oncol* 2025; 16(10): 107877
URL: https://www.wjgnet.com/2218-4333/full/v16/i10/107877.htm
DOI: https://dx.doi.org/10.5306/wjco.v16.i10.107877

INTRODUCTION

Cancer is considered as a main leading cause of death worldwide[1]. The International Agency for Research on Cancer reported an estimated 20 million new cancer cases and 9.7 million cancer deaths in 2022[2]. The hallmarks of cancer were early described to include fourteen biological capabilities which have essential roles in contributing to tumor complexity [3]. Among these are deregulating cellular metabolism, genome instability, tumor-promoting inflammation, and polymorphic microbiomes, which underscore the growing importance of the gut microbiome and inflammation in tumorigenesis.

In the late 19th century, German pathologist Rudolf Virchow proposed that cancer could arise as a consequence of chronic inflammation triggered by persistent exposure to harmful toxic agents, including infections[4]. Around the same time, pioneering research by Robert Koch and Louis Pasteur led to the identification of bacteria within tumor tissues, suggesting a potential link between bacterial infections and cancer development[4]. The term "human microbiome" refers to the diverse community of microorganisms residing within the human body, along with their collective genetic material [5,6].

There is a growing recognition that the complex ecosystems formed by resident bacteria and fungi - the microbiomes - play a crucial role in both health and disease[7]. This understanding has been significantly advanced by the development of next-generation sequencing and bioinformatics, enabling a detailed characterization of microbial populations. In the context of cancer, mounting evidence suggests that inter-individual variability in microbiome composition can profoundly influence cancer phenotypes[8,9]. Currently, approximately 20% of malignancies worldwide are linked to infections[10], accounting for an estimated 1.2 million cases annually[11]. Research into the microbiome, particularly the role of bacteria in cancer pathogenesis, is evolving rapidly, with more than about 100 trillion bacterial cells representing about 10000 species across the human population identified within the human body to date[12,13].

The microbiome has been implicated in tumor development and progression through various mechanisms, including DNA damage, activation of oncogenic pathways and epithelial cell proliferation[14,15], production of carcinogenic metabolites[16], induction of chronic inflammation[17,18], and suppression of antitumor immunity[14,16]. These insights have expanded the understanding of the intricate interactions between the tumor microenvironment and systemic microbial-immune networks, suggesting a broader and more complex influence than previously recognized[19].

Notably, microbial dysbiosis, an imbalance in microbial composition that disrupts host homeostasis, has been shown to significantly affect therapeutic responses to anticancer treatments[20,21]. This is largely attributed to the microbiome's capacity to metabolize drugs, modulate inflammation, and influence immune responses within the tumor microenvironment, all of which play a crucial role in treatment efficacy and drug toxicity[22]. The relationship between the microbiome and anticancer therapy responses has been described as bidirectional, with both factors exerting significant effects on each other[20,23]. This has led to the emergence of "pharmacomicrobiomics", a field dedicated to studying the interaction between drugs and microbial communities[20]. In this context, the role of probiotics and antibiotics, whether used alone or in combination with anticancer agents, is being explored as a strategy to manipulate the microbiome and potentially improve cancer prevention and treatment outcomes[20,24].

Increasing evidence supports the role of bacterial infections in the pathogenesis and progression of various gastrointestinal (GI) malignancies[25,26]. Additionally, substantial data indicate that the microbiome influences tumor responses to anticancer therapies, including conventional chemotherapy and targeted treatments[20,27]. Consequently, the bacterial microbiome represents a promising therapeutic target for the prevention and treatment of GI cancers.

Moreover, dietary patterns play a significant role in shaping gut microbiome composition, serving as a key factor in cancer development[28].

This article explores the current understanding of the intricate relationship between the bacterial microbiome and inflammation in GI malignancies. Particular emphasis is placed on its potential as a therapeutic target, with a specific focus on nutritional interventions as a modifiable factor in disease management.

GUT MICROBIOME, INFLAMMATION AND CARCINOGENESIS IN GI CANCERS

The majority of microorganisms comprising the human microbiome are commensal. The highest microbial diversity is observed in the GI tract, particularly in the cecum and proximal colon. This diversity is shaped by multiple factors, including mode of delivery at birth, infant feeding practices, dietary patterns, lifestyle factors, and host genetics[29]. However, substantial evidence has definitively shown that gut microbiome plays a role in the development of various medical conditions, including inflammatory, hepatic, pancreatic, and respiratory diseases, as well as neurological and dermatological disorders, and cancer[30]. Figure 1 summarizes the most common bacterial species associated with cancers affecting GI tract.

Cancer and the immune system are closely interconnected. Similarly, a robust interaction between gut microbiome and both innate and adaptive immunity has been well-documented. The interplay between bacteria, viruses, parasites, fungi, and mucosal immune cells is regulated by a complex network of cytokines[31].

Germ-free mouse models have demonstrated the critical role of gut microbiome in the development and regulation of various organs and systems, including the immune and endocrine systems, blood, liver, and lungs[32]. Within the intestine, the microbiome maintains epithelial homeostasis and supports the formation of gut-associated lymphoid tissue. Additionally, it promotes the production of epithelial cytokines, which in turn regulate the activity of T and B lymphocytes, macrophages, and polymorphonuclear cells[33,34]. Cytokines like interleukin (IL)-1β, tumor necrosis factor (TNF) α, IL-2, IL-6, IL-15, IL-21, and IL-23 can trigger an inflammatory response, whereas IL-10 and TGF-β exhibit anti-inflammatory properties. The balance between these pro-inflammatory and anti-inflammatory cytokines determines the gut's inflammatory or homeostatic state[35].

Helicobater pylori (*H. pylori*) colonization induces chronic inflammation by overexpressing pro-inflammatory cytokines like IL-1β, IL-8, IL-17, and TNF-α, which increases the risk of gastric cancer (GC)[36]. In patients with gastric adenocarcinoma, higher abundances of *Lactobacillus*, *Bifidobacterium*, *Lactococcus*, and *Streptococcus* have been observed[37]. *Lactic acid bacteria* (LAB) contribute to DNA damage by producing reactive oxygen species (ROS) and reducing nitrates to nitrites, which drive mutagenesis, proto-oncogene overexpression, angiogenesis, and inhibit apoptosis[37]. LAB also plays a key role in epithelial-mesenchymal transition[38]. *Escherichia coli* (*E. coli*) produces colibactin, a compound involved in colorectal carcinoma development[39]. Additionally, *Fusobacterium nucleatum* (*F. nucleatum*), *E. coli NC101*, and *Bacteroides fragilis* promote colorectal cancer (CRC) by activating the Wnt-β-catenin signaling pathway[40]. Increased abundances of genera like *Bacteroides fragilis*, *Campylobacter*, *Enterococcus*, *F. nucleatum*, *Streptococcus*, *Prevotella*, and *Peptostreptococcus*, and decreased abundances of *Bifidobacterium, Clostridium spp.*, *Lactobacillus*, *Ruminococcus*, and *Roseburia* have been noted in CRC patients[41].

Pathogen-associated molecular patterns are recognized by pattern recognition receptors, such as toll-like receptors (TLRs) on macrophages and dendritic cells. TLRs initiate immune responses by activating signaling cascades, including the nuclear factor kappa B (NF-κB), mitogen-activated protein kinase (MAPK), and interferon regulatory factor pathways [42]. For instance, TLR3 and TLR4 engage interferon regulatory factor to induce interferon-beta, while others signal through the myeloid differentiation primary response 88 (MyD88)-interleukin-1 receptor-associated kinase axis, triggering MAPK like p38 and c-Jun N-terminal kinase (JNK) that culminate in the transcription of pro-inflammatory genes[42]. Although TLR-mediated signaling is vital for maintaining epithelial integrity and immune homeostasis, aberrant activation can contribute to tumorigenesis[43-47]. Overexpression of TLRs has been observed in various cancers, and studies in MyD88-deficient mice demonstrate reduced tumor development[48], underscoring the oncogenic potential of dysregulated TLR signaling. Additionally, JNK activation downstream of TLRs may intersect with Ras pathways, promoting apoptosis resistance and increased matrix metalloproteinase expression-hallmarks of cancer progression[17,47,49,50].

The connection between TLR signaling, JNK activation, and Ras-driven oncogenesis in CRC is largely based on *in vitro* evidence using human colon epithelial cell lines. Several studies have shown that activation of TLR4 by bacterial ligands can stimulate the JNK cascade and downstream Ras signaling, resulting in increased expression of pro-survival and proliferative genes[51,52]. However, the relevance of this pathway *in vivo* remains speculative. Animal models have yielded inconsistent results, with some indicating tumor-promoting effects of TLR overactivation, while others report context-dependent roles for JNK that may be either oncogenic or tumor suppressive depending on isoform specificity and the inflammatory milieu[53,54]. Additionally, the crosstalk between TLR/JNK/Ras pathways and host immune responses, microbiota composition, and epithelial integrity is complex and not yet fully characterized in preclinical systems. Thus, while *in vitro* data support mechanistic hypotheses, further *in vivo* studies are required to clarify the functional significance of this signaling axis in colorectal tumorigenesis.

CD8+ cytotoxic T-lymphocytes (CTLs) are crucial for anti-cancer immunity, as they kill malignant cells upon recognizing antigenic peptides[35]. Tumor-specific CTL responses are supported by tumor-associated antigens and the presence of tumor-associated antigen-specific CD8+ T-cells in regressing tumors. In CRC, tumor-infiltrating lymphocytes are primarily CD4+ T cells, producing pro-inflammatory cytokines like induce interferon-γ and IL-17, whereas subsets producing IL-4 may promote oncogenesis[55]. Additionally, natural killer cells at tumor sites in long-surviving patients

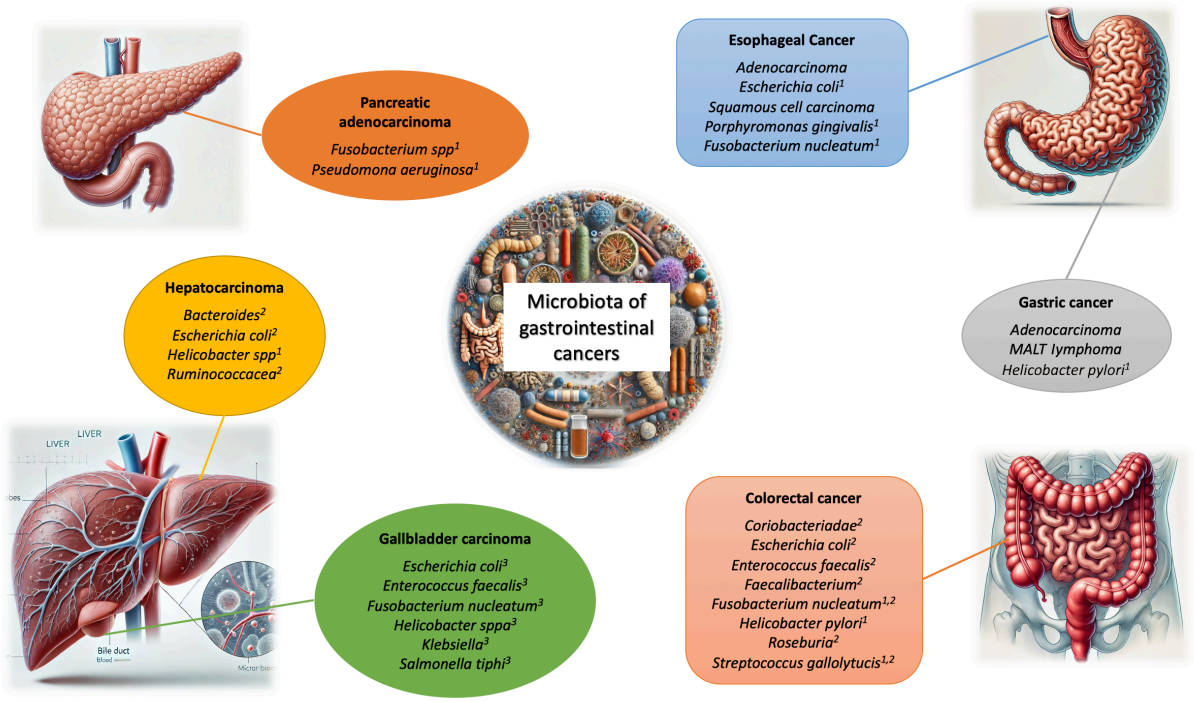

Figure 1 Predominant bacterial microbiota associated with gastrointestinal cancers. Microbiota identified from patients with gastrointestinal tract cancers. [1]Cancerous tissues; [2]Stool samples; [3]Bile secretions.

trigger tumor apoptosis and inhibit proliferation[56].

Cancer cells induce an immunosuppressive microenvironment by producing factors like TGF-β and recruiting regulatory immune cells, such as T-regs, which are inversely correlated with tumor prognosis[57]. T-regs suppress tumor-specific T-lymphocytes by producing IL-10 and TGF-β, consuming IL-2, or expressing CTL-associated protein 4 (CTLA-4). They also inhibit pro-inflammatory CD4+ T-helper (Th) cells and stimulate B cells to produce immunoglobulins. Th17 cells, involved in carcinogenesis by promoting cell proliferation and inhibiting apoptosis, produce cytokines like IL-17 and IL-23, contributing to tumor growth[58-62]. Th17 cells also promote the production of Th1-related cytokines, such as C-X-C motif chemokine ligand (CXCL) 9 and CXCL10, at the tumor site. T-cell exhaustion, a phenomenon where persistent tumor antigen stimulation impairs T-cell function, is a primary mechanism of immune escape, allowing tumors to continue growing despite initial immune responses[63-65]. Figure 2 summarizes how the microbiome promotes carcinogenesis through various mechanisms.

In a healthy state, there is a harmonious balance between the gut microbiome and the immune system at the gut interface[66]. Disruption of this balance leads to a pathological condition called "gut dysbiosis", which fosters the overgrowth of pathogenic bacteria in the intestinal lumen. Dysbiosis can arise from an inflammatory state: In genetically predisposed individuals, factors such as dietary compounds, toxins, and antibiotics can trigger low-grade inflammation, promoting dysbiosis. For instance, high-calorie and high-fat diets common in Western societies have been linked to worsened gut inflammation in patients with inflammatory bowel disease (IBD)[67]. The following sections will develop and analyze the relationship between various treatments for GI tumors and the nutritional strategies that may influence the microbiome and inflammation.

While growing evidence implicates the gut microbiome in the initiation and progression of cancer through mechanisms such as chronic inflammation, genotoxin production, and immune modulation, this pathogenic potential also opens the door to therapeutic opportunities. Among the most accessible and modifiable factors influencing the gut microbiota is diet. The next section explores how targeted nutritional interventions - particularly those involving dietary fiber and microbiota-accessible carbohydrates - can reshape the gut microbial landscape to potentially prevent carcinogenesis and enhance treatment responses.

NUTRITIONAL STRATEGIES MODULATING GUT MICROBIOME AND INFLAMMATION IN GI CANCERS

Probiotics

Probiotics, defined as live microorganisms that, when consumed in sufficient amounts, confer health advantages to the host, have gained attention for their potential role in CRC prevention and treatment. Their beneficial effects are primarily attributed to three mechanisms: Suppression of pathogenic bacterial colonization, modulation of gut immune responses, and reinforcement of intestinal barrier function[68]. The antimicrobial properties of probiotics against pathogenic bacteria have been well-documented. For example, *Bacillus* species were shown to prevent intestinal colonization by *Staphylococcus*

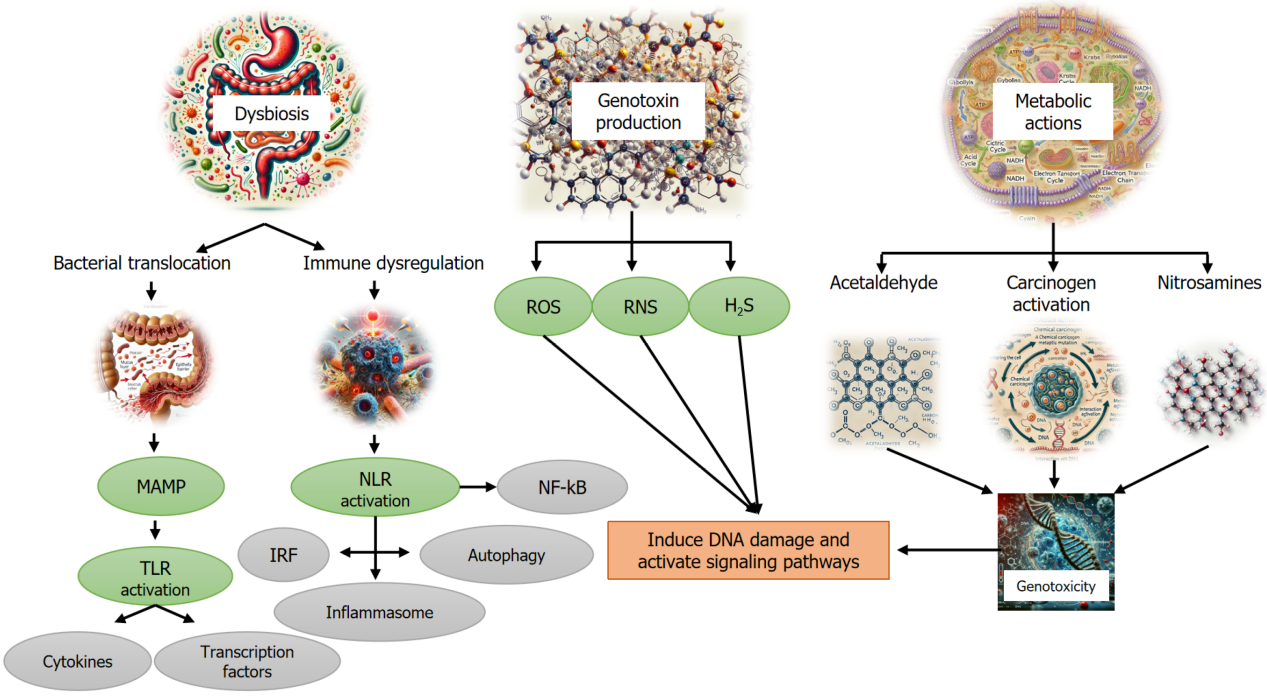

Figure 2 The microbiome contributes to carcinogenesis through various mechanisms. Dysbiosis can promote cancer development through bacterial translocation and immune system disruption. In bacterial translocation, microorganism-associated molecular patterns activate Toll-like receptors, triggering cytokine production and transcription factor activation. On the other hand, immune dysfunction involves the activation of nucleotide-binding oligomerization domain-like receptors, which stimulate multiple signaling pathways, leading to the formation of inflammasomes and/or the activation of nuclear factor kappa B, stress kinases, interferon regulatory factors, inflammatory caspases, and autophagy mechanisms. Additionally, certain genotoxins, such as reactive oxygen species, reactive nitrogen species, and hydrogen sulfide, released by specific bacteria, can have harmful effects. Moreover, bacterial metabolic processes can activate toxins like acetaldehydes and nitrosamines, resulting in a genotoxic impact that may contribute to carcinogenesis. MAMP: Microorganism-associated molecular patterns; TLR: Toll-like receptors; NLR: Nucleotide-binding oligomerization domain-like receptor; NF-κB: Nuclear factor kappa B; IRF: Interferon regulatory factor; ROS: Reactive oxygen species; RNS: Reactive nitrogen species; H_2S: Hydrogen sulfide.

aureus by disrupting its quorum sensing communication system[69]. Similarly, *Clostridium butyricum* suppressed biofilm formation by enterotoxigenic *Bacteroides fragilis* by regulating key virulence and efflux pump-related genes[70]. Certain *Lactobacillus* strains have also exhibited protective effects by preventing bacterial adhesion. *Lactobacillus fermentum* 88 and *Lactobacillus plantarum* 9 demonstrated strong adherence to human enteric cell line HT29 while simultaneously inhibiting *E. coli* attachment[71]. Furthermore, pre-administration of *Lactobacillus rhamnosus* GG in a mouse model of periodontitis provided protection against *F. nucleatum* and *Porphyromonas gingivalis*-induced cecal dysbiosis, significantly mitigating intestinal inflammation[72].

Probiotics are recognized for their immunomodulatory functions in the gut, where they play a crucial role in mitigating colonic inflammation. In an *azoxymethane* and *dextran sulfate sodium*-induced CRC murine model, *Lactobacillus* species were found to suppress Wnt/β-catenin signaling, leading to reduced inflammation and tumor growth[73]. Additionally, a specific strain of *Lactobacillus rhamnosus* demonstrated anti-tumor properties by reducing inflammatory responses and promoting apoptosis, ultimately decreasing tumor incidence[74]. In genetic models of CRC, probiotics have exhibited protective effects. In the *APC Min*/+ mouse model of colon cancer, *Lactobacillus plantarum* strain YYC-3 was shown to inhibit tumor formation, likely by downregulating inflammatory cytokine production and limiting inflammatory cell infiltration[75]. Furthermore, the administration of a probiotic mixture containing *Lactobacillus acidophilus, L. rhamnosus,* and *Bifidobacterium bifidum* significantly reduced colitis and resulted in a 40% decrease in tumor development compared to the control group[76].

Disruptions in tight junction proteins - such as occludin, claudins, junctional adhesion molecules, and zona occludens (ZO) - can lead to increased intestinal permeability, fostering chronic inflammation and heightening the risk of IBD-associated CRC[77]. Probiotics have been shown to enhance gut barrier integrity, providing a potential preventive mechanism. Notably, *E. coli* nissle 1917 improved intestinal barrier function by upregulating and redistributing tight junction proteins, including ZO-1, ZO-2, and claudin-14[78]. The beneficial effects of probiotics on gut barrier integrity have also been observed in colitis models. A probiotic formulation containing *Bifidobacterium, L. acidophilus,* and *Enterococcus* ameliorated colitis in mice by upregulating occludin and claudin-4 expression[79]. Additionally, in a 1,2-dimethylhydrazine dihydrochloride-induced CRC mouse model, supplementation with *L. acidophilus, B. bifidum,* and *Bifidobacterium infantum* strengthened gut mucosal barrier integrity through TLR2 signaling, which was associated with a lower incidence of tumor formation[80].

While some strains of LAB have been reported to generate ROS or contribute to nitrate metabolism under specific conditions, it is important to recognize that most probiotic formulations - particularly those used in clinical and nutritional contexts - employ LAB for their protective effects[81]. For instance, some studies[82-84], highlight the role of

LAB in safeguarding the gastric mucosa, modulating inflammation, and attenuating the toxicity of chemotherapy agents. Thus, while emerging data suggest that certain LAB strains may possess pro-carcinogenic potential under select circumstances, the broader evidence base supports their beneficial role in GI health and cancer therapy support. A nuanced interpretation is warranted to avoid overgeneralizing LAB as solely pro-carcinogenic.

Prebiotics

Prebiotics, such as inulin, fructo-oligosaccharides (FOS), and galactooligosaccharides are non-digestible carbohydrates that selectively stimulate the proliferation of beneficial anaerobic bacteria within the colon. These fibers bypass digestion in the small intestine and undergo fermentation by colonic microbiome, promoting the growth of beneficial bacterial genera, particularly *Bifidobacterium* spp.[85]. Elevated levels of *Bifidobacterium* spp. have been associated with a reduced incidence and progression of tumors[86]. Additionally, inulin and its oligofructose derivatives - characterized by a degree of polymerization ≤ 10 - were observed to decrease the formation of aberrant crypt foci in chemically induced colon carcinogenesis models in mice[87]. Research by Taper *et al*[88-90] explored the impact of dietary supplementation with 15% inulin or oligofructose on chemotherapy efficacy in experimental animals. Findings demonstrated that these prebiotics significantly enhanced the therapeutic efficacy of six commonly used chemotherapeutic agents, including 5-fluorouracil (5-FU) doxorubicin, vincristine, cyclophosphamide, methotrexate, and cytarabine[90].

Consistent with prior investigations from the same research group, inulin notably amplified the therapeutic response to cyclophosphamide by 47%[88]. Moreover, no detrimental interactions or adverse effects were observed when inulin or oligofructose was administered as an adjuvant therapy, highlighting their potential role in optimizing cancer treatment outcomes[90]. A randomized, double-blind, placebo-controlled trial evaluated the effects of a fiber blend (50% inulin and 50% FOS) on gut microbiome in gynecological cancer patients undergoing radiotherapy[91]. Patients receiving the prebiotic mixture exhibited a quicker restoration of *Lactobacillus spp.* and *Bifidobacterium spp.* populations within two weeks after radiotherapy, leading to improved stool consistency compared to the placebo group[91,92]. Diarrhea is a frequent side effect of enteral nutrition, often delaying recovery and prolonging hospital stays, particularly in postoperative GC patients. A study of 120 GC patients, divided into three groups (fiber-free nutrition, fiber-enriched nutrition, and fiber- and probiotic-enriched nutrition), found that hospital stays were shorter in the fiber-supplemented groups, with a significant reduction in diarrhea occurrence compared to the fiber-free group[93].

Recently, a phase II randomized controlled trial was initiated to explore the interactions between gut microbiome and prebiotics in patients with localized anal canal squamous cell carcinoma receiving radiotherapy, aiming to assess their impact on treatment outcomes[94]. Another randomized, double-blind clinical trial examined the effects of prebiotics (FOS, xylooligosaccharides, polydextrose, and resistant dextrin) on gut microbiome and immune function in 140 perioperative CRC patients[95]. In the preoperative phase, prebiotic consumption led to increased levels of *Bifidobacterium* and *Enterococcus*, along with a decrease in *Bacteroides* abundance compared to placebo[95]. Postoperatively, the control group exhibited a rise in *Enterococcus*, *Bacillus*, *Lactococcus*, and *Streptococcus*, whereas the prebiotic group experienced an increase in non-pathogenic *Escherichia-Shigella*. Additionally, microbial richness declined from pre- to post-surgery in patients who did not receive prebiotics[95].

Beyond microbiome modulation, prebiotics significantly influenced immune function. In the preoperative phase, serum levels of immunoglobulin (Ig) G, IgM, and transferrin were elevated, while in the postoperative phase, levels of IgG, IgA, suppressor/cytotoxic T cells (CD3+ CD8+), and total B lymphocytes increased compared to controls[95]. Rowland *et al*[87] examined changes in biological markers following three months of daily FOS supplementation (10 g) in 74 French patients, grouped into those with small colorectal adenomas, large adenomas, or no adenomas. Patients with adenomas exhibited significantly higher butyrate levels after FOS intake, while in patients without adenomas, FOS consumption led to increased levels of cholic acid, chenodeoxycholic acid, total primary bile acids, and ursodeoxycholic acid, as well as decreased fecal lithocholic acid, highlighting its potential role in modulating the colonic environment[96].

Inulin supplementation has been shown to enhance the growth of *Bifidobacterium* spp. and *Akkermansia muciniphila*[97,98]. An *in vitro* study demonstrated that culturing fecal samples with inulin and mucin increased the abundance of microbial species involved in suppressing tumor growth in Rnf5-/- mice[99]. Another study found that inulin consumption supports the enrichment of bacterial taxa associated with anti-tumor immune responses[89]. Remarkably, dietary supplementation with inulin or mucin in C57BL/6 mice triggered anti-tumor immunity, yet mucin alone failed to curb tumor growth in germ-free mice, emphasizing the essential role of gut microbiome in tumor-related immune activation[99]. Preclinical studies suggest that inulin may suppress tumor progression in colon cancer and *NRAS*-mutant melanoma models. Additionally, it has been found to enhance the effectiveness of mitogen-activated protein kinase inhibitors targeting the MAPK/extracellular signal-regulated kinase pathway, which is frequently dysregulated in melanoma[99]. These findings indicate that dietary interventions using inulin or oligofructose could enhance chemotherapy efficacy by modulating gut microbiome and immune function. However, more extensive clinical studies are required to validate these preliminary results[100].

