Secrets Unfold: The Role of Gut Microbiome in Cancer

Ziske Maritska[1][a], Meitria Nur Sabrina[2][b], Rahmanindya Defiyandini Puteri[2][c], Septyan Putra Yusandi[2][d] and Eldi Novriandi[2][e]

[1]*Department of Biology Medicine, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia*
[2]*Department of Internal Medicine, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia*
ziske_maritska@unsri.ac.id

Keywords: Gut Dysbiosis, Gut Microbiome, Microbiota, Cancer

Abstract: The gut microbiota refers to the most diverse and dense complex population of bacteria that live in the gastrointestinal tract and abundantly present approximately 1010-1012 cells per gram of luminal content, which plays a vital role in metabolism and protection. The imbalance of microbial populations in the gut, known as gut dysbiosis, increases the risk of developing numerous types of cancer because it weakens the intestinal epithelial barrier and triggers systemic inflammation. This review wishes to briefly discuss the role of gut microbiome in cancer based on previous studies. This is a literature review where references were obtained from four databases (NCBI, Science Direct, Google Scholar, and Research Gate) for the last five years. Gut dysbiosis is known to be related to insufficient DNA repair mechanisms. A few pathogenic bacteria create genotoxic compounds, raising the chance of mutations and growth of tumors. Identification of several microbial signatures linked to various cancer types leads to advancements in cancer detection, where it can be identified by testing bacterial species or microbial metabolites, which also offer a non-invasive way to monitor and diagnose cancer by examining the microbial DNA or microbial markers in stool or blood samples. By recognizing microbial carcinogens, cancer cases may be treated with antibiotics for modifying gut microbiota. Clinical trials are also being conducted on prebiotics, which show potential in improving antitumor immunity and treatment response in melanoma and colon cancer. A study of patients with colorectal cancer showed that some microbial species were found in individuals with poor prognoses, whereas those with better prognoses were linked to another microbial species. These findings suggest that gut microbiota may provide novel therapeutic targets and serve as a good indicator for predicting cancer prognosis. This unique method has the potential to transform cancer prognosis and therapy.

1 INTRODUCTION

The human microbiome is made up of trillions of bacteria that live in different regions of the body, such as the skin, mouth, and gastrointestinal system. The gut microbiota is the most diverse and dense of these microbial communities, and it plays a critical role in human health. Extensive research has been focused on the gut microbiome and its impact on numerous diseases, including cancer (Yang et al., 2023).

The gut microbiota has been proven to have a significant impact on carcinogenesis, tumor progression, and cancer therapy response. Furthermore, changes in the composition of the gut microbiome have been linked to an increased risk of acquiring some types of cancer. Understanding the complicated relationships between the gut microbiome and cancer could bring useful insights into cancer prevention, diagnosis, and treatment. The goal of this review is to synthesize current understanding about the involvement of the gut microbiome in cancer and offer light on prospective treatment options targeting the gut microbiota (Zhuang et al., 2019).

[a] https://orcid.org/0000-0002-4904-0703
[b] https://orcid.org/0000-0000-0000-0000
[c] https://orcid.org/0000-0000-0000-0000
[d] https://orcid.org/0000-0000-0000-0000
[e] https://orcid.org/0000-0000-0000-0000

Maritska, Z., Sabrina, M. N., Puteri R. D., Yusandi, S. P., Novriandi, E.
Secrets Unfold: The Role of Gut Microbiome in Cancer
1ST International Conference On Medical Science And Health (ICOMESH 2023), pages 123-134

1.1 Briefly Explain the Concept of Gut Microbiome

The complex population of bacteria that live in the gastrointestinal system is referred to as the gut microbiome. It consists of a wide variety of bacteria, viruses, fungi, and other microorganisms that play an important part in the overall health of the human body (Sadrekarimi et al., 2022).

The gut microbiome is crucial for digestion, absorption of nutrients, immune function, and metabolism. It also helps in preventing colonization by harmful bacteria and producing essential vitamins and other beneficial compounds (Zyoud et al., 2022). The composition of the gut microbiome is influenced by a number of factors, including diet, genetics, lifestyle, and exposure to environmental stimuli. Cancer has been associated with dysbiosis, or imbalances or abnormalities in the gut microbiome. Inflammation, the immune system, and the therapeutic response may all be impacted by changes to the gut microbiome, according to a growing body of studies. These changes may then have an impact on how cancer starts and spreads. The development of novel therapeutic strategies that concentrate on these microbial populations may be significantly influenced by knowledge of how the gut microbiome influences cancer (Li et al., 2019).

1.2 The Influence of Gut Microbiome on Cancer Development

Scholars and scientists have devoted increased attention to the gut microbiota's role in cancer in recent years. The phrase "gut microbiome" refers to the complex population of bacteria that live in the gastrointestinal tract and are essential to human health (Rebersek, 2021).

Changes in the makeup and function of the gut microbiome have been related to a number of illnesses, including cancer, according to extensive studies. In a range of malignancies, including colorectal, pancreatic, and breast cancer, the gut microbiome has been found to influence cancer genesis, progression, and response to treatment. Certain bacteria in the gut microbiome, according to study, can either promote or prevent tumor growth by creating various metabolites and influencing immune responses. Understanding the connections between the gut microbiota and cancer may lead to the development of novel therapeutic strategies for preventing or treating cancer by targeting the gut microbiome (Vivarelli et al., 2019).

Extensive research has linked changes in the makeup and function of the gut microbiome to a variety of disorders, including cancer. The gut microbiome has been shown to influence cancer formation, progression, and treatment response in a variety of cancers, including colorectal, pancreatic, and breast cancer. Some bacteria in the gut microbiome, according to research, can either promote or prevent tumor growth by producing various metabolites and regulating immune responses. Understanding the relationships between the gut microbiota and cancer may lead to the development of novel treatment techniques that use the gut microbiome to successfully prevent or treat cancer (Wu et al., 2021).

