

MICROBIAL BIOMARKERS IN CANCER EARLY DETECTION AND PROGNOSTIC BREAKTHROUGHS

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ABSTRACT

Finding microbial biomarkers for cancer has become a ground-breaking strategy in oncology, opening up new possibilities for prognostic evaluation and early identification. The intricate communities of microbes known as microbiomes within the human body are now understood to have a crucial role in the initiation and spread of cancer. Researchers have detected unique microbial signatures linked to different diseases, such as *Helicobacter pylori* in gastric cancer and *Fusobacterium nucleatum* in colorectal cancer, thanks to advancements in metagenomics and next-generation sequencing technology. These micro biomarkers have the potential to be used as non-invasive cancer screening techniques in addition to providing information on the genesis of cancer. Furthermore, as certain microbiome patterns have been connected to patient outcomes, treatment responses, and resistance mechanisms in immunotherapy and chemotherapy, the predictive potential of microbial biomarkers is garnering interest. Personalized cancer treatment might be transformed by incorporating microbiome analysis into clinical practice. This would enable earlier identification, more precise risk assessment, and customized therapeutic approaches based on each patient's microbiome composition. Despite its potential, the field currently needs help with standardizing procedures and figuring out how microbial dysbiosis and carcinogenesis are related. Nonetheless, microbial biomarkers constitute a new area in cancer research, potentially enhancing early diagnosis and prognosis in the coming years.

Keywords: Microbial biomarkers, Cancer detection, Early cancer diagnosis, Prognostic breakthroughs, Cancer progression indicators, Cancer microbiome interactions

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INTRODUCTION

Specific microbes, microbial genes, or metabolites that may be found and measured to act as markers of a particular biological state or disease state are known as microbial biomarkers (Tegl 2015). These biomarkers enable the detection of health or disease signs by offering insightful information about the microbial makeup and activity within the human body. Microbial biomarkers in the cancer setting can indicate the occurrence or risk of malignancies, the course of the disease, or therapy responses. Microbial biomarkers are essential instruments in precision medicine because they aid in early diagnosis, prognosis, and treatment decision-making by monitoring changes in the microbiome or identifying certain microbial species linked to particular cancer types. Various microbes or compounds generated from microbes are known as microbial biomarkers, and they are used as indicators of various biological states, especially about illness. The potential relevance of these biomarkers in cancer diagnosis, monitoring, and understanding is becoming increasingly apparent. The term "cancer microbiome" describes the collective genome of bacteria found in the stomach, malignant tissues, and other bodily regions. It has gained significant attention in scientific circles (Sepich-Poore 2022). The coexisting bacteria, viruses, fungi, and other microorganisms in the human body are collectively called the microbiome.

A growing body of research indicates that changes in the microbiome's makeup and function, often referred to as dysbiosis, can have a major influence on the onset, course, and response to therapy of cancer. Microbial biomarkers play a significant role in cancer as they can affect immune system regulation, inflammation, and metabolism, all of which are important aspects of carcinogenesis (Hanus 2021). Some microbial species, for example, have been connected to a higher risk of colorectal cancer, while others are linked to improved results in melanoma immunotherapy. Moreover, there is increasing interest in the relationship between the microbiome and cancer treatment, specifically in how bacteria may impact the effectiveness of immunotherapy, chemotherapy, and radiation therapy (Liu 2022). Microbial biomarkers provide a promising path for personalized treatment in oncology since they may

be used to predict patient responses to different medicines, monitor disease progression, and predict cancer risk. A comprehensive comprehension of the complex correlation between the microbiome and cancer has the potential to transform methods for cancer prevention, diagnosis, and therapy, hence positioning microbial biomarkers as crucial components in the dynamic field of cancer research (Ullah 2022).