Diet

The ketogenic diet (KD) is a high-fat, isocaloric diet that significantly reduces carbohydrate intake, originally designed for the treatment of epilepsy and glucose transporter type 1 deficiency syndrome deficiency syndrome[101]. As a therapeutic approach, KD aims to trigger ketosis, and it has recently emerged as a potential strategy for cancer treatment[102]. Vander Heiden *et al*[103] found that tumor cells consume glucose at higher rates than surrounding tissue and rely on the aerobic glycolytic pathway to produce lactate. By limiting glucose availability, KD could deprive tumor cells of their primary energy source, potentially inhibiting tumor growth and proliferation. *In vitro* and *in vivo* animal models have shown that KD suppresses glycolysis and cancer cell proliferation, leading to promising anti-tumor effects[104,105]. However, the specific role of the gut microbiome in mediating these anti-tumor effects in cancer therapy remains unclear.

The influence of the microbiome in such effects has been explored in other conditions like autism and epilepsy[106,107]. For example, in mice with autism spectrum disorder, KD was shown to normalize high levels of *Akkermansia muciniphila* and promote a higher Firmicutes/Bacteroidetes ratio[107]. In infants with refractory epilepsy, KD not only reduced seizure frequency but also increased the levels of *Bacteroides* and *Prevotella*, while decreasing *Cronobacter* abundance[106]. Although similar microbiome shifts could be beneficial for cancer patients undergoing treatment, this remains an area for further investigation.

Dietary strategies include: (1) Caloric restriction (CR), which entails a reduction in energy intake by 20%-50% without causing malnutrition or depleting essential nutrients; (2) Time-restricted feeding, where eating is confined to a specific 4- to 12-hour window; (3) Intermittent fasting, which alternates between 24-hour fasting periods and 24-hour ad libitum eating phases; and (4) The fasting-mimicking diet, a five-day period of CR with a low-calorie, vegetable-based diet, followed by a return to regular eating patterns once a month[108]. In recent years, there has been a growing body of research exploring the potential of these dietary approaches to delay the onset and progression of cancer, as well as other chronic diseases[109,110]. A key factor in how dietary restrictions may positively impact metabolism and immune function is the gut microbiome. As previously discussed, the microbiome plays an important role in cancer development and therapy response by influencing gut homeostasis, which in turn affects both the gut barrier and immune system. Therefore, dietary restrictions may help restore gut dysbiosis, improving metabolism and immune responses. Specifically, disruptions in gut permeability and the translocation of bacteria to the mucosal layer can trigger immune dysfunction. Immune homeostasis in the intestines is largely regulated by interactions between epithelial cells and dendritic cells[111]. Thus, by modulating the microbiome, these dietary changes could enhance cancer treatment outcomes. However, reliable data confirming these effects are still lacking. Moreover, it is important to note that interventions like fasting may worsen cachexia syndrome, which impacts nearly half of all cancer patients[112]. Future research should focus on determining the most effective timing and approach for these dietary interventions, considering factors such as gut microbiome composition, cancer type, and the individual characteristics of patients.

High fiber diets

Dietary fiber serves as a key substrate for gut microbial fermentation, leading to the production of short-chain fatty acids, such as butyrate, which have been shown to exert anti-inflammatory and anticancer properties[113]. High-fiber diets have been associated with increased microbiota diversity and favorable shifts in microbial composition, which may enhance antitumor immunity and improve treatment responses[114].

Spencer *et al*[115] reported that melanoma patients consuming high-fiber diets had improved progression-free survival while on immune checkpoint inhibitor (ICI) therapy, potentially mediated by a more favorable gut microbiome profile [115]. Additionally, dietary fiber has been shown to increase microbial metabolites that promote mucosal immunity and inhibit tumor growth in preclinical models[116].

However, the interplay between diet, microbiota, and host immune responses is complex and influenced by multiple factors, including baseline microbiome composition and genetic background. Ongoing studies are investigating the optimal dietary patterns and fiber types for therapeutic benefit in different cancer types[117].

Fecal microbiota transplantation

Fecal microbiota transplantation (FMT) involves the transfer of fecal material from a healthy donor to the GI tract of a recipient, aiming to restore microbial diversity and function[118]. Initially developed for treating recurrent *Clostridioides* difficile infection[119], FMT is now being explored as an adjunct in cancer therapy[120]. Preclinical studies and early-phase clinical trials suggest that FMT can modulate the gut microbiome in a way that enhances the efficacy of ICIs, particularly in melanoma and other solid tumors[121].

For instance, Baruch *et al*[122] demonstrated that FMT from ICI responders could induce clinical responses in melanoma patients previously refractory to anti- programmed death 1 (PD-1) therapy. Similarly, Davar *et al*[123] showed that microbial reprogramming through FMT could overcome primary resistance to immunotherapy in metastatic melanoma. While these findings are promising, further large-scale trials are needed to validate the safety, donor selection criteria, and long-term outcomes of FMT in oncology settings.

GUT MICROBIOME AND THERAPEUTIC APPROACH ACROSS GI MALIGNANCIES

Colon cancer

CRC is the third most prevalent cancer in men and the second in women and the predominant histological subtype is adenocarcinoma[2]. CRC is a multifactorial disease and the main etiology remains complex, environmental factors - including smoking, diet, and lifestyle - significantly influencing individual susceptibility and sporadic cases constitute approximately 80% of cases[124]. Some well-known risk factors are: Age, genetic predispositions, familial CRC history, IBD[125-127]. Gut microbiome alterations and microbial infections have shown an association with CRC pathogenesis and treatment response[128,129].

The human gut hosts over 500 bacterial species, with the densest microbial populations residing in the colon[130]. The microbiome primarily comprises obligate anaerobes such as *Bacteroides*, *Eubacterium*, *Bifidobacterium*, *Fusobacterium*, *Peptostreptococcus*, and *Atopobium*, while facultative anaerobes like *Enterococci*, *Lactobacilli*, *Enterobacteriaceae*, and *Streptococci* constitute a smaller proportion[131,132]. While the primary gut microbiome associated with CRC has not been completely identified, the significance of *F. nucleatum*, *E. coli*, and *Bacteroides fragilis* (*B. fragilis*) in CRC has been established[132,133]. These bacteria can contribute to tumor progression by causing DNA damage and activating various

signaling pathways[134].

F. nucleatum and CRC progression

The *F. nucleatum* protein Fap2 binds to Gal-GalNAc on CRC cells, facilitating bacterial colonization[135]. *F. nucleatum* also interacts with *E-cadherin via* FadA, activating the β-catenin and NF-κB pathways, increasing proinflammatory cytokines (TNF-α, IL-6, IL-8, IL-1β), and promoting immune evasion by binding to TIGIT receptors on natural killer cells and tumor-infiltrating lymphocytes[136,137]. It further enhances CRC progression through TLR4/MyD88 signaling[135,136,138,139].

Bacterial toxins and DNA damage

Research has identified *F. nucleatum* in CRC primary tumors and liver metastases, while *Bacteroides fragilis* and *E. coli* disrupt the colonic mucus barrier. Their toxins cause DNA damage, inflammation, and mutations. *E. coli* also impairs DNA repair *via* EspF and increases ROS, contributing to genetic instability in CRC[140-144].

Additional microbial contributors

Other bacteria linked to CRC include Peptostreptococcus anaerobius, which increases ROS *via* TLR2/TLR4, and seven species (*B. fragilis*, *F. nucleatum*, *Porphyromonas asaccharolytica*, *Parvimonas micra*, *Prevotella intermedia*, *Alistipes finegoldii*, *Thermanaerovibrio acidaminovorans*) associated with lipopolysaccharide (LPS)-induced inflammation and energy biosynthesis pathways. *Atopobium parvulum* and *Actinomyces odontolyticus* are enriched in early CRC and may serve as biomarkers[145,146]. *Enterotoxigenic B. fragilis* (ETBF) drives CRC by inducing IL-17, activating NF-κB, and recruiting myeloid-derived suppressor cells, which suppress CD8+ T-cell activity. ETBF also upregulates matrix metalloproteinase 9 and vascular endothelial growth factor A, further promoting tumor progression *via* CXCL1 and CXCL2[147,148]. Dysbiosis is linked to colorectal diseases, including IBD, colitis, and CRC[149,150]. Several bacteria contribute to CRC development.

Streptococcus gallolyticus: *Streptococcus gallolyticus* (*S. gallolyticus*) is associated with enterococcal endocarditis and cecal carcinoma, with up to 40% of bacteremia cases linked to CRC[151-153]. It promotes tumorigenesis by increasing inflammatory markers and oxidative stress, adhering to colorectal tissues *via* collagen-binding proteins. Colonoscopic screening is recommended for infected patients[153]. While earlier reports suggested an association rate as high as 80%, more recent analyses indicate a lower prevalence. A retrospective cohort study conducted in the Skane Region of Sweden from 2003 to 2018 found that among patients with *S. gallolyticus* subsp. Gallolyticus bacteremia, 7% were diagnosed with CRC within 12 months. This study highlighted a strong association between this specific subspecies and CRC, with a standardized incidence ratio of 59.8 compared to the general population[154]. Additionally, a 2022 study from Iran reported that 60% of patients with CRC had *S. gallolyticus* detected in tumor samples, compared to 29.7% in control subjects without CRC[155].

Bacteroides fragilis: *Bacteroides fragilis* produces fragilysin, which disrupts E-cadherin, activating oncogenic pathways [β-catenin, cellular MYC (c-MYC), cyclin D1][156-159]. Its tumorigenic effects involve signal transducer and activator of transcription 3 activation and a TH17 immune response, which can be mitigated by IL-17/IL-23 blockade[160].

***E. coli* (pks-positive strains):** *E. coli* produce colibactin, a genotoxin that induces DNA damage, mutations, and genomic instability, driving CRC development in mouse models[161,162].

***F. nucleatum*:** *F. nucleatum* is enriched in CRC and correlates with poor survival and metastasis. Its virulence factors, Fap2 and FadA, inhibit immune responses and activate oncogenic signaling (β-catenin, TLR4/NF-κB, miR-21), promoting tumor growth and invasion[136,139,163].

***Enterococcus faecalis*:** *Enterococcus faecalis* (*E. faecalis*) generates reactive oxygen/nitrogen species, leading to DNA damage and chromosomal instability. *H. pylori* may contribute to CRC *via* hypergastrinemia and cytotoxin-associated gene A (CagA)-mediated oncogenic effects, though its role remains unclear[164,165].

Microbial composition shifts in CRC patients include increased *Bacteroides/Prevotella, Fusobacterium, Roseburia,* and *Faecalibacterium* in tumors, with reduced *Enterobacteriaceae* levels[131,132]. Host-microbiome interactions *via* fecal microRNAs influence bacterial gene expression, potentially driving CRC progression[166]. Case-control studies show CRC-associated bacteria (*F. nucleatum, E. faecalis, S. gallolyticus, ETBF*) are enriched in adenomatous polyps, while beneficial bacteria (*Lactobacillus, Roseburia, Bifidobacterium*) are reduced[167,168]. Emerging research suggests gut microbiome profiling combined with machine learning could serve as a non-invasive CRC screening tool, offering accuracy comparable to colonoscopy[150]. A summarized table of the therapeutic approaches related to the gut microbiome in CRC can be found in Table 1[20,133,140,166,169-184].

Pancreatic cancer

Pancreatic cancer is a rapidly progressing and highly fatal disease, with only about 25% of patients surviving beyond one year after diagnosis[185]. Due to late-stage detection in most cases, treatment is often palliative, relying on chemotherapy or radiotherapy rather than surgical intervention. Among the different types, pancreatic ductal adenocarcinoma stands out as the most common and aggressive subtype[186]. Chronic pancreatitis is a well-established risk factor, with incidence rates significantly higher in affected individuals[187]. Studies suggest a strong association between bacterial infections and pancreatic cancer, not necessarily as a direct cause but as contributors to tumor progression, immune modulation, and inflammatory responses[188,189].

Table 1 Therapeutic approaches related to the gut microbiome in colorectal cancer

Therapeutic approach	Description	Key findings
Bacterial eradication	Targeting CRC-associated bacteria using antimicrobial agents	Colibactin-producing *E. coli* inhibited by ClbP inhibitors, reducing tumor growth in mice[169]
		F. nucleatum targeted with metronidazole, lowering bacterial load and tumor proliferation[140]
Probiotics	Using beneficial bacteria to modulate gut microbiome for CRC prevention and chemotherapy support[20,133,170]	*Lactobacillus* and *Bifidobacterium* species reduced preneoplastic lesions in animal models[171,172]
		VSL3 probiotic mix reduced adenoma formation and chemotherapy side effects[173]
		Human studies show mixed results on probiotics' protective effects against CRC[174-176]
FMT	Transplanting healthy microbiome to modify gut composition and potentially prevent CRC[177]	FMT from wild mice improved CRC resistance and inflammation markers in recipient mice[177]
		Clinical evidence remains limited, requiring further studies[178]
Microbiome and chemotherapy resistance	Gut bacteria influence drug resistance and efficacy in CRC treatment[166]	*F. nucleatum* linked to resistance against 5-FU and oxaliplatin *via* immune signaling[166]
		Mycoplasma hyorhinis and *Gammaproteobacteria* impair gemcitabine by enzymatic deactivation[179]
		Ciprofloxacin restored gemcitabine sensitivity[179]
		Antibiotic use may reduce chemotherapy efficacy in some cases[180]
Microbiome and immunotherapy	Gut bacteria influence immune responses to CRC therapies[27]	Microbiome impact responses to immune checkpoint inhibitors (*e.g.*, Ipilimumab)[181]
		Antibiotic-treated mice showed reduced immunotherapy effectiveness[181]
Microbiome and drug toxicity	Bacteria alter drug metabolism, affecting side effects and toxicity	*E. coli* β-glucuronidase reactivates irinotecan, increasing toxicity[182,183]
		Irinotecan alters microbiome, increasing inflammatory bacteria (*Fusobacteria, Proteobacteria*)[182]
		Antibiotic treatment reduced oxaliplatin-induced neuropathy in mice[184]

CRC: Colorectal cancer; ClbP: Colibactin precursor peptidase P; 5-FU: 5-fluorouracil; FMT: Fecal microbiome transplantation; *E. coli*: *Escherichia coli*; *F. nucleatum*: *Fusobacterium nucleatum*.

H. PYLORI AND PANCREATIC CANCER

A growing body of research has associated *H. pylori* infection to pancreatic cancer development[190,191]. Initial case-control studies reported a twofold increased risk in infected individuals, with prospective cohort studies confirming a higher susceptibility in male smokers carrying *H. pylori* antibodies, particularly the CagA-positive strains[192]. Further meta-analyses reinforced these findings, with large cohort studies also establishing a correlation between gastric ulcers (often caused by *H. pylori*) and pancreatic cancer[193,194].

H. pylori is believed to promote pancreatic diseases through its production of ammonia, lipopolysaccharides, and inflammatory mediators. *In vitro* experiments demonstrated increased levels of IL-8 and vascular endothelial growth factor (VEGF) in pancreatic cancer cell lines co-cultured with *H. pylori*, contributing to inflammation and tumor growth [195]. Furthermore, *H. pylori* LPS has been shown to enhance *KRAS* mutations—present in over 90% of pancreatic adenocarcinomas - thereby initiating carcinogenesis[196,197]. Additionally, the infection was found to activate signal transducer and activator of transcription 3, a signaling pathway that promotes cancer progression by upregulating anti-apoptotic and pro-proliferative proteins such as B-cell lymphoma-extra large, myeloid cell leukemia 1, survivin, c-MYC, and cyclin D1[198,199]. While a clear causal relationship has yet to be established, further clinical intervention studies using *H. pylori* eradication therapy may provide insights into its role in pancreatic cancer initiation[200].

ORAL BACTERIA AND PANCREATIC CANCER RISK

Periodontal pathogens have also been implicated in pancreatic cancer risk. *Porphyromonas gingivalis* (*P. gingivalis*), a major

bacterium associated with periodontitis, has been extensively studied in this context[201,202]. The European Prospective Investigation into Cancer cohort reported that individuals with high *P. gingivalis* antibody levels had more than double the risk of developing pancreatic cancer[202]. Though the precise mechanisms remain unclear, *P. gingivalis*' LPS is believed to stimulate the TLR4 signaling pathway, which plays a key role in pancreatic ductal adenocarcinoma (PDAC) by promoting tumor growth, angiogenesis, invasion, and apoptosis suppression.

Additionally, Fusobacterium species have been detected in 8.8% of pancreatic cancer tissues, with their presence linked to poor prognosis[203-205]. These findings suggest Fusobacterium as a potential negative prognostic biomarker for pancreatic cancer[206]. Recent studies have reported a higher prevalence of *F. nucleatum* in PDAC than previously estimated indicating a range of approximately 20% to 30%[207-209]. For instance, a 2024 review highlighted that *F. nucleatum* is present in a significant subset of PDAC tumors, with prevalence rates reaching up to 30% in certain cohorts [209]. This bacterium has been associated with tumor progression and poorer patient outcomes. *F. nucleatum* can promote PDAC cell proliferation and migration through the induction of cytokines such as granulocyte-macrophage colony-stimulating factor, CXCL1, and IL-8, which act *via* autocrine and paracrine signaling pathways[208]. Additionally, it can influence the tumor microenvironment by modulating immune responses, potentially contributing to an immunosuppressive milieu that favors tumor growth[208]. These findings underscore the importance of considering *F. nucleatum* in the context of PDAC pathogenesis and suggest potential avenues for therapeutic intervention targeting the tumor microbiome.

Another emerging bacterial player is *Pseudomonas aeruginosa*, which has been shown to enhance the expression of the *ABCB1* gene, contributing to drug resistance, tumor invasion, and metastasis[210]. Table 2 summarizes recent findings on microbiome-targeted therapies for PDAC[179,189,211,212].

Gastroesophageal cancer

GC is a multifactorial disease influenced by environmental, dietary, host-related, genetic, and epigenetic factors[213,214]. *H. pylori*, designated as a group I carcinogen by the World Health Organization, is a major contributor to GC pathogenesis, colonizing the gastric mucosa in approximately 50% of the global population[215]. The oncogenic potential of *H. pylori* is attributed to two primary mechanisms: Indirect inflammation-mediated pathways and direct bacterial virulence factor interactions[216].

Chronic *H. pylori*-induced inflammation, as described in the Correa model[217], promotes gastric epithelial turnover, increasing the probability of mitotic errors and malignant transformation[218,219]. This pathological cascade progresses from atrophic gastritis to intestinal metaplasia (IM), dysplasia, and ultimately gastric adenocarcinoma[218-220]. The inflammatory response involves complex interactions between the bacterial pathogen, gastric acid secretion, immune cells, and reactive oxygen and nitrogen species, leading to oxidative DNA damage and upregulation of pro-inflammatory mediators[221,222]. Elevated expression of cytokines (IL-1β, IL-6, IL-8, and TNF-α) and cyclooxygenase-2 has been implicated in promoting atrophic mucosal alterations and oncogenic intracellular signaling[223,224]. Furthermore, *H. pylori* infection is associated with epigenetic modifications, including aberrant DNA methylation and gene silencing, affecting key regulatory pathways involved in cell adhesion, proliferation, DNA repair, and immune modulation[223].

Recent high-quality evidence reinforces the protective effect of *H. pylori* eradication therapy in reducing the risk of GC, particularly when administered before the onset of precancerous changes such as IM or dysplasia. A recent meta-analysis published in Frontiers in Microbiology in 2025 evaluated the impact of *H. pylori* eradication on GC risk among patients with IM or dysplasia. The study included 16 randomized controlled trials involving 15027 participants. The findings indicated that *H. pylori* eradication was associated with a 45% reduction in the relative risk (RR) of developing GC compared to no treatment [RR = 0.55; 95% confidence interval (CI): 0.46-0.67; $P < 0.001$]. Subgroup analyses revealed that eradication therapy significantly lowered GC risk in patients with dysplasia (RR = 0.51; 95%CI: 0.32-0.82; $P = 0.005$) and IM (RR = 0.61; 95%CI: 0.40-0.93; $P = 0.022$)[225]. Another recent systematic review and meta-analysis published in Gastroenterology in January 2025 evaluated the impact of *H. pylori* eradication on GC incidence and mortality[226]. The study included 11 randomized controlled trials and 13 observational studies, encompassing a total of 58828 participants. The findings revealed that H. pylori eradication was associated with a 36% reduction in the RR of developing GC (RR = 0.64; 95%CI: 0.48-0.84) and a 22% reduction in GC mortality (RR = 0.78; 95%CI: 0.62-0.98). These results underscore the potential of *H. pylori* eradication as a preventive strategy against GC.

In addition to inflammation-driven carcinogenesis, *H. pylori* exerts direct tumorigenic effects through its virulence factors, particularly CagA and vacuolating cytotoxin A (VacA)[227,228]. CagA disrupts intracellular signaling networks such as the MAPK cascade, NF-κB, phosphoinositide 3-kinase/protein kinase B, and epithelial-mesenchymal transition pathways *via* oncogenic yes-associated protein activation[228,229]. The cag pathogenicity island has also been implicated in *H. pylori*-induced carcinogenesis through mutations in tumor suppressor genes such as *TP53*[230,231]. Meanwhile, VacA facilitates immune evasion by impairing T-cell responses and disrupting epithelial integrity, thereby creating a permissive environment for persistent infection and neoplastic progression[232,233]. Table 3 summarizes recent findings on microbiome-targeted treatment strategies in gastroesophageal cancer[234-244].

Hepatobiliary cancer

Biliary tract cancers include cancers of the bile duct, gallbladder, and ampulla of Vater, with gallbladder cancer (GBC) being the most prevalent[245,246]. While rare in the Western world, GBC is more common in Chile, Central Europe, Thailand, Japan, and parts of India and Pakistan[247,248]. The main risk factors include gallstones, obesity, chronic gallbladder inflammation, genetic predisposition, and environmental factors. Additionally, bacterial infections have been linked to malignant transformation in GBC.

Table 2 Recent findings on microbiome-targeted therapies for pancreatic ductal adenocarcinoma

Therapeutic approach	Description	Key findings
Antibiotic therapy	Targeting tumor-associated bacteria to reduce tumor burden and enhance immunotherapy	Pushalkar *et al*[211] found a 50% tumor burden reduction in PDAC mouse models after oral antibiotic treatment
		Tumor microenvironment reprogrammed, reducing myeloid-derived suppressor cells and increasing M1 macrophages[211]
		Antibiotics improved PD-1 checkpoint inhibitor response, enhancing T-cell activation and reducing tumor size[211]
		A clinical trial is evaluating antibiotic-pembrolizumab combination in locally advanced PDAC[189]
Probiotics and PDAC prevention	Investigating probiotics' role in mitigating PDAC risk factors (*e.g.*, pancreatitis, obesity, diabetes)	*Lactobacillus plantarum* 299 reduced pancreatic sepsis and surgical need in acute pancreatitis patients[212]
		Probiotics reduced fibrosis, inflammation, necrosis, ductal damage, and atypical cellular regeneration, potentially lowering PDAC risk
Microbiome and chemotherapy resistance	Examining bacterial interference with chemotherapy efficacy	*Gammaproteobacteria* enriched in 76% of PDAC samples, degrading gemcitabine into an inactive form[179]
		Microbiome-targeted approaches could enhance chemotherapy effectiveness

PDAC: Pancreatic ductal adenocarcinoma; PD-1: Programmed death 1.

Table 3 Microbiome-targeted treatment strategies in gastroesophageal cancer

Topic	Findings	Key insights
Microbiomes in esophageal cancer treatment	Disrupting microbiome with antibiotics decreases xenograft tumor response to CpG oligonucleotide immunotherapy and platinum-based chemotherapy (*e.g.*, oxaliplatin)[180]	A stable commensal microbiome may enhance cancer therapy effectiveness[180]
	Similar effects observed in germ-free mice[180,234]	Microbiome regulates myeloid-derived cell functions within the tumor microenvironment[234]
		Further clinical research is needed
H. pylori and GC risk	*H. pylori* eradication reduces GC risk but does not guarantee complete prevention [235,236]	Other factors contribute to GC beyond *H. pylori* infection[235]
	A Colombian clinical trial showed no significant GC incidence difference between treated and untreated individuals over six years, but treated individuals had higher precancerous lesion regression rates[235]	Eradication reduces GC risk by about 44% in asymptomatic, infected individuals[236]
Long-term impact of *H. pylori* eradication	A 15-year study showed a 39% reduction in precancerous lesions[237]	Protective effects are strongest in non-atrophic/atrophic gastritis patients[239,240]
	An 8-year study found that atrophic body gastritis reversed in 50% of treated patients[238]	Intestinal metaplasia and dysplasia patients do not experience the same benefit
	Meta-analyses confirmed a significant reduction in GC risk post-eradication[239]	Early eradication is crucial as intestinal metaplasia is irreversible
Epigenetic modifications in GC prevention	DNA demethylating agent (5-azadC) suppresses aberrant methylation and reduces GC incidence in animal models[241]	Developing safer DNA demethylating agents could benefit high-risk individuals [223]
	Clinical use is limited due to high toxicity	
Probiotics and *H. pylori* eradication	Probiotics inhibit *H. pylori* in animal studies[242]	Probiotics may play a role in GC prevention [243,244]
	Clinical trials/meta-analyses show probiotics improve eradication rates, patient compliance, and reduce treatment side effects	Used alongside antibiotics, they enhance treatment efficacy

H. pylori: *Helicobacter pylori*; CpG: Cytosine-phosphate-guanine; GC: Gastric cancer.

KEY BACTERIAL ASSOCIATIONS WITH GBC

Salmonella enterica serovar Typhi (*S. Typhi*): Chronic typhoid carriers have a significantly higher risk of GBC, with some studies reporting up to a 167-fold increased risk. However, recent metagenomic studies in South America found other bacteria (*e.g.*, *E. coli*, *F. nucleatum*, *Enterobacter* species) predominant in GBC patients instead of *S. Typhi*[249-251].

Helicobacter species (*H. bilis, H. hepaticus, H. pylori*)[11,252]: These bile-resistant bacteria can cause chronic inflammation and gallstone formation, contributing to carcinogenesis. Some studies report a 2-3-fold increased risk of GBC in infected individuals. However, more epidemiological studies are needed to confirm causality.

Mixed bacterial infections: *E. coli, Enterobacter, Klebsiella*, and *E. faecalis* have been found in high levels in GBC patients. Given their known role in colon cancer, it is hypothesized they might contribute to GBC through similar mechanisms[253,254].

MECHANISMS OF BACTERIAL-INDUCED CARCINOGENESIS

Gallstones facilitate bacterial colonization, increasing the likelihood of persistent infection. *S. Typhi* infection triggers oncogenic pathways (protein kinase B/MAPK), leading to mutated *p53* and amplified c-MYC - both commonly observed in GBC patients[255,256]. Bacterial glucuronidase enzymes produce carcinogenic metabolites from bile, potentially leading to DNA damage and tumor development[256]. Bacterial enzymes increase secondary bile acids, which are known tumor initiators and promoters in GBC[257].

Hepatocellular carcinoma (HCC), the most common primary liver cancer and a leading cause of cancer-related deaths, is often associated with underlying liver diseases such as cirrhosis, fibrosis, and chronic hepatitis B and C infections[258,259]. Other recognized risk factors include alcoholic liver disease, hemochromatosis, obesity, and non-alcoholic fatty liver disease (NAFLD)[260,261]. While bacterial infections are not traditionally considered a primary cause of HCC, growing evidence suggests that gut and hepatic microbiome may influence its development and progression[262,263]. The liver, though generally sterile, is directly connected to the gut through the hepatic portal system. Disruptions in the gut microbiome can lead to increased intestinal permeability, allowing bacteria and their metabolites - such as lipopolysaccharides - to translocate to the liver[264]. This process contributes to chronic inflammation, immune dysregulation, and liver disease progression[265,266].