2 THE INFLUENCE OF GUT MICROBIOME ON CANCER DEVELOPMENT

In addition, new study has provided light on the link between the gut microbiome and cancer development. Changes in the composition and diversity of the gut microbiota have been linked to the onset and progression of numerous forms of cancer. For example, studies have shown that certain bacteria species in the stomach can produce carcinogenic chemicals, increasing the likelihood of cancer formation (Sun et al., 2023).

Dysbiosis, which is defined as an imbalance or disturbance in the microbiota of the gut, has also been linked to an increase in inflammation and poor immune system regulation, both of which are important contributors to the development of cancer. The gut microbiota also has the power to modify the bioavailability and efficacy of medications and dietary supplements in the treatment and prevention of cancer. These findings underline the need for more study into the intricate link between the gut microbiota and cancer in order to create cutting-edge cancer prevention and treatment strategies (Kim & Lee, 2021).

2.1 Discuss the Potential Impact of Gut Microbiota on Predisposition to Cancer

One potential impact of the gut microbiota on the likelihood of developing cancer is the modification of the immune response. The gut microbiome, which is crucial for managing the immune system, can affect

the development and function of immune cells (Zhao et al., 2023).

Dysbiosis, a microbial imbalance, can lead to chronic inflammation, interfere with immunological homeostasis, and promote the development of carcinogens. The production of pro- or anti inflammatory chemicals by certain gut bacteria can also alter the immune response. For instance, a number of bacteria produce butyrate, a short-chain fatty acid that has been shown to have anti-inflammatory properties and can inhibit the development of colon cancer cells. On the other hand, a few pathogenic bacteria create genotoxic compounds that can harm DNA directly, raise the chance of mutations, and ultimately result in the growth of tumors (Oh et al., 2021).

Understanding the mechanisms by which the gut microbiota regulates immune function as well as the connection between certain microbial species and the formation of cancer is crucial for developing novel therapeutic approaches and treatments (Badal et al., 2020).

Highlight the relationship between gut dysbiosis and increased cancer risk An increased risk of developing numerous types of cancer has been directly linked to an imbalance of microbial populations in the gut, or gut dysbiosis. According to studies, dysbiosis can lead to the gastrointestinal system producing certain chemicals that promote inflammation and cancer (Lee et al., 2021).
Dysbiosis can lead to an overgrowth of some hazardous bacteria, such as Helicobacter pylori, which has been directly related to the onset of stomach cancer. Dysbiosis has also been demonstrated to weaken the intestinal epithelial barrier, allowing dangerous substances to enter the bloodstream and perhaps triggering systemic inflammation, which is a critical element in the emergence and spread of cancer (Chattopadhyay et al., 2021).

Additionally, changes brought on by dysbiosis in the gut's immune system may lessen its capacity to accurately detect and eradicate cancer cells. To create innovative preventative and therapeutic strategies that concentrate on the gut microbiome in cancer therapy, it is essential to acknowledge and address the relationship between gut dysbiosis and increased cancer risk (Gopalakrishnan et al., 2018).

Highlight the Relationship between Gut Dysbiosis and Increased Cancer Risk

An increased risk of developing numerous types of cancer has been directly linked to an imbalance of microbial populations in the gut, or gut dysbiosis. According to studies, dysbiosis can lead to the gastrointestinal system producing certain chemicals that promote inflammation and cancer (Lee et al., 2021).

Dysbiosis can lead to an overgrowth of some hazardous bacteria, such as Helicobacter pylori, which has been directly related to the onset of stomach cancer. Dysbiosis has also been demonstrated to weaken the intestinal epithelial barrier, allowing dangerous substances to enter the bloodstream and perhaps triggering systemic inflammation, which is a critical element in the emergence and spread of cancer (Chattopadhyay et al., 2021).

Additionally, changes brought on by dysbiosis in the gut's immune system may lessen its capacity to accurately detect and eradicate cancer cells. To create innovative preventative and therapeutic strategies that concentrate on the gut microbiome in cancer therapy, it is essential to acknowledge and address the relationship between gut dysbiosis and increased cancer risk (Gopalakrishnan et al., 2018).

Explain How Gut Bacteria Affect DNA Damage and Mutation

Furthermore, it has been shown that gut bacteria play a key role in the degradation and mutation of DNA. A research conducted on mice revealed that some gut bacteria release genotoxins that can damage DNA. These genotoxins have been shown to change the DNA of colon cells, which promotes the spread of cancer (Matson et al., 2021).

It has also been demonstrated that gut bacteria influence the generation of reactive oxygen species (ROS), which may also harm DNA. As an illustration, certain bacteria in the gut have the ability to create large quantities of ROS, which can accumulate DNA damage. Furthermore, gut bacteria can influence the immune system of the host, which in turn influences DNA repair pathways.

Dysbiosis, or an imbalance of gut flora, which promotes the accumulation of mutations and increases the risk of cancer development, has been related to insufficient DNA repair mechanisms. Overall, the intricate connection between gut bacteria and DNA damage highlights the pivotal role the gut microbiome plays in the initiation and progression of cancer (Goodman & Gardner, 2018).

Explain the Role of Gut Microbiome in Tumorigenesis

Furthermore, due to its impact on immunological responses, the gut microbiota has been associated to cancer. There is proof that some gut bacteria have the ability to either activate or block a variety of cell pathways that are essential for the growth of cancer. For instance, a number of bacteria create chemicals that stimulate the immune system and improve the body's defenses against cancer. However, some bacterial species have been linked to the release of inflammatory cytokines, which can encourage an inflammatory milieu that is favorable for the development of cancer. Additionally, by affecting how the immune system reacts to cancer treatments like immunotherapy, the gut microbiota can affect the effectiveness of certain medicines. Emerging intervention techniques that target and utilize the microbiome to enhance cancer outcomes depend on an understanding of the intricate relationships between the gut microbiota, immune responses, and carcinogenesis (Sepich-Poore et al., 2021).