Microbial Signatures in Early Cancer Detection

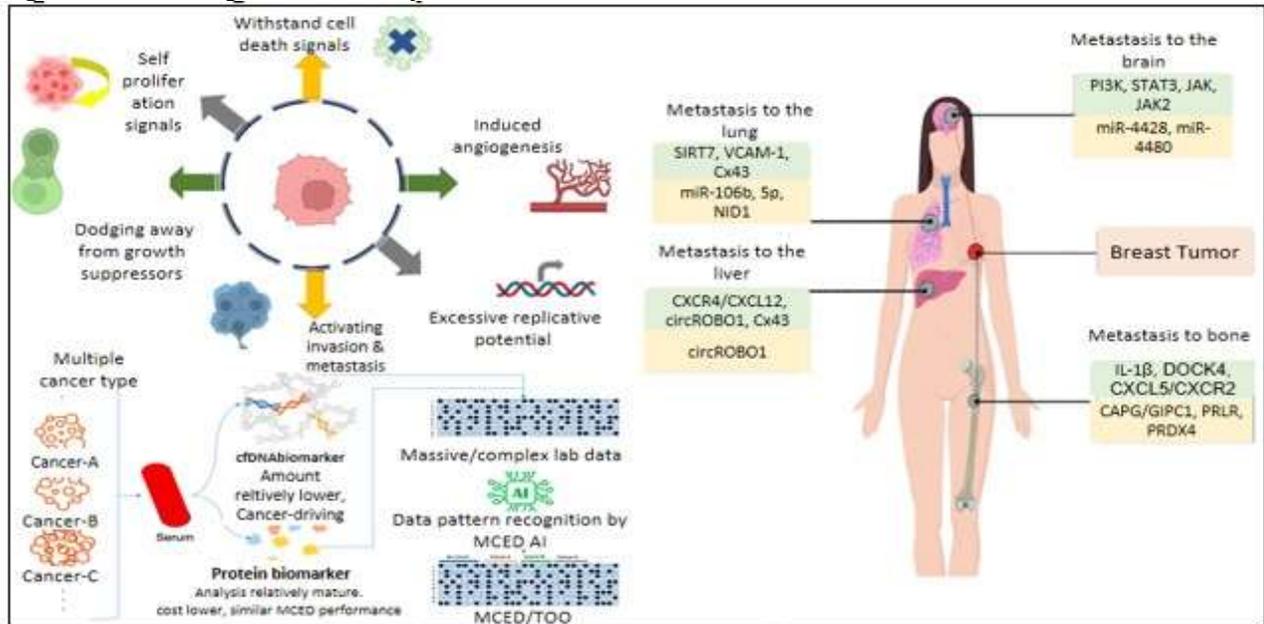
Microbial signatures have emerged as a promising area in early cancer diagnosis, giving a non-invasive method to diagnostics by discovering microbial biomarkers linked with carcinogenesis. The composition of the human microbiome, which is essential for preserving physiological equilibrium, can change significantly due to the development of cancer (Sommariva 2020). These modifications offer distinct microbial biomarkers that can be used for early cancer detection, especially for colorectal, pancreatic, and breast malignancies. For example, research has shown that *Fusobacterium nucleatum* is more prevalent in colorectal cancer, and this is strongly linked to tumor development and metastasis. Similarly, particular microbial taxa, such as *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*, have been related to pancreatic cancer. Even though it has received less attention in this field, breast cancer has demonstrated potential, as the development of tumors is correlated with microbial imbalances in breast tissue. These microbial biomarkers present a promising avenue for non-invasive diagnostics, in which basic biological samples such as blood, saliva, or feces might yield important information about the early stages of cancer development. Technologies such as next-generation sequencing (NGS), polymerase chain reaction (PCR), and metagenomics play crucial roles in identifying these microbial fingerprints with great sensitivity and specificity (Mayo 2014). NGS, for instance, provides a thorough analysis of microbial communities, offering a detailed insight into the microbiome's modifications throughout cancer development. On the other hand, it allows for the quick amplification and identification of certain microbial DNA sequences. In contrast,

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metagenomic techniques provide a more thorough, objective examination of the whole microbial ecology concerning cancer. These innovations, together with the expanding field of bioinformatics, have made microbial-based diagnostics more accessible and dependable. This might lead to a more accurate and non-invasive approach to early cancer diagnosis. The potential of microbial biomarkers as vital instruments for

early intervention, enhancing patient outcomes by detecting malignancies at more manageable stages, is demonstrated by case studies involving various tumors. The field of study on microbial signatures is expanding and may eventually replace or supplement conventional cancer detection techniques (Villéger 2018).