Certain bacterial species have been implicated in HCC development. *E. coli, Atopobium, Bacteroides, Clostridium*, and *Desulfovibrio* were found enriched in the gut microbiome of HCC patients, correlating with increased LPS levels and disease severity[267]. Additionally, obesity-related alterations in gut microbiome contribute to hepatocarcinogenesis through increased production of secondary bile acids, such as deoxycholic acid, which can activate the mammalian target of rapamycin (mTOR) pathway and promote liver tumorigenesis[268]. In high-fat diet-fed mice, elevated deoxycholic acid levels were associated with a higher incidence of HCC, while antibiotic treatment reduced tumor formation. *Helicobacter* species, particularly *Helicobacter hepaticus* and *H. pylori*, have also been linked to HCC[269,270]. *In vivo* studies showed that *H. hepaticus* disrupts enterohepatic homeostasis and activates NF-κB and Wnt signaling pathways, leading to oxidative stress and hepatocyte turnover. Furthermore, *H. pylori* virulence factors such as VacA and CagA were detected in HCC tissues, and its LPS was found to enhance liver cancer cell growth and migration[271,272].

Beyond the gut-liver axis, alterations in oral microbiome have also been observed in HCC patients[273]. A metagenomic analysis of the tongue microbiome identified an increased abundance of *Oribacterium* and *Fusobacterium*, suggesting a potential link between oral and hepatic dysbiosis[273]. Additionally, studies in cirrhosis patients revealed a higher fecal count of *E. coli* in those with HCC, reinforcing the idea that gut microbiome alterations contribute to hepatocarcinogenesis[274]. Recent findings suggest that gut microbiome composition differs in NAFLD-related cirrhosis with and without HCC[275]. Patients with HCC exhibited higher levels of *Bacteroides* and *Ruminococcaceae* while showing reduced levels of beneficial bacteria such as *Bifidobacterium*. These findings indicate that gut microbiome dysbiosis may play a role in the progression from NAFLD and cirrhosis to HCC[275]. Table 4 summarizes recent findings on microbiome-targeted treatment strategies in hepatobiliary cancers[251,255,267,276-282].

Understanding the distinct microbial signatures and dysbiosis patterns across GI cancers such as colorectal, gastric, and pancreatic cancer highlights the intricate role the gut microbiome plays in tumorigenesis and progression. However, the interplay between the microbiome and cancer extends beyond pathogenesis - it also critically influences how patients respond to treatment. The next section explores how common cancer therapies, including chemotherapy, radiotherapy, and immunotherapy, interact with and are modulated by the gut microbiome, shaping both efficacy and toxicity profiles.

CANCER TREATMENTS INFLUENCE GUT MICROBIOME DIVERSITY AND ACTIVITY

Chemotherapy

One of the major side effects of irinotecan, a key anti-cancer drug used for metastatic CRC, is severe diarrhea[283]. A study demonstrated that irinotecan chemotherapy alters the intestinal microbiome in tumor-bearing rats, leading to an increased abundance of Clostridium clusters I, XI, and Enterobacteriaceae, particularly following dose-intensive therapy [284]. Similarly, 5-FU, an anti-metabolite used to treat several cancers, including colorectal, breast, and liver, also induces diarrhea as a frequent side effect[283]. An observational study on breast cancer patients receiving 5-FU, epirubicin, and cyclophosphamide found alterations in intestinal permeability and changes in gut peptides such as glucagon-like peptide-2, ghrelin, and epidermal growth factor. Notably, patients who experienced diarrhea had higher intestinal

Table 4 Microbiome-targeted treatment strategies in hepatobiliary cancers

Topic	Findings	Key insights
Antibiotics, probiotics, and GBC	Limited experimental and clinical evidence on their use for GBC prevention or treatment[255]	*Salmonella* infection may trigger lasting oncogenic changes
	A study by Scanu *et al*[255] found that *Salmonella*-infected mouse embryonic fibroblasts formed tumors even after bacterial eradication with ciprofloxacin	
	Salmonella infection activates Akt/MAPK signaling pathways, potentially sustaining carcinogenesis post-eradication[255]	Further research is needed to explore microbiome-targeted GBC therapies
	Cholecystectomy remains the most effective preventive measure for chronic typhoid carriers at risk of GBC[251]	
Probiotics and HCC prevention	Probiotic-fermented milk and chlorophyllin reduced tumor incidence in AFB1-induced HCC in rats[276]	Probiotics show potential in reducing HCC risk and progression in animal models
	VSL3 probiotic formula inhibited chemically induced HCC, reducing LPS levels, tumor size, and tumor count[267]	
	Prohep (novel probiotic mix) decreased tumor growth by 40%, enhanced anti-inflammatory responses, promoted T-cell activation, and reduced pro-angiogenic factors in mice[277]	Clinical evidence remains limited, requiring large-scale human trials
Probiotics and aflatoxin exposure	Some studies suggest probiotics reduce aflatoxin exposure and toxic DNA adduct formation, potentially lowering HCC risk[278]	Needs further validation in human studies
FMT and liver disease	FMT has shown promise in treating[279]: (1) High-fat diet and alcohol-induced liver injury (animal models)[280]; (2) Severe alcoholic hepatitis (clinical studies)[281]; (3) Chronic hepatitis B[282]; and (4) Advanced liver cirrhosis and hepatic encephalopathy	FMT may help restore gut-liver axis balance[279]
		Its role in HCC prevention and therapy remains unclear, requiring further clinical trials

GBC: Gallbladder cancer; Akt: Protein kinase B; MAPK: Mitogen-activated protein kinase; HCC: Hepatocellular carcinoma; AFB1: Aflatoxin B1; LPS: Lipopolysaccharide; FMT: Fecal microbiome transplantation.

permeability than those who did not[285].

van Vliet *et al*[286] showed that in pediatric patients with acute myeloid leukemia, chemotherapy combined with antimicrobial prophylaxis caused a reduction in anaerobic bacteria and an increase in potentially pathogenic aerobic enterococci. These gut microbiome disturbances may increase the risk of gram-positive infections. Furthermore, a study on paclitaxel-induced neuropathic pain in C57BL/6 (B6) and 129SvEv (129) mice, which display greater neuropathic sensitivity, revealed significant changes in gut microbiome. In particular, paclitaxel chemotherapy led to a decrease in *Akkermansia muciniphila* abundance in the B6 microbiome. The reduction of this beneficial bacterium was linked to gut barrier dysfunction, which might increase systemic exposure to bacterial products and metabolites, contributing to systemic inflammation and pain sensitivity[165,287].

Immunotherapy

Given the close association between gut microbiome and the immune system, immunotherapeutic interventions also exert significant effects on microbial composition and function. In a cohort of HCC patients receiving anti-PD1 therapy, microbial shifts were observed by week 3, with a notable increase in *E. coli* abundance in non-responders' stool samples, while *Lactobacillus*, *Ruminococcaceae*, and *Akkermansia muciniphila* were enriched in responders' microbiome[288]. Similarly, in melanoma patients undergoing anti-CTL-associated protein 4 treatment, there was a decrease in the relative abundance of *Bacteroidales* and *Burkholderiales*, accompanied by a significant increase in *Clostridiales*[289]. Despite these specific alterations in microbial populations, some studies have reported a relatively stable microbial composition throughout the course of immunotherapy[290,291]. A 2022 review discussed how the gut microbiome could reshape the cancer therapy paradigm, emphasizing its influence on immunotherapy, chemotherapy, and radiotherapy responses[292]. Another 2025 narrative review highlighted the interplay between the microbiome and diet in modulating responses to cancer checkpoint immunotherapy, suggesting that dietary interventions could enhance immunotherapy efficacy[293].

Surgery

Recent advancements in cancer surgery have highlighted the significant impact of surgical interventions on gut microbiome, especially in patients with GI cancers. A study examining gastrectomy in GC patients assessed its effects on the gut microbiome and metabolome, exploring the association between microbial changes and post-gastrectomy outcomes. The analysis showed substantial shifts in microbial diversity and richness in patients who underwent gastrectomy, likely due to the reconstruction of the GI tract following surgery. These microbial alterations could influence microbial functions, including nutrient transport and organic compound biosynthesis, which may contribute to changes in post-surgical metabolism[294]. Similarly, a study conducted in China investigated the fecal microbiome of GC patients before and after radical distal gastrectomy[295]. Significant changes were observed in the microbial composition during the perioperative period, with variations in the abundances of *Akkermansia muciniphila, Escherichia/Shigella, Lactobacillus*, and *Dialister*. Post-surgery, there was an increase in *Escherichia/Shigella, Veillonella*, and *Clostridium XVIII*, as well as a

decrease in *Bacteroides*, when compared to healthy controls. These shifts are likely driven by surgical stress and other perioperative factors[295]. Additionally, research has shown that a modified microbiota-accessible carbohydrate diet can positively influence the gut microbiome and clinical symptoms in CRC patients following surgical resection[296].

In CRC surgery, animal studies have shown significant alterations in the gut microbiome following colorectal resection, with a marked reduction in *Bacteroidetes* and *Proteobacteria*, such as *Enterobacteriaceae* and *Rhodospirillaceae*[297]. Moreover, these microbial changes were associated with altered gene expression patterns, including an increase in IL10 and IL12 and a decrease in TNF expression after surgery[297]. In CRC patients, numerous studies have reported post-surgical changes in the gut microbiome, comparing post-surgery samples to those from preoperative CRC patients and healthy controls. These changes include a decrease in *Bacteroides*, *Bifidobacterium, Clostridium, Prevotella, Klebsiella, Faecalibacterium*, and *Parabacteroides*, while *Enterococcus, Pseudomonas, Staphylococcus, Escherichia-Shigella, Enterobacteriaceae*, and *Streptococcus* increased post-surgery[298,299]. In contrast, some studies have shown a decrease in *Escherichia-Shigella* and an increase in *Enterococcus* and *Parabacteroides*[300]. At the phylum level, a reduction in *Firmicutes* and *Bacteroidetes* was observed, alongside a decrease in the *Firmicutes/Bacteroides* ratio and an increase in *Proteobacteria*[301,302]. These microbial changes are likely a consequence of perioperative antibiotic administration, which can alter the gut microbiome, impair immune function, and disrupt metabolic pathways[303]. The resulting disruption in gut barrier integrity, coupled with surgical stress, may contribute to the development of inflammation and other postoperative complications in cancer patients. Recent evidence underscores the benefits of early enteral nutrition and probiotic supplementation in enhancing postoperative recovery for CRC patients.

Early enteral nutrition: Initiating enteral nutrition within 48 hours post-CRC surgery has been associated with improved GI recovery and nutritional status. A retrospective comparative study involving 227 patients in each group demonstrated that early enteral nutrition led to a shorter time to first postoperative flatus, quicker achievement of nutritional goals, and reduced hospital stay, without increasing postoperative complications[304]. Similarly, a randomized controlled trial reported that patients receiving early oral feeding after colorectal surgery experienced faster return of intestinal movements, earlier defecation, and shorter hospital stays compared to those on a regular diet[305].

Probiotic supplementation: Probiotic use in the perioperative period has been shown to reduce postoperative infections and restore beneficial gut microbiota. A systematic review and meta-analysis of randomized controlled trials found that probiotic supplementation significantly decreased the incidence of diarrhea, surgical site infections, urinary infections, and pulmonary infections in CRC patients undergoing surgery[306].

Furthermore, probiotics have been associated with a reduction in postoperative complications such as ileus, abdominal collections, sepsis, and pneumonia. These benefits are attributed to the modulation of gut microbiota, enhancement of intestinal barrier function, and attenuation of inflammatory responses[307].

Radiotherapy

Radiotherapy stimulates anti-tumor responses through immune activation[308], and like other cancer treatments, it induces alterations in gut microbiome composition. In an animal study, irradiated mice exhibited luminal and mucosa-associated dysbiosis compared to controls at two post-radiation time points, which was linked to increased expression of TNF-α, IL-1β, and IL-6[71]. Another recent study on irradiated mice revealed an increase in the *Alistipes* genus and a decrease in *Prevotella* in the large intestine[309]. In human studies, Mitra *et al*[310] reported a reduction in gut microbiome diversity in cervical cancer patients following chemoradiation therapy, while a study of gynecological cancer patients receiving pelvic radiotherapy found a decrease in *Firmicutes* and an increase in *Fusobacterium*[311]. Though further validation is needed, these findings suggest that radiation-induced changes in gut microbiome could lead to alterations in intestinal mucosa, resulting in inflammation[312].

These observations open the door to novel strategies aimed at modulating the gut microbiome to improve cancer treatment outcomes. One such approach is dietary interventions, known to influence gut microbiome composition and functionality[313]. A 2024 study demonstrated that dietary fiber supplementation not only improved tumor control during radiotherapy[314] but also alleviated intestinal radiation toxicity, highlighting the dual benefits of such interventions in cancer therapy[315]. As a result, research into the effects of nutritional interventions during cancer therapy on gut microbiome and clinical outcomes is on the rise. In the following section, we will examine various nutritional strategies that may help optimize gut microbiome and enhance the efficacy of cancer therapies.

The dynamic interplay between cancer therapies and the gut microbiome underscores the bidirectional nature of this relationship - therapies can disrupt microbial homeostasis, while the microbiota, in turn, modulates treatment efficacy and toxicity. These insights not only deepen our mechanistic understanding but also prompt critical questions about how best to leverage the microbiome to optimize clinical outcomes. The following discussion synthesizes these findings, evaluates emerging therapeutic interventions such as dietary modulation and FMT, and highlights future directions for integrating microbiome science into oncology practice.

Targeted therapy and gut microbiome

In addition to standard chemotherapy, several targeted therapies have become integral to the treatment of GI malignancies, including monoclonal antibodies and antibody-drug conjugates. Emerging evidence suggests that the gut microbiota and local inflammatory milieu may significantly influence the efficacy, resistance, and toxicity of these therapies.

ANTIANGIOGENIC THERAPY (BEVACIZUMAB)

Bevacizumab, an anti-VEGF antibody, inhibits tumor angiogenesis and is widely used in combination regimens for metastatic CRC[316,317] and HCC[318]. A recent study investigated the role of the gut microbiota in modulating treatment response by analyzing pretreatment fecal samples from 37 patients[318]. Participants were classified as responders (n = 28) or non-responders (n = 9). Although overall microbial diversity did not differ significantly between the groups, the relative abundance of *Bacteroides stercoris* and *Parabacteroides merdae* was higher in responders. Notably, patients lacking both bacterial species had significantly worse prognoses. These findings suggest that specific gut microbiome may influence the therapeutic efficacy of atezolizumab and bevacizumab in advanced HCC.

While the gut microbiota's impact on chemotherapy in CRC has been studied, its role in targeted therapy remains less understood. Chen *et al*[318] evaluated the association between gut microbiota composition and treatment outcomes in 110 patients with metastatic CRC undergoing combined chemotherapy and targeted therapy. Patients were stratified into anti- epidermal growth factor receptor (EGFR) (cetuximab) and anti-VEGF (bevacizumab) subgroups. Higher gut microbial α-diversity was observed in the partial response group and specifically in the bevacizumab partial response subgroup. β-diversity significantly differed between the bevacizumab partial response and progressive disease groups (P = 0.029)[319]. Notably, *Klebsiella quasipneumoniae* showed the highest fold increase in the progressive disease group, while *F. nucleatum* was about 32 times more abundant in progressive disease *vs* partial response patients. Despite higher diversity being associated with better outcomes, the bacterial profiles were heterogeneous, underscoring the need for further microbiome-based investigations, particularly in East Asian populations.

EGFR MONOCLONAL ANTIBODIES (CETUXIMAB, PANITUMUMAB)

EGFR inhibitors are effective in *RAS* wild-type metastatic CRC. However, the gut microbiota may modulate EGFR pathway activity through inflammation-related mechanisms[319]. As of now, there is limited research directly linking panitumumab or cetuximab - monoclonal antibodies targeting the EGFR - to specific alterations in the gut microbiota in CRC patients[320]. For instance, dysbiosis-induced IL-17 and TNF-α production can interfere with EGFR inhibition and contribute to resistance. Moreover, cetuximab-induced skin toxicity has been linked to microbial alterations, raising the potential for microbiota-based strategies to mitigate adverse effects. A study by Liu *et al*[321] investigated the characteristics of the skin microbiome in patients experiencing severe skin toxicities induced by EGFR inhibitors, such as afatinib. The research revealed that patients with systemic drug-related intertriginous and flexural exanthema-like lesions exhibited significant skin microbial dysbiosis, characterized by reduced microbial diversity and an increased abundance of pathogenic bacteria. These findings suggest that alterations in the skin microbiota are associated with EGFR inhibitor-induced skin toxicities, highlighting the potential for microbiota-based strategies to mitigate such adverse effects. A review article by Ghidini *et al*[322] discusses the impact of tumor sidedness on the efficacy of anti-EGFR agents like panitumumab in metastatic CRC. While the article does not delve deeply into microbiota interactions, it acknowledges that the prognostic role of microbiota in CRC requires further clarification before being integrated into clinical practice.

These findings highlight the bidirectional relationship between the gut microbiota and targeted therapies. Microbial composition may affect drug pharmacokinetics, immune activation, and inflammation, thereby altering clinical outcomes. Integrating microbiome profiling into treatment planning and exploring microbiota-modulating strategies (*e.g.*, probiotics, FMT, diet) alongside targeted agents could represent the next frontier in personalized oncology.

INSIGHTS INTO GUT MICROBIOME, INFLAMMATION, AND NUTRITIONAL STATUS IN GI CANCER

Emerging evidence supports the idea that an altered gut microbiome contributes to the initiation and progression of GI cancers[29]. Inflammation, a hallmark of cancer, plays a significant role in promoting tumorigenesis, and the gut microbiome is crucial in modulating the inflammatory processes within the GI tract[29]. The relationship between gut microbiome and chronic inflammation has been well-documented, with studies showing that dysbiosis can enhance inflammation by disrupting gut barrier integrity, leading to the translocation of bacteria and their metabolites to the systemic circulation[29,206]. This can activate immune cells and trigger inflammatory cascades that ultimately contribute to the development of cancer.

For instance, certain microbial species such as *F. nucleatum* in CRC[163] or *H. pylori* in GC[216] have been associated with chronic inflammation that drives carcinogenesis. These microorganisms can either directly or indirectly manipulate immune responses in the gut, promoting an environment conducive to tumor growth. In CRC, *F. nucleatum* has been shown to induce an inflammatory response that favors the progression of tumors through mechanisms like the activation of NF-κB[163] and the production of pro-inflammatory cytokines. While inflammation is a key driver of cancer progression, it is also an essential component of the immune response to tumors[288]. The immune system relies on a controlled inflammatory response to detect and destroy cancer cells. However, chronic inflammation, induced by dysbiosis or other factors, can impair immune surveillance and promote tumorigenesis[291]. Thus, the goal of nutritional interventions is to strike a balance - modulating inflammation to prevent cancer progression while ensuring that the immune system remains active and capable of combating tumor cells[108].

One of the major challenges in leveraging dietary interventions is understanding how they can modulate the gut microbiome to produce beneficial effects without compromising immune function. For example, while probiotics can be effective in reducing inflammation, overuse of certain strains or imbalanced supplementation could potentially

exacerbate dysbiosis and impair immune responses[24]. Similarly, while fasting can induce beneficial changes in the gut microbiome, excessive or prolonged fasting could worsen conditions like cachexia or malnutrition, which are common in cancer patients[104].

This article has explored the multifaceted role of the gut microbiome in cancer initiation, progression, and response to therapy, emphasizing not only well-established mechanisms but also emerging therapeutic strategies[123,323,324]. A novel contribution of this review is the integration of cutting-edge evidence on interventions such as FMT[120,123] and high-fiber dietary modulation, which have shown promising potential to reshape oncologic outcomes *via* microbiome-targeted approaches. Specifically, the discussion of FMT in immune checkpoint blockade-refractory melanoma offers a timely update on how microbial reprogramming may overcome therapeutic resistance[122,123]. Recent phase I clinical trials have demonstrated that FMT from ICI responders can induce partial and complete responses in previously nonresponsive melanoma patients, marking a significant shift toward microbiome-informed personalized medicine[122,123]. These trials also provide preliminary data on safety and feasibility, although larger, controlled studies are needed to establish standardized protocols, including donor selection and long-term follow-up.

Additionally, this article highlights the underappreciated role of dietary interventions in modulating gut microbial communities to promote favorable cancer immunosurveillance[28,104,115]. Evidence from recent studies suggests that increased fiber intake correlates with enhanced progression-free survival in melanoma patients treated with immunotherapy[115]. These findings are supported by preclinical work indicating that microbial-derived short-chain fatty acids, such as butyrate, can enhance antitumor immunity[116]. However, interindividual variability in microbiota composition underscores the need for personalized dietary recommendations and further interventional trials.

Although the existing evidence on the role of the gut microbiome in cancer and the potential of nutritional interventions to modulate inflammation is promising, there are several challenges that need to be addressed. First, the precise mechanisms by which the gut microbiome influences cancer progression and response to treatment remain unclear. Further research is needed to identify the specific microbial species and metabolic pathways involved in cancer-related inflammation and how dietary interventions can target these pathways. Second, the heterogeneity of cancer types and patient populations makes it difficult to generalize findings across different cancers. The effects of dietary strategies may vary depending on the cancer type, stage, and the individual's microbiome composition. Personalized nutrition, which takes into account the unique gut microbiome and metabolic profile of each patient, could offer a more tailored approach to cancer treatment. Finally, larger clinical trials are needed to validate the findings from preclinical studies and assess the long-term effects of dietary interventions on cancer outcomes. Only through well-designed, rigorous studies can we determine the most effective strategies for using the gut microbiome as a therapeutic target in cancer care.

While there is substantial interest in leveraging the gut microbiome for the prevention and treatment of GI cancers, current findings across studies are not always consistent, highlighting the complexity and nascent stage of this field[236,239,324]. One notable example is the ongoing controversy surrounding *H. pylori* eradication in GC prevention[239,240]. The role of *H. pylori* eradication in GC prevention remains an area of ongoing debate, particularly in relation to the histological stage of gastric mucosal damage. A meta-analysis of randomized controlled trials involving 7955 participants [240] demonstrated that *H. pylori* treatment significantly reduced GC risk overall (RR = 0.64), but the protective effect was notably confined to individuals without advanced mucosal changes - specifically those with non-atrophic or atrophic gastritis. In contrast, patients with IM or dysplasia did not experience a statistically significant reduction in GC risk following eradication, suggesting a "point of no return" beyond which eradication offers limited benefit. These findings were corroborated by a larger systematic review and meta-analysis of 26 studies (52363 subjects), which confirmed a significant reduction in GC risk with *H. pylori* eradication (pooled RR = 0.56)[239]. Subgroup analysis again emphasized that the benefit was primarily observed in patients without IM or dysplasia. Collectively, these studies highlight the critical importance of early *H. pylori* detection and treatment, as the chemopreventive benefit appears to diminish once precancerous lesions are established.

Similarly, the clinical applicability of microbiome-targeted strategies, including FMT, remains hampered by unresolved concerns. Although FMT has shown promise in restoring microbial diversity and enhancing immunotherapy response [122], its long-term safety - particularly in cancer patients with immunocompromised states - remains inadequately studied. Additionally, the efficacy and safety profiles of individual probiotic strains differ markedly[325].

Implementation challenges in clinical practice

While nutritional interventions hold promise in modulating the gut microbiome to improve cancer outcomes, their practical application in clinical settings faces significant challenges. The American Society of Clinical Oncology highlights that the heterogeneity of interventions, patient populations, and cancer stages complicates the translation of evidence into practice, and the benefits of nutritional interventions in advanced cancer and cachexia remain inconsistent and modest at best[326].

Cancer patients, particularly those experiencing cachexia or treatment-induced GI complications, often struggle with dietary compliance due to symptoms like anorexia, nausea, diarrhea, and mucositis[327-329]. These symptoms can limit the tolerance for high-fiber or microbiota-targeted diets, narrowing the therapeutic window for nutritional modulation.

Recent studies highlight these challenges. For instance, a systematic review analyzing appetite and dietary intake endpoints in cancer cachexia clinical trials found considerable variability in assessment methods, underscoring the need for standardized and validated tools to effectively monitor nutritional interventions in this population[330]. Additionally, a randomized controlled trial investigating preoperative immunonutrition in GC patients with cachexia demonstrated that while immunonutrition reduced postoperative infectious complications and improved inflammatory and immune parameters, its implementation requires careful consideration of patient-specific factors and potential GI intolerance[331].

Practical barriers include limited access to registered dietitians, lack of standardized protocols, and patient reluctance or inability to adhere to dietary recommendations due to symptom burden or treatment side effects. Additionally, up to half of patients may pursue unproven or restrictive diets and supplements, increasing the risk of adverse interactions and further nutritional compromise. The American Society of Clinical Oncology recommends referral to a registered dietitian to mitigate these risks and provide individualized support, but acknowledges that such resources are not universally available[326].

For patients with severe GI dysfunction, such as those with nonfunctioning alimentary tracts, parenteral nutrition may be considered, but this approach requires careful patient selection, clear goal-setting, and ongoing evaluation due to its risks, costs, and limited indications1. Multidisciplinary collaboration, early identification of at-risk patients, and patient/caregiver education are essential to optimize feasibility and outcomes in real-world settings[326,332,333].

These findings emphasize the necessity for personalized nutrition approaches that account for individual patient conditions and the integration of dietary planning with oncologic care. Moreover, the development of evidence-based guidelines and the inclusion of dietetic support within multidisciplinary teams are crucial to address the heterogeneity of patient needs and the complexities of clinical practice.

Limitations

Despite growing interest in the gut microbiome and nutritional strategies for GI tumors, several limitations constrain current research. A major challenge lies in the significant individual variability of the gut microbiome, which is shaped by host genetics, diet, environment, medications, and lifestyle factors[324]. This heterogeneity complicates efforts to identify universal microbial biomarkers or design broadly applicable nutritional interventions. Furthermore, while numerous studies have established associations between specific microbial taxa or dietary components and cancer outcomes[12,293,294,334,335], the underlying molecular mechanisms remain largely unresolved. The complexity of the gut ecosystem, involving dynamic interactions between microbes, host immunity, and metabolic pathways, makes it difficult to establish clear causal relationships.

Methodological inconsistencies also limit the comparability of findings across studies[323,324,335]. Variations in sample collection methods, sequencing technologies, bioinformatics pipelines, and data analysis approaches introduce biases and reduce reproducibility. Moreover, much of the current evidence derives from observational studies or preclinical models[150,288,294], with a scarcity of large-scale, well-controlled clinical trials evaluating microbiome-modulating nutritional interventions in GI cancers. These factors highlight the need for more rigorous and standardized research designs to validate initial findings and support clinical translation.

Research gaps and future directions

Despite significant advances in understanding the gut microbiome's role in GI cancers, critical gaps remain that limit translational progress. First, mechanistic insights into microbiota-nutrition-immunity interactions are uneven across GI cancer types. While CRC has been extensively studied, with clear links between diet-modulated microbial metabolites (*e.g.*, short-chain fatty acids) and immune modulation, other GI cancers such as pancreatic[189] and esophageal cancers [334] remain poorly characterized in this context. Detailed mechanistic studies are needed to elucidate how microbiota-derived signals influence tumor immunity and metabolism in these less-studied cancers.

Second, promising microbiota targets for therapeutic intervention - such as *Akkermansia muciniphila* and *Faecalibacterium prausnitzii* - have shown potential in preclinical models for enhancing immunotherapy response and reducing inflammation, yet they lack robust clinical validation[239]. Moreover, FMT trials in GI cancer patients are still limited in scale and often lack standardized protocols, impeding definitive conclusions on efficacy and safety[118,119]. Third, although dietary interventions such as high-fiber diets and microbiota-accessible carbohydrates show promise in modulating the gut ecosystem, the heterogeneity in patient responses and challenges in adherence highlight the need for personalized nutritional strategies guided by microbiome profiling[113].

