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Human Microbiome: Understanding the Role of the Gut Microbiome and Implications for Oncology Nursing Care

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Abstract

Background: The human microbiome plays a critical role in human health and disease. The diversity and composition of the human microbiome varies across human body sites. A dysbiotic gut microbiome is associated with carcinogenesis, therapeutic drug response, and side effects of cancer treatments.

Objectives: This paper aims to demonstrate the role of the gut microbiome in oncology care and nursing implications for clinical cancer care.

Methods: A review of the literature was conducted to determine influencing factors and roles of the gut microbiome in oncology care. The roles of the gut microbiome included treatment-induced dysbiosis of the gut microbiome, treatment-related symptoms such as gastrointestinal and psychoneurological symptoms, and human microbiome-associated interventions, including prebiotics, probiotics, and fecal microbiome transplant.

Practice Implications: By understanding the definition of the human microbiome and its influencing factors, oncology nurses in clinical practice could educate, screen, and monitor cancer patients who have a higher risk of gut microbiome dysbiosis. Knowledge of the gut microbiome and its impact on cancer outcomes can help oncology nurses interpret associations between the gut microbiome and treatment-related toxicities and symptoms. Oncology nurses can guide patients to build a healthy gut microbiome across the trajectory of cancer treatment and survivorship.

Introduction

The human microbiome is defined as a collection of the microorganisms (e.g., bacteria, archaea, eukaryotes, and viruses) and their genomes harbored in or on the human body (Marchesi & Ravel, 2015). The diversity and composition of the human microbiome varies across different body sites. For example, the gastrointestinal tract is primarily dominated by anaerobic microbes, critically associated with food digestion and metabolism, and maintaining homeostasis of the immune system. A healthy vagina is comparatively acidic

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with the dominance of *Lactobacillus species* to prevent yeast infections, sexually transmitted infections, and urinary tract infections. Additionally, the skin has the most variable and least stable microbiome owing to constant exposure to various conditions, including humidity, salinity, and temperature (Kennedy & Chang, 2020).

The human microbiome is a complex subject. Table 1 provides key definitions for terms used throughout this paper. Compared to other body sites, the microbiome in the gut has been studied extensively among cancer populations. The human gut hosts 500 to 1,000 microbial species on average (Knight & Buhler, 2015). A dysbiotic gut microbiome (i.e., loss of keystone taxa, loss of diversity, shifts in metabolic capacity, or increase of pathogens) is associated with carcinogenesis and interference with therapeutic drug metabolism, such as chemotherapy (Roy & Trinchieri, 2017). Recently, dysbiotic gut microbiome is identified as a promising biomarker of toxicities associated with cancer treatment (J. Bai et al., 2020; Touchefeu et al., 2014). Specifically, a disturbed gut microbiome potentially contributes to frequent gastrointestinal symptoms (Touchefeu et al., 2014) and psychoneurological symptoms (J. Bai et al., 2020; Song & Bai, 2020).

Influencing Factors of the Gut Microbiome

Various factors can affect the diversity and composition of the gut microbiome **(**Figure 1**)**. Over 20% of the microbiota variability is shaped by *environmental factors* such as the use of antibiotics, living environment, and anthropometric measurements, while *family factors* such as genetics only explain 2% of taxa variance (Rothschild et al., 2018). The priority effects (i.e., the order and timing of gut microbiota arrival) and microbial transmission (e.g., infant delivery and feeding modalities) can determine the microbial development in early life (Sprockett, Fukami, & Relman, 2018). Both the Human Microbiome Project and the American Gut have identified a series of *individual factors* that change the gut microbiome, including sociodemographic characteristics (e.g., sex, age, and race), health behaviors (e.g., diet and physical activity) (Singh et al., 2017), and chronic conditions such as inflammatory bowel disease. Additionally, the gut microbiome has been explored in various cancers across the continuum of diagnosis, treatment, and survivorship. Cancer treatments such as chemotherapy disrupt the gut microbiome, resulting in gastrointestinal and psychoneurological toxicities and symptoms including gut barrier failure, inflammation, and gut-brain axis (J. Bai et al., 2020; Touchefeu et al., 2014).

Gut Microbiome in Oncology Nursing Care

Treatment-induced gut microbial dysbiosis.