Discuss how gut bacteria can promote inflammation and immune system dysfunction, underlying factors in cancer development. Gut bacteria play a crucial role in promoting inflammation and immune system dysfunction, which are underlying factors in cancer development. Several studies have shown that certain strains of gut bacteria can trigger inflammation in the gut, leading to chronic inflammation throughout the body. This chronic inflammation not only damages healthy cells but also creates an environment that is conducive to the growth and survival of cancer cells. In addition, gut bacteria can influence the immune system's response to cancer cells (Sadrekarimi et al., 2022).

Dysbiosis, an imbalance in the gut microbiome, can lead to a weakened immune system, making it more difficult for the body to recognize and eliminate cancer cells. Furthermore, some strains of gut bacteria produce metabolites that can directly promote the growth and proliferation of cancer cells. Overall, understanding the complex relationship between gut bacteria, inflammation, immune system dysfunction, and cancer development is crucial in developing effective strategies for cancer prevention and treatment (Rebersek, 2021).

Describe the Production of Carcinogens and Tumor-Promoting Compounds by Certain Gut Bacteria

Furthermore, the production of carcinogens and tumor-promoting compounds by certain gut bacteria is a matter of considerable concern. Research has revealed that several species of bacteria within the gut microbiome can produce metabolites that have the potential to induce DNA damage and promote tumorigenesis. For instance, studies have identified the production of genotoxic compounds such as N-nitroso compounds, secondary bile acids, and certain short-chain fatty acids by gut bacteria. N-nitroso compounds are known for their carcinogenic properties and can arise from the metabolism of dietary nitrate and nitrite by certain bacteria (Y. Cheng et al., 2020).

Similar to how primary bile acids are modified by gut bacteria to form secondary bile acids, colorectal cancer growth has also been connected to secondary bile acids. Short-chain fatty acid butyrate can have both pro- and anti-cancerous effects, depending on the situation. When certain gut bacteria break down meal components, butyrate is formed. It is vital to understand how gut bacteria produce these carcinogens and tumor-promoting compounds in order to fully grasp the complex link between the gut microbiome and the development of cancer.Similar to main bile acids, the development of colorectal cancer has also been linked to secondary bile acids produced by gut bacteria by way of modifying primary bile acids. Additionally, the breakdown of food by specific gut bacteria might lead to the (Y. Cheng et al., 2020).

Finally, the intricate relationship between the gut microbiota and cancer is still a dynamic area of research with significant implications for both preventative and therapeutic strategies. The gut microbiota is crucial for maintaining the equilibrium of the body and managing the immune system. Dysbiosis, or an imbalance in the gut microbiome, has been linked to the initiation and development of several types of cancer (Song et al., 2021).

Targeted treatment could be made easier by understanding the methods by which particular microorganisms interact with cancer cells. Exciting research is being done on the possibility of modifying gut flora to enhance the effectiveness of cutting-edge cancer treatments like immunotherapy. Continuous study in this area is expected to result in the development of innovative therapeutic approaches and diagnostic devices, which will ultimately aid in the treatment and prevention of cancer (Akbar et al., 2022).

3 GUT MICROBIOME AND CANCER TREATMENT

In addition, recent studies have revealed that the gut flora may aid in the prevention of cancer. The effect

of the microbiota on how the body reacts to cancer may have an effect on both the effectiveness of immunotherapy and the onset of adverse effects. For instance, it has been demonstrated that the gut flora has a role in how the body responds to immune checkpoint inhibitors, a family of cancer medications that helps the immune system recognize and destroy cancer cells. Particularly, it has been found that the presence of certain strains, particularly Bifidobacterium longum, is associated with the patient's successful response to immunotherapy in the treatment of melanoma. This underlines how important it is to consider the gut microbiota as a potential modifier of the efficacy of cancer treatment (W. Y. Cheng et al., 2020).

Antibiotics and the Cancer Microbiome

Antibiotics are only used to treat or prevent the treatment of recognized microbial carcinogens in cancer cases. This includes administering direct-acting antivirals against active Hepatitis C virus, immunizing against the major human papillomavirus serotypes and the hepatitis B virus, treating gastric lymphomas derived from H. pylori with triple or quadruple antibiotic therapy, and treating gastric lymphomas with H. pylori. The use of antibiotics in solid tumors is supported by anecdotal and inconsistent data, with the exception of antibiotic-derived chemotherapies (such as doxorubicin). Numerous research on lung, colon, and other tissues suggest that removal of intratumoral microbiota may be able to suppress cellular proliferation, alter a tolerogenic TME into an immunogenic state, or stop inflammatory processes that promote tumor growth. Preclinical evidence suggests that the development of leukemia in genetically predisposed hosts may be triggered by either antibiotic usage or gut bacterial translocation in hematologic malignancies (Sánchez-Alcoholado et al., 2020).

Potential exists for prebiotics, postbiotics, and other substances, as well as dietary modifications that alter the microbiota. A new in depth investigation of the role of nutrition in cancer risk found several epidemiological connections but few causal routes. The findings have been compromised by the challenges in gathering dietary information, however metabolomic data that might indicate food consumption and associated small molecule effectors may be helpful in the future. Clinical trials are now being conducted on prebiotics, which show potential in improving antitumor immunity and treatment response in melanoma and colon cancer. Prebiotics are substances that encourage the development of good bacteria. Prebiotics include ingredients including mucin, inulin, and resistant starch. Although there is no proof that postbiotic chemicals (molecules produced from bacteria) might treat cancer, their specific mechanism of action remains (Zyoud et al., 2022).

Other techniques for modifying the gut microbiota of cancer patients include fecal microbiota transplantation (FMT), the addition of particular microbial consortia, and the use of commercial probiotics. Both immunotherapy- and Clostridium difficile (formerly Clostridioides difficile)-induced colitis can be successfully treated with FMT. It is yet unknown if FMT will be stable or effective in the long run. Factors including antibiotic preconditioning, distribution method, frequency of modulation, and dietary recommendations complicate the clinical treatment of gut flora. Whether FMT from donors who benefit from immunotherapy can enhance both clinical and immunological anticancer responses is now being studied in clinical studies. The consequences of transplanting microbial consortia, varying in complexity from multiplexed consortia to monoclonal bacterial strains, are the subject of more clinical investigation. There haven't been many research examining how systemic immunity and anticancer activity are affected by commercially available probiotic formulations; certain formulations have even been suspected of promoting carcinogenesis. In critically unwell individuals, the usage of commercial probiotics may result in bacteremia. As a result, it's suggested that cancer patients stay away from over-the-counter probiotics (Vivarelli et al., 2019).