Addressing these gaps will require multidisciplinary efforts integrating microbiology, immunology, nutrition science, and clinical oncology, alongside longitudinal and interventional clinical trials to translate mechanistic insights into effective therapies. Finally, fostering interdisciplinary collaboration among microbiologists, oncologists, nutritionists, and computational biologists will be essential to translate laboratory discoveries into clinical practice. Collectively, these efforts will pave the way for integrating microbiome-informed nutritional strategies into precision oncology for GI tumors.

CONCLUSION

In conclusion, the interplay between the gut microbiome, inflammation, and cancer development is a complex and evolving area of research. Nutritional strategies that modulate the gut microbiome hold significant potential in enhancing cancer therapy and improving patient outcomes. Probiotics, prebiotics, CR, and fasting-mimicking diets are all promising approaches to managing gut inflammation and promoting a healthy microbiome. However, further research is required to fully understand the mechanisms underlying these effects and to identify the most effective and personalized approaches for cancer patients. By leveraging the gut microbiome's role in inflammation, we may uncover new avenues for improving cancer treatment efficacy and overall patient quality of life.

In summary, the gut microbiome represents a highly dynamic and therapeutically targetable axis in cancer care. By synthesizing recent advances in FMT and diet-based modulation, this review offers a translational perspective that bridges mechanistic microbiome science with actionable clinical strategies. Future directions should prioritize

randomized controlled trials, multi-omics integration, and microbiome-informed precision nutrition to fully realize the promise of microbiome-based interventions in oncology.

FOOTNOTES

Author contributions: Pacheco-Barcia V conceptualized and analyzed the literature, prepared the data to be presented and wrote the review; Mariño-Mendez A and Hernandez-Jimenez E made critical revisions; Jimenez-Fonseca P and Muñoz Martín AJ conducted the literature review; Custodio-Cabello S, Palka-Kotlowska M, and Gonzalez-Diaz I interpreted data; Cabezon-Gutierrez L evaluated the data obtained, wrote review and collaborated in draft of the review; and all authors prepared the draft and approved the submitted version.

Conflict-of-interest statement: Dr. Pacheco Barcia reports grants from FSEOM and MERCK, from Nutricia, from Servier, from LEO Pharma, from PFizer, from Amgen, outside the submitted work.

Country of origin: Spain

ORCID number: Vilma Pacheco-Barcia 0000-0003-0141-1306; Axel Mariño-Mendez 0009-0007-9668-3983; Paula Jimenez-Fonseca 0000-0003-4592-3813; Andrés Jesús Muñoz Martín 0000-0001-6977-8249; Sara Custodio-Cabello 0000-0001-8710-2592; Magda Palka-Kotlowska 0000-0001-6550-2540; Luis Cabezon-Gutierrez 0000-0002-3468-3626.

Corresponding Author's Membership in Professional Societies: Spanish Society of Medical Oncology; European Society of Medical Oncology.

S-Editor: Bai Y
L-Editor: A
P-Editor: Xu ZH

REFERENCES

1 **Torre LA**, Siegel RL, Ward EM, Jemal A. Global Cancer Incidence and Mortality Rates and Trends--An Update. *Cancer Epidemiol Biomarkers Prev* 2016; **25**: 16-27 [*RCA*] [PMID: 26667886 DOI: 10.1158/1055-9965.EPI-15-0578] [FullText]

2 **Bray F**, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2024; **74**: 229-263 [*RCA*] [PMID: 38572751 DOI: 10.3322/caac.21834] [FullText]

3 **Hanahan D**. Hallmarks of Cancer: New Dimensions. *Cancer Discov* 2022; **12**: 31-46 [*RCA*] [PMID: 35022204 DOI: 10.1158/2159-8290.CD-21-1059] [FullText]

4 **Debora C**, Gerardo Antonio Pio N. The bacteria-hypothesis of colorectal cancer: pathogenetic and therapeutic implications. *Transl Gastrointest Cancer* 2014; **3**: 44-53

5 **Turnbaugh PJ**, Ley RE, Hamady M, Fraser-Liggett CM, Knight R, Gordon JI. The human microbiome project. *Nature* 2007; **449**: 804-810 [*RCA*] [PMID: 17943116 DOI: 10.1038/nature06244] [FullText] [Full Text(PDF)]

6 **Lloyd-Price J**, Abu-Ali G, Huttenhower C. The healthy human microbiome. *Genome Med* 2016; **8**: 51 [*RCA*] [PMID: 27122046 DOI: 10.1186/s13073-016-0307-y] [FullText] [Full Text(PDF)]

7 **Thomas S**, Izard J, Walsh E, Batich K, Chongsathidkiet P, Clarke G, Sela DA, Muller AJ, Mullin JM, Albert K, Gilligan JP, DiGuilio K, Dilbarova R, Alexander W, Prendergast GC. The Host Microbiome Regulates and Maintains Human Health: A Primer and Perspective for Non-Microbiologists. *Cancer Res* 2017; **77**: 1783-1812 [*RCA*] [PMID: 28292977 DOI: 10.1158/0008-5472.CAN-16-2929] [FullText]

8 **Dzutsev A**, Badger JH, Perez-Chanona E, Roy S, Salcedo R, Smith CK, Trinchieri G. Microbes and Cancer. *Annu Rev Immunol* 2017; **35**: 199-228 [*RCA*] [PMID: 28142322 DOI: 10.1146/annurev-immunol-051116-052133] [FullText]

9 **Helmink BA**, Khan MAW, Hermann A, Gopalakrishnan V, Wargo JA. The microbiome, cancer, and cancer therapy. *Nat Med* 2019; **25**: 377-388 [*RCA*] [PMID: 30842679 DOI: 10.1038/s41591-019-0377-7] [FullText]

10 **World Health Organization**. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Biological agents. Volume 100 B. Lyon: IARC Publications, 2012

11 **de Martel C**, Franceschi S. Infections and cancer: established associations and new hypotheses. *Crit Rev Oncol Hematol* 2009; **70**: 183-194 [*RCA*] [PMID: 18805702 DOI: 10.1016/j.critrevonc.2008.07.021] [FullText]

12 **Baba Y**, Iwatsuki M, Yoshida N, Watanabe M, Baba H. Review of the gut microbiome and esophageal cancer: Pathogenesis and potential clinical implications. *Ann Gastroenterol Surg* 2017; **1**: 99-104 [*RCA*] [PMID: 29863142 DOI: 10.1002/ags3.12014] [FullText] [Full Text (PDF)]

13 **Bhatt AP**, Redinbo MR, Bultman SJ. The role of the microbiome in cancer development and therapy. *CA Cancer J Clin* 2017; **67**: 326-344 [*RCA*] [PMID: 28481406 DOI: 10.3322/caac.21398] [FullText]

14 **Schwabe RF**, Jobin C. The microbiome and cancer. *Nat Rev Cancer* 2013; **13**: 800-812 [*RCA*] [PMID: 24132111 DOI: 10.1038/nrc3610] [Full Text]

15 **Fulbright LE**, Ellermann M, Arthur JC. The microbiome and the hallmarks of cancer. *PLoS Pathog* 2017; **13**: e1006480 [*RCA*] [PMID:

28934351 DOI: 10.1371/journal.ppat.1006480] [FullText] [Full Text(PDF)]
16 **Johnson CH**, Spilker ME, Goetz L, Peterson SN, Siuzdak G. Metabolite and Microbiome Interplay in Cancer Immunotherapy. *Cancer Res* 2016; **76**: 6146-6152 [*RCA*] [PMID: 27729325 DOI: 10.1158/0008-5472.CAN-16-0309] [FullText]
17 **Dzutsev A**, Goldszmid RS, Viaud S, Zitvogel L, Trinchieri G. The role of the microbiota in inflammation, carcinogenesis, and cancer therapy. *Eur J Immunol* 2015; **45**: 17-31 [*RCA*] [PMID: 25328099 DOI: 10.1002/eji.201444972] [FullText]
18 **Elinav E**, Nowarski R, Thaiss CA, Hu B, Jin C, Flavell RA. Inflammation-induced cancer: crosstalk between tumours, immune cells and microorganisms. *Nat Rev Cancer* 2013; **13**: 759-771 [*RCA*] [PMID: 24154716 DOI: 10.1038/nrc3611] [FullText]
19 **Poutahidis T**, Erdman SE. Commensal bacteria modulate the tumor microenvironment. *Cancer Lett* 2016; **380**: 356-358 [*RCA*] [PMID: 26739062 DOI: 10.1016/j.canlet.2015.12.028] [FullText]
20 **Panebianco C**, Andriulli A, Pazienza V. Pharmacomicrobiomics: exploiting the drug-microbiota interactions in anticancer therapies. *Microbiome* 2018; **6**: 92 [*RCA*] [PMID: 29789015 DOI: 10.1186/s40168-018-0483-7] [FullText] [Full Text(PDF)]
21 **Li W**, Deng Y, Chu Q, Zhang P. Gut microbiome and cancer immunotherapy. *Cancer Lett* 2019; **447**: 41-47 [*RCA*] [PMID: 30684593 DOI: 10.1016/j.canlet.2019.01.015] [FullText]
22 **Gopalakrishnan V**, Helmink BA, Spencer CN, Reuben A, Wargo JA. The Influence of the Gut Microbiome on Cancer, Immunity, and Cancer Immunotherapy. *Cancer Cell* 2018; **33**: 570-580 [*RCA*] [PMID: 29634945 DOI: 10.1016/j.ccell.2018.03.015] [FullText]
23 **Fessler J**, Matson V, Gajewski TF. Exploring the emerging role of the microbiome in cancer immunotherapy. *J Immunother Cancer* 2019; **7**: 108 [*RCA*] [PMID: 30995949 DOI: 10.1186/s40425-019-0574-4] [FullText] [Full Text(PDF)]
24 **Javanmard A**, Ashtari S, Sabet B, Davoodi SH, Rostami-Nejad M, Esmaeil Akbari M, Niaz A, Mortazavian AM. Probiotics and their role in gastrointestinal cancers prevention and treatment; an overview. *Gastroenterol Hepatol Bed Bench* 2018; **11**: 284-295 [*RCA*] [PMID: 30425806] [FullText] [Full Text(PDF)]
25 **Meng C**, Bai C, Brown TD, Hood LE, Tian Q. Human Gut Microbiota and Gastrointestinal Cancer. *Genomics Proteomics Bioinformatics* 2018; **16**: 33-49 [*RCA*] [PMID: 29474889 DOI: 10.1016/j.gpb.2017.06.002] [FullText] [Full Text(PDF)]
26 **Wong SH**, Kwong TNY, Wu CY, Yu J. Clinical applications of gut microbiota in cancer biology. *Semin Cancer Biol* 2019; **55**: 28-36 [*RCA*] [PMID: 29782923 DOI: 10.1016/j.semcancer.2018.05.003] [FullText]
27 **Ma W**, Mao Q, Xia W, Dong G, Yu C, Jiang F. Gut Microbiota Shapes the Efficiency of Cancer Therapy. *Front Microbiol* 2019; **10**: 1050 [*RCA*] [PMID: 31293523 DOI: 10.3389/fmicb.2019.01050] [FullText] [Full Text(PDF)]
28 **David LA**, Maurice CF, Carmody RN, Gootenberg DB, Button JE, Wolfe BE, Ling AV, Devlin AS, Varma Y, Fischbach MA, Biddinger SB, Dutton RJ, Turnbaugh PJ. Diet rapidly and reproducibly alters the human gut microbiome. *Nature* 2014; **505**: 559-563 [*RCA*] [PMID: 24336217 DOI: 10.1038/nature12820] [FullText] [Full Text(PDF)]
29 **Chattopadhyay I**, Gundamaraju R, Jha NK, Gupta PK, Dey A, Mandal CC, Ford BM. Interplay between Dysbiosis of Gut Microbiome, Lipid Metabolism, and Tumorigenesis: Can Gut Dysbiosis Stand as a Prognostic Marker in Cancer? *Dis Markers* 2022; **2022**: 2941248 [*RCA*] [PMID: 35178126 DOI: 10.1155/2022/2941248] [FullText] [Full Text(PDF)]
30 **Cianci R**, Franza L, Schinzari G, Rossi E, Ianiro G, Tortora G, Gasbarrini A, Gambassi G, Cammarota G. The Interplay between Immunity and Microbiota at Intestinal Immunological Niche: The Case of Cancer. *Int J Mol Sci* 2019; **20**: 501 [*RCA*] [PMID: 30682772 DOI: 10.3390/ijms20030501] [FullText] [Full Text(PDF)]
31 **Pagliari D**, Gambassi G, Piccirillo CA, Cianci R. The Intricate Link among Gut "Immunological Niche," Microbiota, and Xenobiotics in Intestinal Pathology. *Mediators Inflamm* 2017; **2017**: 8390595 [*RCA*] [PMID: 29118468 DOI: 10.1155/2017/8390595] [FullText] [Full Text (PDF)]
32 **Al-Asmakh M**, Zadjali F. Use of Germ-Free Animal Models in Microbiota-Related Research. *J Microbiol Biotechnol* 2015; **25**: 1583-1588 [*RCA*] [PMID: 26032361 DOI: 10.4014/jmb.1501.01039] [FullText]
33 **Geem D**, Medina-Contreras O, McBride M, Newberry RD, Koni PA, Denning TL. Specific microbiota-induced intestinal Th17 differentiation requires MHC class II but not GALT and mesenteric lymph nodes. *J Immunol* 2014; **193**: 431-438 [*RCA*] [PMID: 24899505 DOI: 10.4049/jimmunol.1303167] [FullText]
34 **Yoon K**, Kim N. The Effect of Microbiota on Colon Carcinogenesis. *J Cancer Prev* 2018; **23**: 117-125 [*RCA*] [PMID: 30370256 DOI: 10.15430/JCP.2018.23.3.117] [FullText] [Full Text(PDF)]
35 **Cianci R**, Pagliari D, Pietroni V, Landolfi R, Pandolfi F. Tissue infiltrating lymphocytes: the role of cytokines in their growth and differentiation. *J Biol Regul Homeost Agents* 2010; **24**: 239-249 [*RCA*] [PMID: 20846472] [FullText]
36 **Backert S**, Neddermann M, Maubach G, Naumann M. Pathogenesis of Helicobacter pylori infection. *Helicobacter* 2016; **21** Suppl 1: 19-25 [*RCA*] [PMID: 27531534 DOI: 10.1111/hel.12335] [FullText]
37 **Vinasco K**, Mitchell HM, Kaakoush NO, Castaño-Rodríguez N. Microbial carcinogenesis: Lactic acid bacteria in gastric cancer. *Biochim Biophys Acta Rev Cancer* 2019; **1872**: 188309 [*RCA*] [PMID: 31394110 DOI: 10.1016/j.bbcan.2019.07.004] [FullText]
38 **Ohta K**, Kawano R, Ito N. Lactic acid bacteria convert human fibroblasts to multipotent cells. *PLoS One* 2012; **7**: e51866 [*RCA*] [PMID: 23300571 DOI: 10.1371/journal.pone.0051866] [FullText] [Full Text(PDF)]
39 **Dalmasso G**, Cougnoux A, Delmas J, Darfeuille-Michaud A, Bonnet R. The bacterial genotoxin colibactin promotes colon tumor growth by modifying the tumor microenvironment. *Gut Microbes* 2014; **5**: 675-680 [*RCA*] [PMID: 25483338 DOI: 10.4161/19490976.2014.969989] [Full Text]
40 **Jia W**, Xie G, Jia W. Bile acid-microbiota crosstalk in gastrointestinal inflammation and carcinogenesis. *Nat Rev Gastroenterol Hepatol* 2018; **15**: 111-128 [*RCA*] [PMID: 29018272 DOI: 10.1038/nrgastro.2017.119] [FullText]
41 **Chattopadhyay I**, Nandi D, Nag A. The pint- sized powerhouse: Illuminating the mighty role of the gut microbiome in improving the outcome of anti- cancer therapy. *Semin Cancer Biol* 2021; **70**: 98-111 [*RCA*] [PMID: 32739479 DOI: 10.1016/j.semcancer.2020.07.012] [FullText]
42 **Kobe B**, Deisenhofer J. A structural basis of the interactions between leucine-rich repeats and protein ligands. *Nature* 1995; **374**: 183-186 [*RCA*] [PMID: 7877692 DOI: 10.1038/374183a0] [FullText]
43 **Vaishnava S**, Behrendt CL, Ismail AS, Eckmann L, Hooper LV. Paneth cells directly sense gut commensals and maintain homeostasis at the intestinal host-microbial interface. *Proc Natl Acad Sci U S A* 2008; **105**: 20858-20863 [*RCA*] [PMID: 19075245 DOI: 10.1073/pnas.0808723105] [FullText] [Full Text(PDF)]
44 **Menendez A**, Willing BP, Montero M, Wlodarska M, So CC, Bhinder G, Vallance BA, Finlay BB. Bacterial stimulation of the TLR-MyD88 pathway modulates the homeostatic expression of ileal Paneth cell α-defensins. *J Innate Immun* 2013; **5**: 39-49 [*RCA*] [PMID: 22986642 DOI: 10.1159/000341630] [FullText]

45 **Schnare M**, Barton GM, Holt AC, Takeda K, Akira S, Medzhitov R. Toll-like receptors control activation of adaptive immune responses. *Nat Immunol* 2001; **2**: 947-950 [*RCA*] [PMID: 11547333 DOI: 10.1038/ni712] [FullText]

46 **Medzhitov R**, Preston-Hurlburt P, Kopp E, Stadlen A, Chen C, Ghosh S, Janeway CA Jr. MyD88 is an adaptor protein in the hToll/IL-1 receptor family signaling pathways. *Mol Cell* 1998; **2**: 253-258 [*RCA*] [PMID: 9734363 DOI: 10.1016/s1097-2765(00)80136-7] [FullText]

47 **Rakoff-Nahoum S**, Medzhitov R. Regulation of spontaneous intestinal tumorigenesis through the adaptor protein MyD88. *Science* 2007; **317**: 124-127 [*RCA*] [PMID: 17615359 DOI: 10.1126/science.1140488] [FullText]

48 **Rakoff-Nahoum S**, Paglino J, Eslami-Varzaneh F, Edberg S, Medzhitov R. Recognition of commensal microflora by toll-like receptors is required for intestinal homeostasis. *Cell* 2004; **118**: 229-241 [*RCA*] [PMID: 15260992 DOI: 10.1016/j.cell.2004.07.002] [FullText]

49 **Apidianakis Y**, Pitsouli C, Perrimon N, Rahme L. Synergy between bacterial infection and genetic predisposition in intestinal dysplasia. *Proc Natl Acad Sci U S A* 2009; **106**: 20883-20888 [*RCA*] [PMID: 19934041 DOI: 10.1073/pnas.0911797106] [FullText]

50 **von Frieling J**, Fink C, Hamm J, Klischies K, Forster M, Bosch TCG, Roeder T, Rosenstiel P, Sommer F. Grow With the Challenge - Microbial Effects on Epithelial Proliferation, Carcinogenesis, and Cancer Therapy. *Front Microbiol* 2018; **9**: 2020 [*RCA*] [PMID: 30294304 DOI: 10.3389/fmicb.2018.02020] [FullText] [Full Text(PDF)]

51 **Fukata M**, Chen A, Klepper A, Krishnareddy S, Vamadevan AS, Thomas LS, Xu R, Inoue H, Arditi M, Dannenberg AJ, Abreu MT. Cox-2 is regulated by Toll-like receptor-4 (TLR4) signaling: Role in proliferation and apoptosis in the intestine. *Gastroenterology* 2006; **131**: 862-877 [*RCA*] [PMID: 16952555 DOI: 10.1053/j.gastro.2006.06.017] [FullText] [Full Text(PDF)]

52 **Kopp E**, Medzhitov R. Recognition of microbial infection by Toll-like receptors. *Curr Opin Immunol* 2003; **15**: 396-401 [*RCA*] [PMID: 12900270 DOI: 10.1016/s0952-7915(03)00080-3] [FullText]

53 **Das M**, Garlick DS, Greiner DL, Davis RJ. The role of JNK in the development of hepatocellular carcinoma. *Genes Dev* 2011; **25**: 634-645 [*RCA*] [PMID: 21406557 DOI: 10.1101/gad.1989311] [FullText]

54 **Kennedy NJ**, Davis RJ. Role of JNK in tumor development. *Cell Cycle* 2003; **2**: 199-201 [*RCA*] [PMID: 12734425 DOI: 10.4161/cc.2.3.388] [FullText]

55 **Niccolai E**, Ricci F, Russo E, Nannini G, Emmi G, Taddei A, Ringressi MN, Melli F, Miloeva M, Cianchi F, Bechi P, Prisco D, Amedei A. The Different Functional Distribution of "Not Effector" T Cells (Treg/Tnull) in Colorectal Cancer. *Front Immunol* 2017; **8**: 1900 [*RCA*] [PMID: 29375559 DOI: 10.3389/fimmu.2017.01900] [FullText] [Full Text(PDF)]

56 **Zhang M**, Wen B, Anton OM, Yao Z, Dubois S, Ju W, Sato N, DiLillo DJ, Bamford RN, Ravetch JV, Waldmann TA. IL-15 enhanced antibody-dependent cellular cytotoxicity mediated by NK cells and macrophages. *Proc Natl Acad Sci U S A* 2018; **115**: E10915-E10924 [*RCA*] [PMID: 30373815 DOI: 10.1073/pnas.1811615115] [FullText]

57 **Pandolfi F**, Cianci R, Pagliari D, Landolfi R, Cammarota G. Cellular mediators of inflammation: tregs and TH17 cells in gastrointestinal diseases. *Mediators Inflamm* 2009; **2009**: 132028 [*RCA*] [PMID: 20169125 DOI: 10.1155/2009/132028] [FullText] [Full Text(PDF)]

58 **Shahmarvand N**, Nagy A, Shahryari J, Ohgami RS. Mutations in the signal transducer and activator of transcription family of genes in cancer. *Cancer Sci* 2018; **109**: 926-933 [*RCA*] [PMID: 29417693 DOI: 10.1111/cas.13525] [FullText] [Full Text(PDF)]

59 **Hurtado CG**, Wan F, Housseau F, Sears CL. Roles for Interleukin 17 and Adaptive Immunity in Pathogenesis of Colorectal Cancer. *Gastroenterology* 2018; **155**: 1706-1715 [*RCA*] [PMID: 30218667 DOI: 10.1053/j.gastro.2018.08.056] [FullText]

60 **Francescone R**, Hou V, Grivennikov SI. Microbiome, inflammation, and cancer. *Cancer J* 2014; **20**: 181-189 [*RCA*] [PMID: 24855005 DOI: 10.1097/PPO.0000000000000048] [FullText]

61 **Pandolfi F**, Cianci R, Pagliari D, Casciano F, Bagalà C, Astone A, Landolfi R, Barone C. The immune response to tumors as a tool toward immunotherapy. *Clin Dev Immunol* 2011; **2011**: 894704 [*RCA*] [PMID: 22190975 DOI: 10.1155/2011/894704] [FullText] [Full Text(PDF)]

62 **Kryczek I**, Wei S, Szeliga W, Vatan L, Zou W. Endogenous IL-17 contributes to reduced tumor growth and metastasis. *Blood* 2009; **114**: 357-359 [*RCA*] [PMID: 19289853 DOI: 10.1182/blood-2008-09-177360] [FullText]

63 **McCaw TR**, Li M, Starenki D, Cooper SJ, Liu M, Meza-Perez S, Arend RC, Buchsbaum DJ, Forero A, Randall TD. The expression of MHC class II molecules on murine breast tumors delays T-cell exhaustion, expands the T-cell repertoire, and slows tumor growth. *Cancer Immunol Immunother* 2019; **68**: 175-188 [*RCA*] [PMID: 30334128 DOI: 10.1007/s00262-018-2262-5] [FullText]

64 **Wherry EJ**. T cell exhaustion. *Nat Immunol* 2011; **12**: 492-499 [*RCA*] [PMID: 21739672 DOI: 10.1038/ni.2035] [FullText]

65 **Gupta PK**, Godec J, Wolski D, Adland E, Yates K, Pauken KE, Cosgrove C, Ledderose C, Junger WG, Robson SC, Wherry EJ, Alter G, Goulder PJ, Klenerman P, Sharpe AH, Lauer GM, Haining WN. CD39 Expression Identifies Terminally Exhausted CD8+ T Cells. *PLoS Pathog* 2015; **11**: e1005177 [*RCA*] [PMID: 26485519 DOI: 10.1371/journal.ppat.1005177] [FullText] [Full Text(PDF)]

66 **Pagliari D**, Piccirillo CA, Larbi A, Cianci R. The Interactions between Innate Immunity and Microbiota in Gastrointestinal Diseases. *J Immunol Res* 2015; **2015**: 898297 [*RCA*] [PMID: 26078983 DOI: 10.1155/2015/898297] [FullText] [Full Text(PDF)]

67 **Reddavide R**, Rotolo O, Caruso MG, Stasi E, Notarnicola M, Miraglia C, Nouvenne A, Meschi T, De' Angelis GL, Di Mario F, Leandro G. The role of diet in the prevention and treatment of Inflammatory Bowel Diseases. *Acta Biomed* 2018; **89**: 60-75 [*RCA*] [PMID: 30561397 DOI: 10.23750/abm.v89i9-S.7952] [FullText] [Full Text(PDF)]

68 **Fong W**, Li Q, Yu J. Gut microbiota modulation: a novel strategy for prevention and treatment of colorectal cancer. *Oncogene* 2020; **39**: 4925-4943 [*RCA*] [PMID: 32514151 DOI: 10.1038/s41388-020-1341-1] [FullText] [Full Text(PDF)]

69 **Piewngam P**, Zheng Y, Nguyen TH, Dickey SW, Joo HS, Villaruz AE, Glose KA, Fisher EL, Hunt RL, Li B, Chiou J, Pharkjaksu S, Khongthong S, Cheung GYC, Kiratisin P, Otto M. Pathogen elimination by probiotic Bacillus *via* signalling interference. *Nature* 2018; **562**: 532-537 [*RCA*] [PMID: 30305736 DOI: 10.1038/s41586-018-0616-y] [FullText] [Full Text(PDF)]

70 **Shin DS**, Rhee KJ, Eom YB. Effect of Probiotic Clostridium butyricum NCTC 7423 Supernatant on Biofilm Formation and Gene Expression of Bacteroides fragilis. *J Microbiol Biotechnol* 2020; **30**: 368-377 [*RCA*] [PMID: 32066216 DOI: 10.4014/jmb.2001.01027] [FullText]

71 **Gharbi Y**, Fhoula I, Ruas-madiedo P, Afef N, Boudabous A, Gueimonde M, Ouzari H. In-vitro characterization of potentially probiotic Lactobacillus strains isolated from human microbiota: interaction with pathogenic bacteria and the enteric cell line HT29. *Ann Microbiol* 2019; **69**: 61-72 [*RCA*] [DOI: 10.1007/s13213-018-1396-1] [FullText]

72 **Gatej SM**, Bright R, Weyrich LS, Marino V, Christophersen CT, Gibson RJ, Gully N, Zilm P, Bartold PM. Probiotic Lactobacillus Rhamnosus GG Protects Against P. Gingivalis And F. Nucleatum Gut Dysbiosis. *J Int Acad Periodontol* 2020; **22**: 18-27 [*RCA*] [PMID: 32224547] [Full Text]

