RELATION BETWEEN GUT MICROBIOTA AND CANCER

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Abstract

Human has about 100 trillion symbiotic microbes in the gut with 300-1000 different species. Gut microbiota is associated with host metabolism, obesity, diabetes, hepatic disorder, and cancer. Nowadays, studies are focusing on the role of gut microbiota in cancer. Evidence shows that *Fusobacterium* is associated with colorectal cancer when its genome was confirmed by 16SRNA analysis and PCR technique in cancerous cell. The complete mechanism of gut microbe involvement in cancer is still unknown. There may be some association of toxic metabolites of gut microbes, dietary substances, and the immune response. This review will help to attain the brief knowledge about the research till now in the regard of gut microbiota with cancer. The study will also reveal the research of using gut microbes for anticancer therapy. It is examined that *Lactobacillus rhamnosus* in the form of probiotics has a significant role in anticancer therapy. The anticancerous therapeutic and immunogenic role of gut microbiota must be further studied.

Key words: microbiota, colorectal cancer, anticancer therapy, Immune response

I. Introduction:

There are trillions of microbes in the human body, and their synchronized functions are crucial for human survival. Such microbes’ communities are at their densest in the intestinal region, where they together constitute the gut microbiota, a diverse bacterial population that evolves throughout the host's childhood to adulthood. Gut microbiota species can come from any of the three domains of species, namely Archaebacteria, Bacteria, and Eubacteria, as well as viruses and are documented to form complicated trophic interactions with one another and with
their human hosts, varying from symbiosis to parasitic infection. Autochthonous microbes called indigenous microbes, or transitory microbes make up human gut flora. The extensive and diverse representatives of the human gut bacteria play a crucial function in the restoration of human health by supporting the food digestion to release nutrients that are often unreachable to the host, boosting host cellular differentiation, safeguarding the host from pathogenic colonization, and boosting the immunologic mechanism (Milani et al., 2017, Gueimonde et al., 2017).

Carcinoma is the world's second dominant reason for mortality. Cancer is associated with spontaneous mutations in DNA along with environmental conditions and lifestyles of the human. For instance, personal exposure to infective agents, Ultraviolet rays, and toxic materials, as well as one's lifestyle and diet, all have a sturdy impact on cancer hazards. The vulnerability is primarily determined by the dose, period, and mixture of such concussions, as well as one's genetic makeup. Many recent studies have suggested that commensal microbes populate human membranes as predictors of health or pathological diseases, such as cancer (Vivarelli et al., 2019).

**Immunity Connects Bacteria to Metabolism, and Microorganisms Communicate with Host Tissue**

The prevalence of microbes in the organism is detected and monitored by many mechanisms. In the gastrointestinal tract (GI), epithelial cells serve as gatekeepers, transmitting vital knowledge to immune cells in the lamina propria. In reality, pattern recognition receptors (PRRs) including toll-like receptors (TLRs) and NOD-like receptors (NLR) are used by innate immunity to recognize and monitor microorganisms. Pathogen-associated molecular patterns (PAMPs) are recognized by these receptors interacting pathogen or associated biochemical from injured tissues.

The GI tract is the houses the large bulk of the bacteria that live in the human body also houses the body's largest reservoir of immune cells. Importantly the immune system has a strong influence on the microbiota's diversity. As a result, gastrointestinal cells are constantly subjected to a wide range of bacterial antigens and metabolites. Despite such near closeness, we exist in ideal coexistence with microbes. The relationships between gut bacteria and the immune response have contributed to the identification of hitherto undiscovered roles in complement to the traditional immunological aspects (Cani, P. D. 2018).
II. Gut Biota in CRC Patients

The variety of bacteria species in the human gut is thought to be in the thousands. Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria make up the majority of the human intestinal flora. The microbiota of CRC patients is less diversified than that of healthy people. A systematic review of metagenomics from various demographics and populations discovered that patient with colorectal cancer has richer microflora than normal. In analyses of the tumor, surrounding non-tumor mucosa, and stool samples obtained from CRC patients vs. controls, variations in the number of specific microorganisms have been reported. The microbiota and metabolome fluctuate vary in colorectal neoplasia, from adenomatous polyps to initial cancer to metastatic illness, implying that the microbes play pathogenetic and analytical importance. (Almeida et al., 2019; Thomas et al., 2019 and Yachida et al., 2019).

"Eubiosis" refers to healthy bacterial communities inside the human body, with a predominance of varied healthy microbes living in mutual peace. Dysbiosis is characterized by a lack of variety and a prevalence of harmful bacteria. Bacterial toxins, aberrant metabolites, hormonal imbalance, persistent inflammation cause cancers. Immunological modulation, DNA damages, and mutagenesis all have a crucial role in carcinogenesis. The diversity in the metagenome and the richness of microflora in the health and pathology has the role dysbiosis in cancer. Whereas the study began with an emphasis on gut microbiota, it has since grown to include microbial niches in other organs, with the discovery of unique and diverse bacteria in even the most "sterile" tissues including the lungs, breast, prostate, and pancreas. The microbiota impacts cancer development and therapeutic response in chemotherapy and immunotherapy and improved scientific insights are now developing that can aid in treating cancer (Parida et al., 2021).

*Fusobacterium nucleatum*

Two separate investigations found that tumor samples had higher quantities of Fusobacterium DNA and RNA patterns than non-tumor samples. Similar relationships have been discovered in some investigations, including diverse batches of CRC patients around the world. In evidence of *Fusobacterium nucleatum*’s colorectal carcinogenicity, a greater frequency of *F. nucleatum* (found in 10-15% of tumors) has been linked to progressed disease phase, a greater risk of recurrence, and shorter patients surviving periods. *F. nucleatum* levels in malignant cells
have been linked to reduced T cell penetration, corroborating research suggesting *F. nucleatum* suppresses the anti-tumor immune reaction.