Cancer Therapy Using Exogenous Microbiota

Major strides have been made towards engineering exogenous bacterial and viral agents for cancer therapy, particularly as powerful immunotherapy options or neoadjuvants. Two such agents have FDA approval: oncolytic viral therapy for advanced melanoma using talimogene laherparepvec (T-VEC), and bacterial cancer therapy for high-risk, non-muscle invasive bladder cancer using live-attenuated Mycobacterium bovis (BCG vaccine). Because oncolytic viruses are non-commensals and have been reviewed elsewhere in detail, we focus our attention on bacterial cancer therapies (BCTs). Though historically contentious, BCT is re-gaining attention through synthetic biology techniques that programmatically limit systemic toxicities while enhancing regional antitumor immunity. Regulatory challenges for BCT agents are considerable, and despite ongoing clinical trials, they have yet to be commercially surmounted (Song et al., 2021).

3.1 Explore the Influence of Gut Microbiota on Response to Cancer Treatment

Furthermore, recent studies have unveiled the potential role of gut microbiota in impacting the efficacy of cancer treatment. A growing body of evidence suggests that the composition of gut microbiota can affect the response to chemotherapy, immunotherapy, and even radiation therapy. For instance, specific microbial species have been found to enhance or diminish the effectiveness of certain anticancer drugs. Additionally, the presence of certain bacteria in the gut has been associated with a strengthened immune response against tumor cells. Mechanistically, gut microbiota can modulate host immunity, drug metabolism, and tumor microenvironment, thereby influencing the therapeutic outcome. Understanding the complex interplay between gut microbiota and cancer treatment response holds great promise for developing personalized interventions that could optimize treatment outcomes and potentially overcome treatment resistance. However, further in-depth investigations are needed to delineate the exact mecha- nisms underlying these interactions and to develop targeted strategies for manipulating gut microbiota to improve cancer treatment efficacy (Bhatt et al., 2017).

Discuss the Impact of Gut Microbiome on Chemotherapy Outcomes

Antibiotics are only used to treat or prevent the In recent years, researchers have been investigating the impact of gut microbiome on chemotherapy outcomes. The gut microbiome, referring to the trillions of microorganisms residing in the human gas- trointestinal tract, plays a crucial role in various physiological processes, including immune function and drug metabolism. Studies have shown that alterations in the gut microbiome composition can influence the efficacy and toxicity of chemotherapy drugs. For instance, certain bacteria in the gut have been found to enhance the activation of prodrugs, increasing the effectiveness of chemotherapy treatment. Conversely, dysbiosis, or imbalances in the gut microbiome, has been associated with increased drug resistance and adverse effects. Therefore, understanding the intricate relationship between the gut microbiome and chemotherapy outcomes may open up new avenues for personalized cancer treatment strategies. Byconsidering the unique composition of an individual's gut microbiome, medical professionals may be able to optimize chemotherapy regimens, leading to improved patient outcomes and reduced side effects (Matson et al., 2021).

3.1.1 Explain the Role of Gut Bacteria in Immunotherapy Response

The role of gut bacteria in immunotherapy response is becoming an increasingly important area of re-search within the field of cancer treatment. Studies have shown that the composition of an individual's gut microbiome can have a significant impact on their response to immunotherapy. Certain bacteria within the gut have been identified as key players in modulating the immune system and enhancing the effectiveness of immunotherapy drugs. For example, the presence of specific bacteria, such as Akkermansia muciniphila and Bifidobacterium, has been linked to improved treatment outcomes in cancer patients. These bacteria are thought to stimulate the immune system and enhance the anti- tumor response. Furthermore, the gut microbiome has been shown to influence the side effects associated with immunotherapy, with certain bacteria associated with a lower incidence of immune-related adverse events. As a result, understanding the role of gut bacteria in immunotherapy response holds great promise for developing novel approaches to enhance treatment efficacy and reduce treatment-associated side effects in cancer patients (Akbar et al., 2022).

3.2 Highlight the Potential of Using Gut Microbiome Manipulation as a Therapeutic Approach

Antibiotics are only used to treat or prevent the Furthermore, there is an increasing interest in harnessing the potential of gut microbiome manipulation as a therapeutic approach. Research has shown that altering the composition of the gut microbiome can have profound effects on overall health and disease outcomes. For example, certain bacteria have been found to be associated with an increased risk of developing certain cancers, while others have been shown to have anti-tumor effects. Manipulating the gut microbiome through interventions such as probiotics, prebiotics, and fecal microbiota transplantation has been shown to modulate the immune system, reduce inflammation, and even directly affect tumor growth. Additionally, the gut microbiome plays a crucial role in drug metabolism, and its manipulation may enhance the effectiveness of chemotherapy and immunotherapy. While still in its early stages, the potential of using

gut microbiome manipulation as a therapeutic approach is promising and warrants further exploration in the field of cancer research (Ağagündüz et al., 2023).

3.2.1 Discuss the Concept of Fecal Microbiota Transplantation (FMT) in Cancer Treatment

Fecal microbiota transplantation (FMT) is a novel approach that involves the transfer of fecal microbiota from a healthy donor to a recipient in order to restore a healthy gut microbial composition. Although the majority of studies on FMT have focused on its therapeutic potential in the treatment of gastrointestinal disorders such as Clostridium difficile infection, recent evidence suggests that FMT could also have significant implications in cancer treatment. The gut microbiome has been found to play a crucial role in modulating the host immune response and affecting the efficacy of cancer immunotherapy. Studies have shown that certain bacterial species in the gut can enhance anti-tumor immune responses, while others can hinder the effectiveness of immunotherapeutic agents. Therefore, by manipulating the gut microbiota through FMT, it may be possible to optimize cancer treatment outcomes and improve patient responses to immunotherapy (Y. Cheng et al., 2020).