73 **Ghanavati R**, Akbari A, Mohammadi F, Asadollahi P, Javadi A, Talebi M, Rohani M. Lactobacillus species inhibitory effect on colorectal cancer progression through modulating the Wnt/β-catenin signaling pathway. *Mol Cell Biochem* 2020; **470**: 1-13 [*RCA*] [PMID: 32419125 DOI: 10.1007/s11010-020-03740-8] [FullText]

74 **Gamallat Y**, Meyiah A, Kuugbee ED, Hago AM, Chiwala G, Awadasseid A, Bamba D, Zhang X, Shang X, Luo F, Xin Y. Lactobacillus rhamnosus induced epithelial cell apoptosis, ameliorates inflammation and prevents colon cancer development in an animal model. *Biomed Pharmacother* 2016; **83**: 536-541 [*RCA*] [PMID: 27447122 DOI: 10.1016/j.biopha.2016.07.001] [FullText]

75 **Yue Y**, Ye K, Lu J, Wang X, Zhang S, Liu L, Yang B, Nassar K, Xu X, Pang X, Lv J. Probiotic strain Lactobacillus plantarum YYC-3 prevents colon cancer in mice by regulating the tumour microenvironment. *Biomed Pharmacother* 2020; **127**: 110159 [*RCA*] [PMID: 32353824 DOI: 10.1016/j.biopha.2020.110159] [FullText]

76 **Mendes MCS**, Paulino DS, Brambilla SR, Camargo JA, Persinoti GF, Carvalheira JBC. Microbiota modification by probiotic supplementation reduces colitis associated colon cancer in mice. *World J Gastroenterol* 2018; **24**: 1995-2008 [*RCA*] [PMID: 29760543 DOI: 10.3748/wjg.v24.i18.1995] [FullText] [Full Text(PDF)]

77 **Landy J**, Ronde E, English N, Clark SK, Hart AL, Knight SC, Ciclitira PJ, Al-Hassi HO. Tight junctions in inflammatory bowel diseases and inflammatory bowel disease associated colorectal cancer. *World J Gastroenterol* 2016; **22**: 3117-3126 [*RCA*] [PMID: 27003989 DOI: 10.3748/wjg.v22.i11.3117] [FullText] [Full Text(PDF)]

78 **Alvarez CS**, Badia J, Bosch M, Giménez R, Baldomà L. Outer Membrane Vesicles and Soluble Factors Released by Probiotic Escherichia coli Nissle 1917 and Commensal ECOR63 Enhance Barrier Function by Regulating Expression of Tight Junction Proteins in Intestinal Epithelial Cells. *Front Microbiol* 2016; **7**: 1981 [*RCA*] [PMID: 28018313 DOI: 10.3389/fmicb.2016.01981] [FullText] [Full Text(PDF)]

79 **Zhang Y**, Zhao X, Zhu Y, Ma J, Ma H, Zhang H. Probiotic Mixture Protects Dextran Sulfate Sodium-Induced Colitis by Altering Tight Junction Protein Expressions and Increasing Tregs. *Mediators Inflamm* 2018; **2018**: 9416391 [*RCA*] [PMID: 29849501 DOI: 10.1155/2018/9416391] [FullText] [Full Text(PDF)]

80 **Kuugbee ED**, Shang X, Gamallat Y, Bamba D, Awadasseid A, Suliman MA, Zang S, Ma Y, Chiwala G, Xin Y, Shang D. Structural Change in Microbiota by a Probiotic Cocktail Enhances the Gut Barrier and Reduces Cancer *via* TLR2 Signaling in a Rat Model of Colon Cancer. *Dig Dis Sci* 2016; **61**: 2908-2920 [*RCA*] [PMID: 27384052 DOI: 10.1007/s10620-016-4238-7] [FullText]

81 **Feng T**, Wang J. Oxidative stress tolerance and antioxidant capacity of lactic acid bacteria as probiotic: a systematic review. *Gut Microbes* 2020; **12**: 1801944 [*RCA*] [PMID: 32795116 DOI: 10.1080/19490976.2020.1801944] [FullText] [Full Text(PDF)]

82 **Feng J**, Gao M, Zhao C, Yang J, Gao H, Lu X, Ju R, Zhang X, Zhang Y. Oral Administration of Probiotics Reduces Chemotherapy-Induced Diarrhea and Oral Mucositis: A Systematic Review and Meta-Analysis. *Front Nutr* 2022; **9**: 823288 [*RCA*] [PMID: 35299763 DOI: 10.3389/fnut.2022.823288] [FullText] [Full Text(PDF)]

83 **Shen SR**, Chen WJ, Chu HF, Wu SH, Wang YR, Shen TL. Amelioration of 5-fluorouracil-induced intestinal mucositis by Streptococcus thermophilus ST4 in a mouse model. *PLoS One* 2021; **16**: e0253540 [*RCA*] [PMID: 34310611 DOI: 10.1371/journal.pone.0253540] [FullText] [Full Text(PDF)]

84 **López-Gómez L**, Alcorta A, Abalo R. Probiotics and Probiotic-like Agents against Chemotherapy-Induced Intestinal Mucositis: A Narrative Review. *J Pers Med* 2023; **13**: 1487 [*RCA*] [PMID: 37888098 DOI: 10.3390/jpm13101487] [FullText] [Full Text(PDF)]

85 **Gibson GR**, Beatty ER, Wang X, Cummings JH. Selective stimulation of bifidobacteria in the human colon by oligofructose and inulin. *Gastroenterology* 1995; **108**: 975-982 [*RCA*] [PMID: 7698613 DOI: 10.1016/0016-5085(95)90192-2] [FullText]

86 **Reddy BS**, Rivenson A. Inhibitory effect of Bifidobacterium longum on colon, mammary, and liver carcinogenesis induced by 2-amino-3-methylimidazo[4,5-f]quinoline, a food mutagen. *Cancer Res* 1993; **53**: 3914-3918 [*RCA*] [PMID: 8358717] [FullText]

87 **Rowland IR**, Rumney CJ, Coutts JT, Lievense LC. Effect of Bifidobacterium longum and inulin on gut bacterial metabolism and carcinogen-induced aberrant crypt foci in rats. *Carcinogenesis* 1998; **19**: 281-285 [*RCA*] [PMID: 9498277 DOI: 10.1093/carcin/19.2.281] [FullText]

88 **Taper HS**, Roberfroid MB. Possible adjuvant cancer therapy by two prebiotics--inulin or oligofructose. *In Vivo* 2005; **19**: 201-204 [*RCA*] [PMID: 15796175] [FullText]

89 **Taper HS**, Roberfroid MB. Inulin/oligofructose and anticancer therapy. *Br J Nutr* 2002; **87** Suppl 2: S283-S286 [*RCA*] [PMID: 12088530 DOI: 10.1079/BJNBJN/2002549] [FullText]

90 **Taper HS**, Roberfroid MB. Nontoxic potentiation of cancer chemotherapy by dietary oligofructose or inulin. *Nutr Cancer* 2000; **38**: 1-5 [*RCA*] [PMID: 11341034 DOI: 10.1207/S15327914NC381_1] [FullText]

91 **García-Peris P**, Velasco C, Lozano MA, Moreno Y, Paron L, de la Cuerda C, Bretón I, Camblor M, García-Hernández J, Guarner F, Hernández M. Effect of a mixture of inulin and fructo-oligosaccharide on Lactobacillus and Bifidobacterium intestinal microbiota of patients receiving radiotherapy: a randomised, double-blind, placebo-controlled trial. *Nutr Hosp* 2012; **27**: 1908-1915 [*RCA*] [PMID: 23588438 DOI: 10.3305/nh.2012.27.6.5992] [FullText]

92 **Garcia-Peris P**, Velasco C, Hernandez M, Lozano MA, Paron L, de la Cuerda C, Breton I, Camblor M, Guarner F. Effect of inulin and fructo-oligosaccharide on the prevention of acute radiation enteritis in patients with gynecological cancer and impact on quality-of-life: a randomized, double-blind, placebo-controlled trial. *Eur J Clin Nutr* 2016; **70**: 170-174 [*RCA*] [PMID: 26603881 DOI: 10.1038/ejcn.2015.192] [FullText]

93 **Zhao R**, Wang Y, Huang Y, Cui Y, Xia L, Rao Z, Zhou Y, Wu X. Effects of fiber and probiotics on diarrhea associated with enteral nutrition in gastric cancer patients: A prospective randomized and controlled trial. *Medicine (Baltimore)* 2017; **96**: e8418 [*RCA*] [PMID: 29069041 DOI: 10.1097/MD.0000000000008418] [FullText] [Full Text(PDF)]

94 **Straus Farber R**, Walker EL, Diallo F, Onomichi K, Riley C, Zhang L, Zhu W, De Jager PL, Xia Z. A randomized cross-over trial of prebiotics and probiotics in multiple sclerosis: Trial feasibility, supplement tolerability and symptom abatement. *Mult Scler Relat Disord* 2024; **89**: 105762 [*RCA*] [PMID: 39047340 DOI: 10.1016/j.msard.2024.105762] [FullText]

95 **Xie X**, He Y, Li H, Yu D, Na L, Sun T, Zhang D, Shi X, Xia Y, Jiang T, Rong S, Yang S, Ma X, Xu G. Effects of prebiotics on immunologic indicators and intestinal microbiota structure in perioperative colorectal cancer patients. *Nutrition* 2019; **61**: 132-142 [*RCA*] [PMID: 30711862 DOI: 10.1016/j.nut.2018.10.038] [FullText]

96 **Boutron-Ruault MC**, Marteau P, Lavergne-Slove A, Myara A, Gerhardt MF, Franchisseur C, Bornet F; Eripolyp Study Group. Effects of a 3-mo consumption of short-chain fructo-oligosaccharides on parameters of colorectal carcinogenesis in patients with or without small or large colorectal adenomas. *Nutr Cancer* 2005; **53**: 160-168 [*RCA*] [PMID: 16573377 DOI: 10.1207/s15327914nc5302_5] [FullText]

97 **Fehlbaum S**, Prudence K, Kieboom J, Heerikhuisen M, van den Broek T, Schuren FHJ, Steinert RE, Raederstorff D. In Vitro Fermentation of Selected Prebiotics and Their Effects on the Composition and Activity of the Adult Gut Microbiota. *Int J Mol Sci* 2018; **19**: 3097 [*RCA*] [PMID: 30308944 DOI: 10.3390/ijms19103097] [FullText] [Full Text(PDF)]

98 **Everard A**, Belzer C, Geurts L, Ouwerkerk JP, Druart C, Bindels LB, Guiot Y, Derrien M, Muccioli GG, Delzenne NM, de Vos WM, Cani PD. Cross-talk between Akkermansia muciniphila and intestinal epithelium controls diet-induced obesity. *Proc Natl Acad Sci U S A* 2013; **110**: 9066-9071 [*RCA*] [PMID: 23671105 DOI: 10.1073/pnas.1219451110] [FullText]

99 **Li Y**, Tinoco R, Elmén L, Segota I, Xian Y, Fujita Y, Sahu A, Zarecki R, Marie K, Feng Y, Khateb A, Frederick DT, Ashkenazi SK, Kim H, Perez EG, Day CP, Segura Muñoz RS, Schmaltz R, Yooseph S, Tam MA, Zhang T, Avitan-Hersh E, Tzur L, Roizman S, Boyango I, Bar-Sela G, Orian A, Kaufman RJ, Bosenberg M, Goding CR, Baaten B, Levesque MP, Dummer R, Brown K, Merlino G, Ruppin E, Flaherty K, Ramer-Tait A, Long T, Peterson SN, Bradley LM, Ronai ZA. Gut microbiota dependent anti-tumor immunity restricts melanoma growth in Rnf5(-/-) mice. *Nat Commun* 2019; **10**: 1492 [*RCA*] [PMID: 30940817 DOI: 10.1038/s41467-019-09525-y] [FullText] [Full Text(PDF)]

100 **Mazraeh R**, Azizi-Soleiman F, Jazayeri SMHM, Noori SMA. Effect of inulin-type fructans in patients undergoing cancer treatments: A systematic review. *Pak J Med Sci* 2019; **35**: 575-580 [*RCA*] [PMID: 31086553 DOI: 10.12669/pjms.35.2.701] [FullText] [Full Text(PDF)]

101 **Tagliabue A**, Ferraris C, Uggeri F, Trentani C, Bertoli S, de Giorgis V, Veggiotti P, Elli M. Short-term impact of a classical ketogenic diet on gut microbiota in GLUT1 Deficiency Syndrome: A 3-month prospective observational study. *Clin Nutr ESPEN* 2017; **17**: 33-37 [*RCA*] [PMID: 28361745 DOI: 10.1016/j.clnesp.2016.11.003] [FullText]

102 **Chung HY**, Park YK. Rationale, Feasibility and Acceptability of Ketogenic Diet for Cancer Treatment. *J Cancer Prev* 2017; **22**: 127-134 [*RCA*] [PMID: 29018777 DOI: 10.15430/JCP.2017.22.3.127] [FullText] [Full Text(PDF)]

103 **Vander Heiden MG**, Cantley LC, Thompson CB. Understanding the Warburg effect: the metabolic requirements of cell proliferation. *Science* 2009; **324**: 1029-1033 [*RCA*] [PMID: 19460998 DOI: 10.1126/science.1160809] [FullText] [Full Text(PDF)]

104 **Weber DD**, Aminazdeh-Gohari S, Kofler B. Ketogenic diet in cancer therapy. *Aging (Albany NY)* 2018; **10**: 164-165 [*RCA*] [PMID: 29443693 DOI: 10.18632/aging.101382] [FullText] [Full Text(PDF)]

105 **Klement RJ**. Beneficial effects of ketogenic diets for cancer patients: a realist review with focus on evidence and confirmation. *Med Oncol* 2017; **34**: 132 [*RCA*] [PMID: 28653283 DOI: 10.1007/s12032-017-0991-5] [FullText]

106 **Xie G**, Zhou Q, Qiu CZ, Dai WK, Wang HP, Li YH, Liao JX, Lu XG, Lin SF, Ye JH, Ma ZY, Wang WJ. Ketogenic diet poses a significant effect on imbalanced gut microbiota in infants with refractory epilepsy. *World J Gastroenterol* 2017; **23**: 6164-6171 [*RCA*] [PMID: 28970732 DOI: 10.3748/wjg.v23.i33.6164] [FullText] [Full Text(PDF)]

107 **Newell C**, Bomhof MR, Reimer RA, Hittel DS, Rho JM, Shearer J. Ketogenic diet modifies the gut microbiota in a murine model of autism spectrum disorder. *Mol Autism* 2016; **7**: 37 [*RCA*] [PMID: 27594980 DOI: 10.1186/s13229-016-0099-3] [FullText] [Full Text(PDF)]

108 **Rinninella E**, Raoul P, Cintoni M, Palombaro M, Pulcini G, Gasbarrini A, Mele MC. Nutritional Interventions Targeting Gut Microbiota during Cancer Therapies. *Microorganisms* 2021; **9**: 1469 [*RCA*] [PMID: 34361904 DOI: 10.3390/microorganisms9071469] [FullText] [Full Text(PDF)]

109 **Cox LM**, Schafer MJ, Sohn J, Vincentini J, Weiner HL, Ginsberg SD, Blaser MJ. Calorie restriction slows age-related microbiota changes in an Alzheimer's disease model in female mice. *Sci Rep* 2019; **9**: 17904 [*RCA*] [PMID: 31784610 DOI: 10.1038/s41598-019-54187-x] [FullText] [Full Text(PDF)]

110 **Wei S**, Han R, Zhao J, Wang S, Huang M, Wang Y, Chen Y. Intermittent administration of a fasting-mimicking diet intervenes in diabetes progression, restores β cells and reconstructs gut microbiota in mice. *Nutr Metab (Lond)* 2018; **15**: 80 [*RCA*] [PMID: 30479647 DOI: 10.1186/s12986-018-0318-3] [FullText] [Full Text(PDF)]

111 **Rimoldi M**, Chieppa M, Salucci V, Avogadri F, Sonzogni A, Sampietro GM, Nespoli A, Viale G, Allavena P, Rescigno M. Intestinal immune homeostasis is regulated by the crosstalk between epithelial cells and dendritic cells. *Nat Immunol* 2005; **6**: 507-514 [*RCA*] [PMID: 15821737 DOI: 10.1038/ni1192] [FullText]

112 **Tisdale MJ**. Mechanisms of cancer cachexia. *Physiol Rev* 2009; **89**: 381-410 [*RCA*] [PMID: 19342610 DOI: 10.1152/physrev.00016.2008] [FullText]

113 **Barber TM**, Kabisch S, Pfeiffer AFH, Weickert MO. The Health Benefits of Dietary Fibre. *Nutrients* 2020; **12**: 3209 [*RCA*] [PMID: 33096647 DOI: 10.3390/nu12103209] [FullText] [Full Text(PDF)]

114 **Sun L**, Zhang Z, Xu J, Xu G, Liu X. Dietary fiber intake reduces risk for Barrett's esophagus and esophageal cancer. *Crit Rev Food Sci Nutr* 2017; **57**: 2749-2757 [*RCA*] [PMID: 26462851 DOI: 10.1080/10408398.2015.1067596] [FullText]

115 **Spencer CN**, McQuade JL, Gopalakrishnan V, McCulloch JA, Vetizou M, Cogdill AP, Khan MAW, Zhang X, White MG, Peterson CB, Wong MC, Morad G, Rodgers T, Badger JH, Helmink BA, Andrews MC, Rodrigues RR, Morgun A, Kim YS, Roszik J, Hoffman KL, Zheng J, Zhou Y, Medik YB, Kahn LM, Johnson S, Hudgens CW, Wani K, Gaudreau PO, Harris AL, Jamal MA, Baruch EN, Perez-Guijarro E, Day CP, Merlino G, Pazdrak B, Lochmann BS, Szczepaniak-Sloane RA, Arora R, Anderson J, Zobniw CM, Posada E, Sirmans E, Simon J, Haydu LE, Burton EM, Wang L, Dang M, Clise-Dwyer K, Schneider S, Chapman T, Anang NAS, Duncan S, Toker J, Malke JC, Glitza IC, Amaria RN, Tawbi HA, Diab A, Wong MK, Patel SP, Woodman SE, Davies MA, Ross MI, Gershenwald JE, Lee JE, Hwu P, Jensen V, Samuels Y, Straussman R, Ajami NJ, Nelson KC, Nezi L, Petrosino JF, Futreal PA, Lazar AJ, Hu J, Jenq RR, Tetzlaff MT, Yan Y, Garrett WS, Huttenhower C, Sharma P, Watowich SS, Allison JP, Cohen L, Trinchieri G, Daniel CR, Wargo JA. Dietary fiber and probiotics influence the gut microbiome and melanoma immunotherapy response. *Science* 2021; **374**: 1632-1640 [*RCA*] [PMID: 34941392 DOI: 10.1126/science.aaz7015] [FullText]

116 **Zitvogel L**, Daillère R, Roberti MP, Routy B, Kroemer G. Anticancer effects of the microbiome and its products. *Nat Rev Microbiol* 2017; **15**: 465-478 [*RCA*] [PMID: 28529325 DOI: 10.1038/nrmicro.2017.44] [FullText]

117 **Munteanu C**, Schwartz B. Interactions between Dietary Antioxidants, Dietary Fiber and the Gut Microbiome: Their Putative Role in Inflammation and Cancer. *Int J Mol Sci* 2024; **25**: 8250 [*RCA*] [PMID: 39125822 DOI: 10.3390/ijms25158250] [FullText] [Full Text(PDF)]

118 **Porcari S**, Benech N, Valles-Colomer M, Segata N, Gasbarrini A, Cammarota G, Sokol H, Ianiro G. Key determinants of success in fecal microbiota transplantation: From microbiome to clinic. *Cell Host Microbe* 2023; **31**: 712-733 [*RCA*] [PMID: 37167953 DOI: 10.1016/j.chom.2023.03.020] [FullText]

119 **Minkoff NZ**, Aslam S, Medina M, Tanner-Smith EE, Zackular JP, Acra S, Nicholson MR, Imdad A. Fecal microbiota transplantation for the treatment of recurrent Clostridioides difficile (Clostridium difficile). *Cochrane Database Syst Rev* 2023; **4**: CD013871 [*RCA*] [PMID: 37096495 DOI: 10.1002/14651858.CD013871.pub2] [FullText] [Full Text(PDF)]

120 **Yadegar A**, Bar-Yoseph H, Monaghan TM, Pakpour S, Severino A, Kuijper EJ, Smits WK, Terveer EM, Neupane S, Nabavi-Rad A, Sadeghi J, Cammarota G, Ianiro G, Nap-Hill E, Leung D, Wong K, Kao D. Fecal microbiota transplantation: current challenges and future landscapes. *Clin Microbiol Rev* 2024; **37**: e0006022 [*RCA*] [PMID: 38717124 DOI: 10.1128/cmr.00060-22] [FullText]

121 **Routy B**, Lenehan JG, Miller WH Jr, Jamal R, Messaoudene M, Daisley BA, Hes C, Al KF, Martinez-Gili L, Punčochář M, Ernst S, Logan D, Belanger K, Esfahani K, Richard C, Ninkov M, Piccinno G, Armanini F, Pinto F, Krishnamoorthy M, Figueredo R, Thebault P, Takis P, Magrill J, Ramsay L, Derosa L, Marchesi JR, Parvathy SN, Elkrief A, Watson IR, Lapointe R, Segata N, Haeryfar SMM, Mullish BH, Silverman MS, Burton JP, Maleki Vareki S. Fecal microbiota transplantation plus anti-PD-1 immunotherapy in advanced melanoma: a phase I

trial. *Nat Med* 2023; **29**: 2121-2132 [*RCA*] [PMID: 37414899 DOI: 10.1038/s41591-023-02453-x] [FullText]

122 **Baruch EN**, Youngster I, Ben-Betzalel G, Ortenberg R, Lahat A, Katz L, Adler K, Dick-Necula D, Raskin S, Bloch N, Rotin D, Anafi L, Avivi C, Melnichenko J, Steinberg-Silman Y, Mamtani R, Harati H, Asher N, Shapira-Frommer R, Brosh-Nissimov T, Eshet Y, Ben-Simon S, Ziv O, Khan MAW, Amit M, Ajami NJ, Barshack I, Schachter J, Wargo JA, Koren O, Markel G, Boursi B. Fecal microbiota transplant promotes response in immunotherapy-refractory melanoma patients. *Science* 2021; **371**: 602-609 [*RCA*] [PMID: 33303685 DOI: 10.1126/science.abb5920] [FullText]

123 **Davar D**, Dzutsev AK, McCulloch JA, Rodrigues RR, Chauvin JM, Morrison RM, Deblasio RN, Menna C, Ding Q, Pagliano O, Zidi B, Zhang S, Badger JH, Vetizou M, Cole AM, Fernandes MR, Prescott S, Costa RGF, Balaji AK, Morgun A, Vujkovic-Cvijin I, Wang H, Borhani AA, Schwartz MB, Dubner HM, Ernst SJ, Rose A, Najjar YG, Belkaid Y, Kirkwood JM, Trinchieri G, Zarour HM. Fecal microbiota transplant overcomes resistance to anti-PD-1 therapy in melanoma patients. *Science* 2021; **371**: 595-602 [*RCA*] [PMID: 33542131 DOI: 10.1126/science.abf3363] [FullText]

124 **Tan J**, Chen YX. Dietary and Lifestyle Factors Associated with Colorectal Cancer Risk and Interactions with Microbiota: Fiber, Red or Processed Meat and Alcoholic Drinks. *Gastrointest Tumors* 2016; **3**: 17-24 [*RCA*] [PMID: 27722153 DOI: 10.1159/000442831] [FullText]

125 **Kuipers EJ**, Grady WM, Lieberman D, Seufferlein T, Sung JJ, Boelens PG, van de Velde CJ, Watanabe T. Colorectal cancer. *Nat Rev Dis Primers* 2015; **1**: 15065 [*RCA*] [PMID: 27189416 DOI: 10.1038/nrdp.2015.65] [FullText]

126 **Axelrad JE**, Lichtiger S, Yajnik V. Inflammatory bowel disease and cancer: The role of inflammation, immunosuppression, and cancer treatment. *World J Gastroenterol* 2016; **22**: 4794-4801 [*RCA*] [PMID: 27239106 DOI: 10.3748/wjg.v22.i20.4794] [FullText] [Full Text(PDF)]

127 **Vacante M**, Borzì AM, Basile F, Biondi A. Biomarkers in colorectal cancer: Current clinical utility and future perspectives. *World J Clin Cases* 2018; **6**: 869-881 [*RCA*] [PMID: 30568941 DOI: 10.12998/wjcc.v6.i15.869] [FullText] [Full Text(PDF)]

128 **Montalban-Arques A**, Scharl M. Intestinal microbiota and colorectal carcinoma: Implications for pathogenesis, diagnosis, and therapy. *EBioMedicine* 2019; **48**: 648-655 [*RCA*] [PMID: 31631043 DOI: 10.1016/j.ebiom.2019.09.050] [FullText] [Full Text(PDF)]

129 **Garrett WS**. The gut microbiota and colon cancer. *Science* 2019; **364**: 1133-1135 [*RCA*] [PMID: 31221845 DOI: 10.1126/science.aaw2367] [FullText]

130 **Canny GO**, McCormick BA. Bacteria in the intestine, helpful residents or enemies from within? *Infect Immun* 2008; **76**: 3360-3373 [*RCA*] [PMID: 18474643 DOI: 10.1128/IAI.00187-08] [FullText]

131 **Rajilić-Stojanović M**, de Vos WM. The first 1000 cultured species of the human gastrointestinal microbiota. *FEMS Microbiol Rev* 2014; **38**: 996-1047 [*RCA*] [PMID: 24861948 DOI: 10.1111/1574-6976.12075] [FullText] [Full Text(PDF)]

132 **Baliou S**, Adamaki M, Spandidos D, Kyriakopoulos A, Christodoulou I, Zoumpourlis V. The microbiome, its molecular mechanisms and its potential as a therapeutic strategy against colorectal carcinogenesis (Review). *World Acad Sci J* 2018; **1**: 3-19 [DOI: 10.3892/wasj.2018.6] [FullText]

133 **Jahani-Sherafat S**, Alebouyeh M, Moghim S, Ahmadi Amoli H, Ghasemian-Safaei H. Role of gut microbiota in the pathogenesis of colorectal cancer; a review article. *Gastroenterol Hepatol Bed Bench* 2018; **11**: 101-109 [*RCA*] [PMID: 29910850] [FullText] [Full Text(PDF)]

134 **Tilg H**, Adolph TE, Gerner RR, Moschen AR. The Intestinal Microbiota in Colorectal Cancer. *Cancer Cell* 2018; **33**: 954-964 [*RCA*] [PMID: 29657127 DOI: 10.1016/j.ccell.2018.03.004] [FullText]

135 **Gur C**, Ibrahim Y, Isaacson B, Yamin R, Abed J, Gamliel M, Enk J, Bar-On Y, Stanietsky-Kaynan N, Coppenhagen-Glazer S, Shussman N, Almogy G, Cuapio A, Hofer E, Mevorach D, Tabib A, Ortenberg R, Markel G, Miklić K, Jonjic S, Brennan CA, Garrett WS, Bachrach G, Mandelboim O. Binding of the Fap2 protein of Fusobacterium nucleatum to human inhibitory receptor TIGIT protects tumors from immune cell attack. *Immunity* 2015; **42**: 344-355 [*RCA*] [PMID: 25680274 DOI: 10.1016/j.immuni.2015.01.010] [FullText]

136 **Rubinstein MR**, Wang X, Liu W, Hao Y, Cai G, Han YW. Fusobacterium nucleatum promotes colorectal carcinogenesis by modulating E-cadherin/β-catenin signaling *via* its FadA adhesin. *Cell Host Microbe* 2013; **14**: 195-206 [*RCA*] [PMID: 23954158 DOI: 10.1016/j.chom.2013.07.012] [FullText]