Fig 1: Microbial Signatures in Early Cancer Detection



Gut Microbiota and Cancer: The Central Player

Depending on its makeup and activity, the gut microbiota can contribute to cancer risk or act as a protective factor. It has become one of the key players in cancer biology. Microbial community imbalances that are indicative of gut dysbiosis have been closely linked to a higher risk of colorectal and gastrointestinal cancers, among other cancers (Zou 2018). Several different pathways connect the gut microbiota to the development of cancer. The production of metabolites by some microbial species, such as *Enterococcus faecalis* and *Escherichia coli*, can lead to oxidative stress and DNA damage, potentially triggering cancer initiation, making chronic inflammation one of the crucial processes. Furthermore, dysbiosis can alter immunological responses, compromising the body's ability to fight tumors and fostering an environment that is conducive to cancer. It has been demonstrated that certain gut bacteria, such as *Fusobacterium nucleatum*, can avoid immune

recognition, enabling cancer cells to grow unabated (Singh 2023). The gut microbiota also affects medication metabolism and immunological checkpoint pathways, which can affect the effectiveness of cancer treatments, including immunotherapies and chemotherapies. Recent discoveries have revealed gut microbial biomarkers that can act as early indications of cancer, notably in colorectal and gastrointestinal malignancies. For example, early-stage colorectal cancer has been linked to the prevalence of *Fusobacterium* and the concentration of certain microbial metabolites, such as short-chain fatty acids (SCFAs). Using the gut microbiota as a non-invasive diagnostic technique is now possible, which creates new opportunities for risk assessment and early identification. As more research is conducted, it becomes clear that the gut microbiota not only contributes significantly to cancer risk but also offers potential targets for cutting-edge therapeutic approaches like fecal microbiota transplantation (FMT), probiotics, and

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prebiotics to improve the effectiveness of cancer treatments by reestablishing a balanced microbial ecosystem (Kashyap 2023).

Table 1: Mechanisms and Impacts of Gut Microbiota on Cancer Risk and Detection

Aspect	Key Findings/Description	Impact on Cancer	Potential Applications	References
Dietary Influence on Gut Microbiota	Diet alters microbial composition, which in turn affects cancer risk	High-fat or processed diets promote dysbiosis, while fiber-rich diets support protective microbiota	Dietary interventions to modulate the microbiome and reduce cancer risk	Scott (2013)
Genomic Insights into Microbiota-Cancer Interaction	Genomic studies show specific microbial gene functions linked to cancer pathways.	Microbial genes may activate oncogenic pathways or suppress tumor-suppressor genes.	Genomic profiling of microbiota to identify potential cancer-related microbial functions	Xing (2022)
Short-Chain Fatty Acids (SCFAs) and Carcinogenesis	Microbial metabolites like SCFAs can have protective or carcinogenic effects based on microbial composition	SCFAs such as butyrate can suppress inflammation, while other metabolites can promote cancer	Targeting SCFA-producing bacteria for cancer prevention and treatment	Sivaprakasam (2016)
Fecal Microbiota Transplantation (FMT)	Restoring healthy gut microbiota through fecal transplants from healthy donors	Can reverse dysbiosis, improve immune function, and potentially reduce cancer risk	FMT as a novel therapeutic approach for cancer prevention and adjuvant therapy	Brandt (2013)
Probiotics and Prebiotics in Cancer Therapy	Introducing beneficial bacteria or dietary components to support healthy microbiota	Restores microbial balance, potentially reduces cancer progression and enhances treatment efficacy.	Integrating probiotics and prebiotics into cancer prevention and therapeutic protocols	Alam (2022)
Gut Microbiota and Cancer Treatment	The microbiome affects the efficacy of cancer therapies, especially immunotherapies and chemotherapies.	Certain bacteria enhance or reduce the effectiveness of immune checkpoint inhibitors and chemotherapeutics.	Modulating the gut microbiome to improve cancer treatment outcomes (e.g., using probiotics or FMT)	Pouncey (2018)
Microbial Biomarkers for Early Detection	Specific microbial species, such as <i>Fusobacterium</i>	Early detection of microbial shifts may signal the	Development of non-invasive diagnostic tools,	Olovo (2021)