Further research is needed to explore the potential of FMT as a complementary strategy for cancer management. In addition, despite the encouraging results of FMT in the treatment of refractory Clostridium difficile diarrhea, FMT requires consideration of several key factors, especially the choice of an optimal donor. Ideally, the FMT donor should be an individual with a wide variety of microbial compositions, including favorable bacteria. Up to now, Bifidobacteria spp. Akkermansia muciniphilia, E. hirae, and Bacteroides spp. have been regarded as favorable bacteria, which can effectively improve anti-tumor immunity and better control tumor growth in vivo. It is worth noting that the transfer of pathogens is also a potential problem, requiring careful screening regardless of bacteria, viruses or parasites. Some bacteria seem to play a role in the inflammation-induced carcinogenesis (Borella et al., 2021).

3.2.2 Explain Ongoing Research on the Development of Personalized Microbiome-Based Therapies

Ongoing research on the development of personalized microbiome-based therapies holds great potential in addressing various diseases, including cancer. Scientists are investigating the intricate relationship between the gut microbiome and cancer to identify specific bacterial species that can either promote or inhibit tumor growth and progression. By understanding the mechanisms through which these bacteria exert their effects, personalized therapies can be developed to target the specific microbial composition of an individual's gut (Matson et al., 2021).

This involves profiling the gut microbiome through advanced sequencing techniques and analyzing the composition and function of bacterial species. Additionally, researchers are exploring the use of fecal microbiota transplantation (FMT) as a potential therapy for cancer. FMT involves transferring healthy microbiota from a donor to a patient, potentially restoring a balanced gut microbiome and enhancing the efficacy of cancer treatments. Although still in its early stages, ongoing research in this area has the potential to revolutionize cancer treatment approaches by harnessing the power of the microbiome. Additionally, the gut microbiome has emerged as a potential player in the development and progression of various types of cancer (W. Y. Cheng et al., 2020).

Several studies have shown that alterations in the composition and function of the gut microbiota can influence the risk and prognosis of cancer. For instance, certain bacteria have been implicated in the production of carcinogenic metabolites, such as nitrosamines and secondary bile acids, which can promote DNA damage and tumor formation. Moreover, the gut microbiota can modulate the efficacy and toxicity of chemotherapy drugs, affecting treatment outcomes. Furthermore, the immune system plays a crucial role in cancer development and progression, and mounting evidence suggests that the gut microbiota can shape host immune responses to tumors. Thus, understanding the intricate relationship between the gut microbiome and cancer may provide new avenues for the development of novel preventive and therapeutic strategies for various types of cancer (Cullin et al., 2021).

4 GUT MICROBIOME AS A BIOMARKER FOR CANCER DETECTION AND PROGRESSION

Another important aspect of the gut microbiome in relation to cancer is its potential role as a biomarker for cancer detection and progression. Studies have shown that the composition of the gut microbiome differs between individuals with and without cancer, suggesting that changes in the microbiome may be associated with the development of cancer. In addition, specific bacterial species or groups of bacteria have been found to be more abundant or less abundant in patients with certain types of cancer. This suggests that the gut microbiome may have the potential to serve as a diagnostic tool for cancer. Furthermore, recent research has also suggested that the gut microbiome may play a role in the progression of cancer. It has been found that alterations in the gut microbiome can influence the response to cancer therapies, as well as the development of resistance to treatment. Understanding the role of the gut microbiome in cancer detection and progression could have significant implications for the development of personalized cancer therapies and treatment strategies (Sadrekarimi et al., 2022).

4.1 Explore the Potential of Gut Microbiota as a Diagnostic Tool

A fascinating area of cancer research is the possible use of gut bacteria as a diagnostic tool. As previously established, research has revealed a definite link between the gut microbiota and cancer development and progression. The identification of several microbial signatures linked to various cancer types may lead to both advancements in early detection approaches and a revolution in cancer diagnosis. Medical experts may be able to identify individuals who are more likely to acquire various forms of cancer by testing fecal samples for the presence of specific bacterial species or microbial metabolites. By analyzing changes in the gut microbiota over time, it may be feasible to follow the onset of cancer and the success of treatment. To confirm and standardize these microbial signatures, determine their specificity and sensitivity, and implement them into clinical practice, more study is required. The gut microbiota's potential as a non-invasive, readily available diagnostic tool, however, holds promise for enhancing cancer outcomes (Wu et al., 2021).

The gut microbiota is a non-invasive biomarker for cancer and metabolic illnesses that is found in stools. Numerous studies have found that the gut microbiome plays a significant etiological role in the development of CRC and have identified specific fecal microbial indicators of the disease (Song et al., 2021).

The ability of these biomarkers to recognize adenomas or CRC in its early stages is therefore unknown. The associations between the microbiome and colorectal adenoma are also unknown at this time (Goodman & Gardner, 2018).

4.1.1 Discuss the Correlation Between Altered Gut Microbiome and Certain Types of Cancer

Recent study has shed light on the numerous avenues via which gut microbiota dysbiosis may promote carcinogenesis in order to uncover the association between altered gut microbiome and certain types of cancer. It has been claimed that an imbalance in the gut microbial composition may produce inflammation, oxidative stress, and immune system dysfunction, all of which contribute to tumor development and progression. Certain microbial species, for example, have been demonstrated to produce chemicals that directly damage DNA, resulting in genomic instability and tumor formation. Furthermore, dysbiosis-induced inflammation can promote tumor formation by boosting the release of pro-inflammatory cytokines and growth factors (Whisner & Athena Aktipis, 2019).

The capacity of the gut barrier to stop the transmission of possible carcinogens has also been connected to changes in the gut flora. Modern therapeutic strategies that target the microbiota as a manner of cancer therapy and prevention may be made possible by understanding the complex link between changed gut microbiomes and cancer (Sun et al., 2023).