137 **Kashani N**, Bezmin Abadi AT, Rahimi F, Forootan M. FadA-positive Fusobacterium nucleatum is prevalent in biopsy specimens of Iranian patients with colorectal cancer. *New Microbes New Infect* 2020; **34**: 100651 [*RCA*] [PMID: 32025313 DOI: 10.1016/j.nmni.2020.100651] [Full Text] [Full Text(PDF)]

138 **Abed J**, Emgård JE, Zamir G, Faroja M, Almogy G, Grenov A, Sol A, Naor R, Pikarsky E, Atlan KA, Mellul A, Chaushu S, Manson AL, Earl AM, Ou N, Brennan CA, Garrett WS, Bachrach G. Fap2 Mediates Fusobacterium nucleatum Colorectal Adenocarcinoma Enrichment by Binding to Tumor-Expressed Gal-GalNAc. *Cell Host Microbe* 2016; **20**: 215-225 [*RCA*] [PMID: 27512904 DOI: 10.1016/j.chom.2016.07.006] [FullText]

139 **Yang Y**, Weng W, Peng J, Hong L, Yang L, Toiyama Y, Gao R, Liu M, Yin M, Pan C, Li H, Guo B, Zhu Q, Wei Q, Moyer MP, Wang P, Cai S, Goel A, Qin H, Ma Y. Fusobacterium nucleatum Increases Proliferation of Colorectal Cancer Cells and Tumor Development in Mice by Activating Toll-Like Receptor 4 Signaling to Nuclear Factor-κB, and Up-regulating Expression of MicroRNA-21. *Gastroenterology* 2017; **152**: 851-866.e24 [*RCA*] [PMID: 27876571 DOI: 10.1053/j.gastro.2016.11.018] [FullText]

140 **Bullman S**, Pedamallu CS, Sicinska E, Clancy TE, Zhang X, Cai D, Neuberg D, Huang K, Guevara F, Nelson T, Chipashvili O, Hagan T, Walker M, Ramachandran A, Diosdado B, Serna G, Mulet N, Landolfi S, Ramon Y Cajal S, Fasani R, Aguirre AJ, Ng K, Élez E, Ogino S, Tabernero J, Fuchs CS, Hahn WC, Nuciforo P, Meyerson M. Analysis of Fusobacterium persistence and antibiotic response in colorectal cancer. *Science* 2017; **358**: 1443-1448 [*RCA*] [PMID: 29170280 DOI: 10.1126/science.aal5240] [FullText]

141 **Pleguezuelos-Manzano C**, Puschhof J, Rosendahl Huber A, van Hoeck A, Wood HM, Nomburg J, Gurjao C, Manders F, Dalmasso G, Stege PB, Paganelli FL, Geurts MH, Beumer J, Mizutani T, Miao Y, van der Linden R, van der Elst S; Genomics England Research Consortium, Garcia KC, Top J, Willems RJL, Giannakis M, Bonnet R, Quirke P, Meyerson M, Cuppen E, van Boxtel R, Clevers H. Mutational signature in colorectal cancer caused by genotoxic pks(+) E. coli. *Nature* 2020; **580**: 269-273 [*RCA*] [PMID: 32106218 DOI: 10.1038/s41586-020-2080-8] [FullText]

142 **Allen-Vercoe E**, Jobin C. Fusobacterium and Enterobacteriaceae: important players for CRC? *Immunol Lett* 2014; **162**: 54-61 [*RCA*] [PMID: 24972311 DOI: 10.1016/j.imlet.2014.05.014] [FullText]

143 **Maddocks OD**, Scanlon KM, Donnenberg MS. An Escherichia coli effector protein promotes host mutation *via* depletion of DNA mismatch repair proteins. *mBio* 2013; **4**: e00152-e00113 [*RCA*] [PMID: 23781066 DOI: 10.1128/mBio.00152-13] [FullText] [Full Text(PDF)]

144 **Dejea CM**, Fathi P, Craig JM, Boleij A, Taddese R, Geis AL, Wu X, DeStefano Shields CE, Hechenbleikner EM, Huso DL, Anders RA, Giardiello FM, Wick EC, Wang H, Wu S, Pardoll DM, Housseau F, Sears CL. Patients with familial adenomatous polyposis harbor colonic biofilms containing tumorigenic bacteria. *Science* 2018; **359**: 592-597 [*RCA*] [PMID: 29420293 DOI: 10.1126/science.aah3648] [FullText]

145 **Dai Z**, Coker OO, Nakatsu G, Wu WKK, Zhao L, Chen Z, Chan FKL, Kristiansen K, Sung JJY, Wong SH, Yu J. Multi-cohort analysis of

colorectal cancer metagenome identified altered bacteria across populations and universal bacterial markers. *Microbiome* 2018; **6**: 70 [*RCA*] [PMID: 29642940 DOI: 10.1186/s40168-018-0451-2] [FullText] [Full Text(PDF)]

146 **Yachida S**, Mizutani S, Shiroma H, Shiba S, Nakajima T, Sakamoto T, Watanabe H, Masuda K, Nishimoto Y, Kubo M, Hosoda F, Rokutan H, Matsumoto M, Takamaru H, Yamada M, Matsuda T, Iwasaki M, Yamaji T, Yachida T, Soga T, Kurokawa K, Toyoda A, Ogura Y, Hayashi T, Hatakeyama M, Nakagama H, Saito Y, Fukuda S, Shibata T, Yamada T. Metagenomic and metabolomic analyses reveal distinct stage-specific phenotypes of the gut microbiota in colorectal cancer. *Nat Med* 2019; **25**: 968-976 [*RCA*] [PMID: 31171880 DOI: 10.1038/s41591-019-0458-7] [FullText]

147 **Thiele Orberg E**, Fan H, Tam AJ, Dejea CM, Destefano Shields CE, Wu S, Chung L, Finard BB, Wu X, Fathi P, Ganguly S, Fu J, Pardoll DM, Sears CL, Housseau F. The myeloid immune signature of enterotoxigenic Bacteroides fragilis-induced murine colon tumorigenesis. *Mucosal Immunol* 2017; **10**: 421-433 [*RCA*] [PMID: 27301879 DOI: 10.1038/mi.2016.53] [FullText] [Full Text(PDF)]

148 **Chung L**, Thiele Orberg E, Geis AL, Chan JL, Fu K, DeStefano Shields CE, Dejea CM, Fathi P, Chen J, Finard BB, Tam AJ, McAllister F, Fan H, Wu X, Ganguly S, Lebid A, Metz P, Van Meerbeke SW, Huso DL, Wick EC, Pardoll DM, Wan F, Wu S, Sears CL, Housseau F. Bacteroides fragilis Toxin Coordinates a Pro-carcinogenic Inflammatory Cascade *via* Targeting of Colonic Epithelial Cells. *Cell Host Microbe* 2018; **23**: 203-214.e5 [*RCA*] [PMID: 29398651 DOI: 10.1016/j.chom.2018.01.007] [FullText]

149 **Rezasoltani S**, Asadzadeh Aghdaei H, Dabiri H, Akhavan Sepahi A, Modarressi MH, Nazemalhosseini Mojarad E. The association between fecal microbiota and different types of colorectal polyp as precursors of colorectal cancer. *Microb Pathog* 2018; **124**: 244-249 [*RCA*] [PMID: 30142468 DOI: 10.1016/j.micpath.2018.08.035] [FullText]

150 **Dadkhah E**, Sikaroodi M, Korman L, Hardi R, Baybick J, Hanzel D, Kuehn G, Kuehn T, Gillevet PM. Gut microbiome identifies risk for colorectal polyps. *BMJ Open Gastroenterol* 2019; **6**: e000297 [*RCA*] [PMID: 31275588 DOI: 10.1136/bmjgast-2019-000297] [FullText] [Full Text(PDF)]

151 **Pasquereau-Kotula E**, Martins M, Aymeric L, Dramsi S. Significance of Streptococcus gallolyticus subsp. gallolyticus Association With Colorectal Cancer. *Front Microbiol* 2018; **9**: 614 [*RCA*] [PMID: 29666615 DOI: 10.3389/fmicb.2018.00614] [FullText] [Full Text(PDF)]

152 **Abdulamir AS**, Hafidh RR, Abu Bakar F. The association of Streptococcus bovis/gallolyticus with colorectal tumors: the nature and the underlying mechanisms of its etiological role. *J Exp Clin Cancer Res* 2011; **30**: 11 [*RCA*] [PMID: 21247505 DOI: 10.1186/1756-9966-30-11] [FullText] [Full Text(PDF)]

153 **Boleij A**, van Gelder MM, Swinkels DW, Tjalsma H. Clinical Importance of Streptococcus gallolyticus infection among colorectal cancer patients: systematic review and meta-analysis. *Clin Infect Dis* 2011; **53**: 870-878 [*RCA*] [PMID: 21960713 DOI: 10.1093/cid/cir609] [FullText]

154 **Öberg J**, Rasmussen M, Buchwald P, Nilson B, Inghammar M. Streptococcus bovis-bacteremia: subspecies distribution and association with colorectal cancer: a retrospective cohort study. *Epidemiol Infect* 2021; **150**: e8 [*RCA*] [PMID: 38751047 DOI: 10.1017/S0950268821002533] [FullText] [Full Text(PDF)]

155 **Kamali N**, Talebi Bezmin Abadi A, Abadi B, Rahimi F, Forootan M. Identification of Streptococcus gallolyticus in tumor samples of Iranian patients diagnosed with colorectal cancer. *BMC Res Notes* 2022; **15**: 316 [*RCA*] [PMID: 36199123 DOI: 10.1186/s13104-022-06207-9] [Full Text] [Full Text(PDF)]

156 **Purcell RV**, Pearson J, Aitchison A, Dixon L, Frizelle FA, Keenan JI. Colonization with enterotoxigenic Bacteroides fragilis is associated with early-stage colorectal neoplasia. *PLoS One* 2017; **12**: e0171602 [*RCA*] [PMID: 28151975 DOI: 10.1371/journal.pone.0171602] [FullText] [Full Text(PDF)]

157 **Wu S**, Morin PJ, Maouyo D, Sears CL. Bacteroides fragilis enterotoxin induces c-Myc expression and cellular proliferation. *Gastroenterology* 2003; **124**: 392-400 [*RCA*] [PMID: 12557145 DOI: 10.1053/gast.2003.50047] [FullText]

158 **Toprak NU**, Yagci A, Gulluoglu BM, Akin ML, Demirkalem P, Celenk T, Soyletir G. A possible role of Bacteroides fragilis enterotoxin in the aetiology of colorectal cancer. *Clin Microbiol Infect* 2006; **12**: 782-786 [*RCA*] [PMID: 16842574 DOI: 10.1111/j.1469-0691.2006.01494.x] [FullText]

159 **Boleij A**, Hechenbleikner EM, Goodwin AC, Badani R, Stein EM, Lazarev MG, Ellis B, Carroll KC, Albesiano E, Wick EC, Platz EA, Pardoll DM, Sears CL. The Bacteroides fragilis toxin gene is prevalent in the colon mucosa of colorectal cancer patients. *Clin Infect Dis* 2015; **60**: 208-215 [*RCA*] [PMID: 25305284 DOI: 10.1093/cid/ciu787] [FullText]

160 **Wu S**, Rhee KJ, Albesiano E, Rabizadeh S, Wu X, Yen HR, Huso DL, Brancati FL, Wick E, McAllister F, Housseau F, Pardoll DM, Sears CL. A human colonic commensal promotes colon tumorigenesis *via* activation of T helper type 17 T cell responses. *Nat Med* 2009; **15**: 1016-1022 [*RCA*] [PMID: 19701202 DOI: 10.1038/nm.2015] [FullText]

161 **Maddocks OD**, Short AJ, Donnenberg MS, Bader S, Harrison DJ. Attaching and effacing Escherichia coli downregulate DNA mismatch repair protein in vitro and are associated with colorectal adenocarcinomas in humans. *PLoS One* 2009; **4**: e5517 [*RCA*] [PMID: 19436735 DOI: 10.1371/journal.pone.0005517] [FullText] [Full Text(PDF)]

162 **Cuevas-Ramos G**, Petit CR, Marcq I, Boury M, Oswald E, Nougayrède JP. Escherichia coli induces DNA damage in vivo and triggers genomic instability in mammalian cells. *Proc Natl Acad Sci U S A* 2010; **107**: 11537-11542 [*RCA*] [PMID: 20534522 DOI: 10.1073/pnas.1001261107] [FullText]

163 **Wu J**, Li Q, Fu X. Fusobacterium nucleatum Contributes to the Carcinogenesis of Colorectal Cancer by Inducing Inflammation and Suppressing Host Immunity. *Transl Oncol* 2019; **12**: 846-851 [*RCA*] [PMID: 30986689 DOI: 10.1016/j.tranon.2019.03.003] [FullText] [Full Text(PDF)]

164 **Pillar CM**, Gilmore MS. Enterococcal virulence--pathogenicity island of E. Faecalis. *Front Biosci* 2004; **9**: 2335-2346 [*RCA*] [PMID: 15353291 DOI: 10.2741/1400] [FullText]

165 **Balamurugan R**, Rajendiran E, George S, Samuel GV, Ramakrishna BS. Real-time polymerase chain reaction quantification of specific butyrate-producing bacteria, Desulfovibrio and Enterococcus faecalis in the feces of patients with colorectal cancer. *J Gastroenterol Hepatol* 2008; **23**: 1298-1303 [*RCA*] [PMID: 18624900 DOI: 10.1111/j.1440-1746.2008.05490.x] [FullText]

166 **Yu T**, Guo F, Yu Y, Sun T, Ma D, Han J, Qian Y, Kryczek I, Sun D, Nagarsheth N, Chen Y, Chen H, Hong J, Zou W, Fang JY. Fusobacterium nucleatum Promotes Chemoresistance to Colorectal Cancer by Modulating Autophagy. *Cell* 2017; **170**: 548-563.e16 [*RCA*] [PMID: 28753429 DOI: 10.1016/j.cell.2017.07.008] [FullText]

167 **Shah MS**, DeSantis T, Yamal JM, Weir T, Ryan EP, Cope JL, Hollister EB. Re-purposing 16S rRNA gene sequence data from within case paired tumor biopsy and tumor-adjacent biopsy or fecal samples to identify microbial markers for colorectal cancer. *PLoS One* 2018; **13**: e0207002 [*RCA*] [PMID: 30412600 DOI: 10.1371/journal.pone.0207002] [FullText] [Full Text(PDF)]

168 **Liu S**, da Cunha AP, Rezende RM, Cialic R, Wei Z, Bry L, Comstock LE, Gandhi R, Weiner HL. The Host Shapes the Gut Microbiota *via*

Fecal MicroRNA. *Cell Host Microbe* 2016; **19**: 32-43 [*RCA*] [PMID: 26764595 DOI: 10.1016/j.chom.2015.12.005] [FullText]
169 **Faïs T**, Delmas J, Cougnoux A, Dalmasso G, Bonnet R. Targeting colorectal cancer-associated bacteria: A new area of research for personalized treatments. *Gut Microbes* 2016; **7**: 329-333 [*RCA*] [PMID: 27007710 DOI: 10.1080/19490976.2016.1155020] [FullText]
170 **Drago L**. Probiotics and Colon Cancer. *Microorganisms* 2019; **7**: 66 [*RCA*] [PMID: 30823471 DOI: 10.3390/microorganisms7030066] [Full Text] [Full Text(PDF)]
171 **Bassaganya-Riera J**, Viladomiu M, Pedragosa M, De Simone C, Hontecillas R. Immunoregulatory mechanisms underlying prevention of colitis-associated colorectal cancer by probiotic bacteria. *PLoS One* 2012; **7**: e34676 [*RCA*] [PMID: 22511958 DOI: 10.1371/journal.pone.0034676] [FullText] [Full Text(PDF)]
172 **Molska M**, Reguła J. Potential Mechanisms of Probiotics Action in the Prevention and Treatment of Colorectal Cancer. *Nutrients* 2019; **11**: 2453 [*RCA*] [PMID: 31615096 DOI: 10.3390/nu11102453] [FullText] [Full Text(PDF)]
173 **Bowen JM**, Stringer AM, Gibson RJ, Yeoh AS, Hannam S, Keefe DM. VSL#3 probiotic treatment reduces chemotherapy-induced diarrhea and weight loss. *Cancer Biol Ther* 2007; **6**: 1449-1454 [*RCA*] [PMID: 17881902 DOI: 10.4161/cbt.6.9.4622] [FullText]
174 **Malhotra SL**. Dietary factors in a study of cancer colon from Cancer Registry, with special reference to the role of saliva, milk and fermented milk products and vegetable fibre. *Med Hypotheses* 1977; **3**: 122-126 [*RCA*] [PMID: 578288 DOI: 10.1016/0306-9877(77)90024-x] [FullText]
175 **Peters RK**, Pike MC, Garabrant D, Mack TM. Diet and colon cancer in Los Angeles County, California. *Cancer Causes Control* 1992; **3**: 457-473 [*RCA*] [PMID: 1525327 DOI: 10.1007/BF00051359] [FullText]
176 **Young TB**, Wolf DA. Case-control study of proximal and distal colon cancer and diet in Wisconsin. *Int J Cancer* 1988; **42**: 167-175 [*RCA*] [PMID: 3403062 DOI: 10.1002/ijc.2910420205] [FullText]
177 **Rosshart SP**, Vassallo BG, Angeletti D, Hutchinson DS, Morgan AP, Takeda K, Hickman HD, McCulloch JA, Badger JH, Ajami NJ, Trinchieri G, Pardo-Manuel de Villena F, Yewdell JW, Rehermann B. Wild Mouse Gut Microbiota Promotes Host Fitness and Improves Disease Resistance. *Cell* 2017; **171**: 1015-1028.e13 [*RCA*] [PMID: 29056339 DOI: 10.1016/j.cell.2017.09.016] [FullText]
178 **Filip M**, Tzaneva V, Dumitrascu DL. Fecal transplantation: digestive and extradigestive clinical applications. *Clujul Med* 2018; **91**: 259-265 [*RCA*] [PMID: 30093802 DOI: 10.15386/cjmed-946] [FullText] [Full Text(PDF)]
179 **Geller LT**, Barzily-Rokni M, Danino T, Jonas OH, Shental N, Nejman D, Gavert N, Zwang Y, Cooper ZA, Shee K, Thaiss CA, Reuben A, Livny J, Avraham R, Frederick DT, Ligorio M, Chatman K, Johnston SE, Mosher CM, Brandis A, Fuks G, Gurbatri C, Gopalakrishnan V, Kim M, Hurd MW, Katz M, Fleming J, Maitra A, Smith DA, Skalak M, Bu J, Michaud M, Trauger SA, Barshack I, Golan T, Sandbank J, Flaherty KT, Mandinova A, Garrett WS, Thayer SP, Ferrone CR, Huttenhower C, Bhatia SN, Gevers D, Wargo JA, Golub TR, Straussman R. Potential role of intratumor bacteria in mediating tumor resistance to the chemotherapeutic drug gemcitabine. *Science* 2017; **357**: 1156-1160 [*RCA*] [PMID: 28912244 DOI: 10.1126/science.aah5043] [FullText]
180 **Iida N**, Dzutsev A, Stewart CA, Smith L, Bouladoux N, Weingarten RA, Molina DA, Salcedo R, Back T, Cramer S, Dai RM, Kiu H, Cardone M, Naik S, Patri AK, Wang E, Marincola FM, Frank KM, Belkaid Y, Trinchieri G, Goldszmid RS. Commensal bacteria control cancer response to therapy by modulating the tumor microenvironment. *Science* 2013; **342**: 967-970 [*RCA*] [PMID: 24264989 DOI: 10.1126/science.1240527] [FullText]
181 **Vétizou M**, Pitt JM, Daillère R, Lepage P, Waldschmitt N, Flament C, Rusakiewicz S, Routy B, Roberti MP, Duong CP, Poirier-Colame V, Roux A, Becharef S, Formenti S, Golden E, Cording S, Eberl G, Schlitzer A, Ginhoux F, Mani S, Yamazaki T, Jacquelot N, Enot DP, Bérard M, Nigou J, Opolon P, Eggermont A, Woerther PL, Chachaty E, Chaput N, Robert C, Mateus C, Kroemer G, Raoult D, Boneca IG, Carbonnel F, Chamaillard M, Zitvogel L. Anticancer immunotherapy by CTLA-4 blockade relies on the gut microbiota. *Science* 2015; **350**: 1079-1084 [*RCA*] [PMID: 26541610 DOI: 10.1126/science.aad1329] [FullText]
182 **Wallace BD**, Wang H, Lane KT, Scott JE, Orans J, Koo JS, Venkatesh M, Jobin C, Yeh LA, Mani S, Redinbo MR. Alleviating cancer drug toxicity by inhibiting a bacterial enzyme. *Science* 2010; **330**: 831-835 [*RCA*] [PMID: 21051639 DOI: 10.1126/science.1191175] [FullText] [Full Text(PDF)]
183 **Xu Y**, Villalona-Calero MA. Irinotecan: mechanisms of tumor resistance and novel strategies for modulating its activity. *Ann Oncol* 2002; **13**: 1841-1851 [*RCA*] [PMID: 12453851 DOI: 10.1093/annonc/mdf337] [FullText]
184 **Shen S**, Lim G, You Z, Ding W, Huang P, Ran C, Doheny J, Caravan P, Tate S, Hu K, Kim H, McCabe M, Huang B, Xie Z, Kwon D, Chen L, Mao J. Gut microbiota is critical for the induction of chemotherapy-induced pain. *Nat Neurosci* 2017; **20**: 1213-1216 [*RCA*] [PMID: 28714953 DOI: 10.1038/nn.4606] [FullText] [Full Text(PDF)]
185 **Weledji EP**, Enoworock G, Mokake M, Sinju M. How Grim is Pancreatic Cancer? *Oncol Rev* 2016; **10**: 294 [*RCA*] [PMID: 27471581 DOI: 10.4081/oncol.2016.294] [FullText] [Full Text(PDF)]
186 **Adamska A**, Domenichini A, Falasca M. Pancreatic Ductal Adenocarcinoma: Current and Evolving Therapies. *Int J Mol Sci* 2017; **18**: 1338 [*RCA*] [PMID: 28640192 DOI: 10.3390/ijms18071338] [FullText] [Full Text(PDF)]
187 **Yadav D**, Lowenfels AB. The epidemiology of pancreatitis and pancreatic cancer. *Gastroenterology* 2013; **144**: 1252-1261 [*RCA*] [PMID: 23622135 DOI: 10.1053/j.gastro.2013.01.068] [FullText]
188 **Wang C**, Li J. Pathogenic Microorganisms and Pancreatic Cancer. *Gastrointest Tumors* 2015; **2**: 41-47 [*RCA*] [PMID: 26673459 DOI: 10.1159/000380896] [FullText]
189 **Wei MY**, Shi S, Liang C, Meng QC, Hua J, Zhang YY, Liu J, Zhang B, Xu J, Yu XJ. The microbiota and microbiome in pancreatic cancer: more influential than expected. *Mol Cancer* 2019; **18**: 97 [*RCA*] [PMID: 31109338 DOI: 10.1186/s12943-019-1008-0] [FullText] [Full Text (PDF)]
190 **Raderer M**, Wrba F, Kornek G, Maca T, Koller DY, Weinlaender G, Hejna M, Scheithauer W. Association between Helicobacter pylori infection and pancreatic cancer. *Oncology* 1998; **55**: 16-19 [*RCA*] [PMID: 9428370 DOI: 10.1159/000011830] [FullText]
191 **Gravina AG**, Zagari RM, De Musis C, Romano L, Loguercio C, Romano M. Helicobacter pylori and extragastric diseases: A review. *World J Gastroenterol* 2018; **24**: 3204-3221 [*RCA*] [PMID: 30090002 DOI: 10.3748/wjg.v24.i29.3204] [FullText] [Full Text(PDF)]
192 **Stolzenberg-Solomon RZ**, Blaser MJ, Limburg PJ, Perez-Perez G, Taylor PR, Virtamo J, Albanes D; ATBC Study. Helicobacter pylori seropositivity as a risk factor for pancreatic cancer. *J Natl Cancer Inst* 2001; **93**: 937-941 [*RCA*] [PMID: 11416115 DOI: 10.1093/jnci/93.12.937] [FullText]
193 **Bao Y**, Spiegelman D, Li R, Giovannucci E, Fuchs CS, Michaud DS. History of peptic ulcer disease and pancreatic cancer risk in men. *Gastroenterology* 2010; **138**: 541-549 [*RCA*] [PMID: 19818786 DOI: 10.1053/j.gastro.2009.09.059] [FullText]
194 **Luo J**, Nordenvall C, Nyrén O, Adami HO, Permert J, Ye W. The risk of pancreatic cancer in patients with gastric or duodenal ulcer disease. *Int J Cancer* 2007; **120**: 368-372 [*RCA*] [PMID: 17044024 DOI: 10.1002/ijc.22123] [FullText]

195 **Manes G**, Balzano A, Vaira D. Helicobacter pylori and pancreatic disease. *JOP* 2003; **4**: 111-116 [*RCA*] [PMID: 12743416] [FullText]

196 **Huang H**, Daniluk J, Liu Y, Chu J, Li Z, Ji B, Logsdon CD. Oncogenic K-Ras requires activation for enhanced activity. *Oncogene* 2014; **33**: 532-535 [*RCA*] [PMID: 23334325 DOI: 10.1038/onc.2012.619] [FullText]

197 **Daniluk J**, Liu Y, Deng D, Chu J, Huang H, Gaiser S, Cruz-Monserrate Z, Wang H, Ji B, Logsdon CD. An NF-κB pathway-mediated positive feedback loop amplifies Ras activity to pathological levels in mice. *J Clin Invest* 2012; **122**: 1519-1528 [*RCA*] [PMID: 22406536 DOI: 10.1172/JCI59743] [FullText]

198 **Yu H**, Pardoll D, Jove R. STATs in cancer inflammation and immunity: a leading role for STAT3. *Nat Rev Cancer* 2009; **9**: 798-809 [*RCA*] [PMID: 19851315 DOI: 10.1038/nrc2734] [FullText]

199 **Lesina M**, Kurkowski MU, Ludes K, Rose-John S, Treiber M, Klöppel G, Yoshimura A, Reindl W, Sipos B, Akira S, Schmid RM, Algül H. Stat3/Socs3 activation by IL-6 transsignaling promotes progression of pancreatic intraepithelial neoplasia and development of pancreatic cancer. *Cancer Cell* 2011; **19**: 456-469 [*RCA*] [PMID: 21481788 DOI: 10.1016/j.ccr.2011.03.009] [FullText]

200 **Michaud DS**. Role of bacterial infections in pancreatic cancer. *Carcinogenesis* 2013; **34**: 2193-2197 [*RCA*] [PMID: 23843038 DOI: 10.1093/carcin/bgt249] [FullText]

201 **Tribble GD**, Kerr JE, Wang BY. Genetic diversity in the oral pathogen Porphyromonas gingivalis: molecular mechanisms and biological consequences. *Future Microbiol* 2013; **8**: 607-620 [*RCA*] [PMID: 23642116 DOI: 10.2217/fmb.13.30] [FullText]

202 **Michaud DS**, Izard J, Wilhelm-Benartzi CS, You DH, Grote VA, Tjønneland A, Dahm CC, Overvad K, Jenab M, Fedirko V, Boutron-Ruault MC, Clavel-Chapelon F, Racine A, Kaaks R, Boeing H, Foerster J, Trichopoulou A, Lagiou P, Trichopoulos D, Sacerdote C, Sieri S, Palli D, Tumino R, Panico S, Siersema PD, Peeters PH, Lund E, Barricarte A, Huerta JM, Molina-Montes E, Dorronsoro M, Quirós JR, Duell EJ, Ye W, Sund M, Lindkvist B, Johansen D, Khaw KT, Wareham N, Travis RC, Vineis P, Bueno-de-Mesquita HB, Riboli E. Plasma antibodies to oral bacteria and risk of pancreatic cancer in a large European prospective cohort study. *Gut* 2013; **62**: 1764-1770 [*RCA*] [PMID: 22990306 DOI: 10.1136/gutjnl-2012-303006] [FullText]