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	<i>nucleatum</i> , linked with colorectal cancer	onset of colorectal and gastrointestinal cancers.	gut microbial profiling for early-stage cancer detection	
Immune Modulation by Gut Microbiota	Microbiota modulate immune responses by either stimulating or suppressing the immune.	Suppression of antitumor immunity and promotion of tumor growth, e.g., by <i>Fusobacterium nucleatum</i>	Immune-boosting probiotics to enhance anti-tumor responses	Amoroso (2020)
Microbial Influence on Inflammation	Certain gut microbes (e.g., <i>Escherichia coli</i> , <i>Enterococcus faecalis</i>) induce inflammation and DNA damage.	Prolonged inflammation supports the tumor microenvironment and encourages malignant transformation.	Anti-inflammatory therapies targeting microbial-induced inflammation	Sartor (2008)
Gut Dysbiosis and Cancer Risk	Imbalance in gut microbiota (e.g., overgrowth of pathogenic bacteria) linked to increased cancer susceptibility	Dysbiosis leads to chronic inflammation, oxidative stress, and immune dysregulation, promoting carcinogenesis.	Identifying dysbiosis patterns for cancer risk screening	Biragyn (2018)

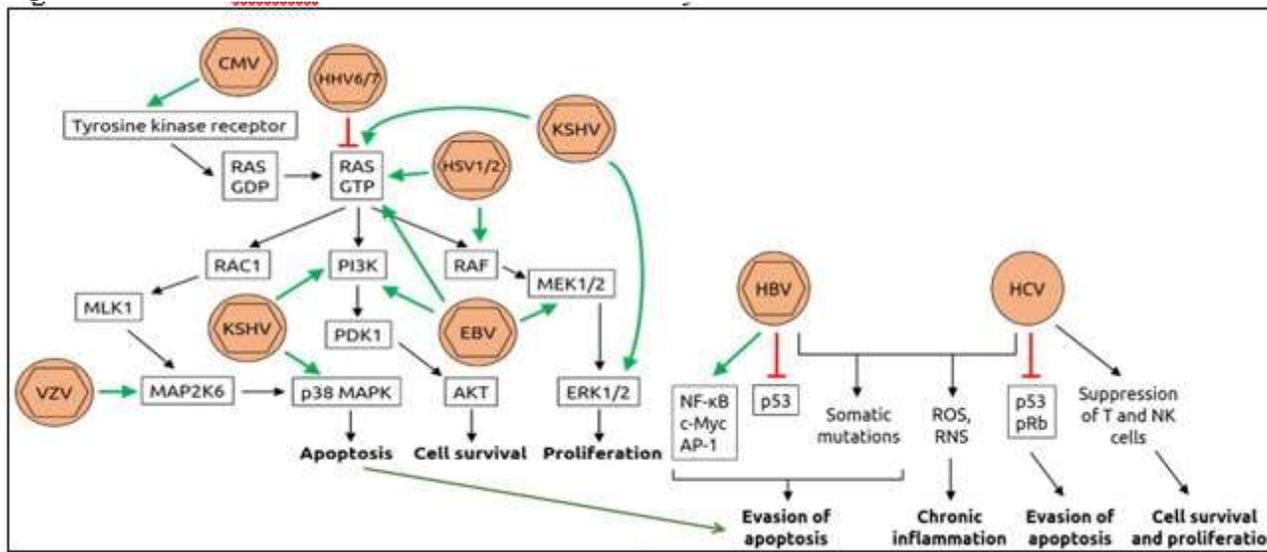
Oral Microbiome and Head and Neck Cancers

The oral microbiome significantly influences head and neck cancers (HNC), which provides a diverse microbial landscape reflecting both healthy and pathological states. A diverse range of bacteria, viruses, fungus, and other microbes live in the human mouth cavity and constitute a dynamic ecosystem (Ali 2012). Changes in this microbial makeup in the setting of head and neck tumors are becoming more widely acknowledged as both an effect of and a possible cause of oncogenic processes. Research indicates that changes in the diversity of microorganisms, namely a decrease in the number of beneficial bacteria and an increase in harmful species, might be precursors to cancerous development. *Porphyromonas gingivalis* and *Fusobacterium nucleatum*, for example, have been linked to increased inflammation and the advancement of cancer, suggesting that mouth infections may play a role in the development of tumors. Salivary indicators produced from these microbial communities are emerging as important tools in non-invasive