The gut microbiota interacts with both gut and immunological cells through activating inflammasomes. Importantly, depending on the gut flora, the type of inflammasome activation may affect the outcome. We now have a limited understanding of the pathways that result in inflammasome activation during tumor formation (Zhuang et al., 2019).

4.1.2 Explain the Emergence of Microbiome-Based Diagnostic Tests

One of the newest fields of medical research is the use of microbiome-based diagnostic techniques. It has been shown that the gut microbiota has a substantial impact on a number of diseases, including cancer. Due to technological developments in DNA sequencing and bioinformatics, the composition and function of the gut microbiome have been widely

researched. Dysbiosis, which has been connected to a higher risk of developing a number of cancer types, has been seen to be caused by alterations in the gut microbiota (Rebersek, 2021).

Using innate sensors such inflammasomal NLRs, innate immune cells and epithelial cells may detect commensal microorganisms and their metabolites. The IL-18 that inflammasomes produce is crucial for maintaining the gastro-intestinal barrier and specifically for altering intestinal tissue. Commensal bacteria and their byproducts prevent dysbiosis and intestinal barrier disruption by activating inflammasomes and triggering the release of IL-18 in the gut. The intestinal barrier is compromised because less IL-18 is produced when an inflammasome component is absent. Such damage increases inflammation and commensal bacterial penetration, both of which have the potential to lead to cancer in the long run (Borella et al., 2021).

These changes are intended to be recognized by microbiome-based diagnostic tests, which also offer a non-invasive way to monitor and diagnose cancer early on. These tests can offer useful information on the existence, development, and response to cancer treatment by examining the microbial DNA or certain microbial markers in stool or blood samples of patients. Furthermore, microbiome-based diagnostics may contribute to customized medicine by identifying people who are more likely to react to particular therapies based on their gut microbial makeup (Badal et al., 2020).

4.2 Highlight the Role of Gut Microbiome in Predicting Cancer Prognosis

A new area of study that offers considerable promise for bettering patient outcomes is the function of the gut microbiota in determining the prognosis for cancer. The gut microbiome's makeup and the likelihood of developing cancer are clearly related, according to several research. For instance, in a study of patients with colorectal cancer, it was shown that some microbial species were concentrated in individuals with poor prognosis, but other microbial species were linked to better results. In addition, the presence of certain microbial metabolites, such short-chain fatty acids, has been connected to a better prognosis in a number of cancer types (Matson et al., 2021).

These results suggest that the gut microbiota may provide novel therapeutic targets and serve as a good indicator for predicting cancer prognosis. Even though additional study is necessary to fully comprehend the complex connection between the gut microbiota and cancer prognosis, the exciting possibilities for customized treatment and improved patient care are worth investigating (Olvera-Rosales et al., 2021).

4.2.1 Discuss Studies on the Association Between Specific Microbial Compositions and Cancer Prognosis

The relationship between certain microbial assemblages and cancer prognosis has been investigated in a number of research. A research by Geller and colleagues examined the gut microbiota in people with colorectal cancer and assessed its potential as a predictive marker. Researchers discovered that patients' prognoses were much worse for those with greater levels of Fusobacterium nucleatum than for those with lower levels. In a related study, Chang and colleagues looked at the relationship between oral microbiome and the prognosis for head and neck squamous cell cancer (HNSCC). The researchers discovered that individuals with HNSCC who had greater concentrations of certain bacteria, such as Prevotel-la melaninogenica and Streptococcus anginosus, had worse prognoses and more recurrences. These findings emphasize the potential relevance of certain microbial compositions in cancer prognosis prediction and imply that modulating the gut and oral microbiome may have therapeutic implications for cancer therapy (Song et al., 2021).

The inflammasomes protect animals from CRC brought on by colitis, as demonstrated by several studies utilizing mice lacking in various inflammasome components, including NLRP3, NLRP1, NLRP6, NLRC4, and Caspase-1. Notably, IL-18, an effector of inflammasomes, is needed to control colitis instead of IL-1. Actually, colitis-associated CRC is also highly common in IL-18 KO or IL-18R KO mice (Sun et al., 2023).

In particular, the preservation of the gastro-intestinal barrier and intestinal tissue remodeling depend on the production of IL-18 by inflammasomes. Commensal bacteria and their byproducts, which serve to prevent dysbiosis and disruption of the intestinal barrier, activate inflammasomes and create IL-18 in the gut. Reduced IL-18 production brought on by an inflammasome component deficit weakens the intestinal barrier. Such harm causes a rise in inflammation and a deeper penetration of commensal bacteria, both of which may eventually end in cancer (Akbar et al., 2022).

Mice lacking inflammasome components such NLRP6, ASC, caspase-1, and IL-18 have been shown to have dysbiosis [131–134]. It is significant to note that it has been suggested that inflammasomal NLRP6 is necessary for the homeostasis of commensal bacteria. Dysbiosis and an increase in CRCs linked to inflammation are shown in NLRP6 KO mice. Inflammasomes and IL-18 offer protection against CRC brought on by inflammation. Additional research is required to determine if inflammasomes and/or IL-18 prevent the growth of CRC in genetic CRC models (such as the APC/min mice) and in human CRC. Inflammasomes can be activated by Lactobacilli in primary human macrophages and primary mammalian gut epithelial cells as a defensive mechanism against viral infection or epithelial damage. As a result, inflammasomes in carcinogenesis are a double-edged sword and the gut microbiota may have an impact on how a particular inflammasome is activated during tumorigenesis. Inflammasome activation in CRC has a protective function, but in breast and skin malignancies it plays a harmful effect (Chattopadhyay et al., 2021).