Cancer treatments, particularly chemotherapy and radiation therapy (RT), can influence the diversity and composition of the gut microbiome **(**Table 2**)**. Adult patients' gut microbiome was significantly disrupted across chemotherapy, with decreases in the abundance of healthy gut microbiotas, including *Firmicutes, Actinobacteria*, *Bacteroides, Bifidobacteria, Clostridium cluster IV* and *XIVa*, and increases in pathological microbes such as *Proteobacteria* and *Enterobacteriaceae* (Montassier et al., 2014). Similarly, a marked reduction in the number of anaerobic bacteria (e.g., *Bifidobacteria, Clostridium cluster XIVa, Faecalibacterium, Lactobacillus,* and *Streptococci*) and an increase in

Enterococci were found in children with cancer receiving chemotherapy (Rajagopala et al., 2016; van Vliet et al., 2009). RT can also influence the gut microbiome diversity and composition. The reduced richness of the gut microbiome community, as well as a decreased abundance of *Firmicutes* and increased abundance of *Fusobacteria*, were observed in gynecologic cancer patients treated with RT. Moreover, the overall gut microbiome pattern can be remodeled after the completion of RT. Studies in pelvic cancer patients demonstrate that RT could lead to an increased abundance of *Clostridium_XIVa, Proteobacteria,* and *Gammaproteobacteria* and a decreased abundance of *Faecalibacterium, Lachnospiracea, Oscillibacter, Roseburia,* and *Streptococcus (*Wang et al., 2019*).* Among pediatric cancer patients, the reduced microbiome diversity was observed throughout RT; for instance, decreased relative abundance of *Firmicutes* and increased relative abundance of *Proteobacteria, Streptococcus, Bacteroides, Dorea, Subdoligranulum*, and *Escherichia-Shigella* were reported after RT completion (Sahly, Moustafa, Zaghloul, & Salem, 2019). Understanding how gut microbiome dysbiosis at the time of the treatment may influence cancer treatment toxicities and symptoms requires further investigation.

Gastrointestinal symptoms.

Gastrointestinal symptoms such as diarrhea, constipation, and oral mucositis, frequently occur in cancer patients owing to cytotoxic treatments. Patients with significant gastrointestinal symptoms may have a decreased diversity of healthy microbial communities, such as a lower abundance of *Actinobacteria, Lactobacillus, Faecalibacterium, Roseburia,* and *Bifidobacterium,* and an increase in pathologically relevant microbiome species, such as *Escherichia coli, Enterobacter,* and *Staphylococcus* (Montassier et al., 2015). Among cancer patients who developed gastrointestinal symptoms during RT, a modified bacterial profile with a higher abundance of *Phascolarctobacterium, Lachnospiraceae, Erysipelotrichaceae*, *Clostridium XI* and *XVIII,* and *Fecalitalea* was reported (Mitra et al., 2020). Relationships between the gut microbiome and gastrointestinal symptoms are still unknown in childhood cancer patients. The pathogenesis of gut microbiome for cancer treatment-related gastrointestinal symptoms may be associated with the following pathways: inflammatory cytokines; intestinal permeability; bacteria translocation; changes in the epithelial surface microbiota pattern, intestinal protection from noxious stimuli, epithelial repair mechanisms; and the release of immune cells and molecules (van Vliet, Harmsen, de Bont, & Tissing, 2010).

Psychoneurological symptoms (PNS).

PNS, including pain, fatigue, anxiety, depression, sleep disturbance, and cognitive impairment, are prevalent among cancer populations undergoing cancer treatments. Recent studies have demonstrated associations between the gut microbiome and PNS (J. Bai et al., 2020; González-Mercado et al., 2020). Higher PNS was associated with decreased microbial diversity, a lower abundance of *Firmicutes, Ruminiclostridium, Phascolarctobacterium, Subdoligranulum*, but a higher abundance of *Bacteroidetes, Anaerofustis, Tyzzerella, Intestinimonas*, and Family *XIII AD3011*. Patients with lower PNS had a higher abundance of *Lactococcus, Phascolarctobacterium, Acidaminococcaceae,* and *Desulfovibrio* than those with a higher PNS (J. Bai et al., 2020). In rectal cancer patients treated with chemoradiation therapy, an enriched abundance *of Bacteroides, Blautia1, Ruminococcaceae, Oscillibacter*,

and *Lactobacillus* was observed among patients with no symptoms. In contrast, lower alpha diversity and higher abundance of *Blautia2* were reported among patients with two or more PNS (González-Mercado et al., 2020). Associations between the gut microbiome and PNS in children undergoing chemotherapy and RT are limited and require further studies. The gut microbiome may modulate the occurrence and severity of PNS via endocrine, immune, and neural pathways through the microbiome-gut-brain axis (Song & Bai, 2020), a bi-directional network to connect the communications between the gut and the brain.