screening approaches. A less intrusive option to conventional biopsy techniques, using saliva to identify certain microbial signatures and other molecular alterations, such as DNA mutations, protein markers, and metabolites, shows promise for the early diagnosis of HNC (Kumar 2024). Researchers can better understand the path from a healthy condition to precancerous lesions and ultimately to full-blown malignancy by examining microbial diversity and its alterations. Dysbiosis in the oral environment is generally indicated by a rise in the dominance of carcinogenic microorganisms and a reduction in the variety of bacteria. This dysbiosis not only makes inflammation worse but also alters the immune system, creating a setting that is favorable to the growth of cancer. Further investigation of the complex link between head and neck malignancies and the oral microbiome may yield new insights into the microbial foundations of cancer and innovative approaches to diagnosis and treatment (Burcher 2022).

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Fig 2: Oral Microbiome and Head and Neck Cancers



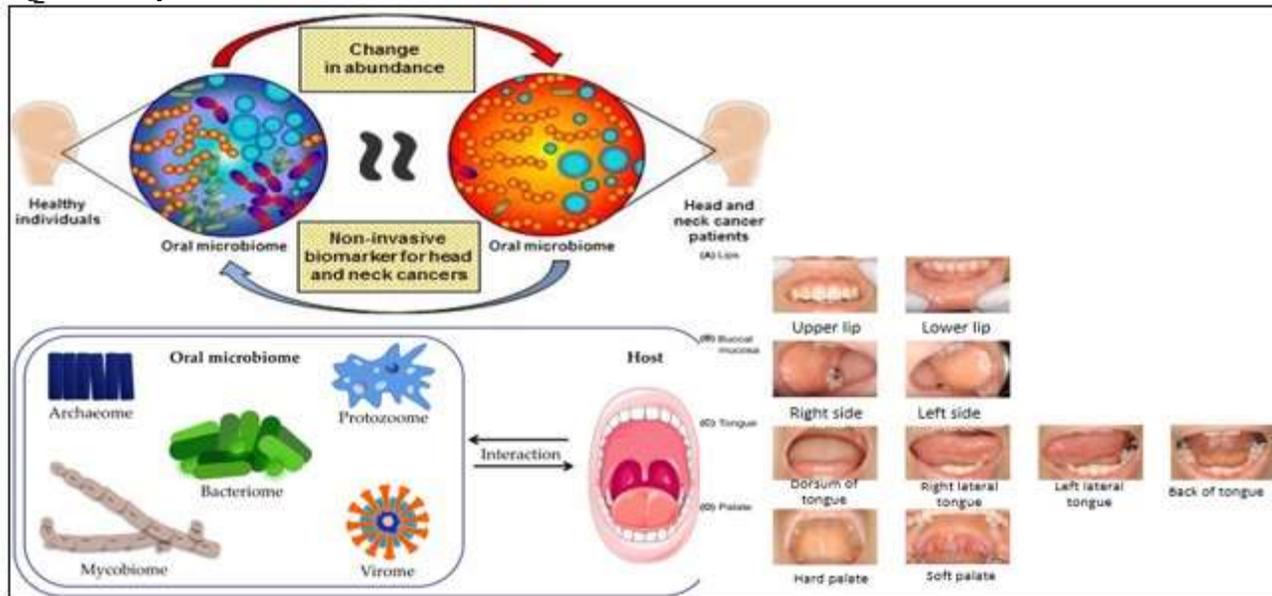
Urinary Microbiome in Urothelial and Prostate Cancer Detection