4.2.2 Explain the Potential of Using Gut Microbiome Biomarkers for Personalized Treatment Decisions

One such use is the use of gut microbiota markers in custom treatment programs. Studies have shown that the composition of the gut microbiota can influence the efficacy of cancer medicines including chemotherapy and immunotherapy. By examining the distinct bacterial species that are present in a patient's stomach, clinicians may be able to identify biomarkers that help forecast therapeutic response. For instance, it has been demonstrated that certain stomach bacteria can enhance the effectiveness of immunotherapy drugs by regulating the immune system's response. Similar to this, the presence of certain microbes has been related to cancer patients' resistance to chemotherapy. Clinicians can better treat patients and increase the chance of success by customizing treatment programs based on these indicators. By enhancing patient results and minimizing adverse effects, this unique method has the potential to transform cancer therapy. However, further investigation is required to completely comprehend the intricate relationships between the gut microbiota and cancer therapies as well as to create trustworthy biomarkers for individualized therapy choices (Huang & Mao, 2022).

Understanding the function of the gut microbiome in the onset and spread of cancer has drawn more and more interest from researchers in recent years. The billions of microorganisms that live in the gastrointestinal tract that make up the gut microbiome are essential for maintaining a healthy immune system and metabolic processes. However, dysbiosis—an imbalance in the gut microbiome—has been linked to a number of illnesses, including cancer. According to studies, certain bacteria in the stomach can create metabolites and toxins that cause DNA damage and inflammation, both of which have been linked to the development of cancer (Badal et al., 2020).

5 CONCLUSION

In conclusion, gut microbiota have a significant impact on how cancer develops and spreads. Data suggest that physiological disturbances or imbalances in the gut microbial community may promote cancer cell growth and impair the immune system's ability to fight cancer. Much remains to be understood about the specific mechanisms by which the gut microbiome affects cancer. Future research should mainly focus on the therapeutic potential of the gut microbiota in cancer prevention and treatment. Studies evaluating the impact of dietary interventions, such as increased fiber or probiotic use, on the gut microbiome and its role in cancer prevention mail is also needed.

REFERENCES

Ağagündüz, D., Cocozza, E., Cemali, Ö., Bayazıt, A. D., Nanì, M. F., Cerqua, I., Morgillo, F., Saygılı, S. K., Berni Canani, R., Amero, P., & Capasso, R. (2023). Understanding the role of the gut microbiome in gastrointestinal cancer: A review. *Frontiers in Pharmacology*, *14*, 1130562. https://doi.org/10.3389/fphar.2023.1130562

Akbar, N., Khan, N. A., Muhammad, J. S., & Siddiqui, R. (2022). The role of gut microbiome in cancer genesis and cancer prevention. *Health Sciences Review*, *2*, 100010. https://doi.org/https://doi.org/10.1016/j.hsr.2021.100010

Badal, V. D., Vaccariello, E. D., Murray, E. R., Yu, K. E., Knight, R., Jeste, D. V, & Nguyen, T. T. (2020). The Gut Microbiome, Aging, and Longevity: A Systematic Review. *Nutrients*, *12*(12). https://doi.org/10.3390/nu12123759

Bhatt, A. P., Redinbo, M. R., & Bultman, S. J. (2017). The role of the microbiome in cancer development and therapy. *CA: A Cancer Journal for Clinicians*, *67*(4), 326–344. https://doi.org/10.3322/caac.21398

Borella, F., Carosso, A. R., Cosma, S., Preti, M., Collemi, G., Cassoni, P., Bertero, L., & Benedetto, C. (2021). Gut Microbiota and Gynecological Cancers: A Summary of Pathogenetic Mechanisms and Future Directions. *ACS Infectious Diseases*, *7*(5), 987–1009. https://doi.org/10.1021/acsinfecdis.0c00839

Chattopadhyay, I., Dhar, R., Pethusamy, K., Seethy, A., Srivastava, T., Sah, R., Sharma, J., & Karmakar, S. (2021). Exploring the Role of Gut Microbiome in Colon Cancer. *Applied Biochemistry and Biotechnology*, *193*(6), 1780–1799. https://doi.org/10.1007/s12010-021-03498-9

Cheng, W. Y., Wu, C.-Y., & Yu, J. (2020). The role of gut microbiota in cancer treatment: friend or foe? *Gut*, *69*(10), 1867 LP – 1876. https://doi.org/10.1136/gutjnl-2020-321153

Cheng, Y., Ling, Z., & Li, L. (2020). The Intestinal Microbiota and Colorectal Cancer. *Frontiers in Immunology*, *11*. https://doi.org/10.3389/fimmu.2020.615056

Cullin, N., Azevedo Antunes, C., Straussman, R., Stein-Thoeringer, C. K., & Elinav, E. (2021). Microbiome and cancer. *Cancer Cell*, *39*(10), 1317–1341. https://doi.org/10.1016/j.ccell.2021.08.006

Goodman, B., & Gardner, H. (2018). The microbiome and cancer. *The Journal of Pathology*, *244*(5), 667–676. https://doi.org/10.1002/path.5047

Gopalakrishnan, V., Helmink, B. A., Spencer, C. N., Reuben, A., & Wargo, J. A. (2018). The Influence of the Gut Microbiome on Cancer, Immunity, and Cancer Immunotherapy. *Cancer Cell*, *33*(4), 570–580. https://doi.org/10.1016/j.ccell.2018.03.015

Huang, J.-T., & Mao, Y.-Q. (2022). The impact of the microbiome in cancer: Targeting metabolism of cancer cells and host. *Frontiers in Oncology*, *12*, 1029033. https://doi.org/10.3389/fonc.2022.1029033

Kim, J., & Lee, H. K. (2021). Potential Role of the Gut Microbiome In Colorectal Cancer Progression. *Frontiers in Immunology*, *12*, 807648. https://doi.org/10.3389/fimmu.2021.807648

Lee, K. A., Luong, M. K., Shaw, H., Nathan, P., Bataille, V., & Spector, T. D. (2021). The gut microbiome: what the oncologist ought to know. *British Journal of Cancer*, *125*(9), 1197–1209. https://doi.org/10.1038/s41416-021-01467-x

Li, W., Deng, Y., Chu, Q., & Zhang, P. (2019). Gut microbiome and cancer immunotherapy. *Cancer Letters*, *447*, 41–47. https://doi.org/10.1016/j.canlet.2019.01.015