Human microbiome-related interventions.

Several interventions, including probiotics, prebiotics, or fecal microbiome transplant (FMT), have been studied and found to prevent or treat dysbiotic gut microbiome in various chronic conditions, including cancer **(**Figure 2**)**. Probiotics, defined as living bacteria that can benefit the host's health via changing the gut microbiome, can positively affect cancer patients by reducing their experience of PNS. A 12-week probiotics treatment (i.e., *Lacidofil*) in colorectal cancer patients resulted in a significant reduction in patients suffering from irritable bowel symptoms and improved colorectal cancer-related anxiety, depression, and quality of life (QOL) (Lee et al., 2014). Prebiotics are defined as non-digestible food ingredients that can benefit the hosts' health by changing the composition and function of the gut microbiome. The effects of prebiotics, such as enteral formula containing fermentable dietary fibers (i.e., fructooligosaccharides), have been examined in the gut microbiome dysbiosis in childhood cancer patients (Zheng et al., 2006). In contrast, FMT is rarely examined in cancer populations. Further studies are needed to understand the mechanism by which prebiotics, probiotics, or FMT mediate protection against cancer therapy symptoms and to help define specific interventions to diminish the adverse effects of cancer treatments.

Nursing Implications

Understanding the role of the gut microbiome in oncology care helps provide nurses with the tools to monitor risks for dysbiotic gut microbiome, screen cancer treatment-related gastrointestinal symptoms and PNS, and prompts nurses to educate patients on interventions that can improve gut health. First, oncology nurses need to understand the potential risk factors for gut microbiome dysbiosis. Many cancer treatments increase the risk of gut microbiome dysbiosis. Second, oncology nurses can use the gut microbiome to screen and monitor cancer treatment-related gastrointestinal and PNS symptoms that may affect cancer patients' QOL. Third, oncology nurses can guide patients to maintain a healthy gut microbiome. While personalized interventions, such as FMT, are still under development, nurses can educate patients on how to maintain a healthy gut microbiome by using a healthy diet and lifestyle, prebiotics, and probiotics.

Conclusion

Cancer treatment can lead to a dysbiotic gut microbiome, specifically associated with gastrointestinal symptoms and PNS, leading to a decrease in a patient's QOL. By understanding the role of the gut microbiome, oncology nurses can screen patients with a dysbiotic gut microbiome, examine associations between the gut microbiome and treatment

toxicities and symptoms, and guide patients to adjust their diet or to consider use of probiotics to build a healthy gut microbiome.