203 **Zhang JJ**, Wu HS, Wang L, Tian Y, Zhang JH, Wu HL. Expression and significance of TLR4 and HIF-1alpha in pancreatic ductal adenocarcinoma. *World J Gastroenterol* 2010; **16**: 2881-2888 [*RCA*] [PMID: 20556833 DOI: 10.3748/wjg.v16.i23.2881] [FullText] [Full Text (PDF)]

204 **Ikebe M**, Kitaura Y, Nakamura M, Tanaka H, Yamasaki A, Nagai S, Wada J, Yanai K, Koga K, Sato N, Kubo M, Tanaka M, Onishi H, Katano M. Lipopolysaccharide (LPS) increases the invasive ability of pancreatic cancer cells through the TLR4/MyD88 signaling pathway. *J Surg Oncol* 2009; **100**: 725-731 [*RCA*] [PMID: 19722233 DOI: 10.1002/jso.21392] [FullText]

205 **Ochi A**, Nguyen AH, Bedrosian AS, Mushlin HM, Zarbakhsh S, Barilla R, Zambirinis CP, Fallon NC, Rehman A, Pylayeva-Gupta Y, Badar S, Hajdu CH, Frey AB, Bar-Sagi D, Miller G. MyD88 inhibition amplifies dendritic cell capacity to promote pancreatic carcinogenesis *via* Th2 cells. *J Exp Med* 2012; **209**: 1671-1687 [*RCA*] [PMID: 22908323 DOI: 10.1084/jem.20111706] [FullText] [Full Text(PDF)]

206 **Zhang H**, Sun L. When human cells meet bacteria: precision medicine for cancers using the microbiota. *Am J Cancer Res* 2018; **8**: 1157-1175 [*RCA*] [PMID: 30094091 DOI: 10.1158/1538-7445.AM2018-1157] [FullText]

207 **Udayasuryan B**, Ahmad RN, Nguyen TTD, Umaña A, Monét Roberts L, Sobol P, Jones SD, Munson JM, Slade DJ, Verbridge SS. Fusobacterium nucleatum induces proliferation and migration in pancreatic cancer cells through host autocrine and paracrine signaling. *Sci Signal* 2022; **15**: eabn4948 [*RCA*] [PMID: 36256708 DOI: 10.1126/scisignal.abn4948] [FullText]

208 **Hayashi M**, Ikenaga N, Nakata K, Luo H, Zhong P, Date S, Oyama K, Higashijima N, Kubo A, Iwamoto C, Torata N, Abe T, Yamada Y, Ohuchida K, Oda Y, Nakamura M. Intratumor Fusobacterium nucleatum promotes the progression of pancreatic cancer *via* the CXCL1-CXCR2 axis. *Cancer Sci* 2023; **114**: 3666-3678 [*RCA*] [PMID: 37438965 DOI: 10.1111/cas.15901] [FullText] [Full Text(PDF)]

209 **D'Antonio DL**, Zenoniani A, Umme S, Piattelli A, Curia MC. Intratumoral Fusobacterium nucleatum in Pancreatic Cancer: Current and Future Perspectives. *Pathogens* 2024; **14**: 2 [*RCA*] [PMID: 39860963 DOI: 10.3390/pathogens14010002] [FullText] [Full Text(PDF)]

210 **Gaida MM**, Mayer C, Dapunt U, Stegmaier S, Schirmacher P, Wabnitz GH, Hänsch GM. Expression of the bitter receptor T2R38 in pancreatic cancer: localization in lipid droplets and activation by a bacteria-derived quorum-sensing molecule. *Oncotarget* 2016; **7**: 12623-12632 [*RCA*] [PMID: 26862855 DOI: 10.18632/oncotarget.7206] [FullText] [Full Text(PDF)]

211 **Pushalkar S**, Hundeyin M, Daley D, Zambirinis CP, Kurz E, Mishra A, Mohan N, Aykut B, Usyk M, Torres LE, Werba G, Zhang K, Guo Y, Li Q, Akkad N, Lall S, Wadowski B, Gutierrez J, Kochen Rossi JA, Herzog JW, Diskin B, Torres-Hernandez A, Leinwand J, Wang W, Taunk PS, Savadkar S, Janal M, Saxena A, Li X, Cohen D, Sartor RB, Saxena D, Miller G. The Pancreatic Cancer Microbiome Promotes Oncogenesis by Induction of Innate and Adaptive Immune Suppression. *Cancer Discov* 2018; **8**: 403-416 [*RCA*] [PMID: 29567829 DOI: 10.1158/2159-8290.CD-17-1134] [FullText]

212 **Oláh A**, Romics L Jr. Early enteral nutrition in acute pancreatitis--benefits and limitations. *Langenbecks Arch Surg* 2008; **393**: 261-269 [*RCA*] [PMID: 18266002 DOI: 10.1007/s00423-008-0291-9] [FullText]

213 **Zabaleta J**. Multifactorial etiology of gastric cancer. *Methods Mol Biol* 2012; **863**: 411-435 [*RCA*] [PMID: 22359309 DOI: 10.1007/978-1-61779-612-8_26] [FullText]

214 **Ishaq S**, Nunn L. Helicobacter pylori and gastric cancer: a state of the art review. *Gastroenterol Hepatol Bed Bench* 2015; **8**: S6-S14 [*RCA*] [PMID: 26171139] [FullText] [Full Text(PDF)]

215 **Pucułek M**, Machlowska J, Wierzbicki R, Baj J, Maciejewski R, Sitarz R. Helicobacter pylori associated factors in the development of gastric cancer with special reference to the early-onset subtype. *Oncotarget* 2018; **9**: 31146-31162 [*RCA*] [PMID: 30123433 DOI: 10.18632/oncotarget.25757] [FullText] [Full Text(PDF)]

216 **Zhang RG**, Duan GC, Fan QT, Chen SY. Role of Helicobacter pylori infection in pathogenesis of gastric carcinoma. *World J Gastrointest Pathophysiol* 2016; **7**: 97-107 [*RCA*] [PMID: 26909232 DOI: 10.4291/wjgp.v7.i1.97] [FullText] [Full Text(PDF)]

217 **Correa P**, Haenszel W, Cuello C, Tannenbaum S, Archer M. A model for gastric cancer epidemiology. *Lancet* 1975; **2**: 58-60 [*RCA*] [PMID: 49653 DOI: 10.1016/s0140-6736(75)90498-5] [FullText]

218 **Watari J**, Chen N, Amenta PS, Fukui H, Oshima T, Tomita T, Miwa H, Lim KJ, Das KM. Helicobacter pylori associated chronic gastritis, clinical syndromes, precancerous lesions, and pathogenesis of gastric cancer development. *World J Gastroenterol* 2014; **20**: 5461-5473 [*RCA*] [PMID: 24833876 DOI: 10.3748/wjg.v20.i18.5461] [FullText] [Full Text(PDF)]

219 **Moss SF**. The Clinical Evidence Linking Helicobacter pylori to Gastric Cancer. *Cell Mol Gastroenterol Hepatol* 2017; **3**: 183-191 [*RCA*] [PMID: 28275685 DOI: 10.1016/j.jcmgh.2016.12.001] [FullText] [Full Text(PDF)]

220 **Song H**, Ekheden IG, Zheng Z, Ericsson J, Nyrén O, Ye W. Incidence of gastric cancer among patients with gastric precancerous lesions: observational cohort study in a low risk Western population. *BMJ* 2015; **351**: h3867 [*RCA*] [PMID: 26215280 DOI: 10.1136/bmj.h3867] [Full

Text] [Full Text(PDF)]

221 **Bhattacharyya A**, Chattopadhyay R, Mitra S, Crowe SE. Oxidative stress: an essential factor in the pathogenesis of gastrointestinal mucosal diseases. *Physiol Rev* 2014; **94**: 329-354 [*RCA*] [PMID: 24692350 DOI: 10.1152/physrev.00040.2012] [FullText]

222 **Tsai HF**, Hsu PN. Interplay between Helicobacter pylori and immune cells in immune pathogenesis of gastric inflammation and mucosal pathology. *Cell Mol Immunol* 2010; **7**: 255-259 [*RCA*] [PMID: 20190789 DOI: 10.1038/cmi.2010.2] [FullText]

223 **Maeda M**, Moro H, Ushijima T. Mechanisms for the induction of gastric cancer by Helicobacter pylori infection: aberrant DNA methylation pathway. *Gastric Cancer* 2017; **20**: 8-15 [*RCA*] [PMID: 27718135 DOI: 10.1007/s10120-016-0650-0] [FullText]

224 **Muhammad JS**, Eladl MA, Khoder G. Helicobacter pylori-induced DNA Methylation as an Epigenetic Modulator of Gastric Cancer: Recent Outcomes and Future Direction. *Pathogens* 2019; **8**: 23 [*RCA*] [PMID: 30781778 DOI: 10.3390/pathogens8010023] [FullText] [Full Text (PDF)]

225 **Fu Q**, Yu H, Liu M, Chen L, Chen W, Wang Z, Li W. Effect of Helicobacter pylori eradication on gastric cancer risk in patients with intestinal metaplasia or dysplasia: a meta-analysis of randomized controlled trials. *Front Microbiol* 2025; **16**: 1530549 [*RCA*] [PMID: 40143868 DOI: 10.3389/fmicb.2025.1530549] [FullText]

226 **Ford AC**, Yuan Y, Park JY, Forman D, Moayyedi P. Eradication Therapy to Prevent Gastric Cancer in Helicobacterpylori-Positive Individuals: Systematic Review and Meta-Analysis of Randomized Controlled Trials and Observational Studies. *Gastroenterology* 2025; **169**: 261-276 [*RCA*] [PMID: 39824392 DOI: 10.1053/j.gastro.2024.12.033] [FullText]

227 **Kikuchi S**, Crabtree JE, Forman D, Kurosawa M. Association between infections with CagA-positive or -negative strains of Helicobacter pylori and risk for gastric cancer in young adults. Research Group on Prevention of Gastric Carcinoma Among Young Adults. *Am J Gastroenterol* 1999; **94**: 3455-3459 [*RCA*] [PMID: 10606302 DOI: 10.1111/j.1572-0241.1999.01607.x] [FullText]

228 **Yong X**, Tang B, Li BS, Xie R, Hu CJ, Luo G, Qin Y, Dong H, Yang SM. Helicobacter pylori virulence factor CagA promotes tumorigenesis of gastric cancer *via* multiple signaling pathways. *Cell Commun Signal* 2015; **13**: 30 [*RCA*] [PMID: 26160167 DOI: 10.1186/s12964-015-0111-0] [FullText] [Full Text(PDF)]

229 **Li N**, Feng Y, Hu Y, He C, Xie C, Ouyang Y, Artim SC, Huang D, Zhu Y, Luo Z, Ge Z, Lu N. Helicobacter pylori CagA promotes epithelial mesenchymal transition in gastric carcinogenesis *via* triggering oncogenic YAP pathway. *J Exp Clin Cancer Res* 2018; **37**: 280 [*RCA*] [PMID: 30466467 DOI: 10.1186/s13046-018-0962-5] [FullText] [Full Text(PDF)]

230 **Wei J**, Noto J, Zaika E, Romero-Gallo J, Correa P, El-Rifai W, Peek RM, Zaika A. Pathogenic bacterium Helicobacter pylori alters the expression profile of p53 protein isoforms and p53 response to cellular stresses. *Proc Natl Acad Sci U S A* 2012; **109**: E2543-E2550 [*RCA*] [PMID: 22927405 DOI: 10.1073/pnas.1205664109] [FullText]

231 **Shibata A**, Parsonnet J, Longacre TA, Garcia MI, Puligandla B, Davis RE, Vogelman JH, Orentreich N, Habel LA. CagA status of Helicobacter pylori infection and p53 gene mutations in gastric adenocarcinoma. *Carcinogenesis* 2002; **23**: 419-424 [*RCA*] [PMID: 11895856 DOI: 10.1093/carcin/23.3.419] [FullText]

232 **Torres VJ**, VanCompernolle SE, Sundrud MS, Unutmaz D, Cover TL. Helicobacter pylori vacuolating cytotoxin inhibits activation-induced proliferation of human T and B lymphocyte subsets. *J Immunol* 2007; **179**: 5433-5440 [*RCA*] [PMID: 17911630 DOI: 10.4049/jimmunol.179.8.5433] [FullText]

233 **Palframan SL**, Kwok T, Gabriel K. Vacuolating cytotoxin A (VacA), a key toxin for Helicobacter pylori pathogenesis. *Front Cell Infect Microbiol* 2012; **2**: 92 [*RCA*] [PMID: 22919683 DOI: 10.3389/fcimb.2012.00092] [FullText] [Full Text(PDF)]

234 **Goldszmid RS**, Dzutsev A, Viaud S, Zitvogel L, Restifo NP, Trinchieri G. Microbiota modulation of myeloid cells in cancer therapy. *Cancer Immunol Res* 2015; **3**: 103-109 [*RCA*] [PMID: 25660553 DOI: 10.1158/2326-6066.CIR-14-0225] [FullText]

235 **Correa P**, Fontham ET, Bravo JC, Bravo LE, Ruiz B, Zarama G, Realpe JL, Malcom GT, Li D, Johnson WD, Mera R. Chemoprevention of gastric dysplasia: randomized trial of antioxidant supplements and anti-helicobacter pylori therapy. *J Natl Cancer Inst* 2000; **92**: 1881-1888 [*RCA*] [PMID: 11106679 DOI: 10.1093/jnci/92.23.1881] [FullText]

236 **Ford AC**, Forman D, Hunt RH, Yuan Y, Moayyedi P. Helicobacter pylori eradication therapy to prevent gastric cancer in healthy asymptomatic infected individuals: systematic review and meta-analysis of randomised controlled trials. *BMJ* 2014; **348**: g3174 [*RCA*] [PMID: 24846275 DOI: 10.1136/bmj.g3174] [FullText] [Full Text(PDF)]

237 **Ma JL**, Zhang L, Brown LM, Li JY, Shen L, Pan KF, Liu WD, Hu Y, Han ZX, Crystal-Mansour S, Pee D, Blot WJ, Fraumeni JF Jr, You WC, Gail MH. Fifteen-year effects of Helicobacter pylori, garlic, and vitamin treatments on gastric cancer incidence and mortality. *J Natl Cancer Inst* 2012; **104**: 488-492 [*RCA*] [PMID: 22271764 DOI: 10.1093/jnci/djs003] [FullText]

238 **Vannella L**, Lahner E, Bordi C, Pilozzi E, Di Giulio E, Corleto VD, Osborn J, Delle Fave G, Annibale B. Reversal of atrophic body gastritis after H. pylori eradication at long-term follow-up. *Dig Liver Dis* 2011; **43**: 295-299 [*RCA*] [PMID: 21112822 DOI: 10.1016/j.dld.2010.10.012] [FullText]

239 **Chen HN**, Wang Z, Li X, Zhou ZG. Helicobacter pylori eradication cannot reduce the risk of gastric cancer in patients with intestinal metaplasia and dysplasia: evidence from a meta-analysis. *Gastric Cancer* 2016; **19**: 166-175 [*RCA*] [PMID: 25609452 DOI: 10.1007/s10120-015-0462-7] [FullText]

240 **Rokkas T**, Rokka A, Portincasa P. A systematic review and meta-analysis of the role of Helicobacter pylori eradication in preventing gastric cancer. *Ann Gastroenterol* 2017; **30**: 414-423 [*RCA*] [PMID: 28655977 DOI: 10.20524/aog.2017.0144] [FullText] [Full Text(PDF)]

241 **Niwa T**, Toyoda T, Tsukamoto T, Mori A, Tatematsu M, Ushijima T. Prevention of Helicobacter pylori-induced gastric cancers in gerbils by a DNA demethylating agent. *Cancer Prev Res (Phila)* 2013; **6**: 263-270 [*RCA*] [PMID: 23559452 DOI: 10.1158/1940-6207.CAPR-12-0369] [FullText]

242 **Araya M**, Morelli L, Reid G, Sanders ME, Stanton C, Pineiro M, Ben Embarek P. Guidelines for the evaluation of probiotics in food. 2002. [cited 3 August 2021]. Available from: https://www.researchgate.net/publication/284392003_Guidelines_for_the_evaluation_of_probiotics_in_food

243 **Losurdo G**, Cubisino R, Barone M, Principi M, Leandro G, Ierardi E, Di Leo A. Probiotic monotherapy and Helicobacter pylori eradication: A systematic review with pooled-data analysis. *World J Gastroenterol* 2018; **24**: 139-149 [*RCA*] [PMID: 29358890 DOI: 10.3748/wjg.v24.i1.139] [FullText] [Full Text(PDF)]

244 **Zhu R**, Chen K, Zheng YY, Zhang HW, Wang JS, Xia YJ, Dai WQ, Wang F, Shen M, Cheng P, Zhang Y, Wang CF, Yang J, Li JJ, Lu J, Zhou YQ, Guo CY. Meta-analysis of the efficacy of probiotics in Helicobacter pylori eradication therapy. *World J Gastroenterol* 2014; **20**: 18013-18021 [*RCA*] [PMID: 25548501 DOI: 10.3748/wjg.v20.i47.18013] [FullText] [Full Text(PDF)]

245 **Marsh Rde W**, Alonzo M, Bajaj S, Baker M, Elton E, Farrell TA, Gore RM, Hall C, Nowak J, Roy H, Shaikh A, Talamonti MS.

Comprehensive review of the diagnosis and treatment of biliary tract cancer 2012. Part I: diagnosis-clinical staging and pathology. *J Surg Oncol* 2012; **106**: 332-338 [*RCA*] [PMID: 22488652 DOI: 10.1002/jso.23028] [FullText]

246 **Rakić M**, Patrlj L, Kopljar M, Kliček R, Kolovrat M, Loncar B, Busic Z. Gallbladder cancer. *Hepatobiliary Surg Nutr* 2014; **3**: 221-226 [*RCA*] [PMID: 25392833 DOI: 10.3978/j.issn.2304-3881.2014.09.03] [FullText]

247 **Andia ME**, Hsing AW, Andreotti G, Ferreccio C. Geographic variation of gallbladder cancer mortality and risk factors in Chile: a population-based ecologic study. *Int J Cancer* 2008; **123**: 1411-1416 [*RCA*] [PMID: 18566990 DOI: 10.1002/ijc.23662] [FullText] [Full Text(PDF)]

248 **Hundal R**, Shaffer EA. Gallbladder cancer: epidemiology and outcome. *Clin Epidemiol* 2014; **6**: 99-109 [*RCA*] [PMID: 24634588 DOI: 10.2147/CLEP.S37357] [FullText] [Full Text(PDF)]

249 **Ruby T**, McLaughlin L, Gopinath S, Monack D. Salmonella's long-term relationship with its host. *FEMS Microbiol Rev* 2012; **36**: 600-615 [*RCA*] [PMID: 22335190 DOI: 10.1111/j.1574-6976.2012.00332.x] [FullText]

250 **Koshiol J**, Wozniak A, Cook P, Adaniel C, Acevedo J, Azócar L, Hsing AW, Roa JC, Pasetti MF, Miquel JF, Levine MM, Ferreccio C; Gallbladder Cancer Chile Working Group. Salmonella enterica serovar Typhi and gallbladder cancer: a case-control study and meta-analysis. *Cancer Med* 2016; **5**: 3310-3235 [*RCA*] [PMID: 27726295 DOI: 10.1002/cam4.915] [FullText] [Full Text(PDF)]

251 **Gunn JS**, Marshall JM, Baker S, Dongol S, Charles RC, Ryan ET. Salmonella chronic carriage: epidemiology, diagnosis, and gallbladder persistence. *Trends Microbiol* 2014; **22**: 648-655 [*RCA*] [PMID: 25065707 DOI: 10.1016/j.tim.2014.06.007] [FullText]

252 **Tsuchiya Y**, Loza E, Villa-Gomez G, Trujillo CC, Baez S, Asai T, Ikoma T, Endoh K, Nakamura K. Metagenomics of Microbial Communities in Gallbladder Bile from Patients with Gallbladder Cancer or Cholelithiasis. *Asian Pac J Cancer Prev* 2018; **19**: 961-967 [*RCA*] [PMID: 29693356 DOI: 10.22034/APJCP.2018.19.4.961] [FullText] [Full Text(PDF)]

253 **Kumar S**, Kumar S, Kumar S. Infection as a risk factor for gallbladder cancer. *J Surg Oncol* 2006; **93**: 633-639 [*RCA*] [PMID: 16724347 DOI: 10.1002/jso.20530] [FullText]

254 **Csendes A**, Becerra M, Burdiles P, Demian I, Bancalari K, Csendes P. Bacteriological studies of bile from the gallbladder in patients with carcinoma of the gallbladder, cholelithiasis, common bile duct stones and no gallstones disease. *Eur J Surg* 1994; **160**: 363-367 [*RCA*] [PMID: 7948355] [FullText]

255 **Scanu T**, Spaapen RM, Bakker JM, Pratap CB, Wu LE, Hofland I, Broeks A, Shukla VK, Kumar M, Janssen H, Song JY, Neefjes-Borst EA, te Riele H, Holden DW, Nath G, Neefjes J. Salmonella Manipulation of Host Signaling Pathways Provokes Cellular Transformation Associated with Gallbladder Carcinoma. *Cell Host Microbe* 2015; **17**: 763-774 [*RCA*] [PMID: 26028364 DOI: 10.1016/j.chom.2015.05.002] [FullText]

256 **Kinoshita H**, Nagata E, Hirohashi K, Sakai K, Kobayashi Y. Carcinoma of the gallbladder with an anomalous connection between the choledochus and the pancreatic duct. Report of 10 cases and review of the literature in Japan. *Cancer* 1984; **54**: 762-769 [*RCA*] [PMID: 6744208 DOI: 10.1002/1097-0142(1984)54:4<762::aid-cncr2820540429>3.0.co;2-k] [FullText]

257 **Sharma V**, Chauhan VS, Nath G, Kumar A, Shukla VK. Role of bile bacteria in gallbladder carcinoma. *Hepatogastroenterology* 2007; **54**: 1622-1625 [*RCA*] [PMID: 18019679] [FullText]

258 **White DL**, Kanwal F, Jiao L, El-serag HB. Epidemiology of Hepatocellular Carcinoma. In: Carr B, editor. Hepatocellular Carcinoma. Current Clinical Oncology. New York: Springer, 2016

259 **Wu CH**, Chiu NC, Yeh YC, Kuo Y, Yu SS, Weng CY, Liu CA, Chou YH, Chiou YY. Uncommon liver tumors: Case report and literature review. *Medicine (Baltimore)* 2016; **95**: e4952 [*RCA*] [PMID: 27684838 DOI: 10.1097/MD.0000000000004952] [FullText] [Full Text(PDF)]

260 **Blonski W**, Kotlyar DS, Forde KA. Non-viral causes of hepatocellular carcinoma. *World J Gastroenterol* 2010; **16**: 3603-3615 [*RCA*] [PMID: 20677332 DOI: 10.3748/wjg.v16.i29.3603] [FullText] [Full Text(PDF)]

261 **Balogh J**, Victor D 3rd, Asham EH, Burroughs SG, Boktour M, Saharia A, Li X, Ghobrial RM, Monsour HP Jr. Hepatocellular carcinoma: a review. *J Hepatocell Carcinoma* 2016; **3**: 41-53 [*RCA*] [PMID: 27785449 DOI: 10.2147/JHC.S61146] [FullText] [Full Text(PDF)]

262 **Mittal S**, El-Serag HB. Epidemiology of hepatocellular carcinoma: consider the population. *J Clin Gastroenterol* 2013; **47** Suppl: S2-S6 [*RCA*] [PMID: 23632345 DOI: 10.1097/MCG.0b013e3182872f29] [FullText]

263 **Sanduzzi Zamparelli M**, Rocco A, Compare D, Nardone G. The gut microbiota: A new potential driving force in liver cirrhosis and hepatocellular carcinoma. *United European Gastroenterol J* 2017; **5**: 944-953 [*RCA*] [PMID: 29163959 DOI: 10.1177/2050640617705576] [FullText]

264 **Gupta H**, Youn GS, Shin MJ, Suk KT. Role of Gut Microbiota in Hepatocarcinogenesis. *Microorganisms* 2019; **7**: 121 [*RCA*] [PMID: 31060311 DOI: 10.3390/microorganisms7050121] [FullText] [Full Text(PDF)]

265 **Schnabl B**, Brenner DA. Interactions between the intestinal microbiome and liver diseases. *Gastroenterology* 2014; **146**: 1513-1524 [*RCA*] [PMID: 24440671 DOI: 10.1053/j.gastro.2014.01.020] [FullText]

266 **Yu LX**, Schwabe RF. The gut microbiome and liver cancer: mechanisms and clinical translation. *Nat Rev Gastroenterol Hepatol* 2017; **14**: 527-539 [*RCA*] [PMID: 28676707 DOI: 10.1038/nrgastro.2017.72] [FullText]

267 **Zhang HL**, Yu LX, Yang W, Tang L, Lin Y, Wu H, Zhai B, Tan YX, Shan L, Liu Q, Chen HY, Dai RY, Qiu BJ, He YQ, Wang C, Zheng LY, Li YQ, Wu FQ, Li Z, Yan HX, Wang HY. Profound impact of gut homeostasis on chemically-induced pro-tumorigenic inflammation and hepatocarcinogenesis in rats. *J Hepatol* 2012; **57**: 803-812 [*RCA*] [PMID: 22727732 DOI: 10.1016/j.jhep.2012.06.011] [FullText]

268 **Yoshimoto S**, Loo TM, Atarashi K, Kanda H, Sato S, Oyadomari S, Iwakura Y, Oshima K, Morita H, Hattori M, Honda K, Ishikawa Y, Hara E, Ohtani N. Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome. *Nature* 2013; **499**: 97-101 [*RCA*] [PMID: 23803760 DOI: 10.1038/nature12347] [FullText]

269 **Huang Y**, Fan XG, Wang ZM, Zhou JH, Tian XF, Li N. Identification of helicobacter species in human liver samples from patients with primary hepatocellular carcinoma. *J Clin Pathol* 2004; **57**: 1273-1277 [*RCA*] [PMID: 15563667 DOI: 10.1136/jcp.2004.018556] [FullText]

270 **Dore MP**, Realdi G, Mura D, Graham DY, Sepulveda AR. Helicobacter infection in patients with HCV-related chronic hepatitis, cirrhosis, and hepatocellular carcinoma. *Dig Dis Sci* 2002; **47**: 1638-1643 [*RCA*] [PMID: 12141829 DOI: 10.1023/a:1015848009444] [FullText]

271 **Queiroz DM**, Rocha AM, Rocha GA, Cinque SM, Oliveira AG, Godoy A, Tanno H. Association between Helicobacter pylori infection and cirrhosis in patients with chronic hepatitis C virus. *Dig Dis Sci* 2006; **51**: 370-373 [*RCA*] [PMID: 16534683 DOI: 10.1007/s10620-006-3150-y] [FullText]

272 **Liu X**, Liang J, Li G. Lipopolysaccharide promotes adhesion and invasion of hepatoma cell lines HepG2 and HepG2.2.15. *Mol Biol Rep* 2010; **37**: 2235-2239 [*RCA*] [PMID: 19680784 DOI: 10.1007/s11033-009-9710-4] [FullText]