Matson, V., Chervin, C. S., & Gajewski, T. F. (2021). Cancer and the Microbiome-Influence of the Commensal Microbiota on Cancer, Immune Responses, and Immunotherapy. *Gastroenterology*, *160*(2), 600–613. https://doi.org/10.1053/j.gastro.2020.11.041

Oh, B., Boyle, F., Pavlakis, N., Clarke, S., Eade, T., Hruby, G., Lamoury, G., Carroll, S., Morgia, M., Kneebone, A., Stevens, M., Liu, W., Corless, B., Molloy, M., Kong, B., Libermann, T., Rosenthal, D., & Back, M. (2021). The Gut Microbiome and Cancer Immunotherapy: Can We Use the Gut Microbiome as a Predictive Biomarker for Clinical Response in Cancer Immunotherapy? *Cancers*, *13*(19). https://doi.org/10.3390/cancers13194824

Olvera-Rosales, L.-B., Cruz-Guerrero, A.-E., Ramírez-Moreno, E., Quintero-Lira, A., Contreras-López, E., Jaimez-Ordaz, J., Castañeda-Ovando, A., Añorve-Morga, J., Calderón-Ramos, Z.-G., Arias-Rico, J., & González-Olivares, L.-G. (2021). Impact of the Gut Microbiota Balance on the Health-Disease Relationship: The Importance of Consuming Probiotics and Prebiotics. *Foods (Basel, Switzerland)*, *10*(6). https://doi.org/10.3390/foods10061261

Rebersek, M. (2021). Gut microbiome and its role in colorectal cancer. *BMC Cancer*, *21*(1), 1325. https://doi.org/10.1186/s12885-021-09054-2

Sadrekarimi, H., Gardanova, Z. R., Bakhshesh, M., Ebrahimzadeh, F., Yaseri, A. F., Thangavelu, L., Hasanpoor, Z., Zadeh, F. A., & Kahrizi, M. S. (2022). Emerging role of human microbiome in cancer development and response to therapy: special focus on intestinal microflora. *Journal of Translational Medicine*, *20*(1), 301. https://doi.org/10.1186/s12967-022-03492-7

Sánchez-Alcoholado, L., Ramos-Molina, B., Otero, A., Laborda-Illanes, A., Ordóñez, R., Medina, J. A., Gómez-Millán, J., & Queipo-Ortuño, M. I. (2020). The Role of the Gut Microbiome in Colorectal Cancer Development and Therapy Response. *Cancers*, *12*(6). https://doi.org/10.3390/cancers12061406

Sepich-Poore, G. D., Zitvogel, L., Straussman, R., Hasty, J., Wargo, J. A., & Knight, R. (2021). The microbiome and human cancer. *Science (New York, N.Y.)*, *371*(6536). https://doi.org/10.1126/science.abc4552

Song, P., Wang, Q.-B., Liang, B., & Jiang, S.-J. (2021). Advances in research on the relationship between the gut microbiome and cancer. *European Review for Medical and Pharmacological Sciences*, *25*(16), 5104–5112. https://doi.org/10.26355/eurrev_202108_26521

Sun, J., Chen, F., & Wu, G. (2023). Potential effects of gut microbiota on host cancers: focus on immunity, DNA damage, cellular pathways, and anticancer therapy. *The ISME Journal*, *17*(10), 1535–1551. https://doi.org/10.1038/s41396-023-01483-0

Vivarelli, S., Salemi, R., Candido, S., Falzone, L., Santagati, M., Stefani, S., Torino, F., Banna, G. L., Tonini, G., & Libra, M. (2019). Gut Microbiota and Cancer: From Pathogenesis to Therapy. *Cancers*, *11*(1). https://doi.org/10.3390/cancers11010038

Whisner, C. M., & Athena Aktipis, C. (2019). The Role of the Microbiome in Cancer Initiation and Progression: How Microbes and Cancer Cells Utilize Excess Energy and Promote One Another's Growth. *Current Nutrition Reports*, *8*(1), 42–51. https://doi.org/10.1007/s13668-019-0257-2

Wu, Y., Jiao, N., Zhu, R., Zhang, Y., Wu, D., Wang, A.-J., Fang, S., Tao, L., Li, Y., Cheng, S., He, X., Lan, P., Tian, C., Liu, N.-N., & Zhu, L. (2021). Identification of microbial markers across populations in early detection of colorectal cancer. *Nature Communications*, *12*(1), 3063. https://doi.org/10.1038/s41467-021-23265-y

Yang, Q., Wang, B., Zheng, Q., Li, H., Meng, X., Zhou, F., & Zhang, L. (2023). A Review of Gut Microbiota-Derived Metabolites in Tumor Progression and Cancer Therapy. *Advanced Science*, *10*(15), 2207366. https://doi.org/https://doi.org/10.1002/advs.202207366

Zhao, L.-Y., Mei, J.-X., Yu, G., Lei, L., Zhang, W.-H., Liu, K., Chen, X.-L., Kołat, D., Yang, K., & Hu, J.-K. (2023). Role of the gut microbiota in anticancer therapy: from molecular mechanisms to clinical applications. *Signal Transduction and Targeted Therapy*, *8*(1), 201. https://doi.org/10.1038/s41392-023-01406-7

Zhuang, H., Cheng, L., Wang, Y., Zhang, Y.-K., Zhao, M.-F., Liang, G.-D., Zhang, M.-C., Li, Y.-G., Zhao, J.-B., Gao, Y.-N., Zhou, Y.-J., & Liu, S.-L. (2019). Dysbiosis of the Gut Microbiome in Lung Cancer. *Frontiers in Cellular and Infection Microbiology*, *9*, 112. https://doi.org/10.3389/fcimb.2019.00112

Zyoud, S. H., Al-Jabi, S. W., Amer, R., Shakhshir, M., Shahwan, M., Jairoun, A. A., Akkawi, M., & Abu Taha, A. (2022). Global research trends on the links between the gut microbiome and cancer: a visualization analysis. *Journal of Translational Medicine*, *20*(1), 83. https://doi.org/10.1186/s12967-022-03293-y