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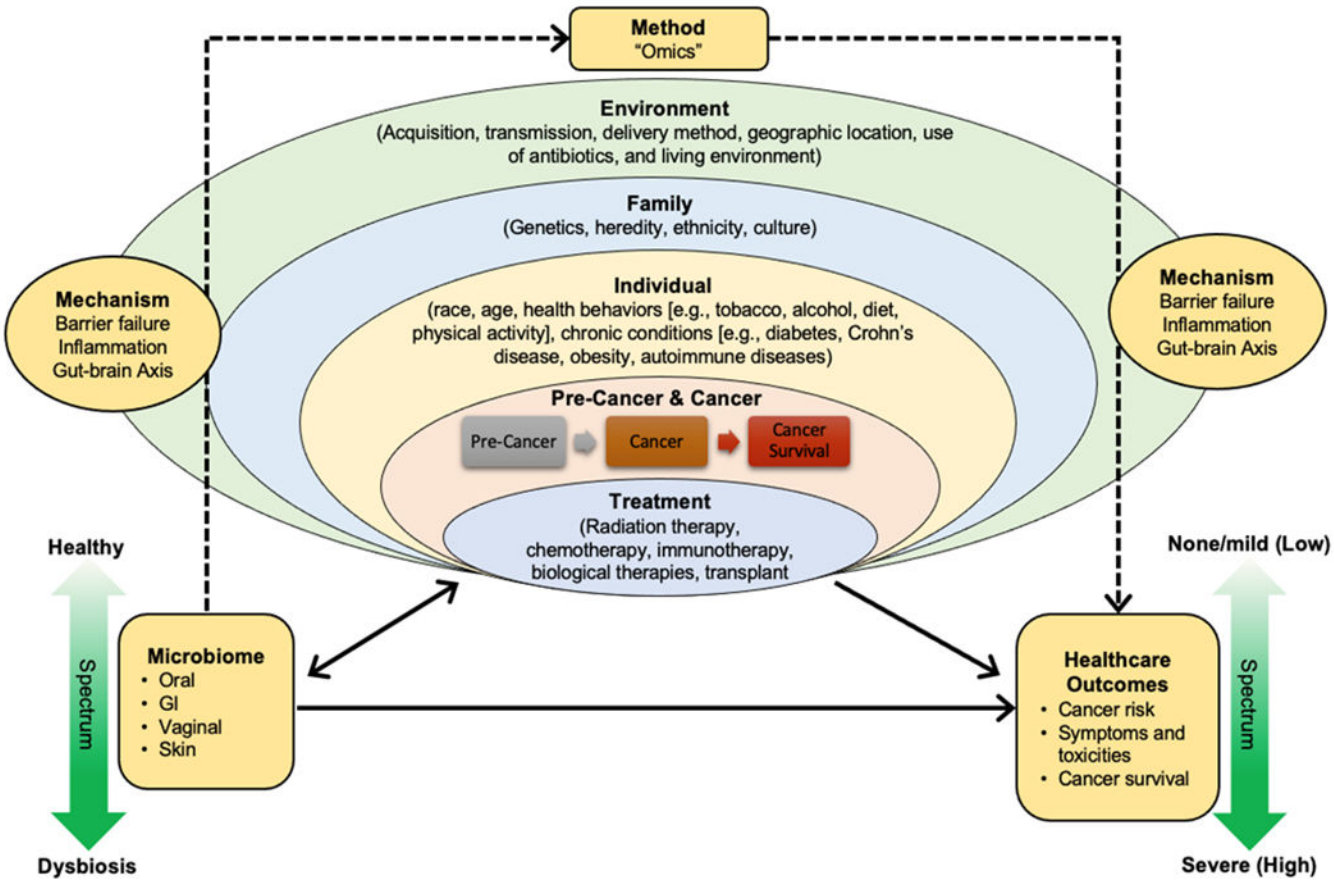

Figure 1.
Influencing Factors of the Gut Microbiome in Cancer

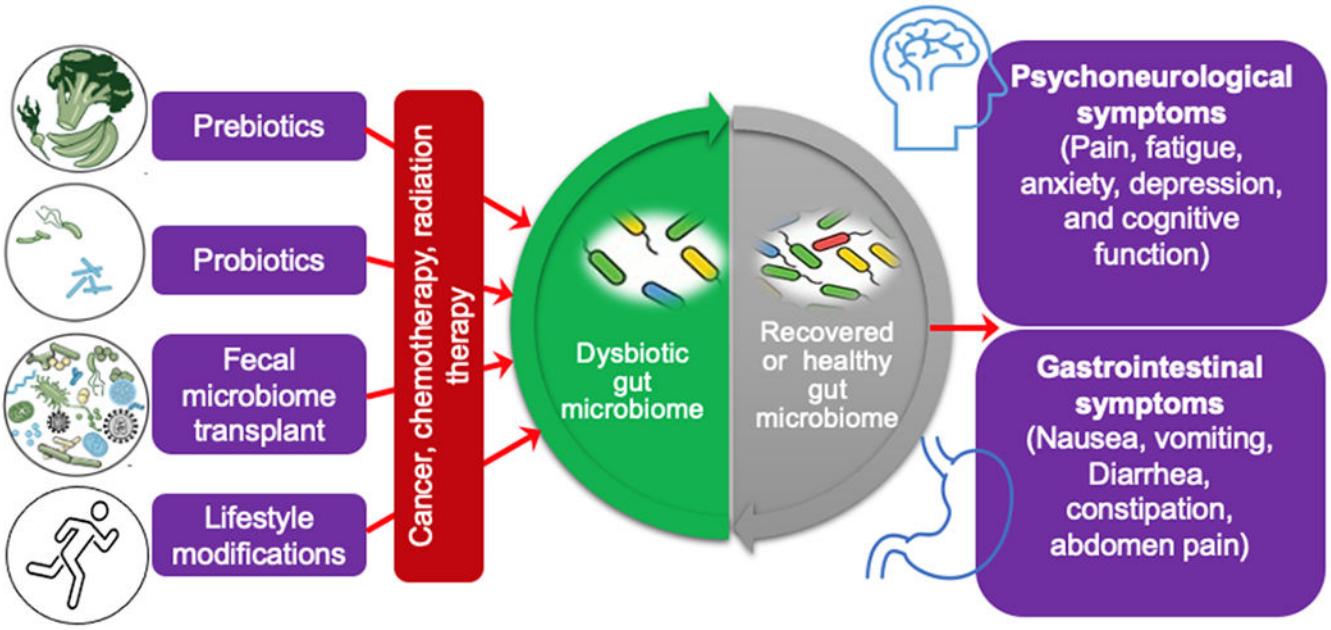

Figure 2.