273 **Lu H**, Ren Z, Li A, Zhang H, Jiang J, Xu S, Luo Q, Zhou K, Sun X, Zheng S, Li L. Deep sequencing reveals microbiota dysbiosis of tongue coat in patients with liver carcinoma. *Sci Rep* 2016; **6**: 33142 [*RCA*] [PMID: 27605161 DOI: 10.1038/srep33142] [FullText] [Full Text(PDF)]

274 **Grąt M**, Wronka KM, Krasnodębski M, Masior Ł, Lewandowski Z, Kosińska I, Grąt K, Stypułkowski J, Rejowski S, Wasilewicz M, Gałęcka

M, Szachta P, Krawczyk M. Profile of Gut Microbiota Associated With the Presence of Hepatocellular Cancer in Patients With Liver Cirrhosis. *Transplant Proc* 2016; **48**: 1687-1691 [*RCA*] [PMID: 27496472 DOI: 10.1016/j.transproceed.2016.01.077] [FullText]

275 **Ponziani FR**, Bhoori S, Castelli C, Putignani L, Rivoltini L, Del Chierico F, Sanguinetti M, Morelli D, Paroni Sterbini F, Petito V, Reddel S, Calvani R, Camisaschi C, Picca A, Tuccitto A, Gasbarrini A, Pompili M, Mazzaferro V. Hepatocellular Carcinoma Is Associated With Gut Microbiota Profile and Inflammation in Nonalcoholic Fatty Liver Disease. *Hepatology* 2019; **69**: 107-120 [*RCA*] [PMID: 29665135 DOI: 10.1002/hep.30036] [FullText]

276 **Wan MLY**, El-Nezami H. Targeting gut microbiota in hepatocellular carcinoma: probiotics as a novel therapy. *Hepatobiliary Surg Nutr* 2018; **7**: 11-20 [*RCA*] [PMID: 29531939 DOI: 10.21037/hbsn.2017.12.07] [FullText]

277 **Li J**, Sung CY, Lee N, Ni Y, Pihlajamäki J, Panagiotou G, El-Nezami H. Probiotics modulated gut microbiota suppresses hepatocellular carcinoma growth in mice. *Proc Natl Acad Sci U S A* 2016; **113**: E1306-E1315 [*RCA*] [PMID: 26884164 DOI: 10.1073/pnas.1518189113] [FullText]

278 **El-Nezami HS**, Polychronaki NN, Ma J, Zhu H, Ling W, Salminen EK, Juvonen RO, Salminen SJ, Poussa T, Mykkänen HM. Probiotic supplementation reduces a biomarker for increased risk of liver cancer in young men from Southern China. *Am J Clin Nutr* 2006; **83**: 1199-1203 [*RCA*] [PMID: 16685066 DOI: 10.1093/ajcn/83.5.1199] [FullText]

279 **Bajaj JS**, Kassam Z, Fagan A, Gavis EA, Liu E, Cox IJ, Kheradman R, Heuman D, Wang J, Gurry T, Williams R, Sikaroodi M, Fuchs M, Alm E, John B, Thacker LR, Riva A, Smith M, Taylor-Robinson SD, Gillevet PM. Fecal microbiota transplant from a rational stool donor improves hepatic encephalopathy: A randomized clinical trial. *Hepatology* 2017; **66**: 1727-1738 [*RCA*] [PMID: 28586116 DOI: 10.1002/hep.29306] [FullText]

280 **Ferrere G**, Wrzosek L, Cailleux F, Turpin W, Puchois V, Spatz M, Ciocan D, Rainteau D, Humbert L, Hugot C, Gaudin F, Noordine ML, Robert V, Berrebi D, Thomas M, Naveau S, Perlemuter G, Cassard AM. Fecal microbiota manipulation prevents dysbiosis and alcohol-induced liver injury in mice. *J Hepatol* 2017; **66**: 806-815 [*RCA*] [PMID: 27890791 DOI: 10.1016/j.jhep.2016.11.008] [FullText]

281 **Philips CA**, Pande A, Shasthry SM, Jamwal KD, Khillan V, Chandel SS, Kumar G, Sharma MK, Maiwall R, Jindal A, Choudhary A, Hussain MS, Sharma S, Sarin SK. Healthy Donor Fecal Microbiota Transplantation in Steroid-Ineligible Severe Alcoholic Hepatitis: A Pilot Study. *Clin Gastroenterol Hepatol* 2017; **15**: 600-602 [*RCA*] [PMID: 27816755 DOI: 10.1016/j.cgh.2016.10.029] [FullText]

282 **Ren YD**, Ye ZS, Yang LZ, Jin LX, Wei WJ, Deng YY, Chen XX, Xiao CX, Yu XF, Xu HZ, Xu LZ, Tang YN, Zhou F, Wang XL, Chen MY, Chen LG, Hong MZ, Ren JL, Pan JS. Fecal microbiota transplantation induces hepatitis B virus e-antigen (HBeAg) clearance in patients with positive HBeAg after long-term antiviral therapy. *Hepatology* 2017; **65**: 1765-1768 [*RCA*] [PMID: 28027582 DOI: 10.1002/hep.29008] [Full Text]

283 **Stein A**, Voigt W, Jordan K. Chemotherapy-induced diarrhea: pathophysiology, frequency and guideline-based management. *Ther Adv Med Oncol* 2010; **2**: 51-63 [*RCA*] [PMID: 21789126 DOI: 10.1177/1758834009355164] [FullText]

284 **Lin XB**, Dieleman LA, Ketabi A, Bibova I, Sawyer MB, Xue H, Field CJ, Baracos VE, Gänzle MG. Irinotecan (CPT-11) chemotherapy alters intestinal microbiota in tumour bearing rats. *PLoS One* 2012; **7**: e39764 [*RCA*] [PMID: 22844397 DOI: 10.1371/journal.pone.0039764] [Full Text] [Full Text(PDF)]

285 **Russo F**, Linsalata M, Clemente C, D'Attoma B, Orlando A, Campanella G, Giotta F, Riezzo G. The effects of fluorouracil, epirubicin, and cyclophosphamide (FEC60) on the intestinal barrier function and gut peptides in breast cancer patients: an observational study. *BMC Cancer* 2013; **13**: 56 [*RCA*] [PMID: 23379680 DOI: 10.1186/1471-2407-13-56] [FullText] [Full Text(PDF)]

286 **van Vliet MJ**, Tissing WJ, Dun CA, Meessen NE, Kamps WA, de Bont ES, Harmsen HJ. Chemotherapy treatment in pediatric patients with acute myeloid leukemia receiving antimicrobial prophylaxis leads to a relative increase of colonization with potentially pathogenic bacteria in the gut. *Clin Infect Dis* 2009; **49**: 262-270 [*RCA*] [PMID: 19514856 DOI: 10.1086/599346] [FullText]

287 **Reunanen J**, Kainulainen V, Huuskonen L, Ottman N, Belzer C, Huhtinen H, de Vos WM, Satokari R. Akkermansia muciniphila Adheres to Enterocytes and Strengthens the Integrity of the Epithelial Cell Layer. *Appl Environ Microbiol* 2015; **81**: 3655-3662 [*RCA*] [PMID: 25795669 DOI: 10.1128/AEM.04050-14] [FullText]

288 **Zheng Y**, Wang T, Tu X, Huang Y, Zhang H, Tan D, Jiang W, Cai S, Zhao P, Song R, Li P, Qin N, Fang W. Gut microbiome affects the response to anti-PD-1 immunotherapy in patients with hepatocellular carcinoma. *J Immunother Cancer* 2019; **7**: 193 [*RCA*] [PMID: 31337439 DOI: 10.1186/s40425-019-0650-9] [FullText] [Full Text(PDF)]

289 **Wortelboer K**, Nieuwdorp M, Herrema H. Fecal microbiota transplantation beyond Clostridioides difficile infections. *EBioMedicine* 2019; **44**: 716-729 [*RCA*] [PMID: 31201141 DOI: 10.1016/j.ebiom.2019.05.066] [FullText] [Full Text(PDF)]

290 **Tanoue T**, Morita S, Plichta DR, Skelly AN, Suda W, Sugiura Y, Narushima S, Vlamakis H, Motoo I, Sugita K, Shiota A, Takeshita K, Yasuma-Mitobe K, Riethmacher D, Kaisho T, Norman JM, Mucida D, Suematsu M, Yaguchi T, Bucci V, Inoue T, Kawakami Y, Olle B, Roberts B, Hattori M, Xavier RJ, Atarashi K, Honda K. A defined commensal consortium elicits CD8 T cells and anti-cancer immunity. *Nature* 2019; **565**: 600-605 [*RCA*] [PMID: 30675064 DOI: 10.1038/s41586-019-0878-z] [FullText]

291 **Frankel AE**, Coughlin LA, Kim J, Froehlich TW, Xie Y, Frenkel EP, Koh AY. Metagenomic Shotgun Sequencing and Unbiased Metabolomic Profiling Identify Specific Human Gut Microbiota and Metabolites Associated with Immune Checkpoint Therapy Efficacy in Melanoma Patients. *Neoplasia* 2017; **19**: 848-855 [*RCA*] [PMID: 28923537 DOI: 10.1016/j.neo.2017.08.004] [FullText] [Full Text(PDF)]

292 **Liu L**, Shah K. The Potential of the Gut Microbiome to Reshape the Cancer Therapy Paradigm: A Review. *JAMA Oncol* 2022; **8**: 1059-1067 [*RCA*] [PMID: 35482355 DOI: 10.1001/jamaoncol.2022.0494] [FullText]

293 **Gamrath L**, Pedersen TB, Møller MV, Volmer LM, Holst-Christensen L, Vestermark LW, Donskov F. Role of the Microbiome and Diet for Response to Cancer Checkpoint Immunotherapy: A Narrative Review of Clinical Trials. *Curr Oncol Rep* 2025; **27**: 45-58 [*RCA*] [PMID: 39753816 DOI: 10.1007/s11912-024-01622-6] [FullText] [Full Text(PDF)]

294 **Erawijantari PP**, Mizutani S, Shiroma H, Shiba S, Nakajima T, Sakamoto T, Saito Y, Fukuda S, Yachida S, Yamada T. Influence of gastrectomy for gastric cancer treatment on faecal microbiome and metabolome profiles. *Gut* 2020; **69**: 1404-1415 [*RCA*] [PMID: 31953253 DOI: 10.1136/gutjnl-2019-319188] [FullText] [Full Text(PDF)]

295 **Liang W**, Yang Y, Wang H, Wang H, Yu X, Lu Y, Shen S, Teng L. Gut microbiota shifts in patients with gastric cancer in perioperative period. *Medicine (Baltimore)* 2019; **98**: e16626 [*RCA*] [PMID: 31464899 DOI: 10.1097/MD.0000000000016626] [FullText] [Full Text(PDF)]

296 **Hu Y**, Zhou P, Deng K, Zhou Y, Hu K. Targeting the gut microbiota: a new strategy for colorectal cancer treatment. *J Transl Med* 2024; **22**: 915 [*RCA*] [PMID: 39379983 DOI: 10.1186/s12967-024-05671-0] [FullText] [Full Text(PDF)]

297 **Lapthorne S**, Bines JE, Fouhy F, Dellios NL, Wilson G, Thomas SL, Scurr M, Stanton C, Cotter PD, Pereira-Fantini PM. Changes in the colon microbiota and intestinal cytokine gene expression following minimal intestinal surgery. *World J Gastroenterol* 2015; **21**: 4150-4158 [*RCA*] [PMID: 25892864 DOI: 10.3748/wjg.v21.i14.4150] [FullText] [Full Text(PDF)]

298 **Kong C**, Gao R, Yan X, Huang L, He J, Li H, You J, Qin H. Alterations in intestinal microbiota of colorectal cancer patients receiving radical surgery combined with adjuvant CapeOx therapy. *Sci China Life Sci* 2019; **62**: 1178-1193 [*RCA*] [PMID: 30796721 DOI: 10.1007/s11427-018-9456-x] [FullText]

299 **Ohigashi S**, Sudo K, Kobayashi D, Takahashi T, Nomoto K, Onodera H. Significant changes in the intestinal environment after surgery in patients with colorectal cancer. *J Gastrointest Surg* 2013; **17**: 1657-1664 [*RCA*] [PMID: 23807702 DOI: 10.1007/s11605-013-2270-x] [Full Text]

300 **Liu CJ**, Zhang YL, Shang Y, Wu B, Yang E, Luo YY, Li XR. Intestinal bacteria detected in cancer and adjacent tissue from patients with colorectal cancer. *Oncol Lett* 2019; **17**: 1115-1127 [*RCA*] [PMID: 30655873 DOI: 10.3892/ol.2018.9714] [FullText] [Full Text(PDF)]

301 **Cong J**, Zhu H, Liu D, Li T, Zhang C, Zhu J, Lv H, Liu K, Hao C, Tian Z, Zhang J, Zhang X. A Pilot Study: Changes of Gut Microbiota in Post-surgery Colorectal Cancer Patients. *Front Microbiol* 2018; **9**: 2777 [*RCA*] [PMID: 30515141 DOI: 10.3389/fmicb.2018.02777] [FullText] [Full Text(PDF)]

302 **Deng Y**, Ding X, Song Q, Zhao G, Han L, Ding B, Wang X, Hao X, Li H. Alterations in mucosa-associated microbiota in the stomach of patients with gastric cancer. *Cell Oncol (Dordr)* 2021; **44**: 701-714 [*RCA*] [PMID: 33770413 DOI: 10.1007/s13402-021-00596-y] [FullText] [Full Text(PDF)]

303 **Francino MP**. Antibiotics and the Human Gut Microbiome: Dysbioses and Accumulation of Resistances. *Front Microbiol* 2015; **6**: 1543 [*RCA*] [PMID: 26793178 DOI: 10.3389/fmicb.2015.01543] [FullText] [Full Text(PDF)]

304 **Wang WY**, Chen CW, Wang TJ, Lin KL, Liu CY. Outcomes of early enteral feeding in patients after curative colorectal cancer surgery: A retrospective comparative study. *Eur J Oncol Nurs* 2021; **54**: 101970 [*RCA*] [PMID: 34496304 DOI: 10.1016/j.ejon.2021.101970] [FullText]

305 **Dag A**, Colak T, Turkmenoglu O, Gundogdu R, Aydin S. A randomized controlled trial evaluating early versus traditional oral feeding after colorectal surgery. *Clinics (Sao Paulo)* 2011; **66**: 2001-2005 [*RCA*] [PMID: 22189721 DOI: 10.1590/s1807-59322011001200001] [FullText] [Full Text(PDF)]

306 **Persson JE**, Viana P, Persson M, Relvas JH, Danielski LG. Perioperative or Postoperative Probiotics Reduce Treatment-Related Complications in Adult Colorectal Cancer Patients Undergoing Surgery: A Systematic Review and Meta-analysis. *J Gastrointest Cancer* 2024; **55**: 740-748 [*RCA*] [PMID: 38231290 DOI: 10.1007/s12029-024-01016-8] [FullText]

307 **Araújo MM**, Montalvão-Sousa TM, Teixeira PDC, Figueiredo ACMG, Botelho PB. The effect of probiotics on postsurgical complications in patients with colorectal cancer: a systematic review and meta-analysis. *Nutr Rev* 2023; **81**: 493-510 [*RCA*] [PMID: 36106795 DOI: 10.1093/nutrit/nuac069] [FullText]

308 **Zhang S**, Wang Q, Zhou C, Chen K, Chang H, Xiao W, Gao Y. Colorectal cancer, radiotherapy and gut microbiota. *Chin J Cancer Res* 2019; **31**: 212-222 [*RCA*] [PMID: 30996579 DOI: 10.21147/j.issn.1000-9604.2019.01.16] [FullText] [Full Text(PDF)]

309 **Kim YS**, Kim J, Park SJ. High-throughput 16S rRNA gene sequencing reveals alterations of mouse intestinal microbiota after radiotherapy. *Anaerobe* 2015; **33**: 1-7 [*RCA*] [PMID: 25600706 DOI: 10.1016/j.anaerobe.2015.01.004] [FullText]

310 **Mitra A**, Grossman Biegert GW, Delgado AY, Karpinets TV, Solley TN, Mezzari MP, Yoshida-Court K, Petrosino JF, Mikkelson MD, Lin L, Eifel P, Zhang J, Ramondetta LM, Jhingran A, Sims TT, Schmeler K, Okhuysen P, Colbert LE, Klopp AH. Microbial Diversity and Composition Is Associated with Patient-Reported Toxicity during Chemoradiation Therapy for Cervical Cancer. *Int J Radiat Oncol Biol Phys* 2020; **107**: 163-171 [*RCA*] [PMID: 31987960 DOI: 10.1016/j.ijrobp.2019.12.040] [FullText]

311 **Nam YD**, Kim HJ, Seo JG, Kang SW, Bae JW. Impact of pelvic radiotherapy on gut microbiota of gynecological cancer patients revealed by massive pyrosequencing. *PLoS One* 2013; **8**: e82659 [*RCA*] [PMID: 24367534 DOI: 10.1371/journal.pone.0082659] [FullText] [Full Text (PDF)]

312 **Gerassy-Vainberg S**, Blatt A, Danin-Poleg Y, Gershovich K, Sabo E, Nevelsky A, Daniel S, Dahan A, Ziv O, Dheer R, Abreu MT, Koren O, Kashi Y, Chowers Y. Radiation induces proinflammatory dysbiosis: transmission of inflammatory susceptibility by host cytokine induction. *Gut* 2018; **67**: 97-107 [*RCA*] [PMID: 28438965 DOI: 10.1136/gutjnl-2017-313789] [FullText]

313 **Singh RK**, Chang HW, Yan D, Lee KM, Ucmak D, Wong K, Abrouk M, Farahnik B, Nakamura M, Zhu TH, Bhutani T, Liao W. Influence of diet on the gut microbiome and implications for human health. *J Transl Med* 2017; **15**: 73 [*RCA*] [PMID: 28388917 DOI: 10.1186/s12967-017-1175-y] [FullText] [Full Text(PDF)]

314 **Then CK**, Paillas S, Moomin A, Misheva MD, Moir RA, Hay SM, Bremner D, Roberts Nee Nellany KS, Smith EE, Heidari Z, Sescu D, Wang X, Suárez-Bonnet A, Hay N, Murdoch SL, Saito R, Collie-Duguid ESR, Richardson S, Priestnall SL, Wilson JM, Gurumurthy M, Royle JS, Samuel LM, Ramsay G, Vallis KA, Foster KR, McCullagh JSO, Kiltie AE. Dietary fibre supplementation enhances radiotherapy tumour control and alleviates intestinal radiation toxicity. *Microbiome* 2024; **12**: 89 [*RCA*] [PMID: 38745230 DOI: 10.1186/s40168-024-01804-1] [FullText]

315 **Qu CY**, Zheng Y, Zhou M, Zhang Y, Shen F, Cao J, Xu LM. Value of bevacizumab in treatment of colorectal cancer: A meta-analysis. *World J Gastroenterol* 2015; **21**: 5072-5080 [*RCA*] [PMID: 25945023 DOI: 10.3748/wjg.v21.i16.5072] [FullText] [Full Text(PDF)]

316 **Prager GW**, Taieb J, Fakih M, Ciardiello F, Van Cutsem E, Elez E, Cruz FM, Wyrwicz L, Stroyakovskiy D, Pápai Z, Poureau PG, Liposits G, Cremolini C, Bondarenko I, Modest DP, Benhadji KA, Amellal N, Leger C, Vidot L, Tabernero J; SUNLIGHT Investigators. Trifluridine-Tipiracil and Bevacizumab in Refractory Metastatic Colorectal Cancer. *N Engl J Med* 2023; **388**: 1657-1667 [*RCA*] [PMID: 37133585 DOI: 10.1056/NEJMoa2214963] [FullText]

317 **Finn RS**, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY, Kudo M, Breder V, Merle P, Kaseb AO, Li D, Verret W, Xu DZ, Hernandez S, Liu J, Huang C, Mulla S, Wang Y, Lim HY, Zhu AX, Cheng AL; IMbrave150 Investigators. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. *N Engl J Med* 2020; **382**: 1894-1905 [*RCA*] [PMID: 32402160 DOI: 10.1056/NEJMoa1915745] [FullText]

318 **Chen YC**, Chuang CH, Miao ZF, Yip KL, Liu CJ, Li LH, Wu DC, Cheng TL, Lin CY, Wang JY. Gut microbiota composition in chemotherapy and targeted therapy of patients with metastatic colorectal cancer. *Front Oncol* 2022; **12**: 955313 [*RCA*] [PMID: 36212420 DOI: 10.3389/fonc.2022.955313] [FullText] [Full Text(PDF)]

319 **Martini G**, Ciardiello D, Dallio M, Famiglietti V, Esposito L, Corte CMD, Napolitano S, Fasano M, Gravina AG, Romano M, Loguercio C, Federico A, Maiello E, Tuccillo C, Morgillo F, Troiani T, Di Maio M, Martinelli E, Ciardiello F. Gut microbiota correlates with antitumor activity in patients with mCRC and NSCLC treated with cetuximab plus avelumab. *Int J Cancer* 2022; **151**: 473-480 [*RCA*] [PMID: 35429341 DOI: 10.1002/ijc.34033] [FullText] [Full Text(PDF)]

320 **Liu W**, Peng L, Chen L, Wan J, Lou S, Yang T, Shen Z. Skin microbial dysbiosis is a characteristic of systemic drug-related intertriginous and flexural exanthema-like lesions induced by EGFR inhibitor. *Heliyon* 2023; **9**: e21690 [*RCA*] [PMID: 38028014 DOI: 10.1016/j.heliyon.2023.e21690] [FullText] [Full Text(PDF)]

321 **Liu Y**, Baba Y, Ishimoto T, Gu X, Zhang J, Nomoto D, Okadome K, Baba H, Qiu P. Gut microbiome in gastrointestinal cancer: a friend or

foe? *Int J Biol Sci* 2022; **18**: 4101-4117 [*RCA*] [PMID: 35844804 DOI: 10.7150/ijbs.69331] [FullText] [Full Text(PDF)]

322 **Ghidini M**, Petrelli F, Tomasello G. Right Versus Left Colon Cancer: Resectable and Metastatic Disease. *Curr Treat Options Oncol* 2018; **19**: 31 [*RCA*] [PMID: 29796712 DOI: 10.1007/s11864-018-0544-y] [FullText]

323 **Wieërs G**, Belkhir L, Enaud R, Leclercq S, Philippart de Foy JM, Dequenne I, de Timary P, Cani PD. How Probiotics Affect the Microbiota. *Front Cell Infect Microbiol* 2019; **9**: 454 [*RCA*] [PMID: 32010640 DOI: 10.3389/fcimb.2019.00454] [FullText] [Full Text(PDF)]

324 **Roeland EJ**, Bohlke K, Baracos VE, Bruera E, Del Fabbro E, Dixon S, Fallon M, Herrstedt J, Lau H, Platek M, Rugo HS, Schnipper HH, Smith TJ, Tan W, Loprinzi CL. Management of Cancer Cachexia: ASCO Guideline. *J Clin Oncol* 2020; **38**: 2438-2453 [*RCA*] [PMID: 32432946 DOI: 10.1200/JCO.20.00611] [FullText]

325 **Sánchez-Sánchez E**, Orúe I, Guerra JA, Estornell MA, Barragán B, Blanco M, Comellas M, Cancer E. Nutritional management of cancer patients in clinical practice in Spain: patients' and multidisciplinary health care professionals' perceptions. *Eur J Clin Nutr* 2023; **77**: 454-459 [*RCA*] [PMID: 36550218 DOI: 10.1038/s41430-022-01251-x] [FullText]

326 **Lidoriki I**, Frountzas M, Karanikki E, Katsarlinou E, Tsikrikou I, Toutouzas KG, Schizas D. Adherence to Oral Nutrition Supplementation in Gastrointestinal Cancer Patients: A Systematic Review of the Literature. *Nutr Cancer* 2024; **76**: 31-41 [*RCA*] [PMID: 37946396 DOI: 10.1080/01635581.2023.2277519] [FullText]

327 **Bozzetti F**, Cozzaglio L, Gavazzi C, Bidoli P, Bonfanti G, Montalto F, Soto Parra H, Valente M, Zucali R. Nutritional support in patients with cancer of the esophagus: impact on nutritional status, patient compliance to therapy, and survival. *Tumori* 1998; **84**: 681-686 [*RCA*] [PMID: 10080677 DOI: 10.1177/030089169808400614] [FullText]

328 **Vagnildhaug OM**, Balstad TR, Ottestad I, Bye A, Greil C, Arends J, Baracos V, Brown LR, Dajani OF, Dolan RD, Fallon M, Fraser E, Grzyb A, Hjermstad MJ, Jakobsen G, Kaasa S, McDonald J, Philips I, Sayers J, Simpson MR, Sousa MS, Skipworth RJE, Laird BJA, Solheim TS; Cancer Cachexia Endpoints Working Group. Appetite and dietary intake endpoints in cancer cachexia clinical trials: Systematic Review 2 of the cachexia endpoints series. *J Cachexia Sarcopenia Muscle* 2024; **15**: 513-535 [*RCA*] [PMID: 38343065 DOI: 10.1002/jcsm.13434] [Full Text]

329 **Yu J**, Yuan A, Liu Q, Wang W, Sun Y, Li Z, Meng C, Zhou Y, Cao S. Effect of preoperative immunonutrition on postoperative short-term clinical outcomes in patients with gastric cancer cachexia: a prospective randomized controlled trial. *World J Surg Oncol* 2024; **22**: 101 [*RCA*] [PMID: 38632641 DOI: 10.1186/s12957-024-03348-y] [FullText] [Full Text(PDF)]

330 **Bianchini C**, Bonomo P, Bossi P, Caccialanza R, Fabi A. Bridging gaps in cancer cachexia Care: Current insights and future perspectives. *Cancer Treat Rev* 2024; **125**: 102717 [*RCA*] [PMID: 38518714 DOI: 10.1016/j.ctrv.2024.102717] [FullText]

331 **Garutti M**, Noto C, Pastò B, Cucciniello L, Alajmo M, Casirati A, Pedrazzoli P, Caccialanza R, Puglisi F. Nutritional Management of Oncological Symptoms: A Comprehensive Review. *Nutrients* 2023; **15**: 5068 [*RCA*] [PMID: 38140327 DOI: 10.3390/nu15245068] [FullText]

332 **Zhou J**, Sun S, Luan S, Xiao X, Yang Y, Mao C, Chen L, Zeng X, Zhang Y, Yuan Y. Gut Microbiota for Esophageal Cancer: Role in Carcinogenesis and Clinical Implications. *Front Oncol* 2021; **11**: 717242 [*RCA*] [PMID: 34733778 DOI: 10.3389/fonc.2021.717242] [Full Text] [Full Text(PDF)]

333 **Elsalem L**, Jum'ah AA, Alfaqih MA, Aloudat O. The Bacterial Microbiota of Gastrointestinal Cancers: Role in Cancer Pathogenesis and Therapeutic Perspectives. *Clin Exp Gastroenterol* 2020; **13**: 151-185 [*RCA*] [PMID: 32440192 DOI: 10.2147/CEG.S243337] [FullText] [Full Text(PDF)]

334 **Loke YL**, Chew MT, Ngeow YF, Lim WWD, Peh SC. Colon Carcinogenesis: The Interplay Between Diet and Gut Microbiota. *Front Cell Infect Microbiol* 2020; **10**: 603086 [*RCA*] [PMID: 33364203 DOI: 10.3389/fcimb.2020.603086] [FullText] [Full Text(PDF)]

335 **Kok CR**, Rose D, Hutkins R. Predicting Personalized Responses to Dietary Fiber Interventions: Opportunities for Modulation of the Gut Microbiome to Improve Health. *Annu Rev Food Sci Technol* 2023; **14**: 157-182 [*RCA*] [PMID: 36446139 DOI: 10.1146/annurev-food-060721-015516] [FullText]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com