Due to the discovery of distinct microbial patterns linked to prostate and urothelial cancers, the urine microbiome has become a potentially useful tool for identifying these tumors. Research has indicated that people with bladder and prostate tumors have a considerably different microbial makeup of the urinary system than healthy persons (Karam 2022). This suggests that certain bacteria or changes in microbial communities may act as markers for cancer development. Tumor growth can be facilitated by immunological dysregulation and inflammation, for example, associated with changes in microbial diversity and certain pathogens. According to these results, urine microbiota may be used as a non-invasive diagnostic tool, especially in the early identification of prostate and urothelial malignancies. Urine sampling is comparatively simple to acquire and provides a plethora of molecular information, including metabolites and microbial DNA, that can serve as biomarkers in contrast to more conventional approaches like

biopsies or imaging. Technological developments in high-throughput sequencing and bioinformatics have made it easier to identify these biomarkers, which aid in distinguishing between benign urinary tract disorders and malignant changes (Adam 2001). Nonetheless, standardized urine microbiome sampling and analysis still face several obstacles. Factors such as sample contamination, changes in microbial populations owing to food, antibiotics, or other external factors, and the necessity for large, well-defined clinical cohorts pose challenges to the general clinical use of urine microbiota-based diagnostics. However, research is moving forward to break through these obstacles, and new tools like machine learning algorithms and microfluidic devices are making it easier to identify microbial fingerprints precisely. The urine microbiome has the potential to revolutionize the detection of bladder and prostate cancers by providing individualized treatment plans based on each patient's microbial profile and earlier, more accurate diagnosis as these technologies advance (Dinges 2019).

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Fig 3: Urinary Microbiome in Urothelial and Prostate Cancer Detection



Microbiome-Based Prognostic Biomarkers: Predicting Cancer Outcomes

As a predictive tool in cancer, the human microbiome, a complex ecology of bacteria living within the body, has attracted much interest. Recent research emphasizes how patient outcomes may be predicted by changes in the microbiota after cancer therapies, including immunotherapy, chemotherapy, and surgery. Changes in the variety, makeup, and functioning of microbes after therapy provide important information about how the body reacts to cancer treatments (Bhatt 2017). For example, some bacterial strains are known to multiply after chemotherapy, which may result in resistance to therapy or immune suppression. In contrast, other strains may promote the effectiveness of treatment and immunological recovery. It is becoming increasingly important to correlate microbial alterations with patient survival and recurrence rates. For instance, decreased microbial diversity has been associated with worse survival rates and increased recurrence rates in several malignancies, such as pancreatic and

colorectal cancer. Certain microbial biomarkers, such as *Fusobacterium nucleatum* in colorectal cancer, have been linked to the development and recurrence of the illness, making them crucial markers for tracking long-term results (Villéger 2018). Moreover, physicians may classify patients depending on their prognosis or likelihood of recurrence by incorporating microbiome-based biomarkers into risk stratification models. To create individualized treatment plans that are less hazardous for patients with a favorable microbiological profile or more active intervention for high-risk patients, stratification is essential. Personalized cancer care might be improved, and existing prediction models could be more accurate if microbiome profiles were used as prognostic indicators. By discovering microbial patterns associated with treatment response and long-term outcomes, researchers are pioneering a unique paradigm in cancer prediction, where microbiome data combines genetic and clinical indicators to advance precision therapy (Barone 2022).

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Table 2: Microbiome-Based Prognostic Biomarkers in Cancer Care

Cancer Type	Microbial Biomarkers	Post-Treatment Changes	Correlation with Prognosis	Prognostic Implications	Tailored Treatment Strategies
Colorectal Cancer	<i>Fusobacterium nucleatum</i>	Increase post-chemotherapy	Higher recurrence rates, poorer survival	Monitoring microbial shifts can aid in predicting the recurrence	Aggressive therapy in high-risk patients, microbial-targeted treatments
Pancreatic Cancer	<i>Streptococcus</i> species	Decreased diversity post-surgery	Linked to lower survival rates	Microbial biomarkers offer predictive value for patient stratification	Personalized chemotherapy regimens based on microbial profiles
Breast Cancer	<i>Lactobacillus</i> species	Altered microbial composition post-immunotherapy	Associated with favorable immune response	Improved survival in patients with favorable microbiome signatures	Optimizing immunotherapy for patients with beneficial microbiome
Lung Cancer	<i>Veillonella</i> species	Reduced microbial diversity post-chemotherapy	Correlated with immune suppression and poor prognosis	Utilizing microbial markers for risk assessment	Microbial supplementation for enhancing immune recovery
Ovarian Cancer	<i>Bifidobacterium</i> species	Post-treatment disruption in microbial homeostasis	Implicated in recurrence and treatment resistance	Biomarkers guide prognosis and recurrence monitoring	Tailored treatments based on microbial risk profiles
Melanoma	<i>Bacteroides fragilis</i>	Post-immunotherapy increase in beneficial microbes	Linked to improved survival outcomes	Microbiome biomarkers integrated into risk stratification	Immunotherapy enhancement in patients with favorable microbial responses
Prostate Cancer	<i>Prevotella</i> species	Changes in gut microbiome post-therapy	Impact on systemic inflammation and survival	Prognostic value in survival and treatment response	Customizing anti-inflammatory therapies based on microbiome profiles
Gastric Cancer	<i>Helicobacter pylori</i>	Persistence post-surgery	Associated with recurrence	Targeting microbial persistence	Incorporating microbial eradication into