Target the gut microbiome for therapeutic management of cancer treatment-related symptoms. Based on the current knowledge of the bacterial microbiome in cancer treatment-related symptoms, prebiotics, probiotics, fecal microbiome transplantation, and lifestyle changes are suggested approaches for the early prevention and management of cancer treatment-related symptoms via adjusting the gut microbiome.

Table 1.

Concepts for the Human Microbiome

Concept	Description/Definition
Alpha diversity	Diversity within an individual site or sample diversity
Archaea	A domain of single-celled organisms which lack cell nuclei
Beta diversity	Diversity between separate samples
Eukaryotes	Organisms whose cells have a nucleus enclosed within a nuclear envelope
Fecal microbiome transplant	An investigational treatment in which a fecal preparation from a carefully screened, healthy stool donor is transplanted into the colon of the patient via multiple routes, such as colonoscopy, naso-enteric tube, and capsules
Genome	All genetic material of an organism
Gut microbial dysbiosis	A disrupted profile of the gut microbiome, including loss of keystone taxa, loss of diversity, shifts in metabolic capacity, or increase of pathogens
Gut microbiome	Microbes and their microbial genomes in the gastrointestinal tract
Microbiome	The collection of microbes and their microbial genomes at a given site (e.g., vagina or gastrointestinal tract)
Gut-brain axis	The bidirectional network involving multiple biological systems that allows communication between gut bacteria and the brain
Microbiota	The microbial taxa associated with humans. The human body is colonized by a vast number of microbes, collectively called the human microbiota
Prebiotics	Non-digestible food ingredients that can benefit the host's health via changing the composition and function of the gut microbiome
Probiotics	Living bacteria that can benefit the host's health via changing the gut microbiome
Psychoneurological symptoms (PNS)	A cluster of co-occurring symptoms with potentially common biological or pathophysiological mechanisms, including pain, fatigue, anxiety, depression, sleep disturbance, and cognitive dysfunction
Taxa	A population of phylogenetically related organisms

Note: Based on references of Marchesi & Ravel, 2015; Roy & Trinchieri, 2017; Bai et al., 2020; Touchefeu et al., 2014

Table 2.

Taxa Associated with Cancer and Cancer Treatment-related Symptoms

Outcomes or Toxicities	Key Taxa
Patients with cancer (vs healthy controls)	• Decrease in *Firmicutes, Actinobacteria, Bacteroides, Bifidobacteria, Clostridium cluster IV* and *XIVa, Faecalibacterium, Lactobacillus, Faecalibacterium, Lachnospiracea, Oscillibacter*, and *Roseburia* • Increase in *Proteobacteria, Enterobacteriaceae, Enterococci, Fusobacteria, Gammaproteobacteria, Streptococcus, Dorea, Subdoligranulum*, and *Escherichia-Shigella*
High gastrointestinal symptoms (vs low gastrointestinal symptoms)	• Decrease in *Actinobacteria, Lactobacillus, Faecalibacterium, Roseburia*, and *Bifidobacterium* • Increase in *Escherichia coli, Enterobacter, Staphylococcus, Phascolarctobacterium, Lachnospiraceae, Erysipelotrichaceae, Clostridium XI* and *XVIII*, and *Fecalitalea*
High psychoneurological symptoms (vs low psychoneurological symptoms)	• Decrease in *Firmicutes, Ruminiclostridium, Phascolarctobacterium*, and *Subdoligranulum* • Increase in *Bacteroidetes, Anaerofustis, Tyzzerella, Intestinimonas*, and Family *XIII AD3011*
Low psychoneurological symptoms (vs high psychoneurological symptoms)	• Increase in *Lactococcus, Lactobacillus, Phascolarctobacterium, Acidaminococcaceae, Desulfovibrio, Bacteroides, Blautia1, Ruminococcaceae*, and *Oscillibacter*