*F. nucleatum* has been linked to diagnostic and genetic aspects in individuals with CRC or precancerous lesions. It includes BRAF mutations and hypermutation with microsatellite instabilities, according to epidemiologic research. Considering that these characteristics characterize recurrent neoplasia, *F. nucleatum* could have a role in CRC establishment via the serrated route (Mima *et al.*, 2016; Yu *et al.*, 2017; Rashtak *et al.*, 2017; Purcell *et al.*, 2017; Bullman *et al.*, 2017). Figure 1 (a) depicts that in some chemotherapy or immunotherapy individuals, higher microbial richness is linked to an improving patient therapeutic response and

![Figure 1](image.png)

**Fig 1**: Control of the microbiome during cancer therapy

a lower risk of infection. (b) In some cancer victims, lower microbial richness is linked to poorer clinical therapeutic responses, higher toxicity, and high mortality and death. (c) In the approach, microbiota control by fecal microbiota transplant (FMT), probiotics, prebiotics, and other nutritional microbial component regulators may be employed as a treatment adjuvant to modify bacterial ecology in people with cancer.
Colonic Microbe Exploitation as an Effective Alternative for Cancer Care

The growing body of research supporting the involvement of the microbiota in cancer incidence, clinical presentation, and therapy increases the possibility of using the microbiome as a preventative or treatment adjuvant. Additives with individual species (probiotics or living biotherapeutics), alone and in combo, nutritional moderators of microbiota population, or entire microbial transplants can all be used to manipulate the microbiome. Probiotics are typically harmless and particularly effective in lowering treatment-related diarrhea, according to a comprehensive analysis of probiotic administration in pelvic and colorectal cancer sufferers having chemotherapy-induced diarrhea (Wang et al., 2016). In rats with 5-fluorouracil-induced oral thrush, probiotics such as Lactobacillus casei, Lactobacillus acidophilus, and Bifidobacterium bifidum reduced inflammation reactions and improved therapeutically relevant diarrhea (Yeung et al., 2015).

III. Animal Studies in Cancer Therapy

Mice given a combination of L. acidophilus and Cisplatin showed a better survival. (Gui et al., 2015). Mice administered with Lactobacillus rhamnosus during HSCT had enhanced safety and lower acute mortality. A tiny preliminary study of four FMTs after HSCT in individuals with steroid-refractory GVHD found that 75 percent of patients showed GVHD remission (Kakihana et al., 2016).

Preliminary research in animal studies has shown promise in improving the efficiency of immunotherapy in weak respondents or germ-free mice by manipulating the microbiome through oral supplements or using FMT from human medication respondents. Whereas initial research in this field is promising (Banna et al., 2017), the majority of studies have been conducted in murine models, which may not adequately describe the human microbiota or physiologic consequences. To enhance the effectiveness and optimum manner of microbiota alteration as an adjuvant to chemotherapy agents, substantial, appropriately controlled clinical studies in people with cancer are necessary, with some pertinent studies presently underway. More illustrations are given in Figure 2 (FMT 2018 and FMT 2017). This diagram depicts the significance of the microbiome in prospective immunological effectiveness, prognosis, and toxicity indicators. It also has precise modification techniques such as probiotics, vaccines, fecal microbiota.
transplantation (FMT), bacterial bioengineering, antibiotics, and prebiotics. Yet, further study will need to address several limitations and issues.

The massive microbial population invading the intestine, their molecules, the host immune response, and cancers have a complicated relationship. Intestinal microflora and their compounds influence host defense from the inside by influencing host immunological diseases, as a result, regulating tumor development and development.

Extremely, the host immune system influences tumor monitoring by modifying microbe-related communication or biochemical activities. Immune dodging promotes or inhibits carcinogenesis. Cancer can be induced by intestinal microbiota through various pathways like inflammation, genotoxicity, and metabolic activity. Cancer changes the intestinal flora to increase or decrease reactions to immune-based therapies like immune-checkpoint blockade (ICB). ICB can cause immune-related adverse effects (irAEs) or toxicity in the recipient. The most serious of these is immunity-associated colitis.

**Fig 2:** The interaction of gut flora, cancer immunological activation, and cancer immunology, as well as future prospects for accurate microbiota regulation.
IV. Conclusion

Gut bacteria play an important role in cancer treatment and immune function. Microbiome targeted therapy, which includes FMT, probiotics, antimicrobials, prebiotics, and vaccinations, has been recommended as the optimum bacterial clinical intervention in cancer care as it provides a more precise and safer bacterial prescription for immune cell eradication. Numerous approaches are now being evaluated in clinical experiments as more live immunostimulatory microbes and antimicrobials that influence unfriendly microbes. Genetically engineered vaccines with microorganism preservatives, monoclonal bacterial ingredients, probiotics, FMT, prebiotics, or nutritional immunoenergising ingredients and adjuvants might improve the anticancer effects of microbes. The characterization of specific microbial isolates or genetic manipulation of test organisms to transport materials or medications to target sites could be the focus of microbiome-based treatments. It has been suggested that synthetic microbial treatment, in which bioartificial anticancer bacterial species improve the adaptive and innate immune systems, has been suggested. Furthermore, widespread delivery of microbial outer membrane vesicles (OMVs) may constitute a novel cancer treatment technique for producing anticancer cytokines with minimal side reactions.

Abbreviations

 allo-HSCT stands for allo-hematopoietic stem cell transplantation; CpG-ODN stands for CpGoligodeoxynucleotides, and TBI stands for total body irradiation.

References