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			and poor survival	can improve prognosis	treatment protocols
Esophageal Cancer	<i>Porphyromonas gingivalis</i>	Disruption of microbiome post-treatment	Linked to poor immune response and higher mortality	Biomarkers enable the monitoring of immune recovery	Personalized immunotherapy approaches based on microbial signatures
Liver Cancer	<i>Clostridium species</i>	Shifts in microbiome composition post-therapy	Associated with liver dysfunction and recurrence	Microbiome changes provide early prognostic indicators	Tailored treatments based on liver-microbiome interactions

The Role of Virome in Cancer Biomarker Discovery

The importance of the virome in identifying cancer biomarkers has come to light as researchers learn more about the intricate relationships between viral components and tumor biology. Human papillomavirus (HPV) and Epstein-Barr virus (EBV), in particular, have been linked for a long time to some malignancies, including cervical cancer (HPV) and nasopharyngeal carcinoma (EBV). These viruses are useful as prognostic and diagnostic indicators because they integrate into host genomes, induce mutations, or alter immune responses, contributing to oncogenesis (Mui 2017). For instance, HPV DNA detection is frequently employed in the screening process for cervical cancer, and the EBV viral load serves as a trustworthy marker for the treatment of nasopharyngeal carcinoma. Beyond these well-known viruses, there is growing interest in studying other members of the human virome, which is the entirety of viral communities in the human body. Examples of these include the human polyomaviruses, which are linked to some brain tumors, and the hepatitis B and C viruses, which are related to hepatocellular carcinoma. These viral fingerprints can help with early identification, therapy selection, and therapeutic response

monitoring by providing insights into the molecular mechanisms underlying the onset and progression of cancer (Syn 2016). Furthermore, new studies are investigating the function of viruses called bacteriophages, which infect bacteria when diagnosing cancer. Because of their impact on the human microbiome, which is increasingly understood to be involved in the pathophysiology of cancer, bacteriophages considered unimportant to human health are now being studied for their potential as indirect cancer biomarkers. Phage populations might provide a new way to find biomarkers by reflecting changes in microbial communities that support carcinogenesis. Integrating the human virome into cancer diagnostics is a cutting-edge technique, promising to enhance the precision of biomarker-based treatments and improve cancer outcomes by identifying viral components that are either causative of or sensitive to cancer development. The virome has enormous potential to transform the hunt for cancer biomarkers and broaden the arsenal for early diagnosis and customized therapy as studies unfold the complex functions of viruses and phages in the tumor microenvironment (Zhang 2024).

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individual's potential response to immunotherapy, chemotherapy, or targeted therapies. The synergy between AI-driven analysis and multi-omics platforms reveals new possibilities in microbial biomarker discovery, expediting the transfer from research to clinical application (Huo 2024).

Challenges and Limitations in the Clinical Application of Microbial Biomarkers

The first set of difficulties and constraints in the therapeutic use of microbial biomarkers is microbial samples' unpredictability and standardization problems. Microbiomes are dynamic and can change in response to various circumstances, including medicine, environment, and food. Because of this, it is challenging to get reliable microbiological samples, and standardizing these samples across multiple demographics and clinical contexts is a major challenge. Furthermore, the need for well-recognized sample collection, processing, and preservation procedures makes microbial biomarker-based diagnostics even less reliable. Developing microbial biomarker-based diagnostic assays necessitates stringent validation and approval procedures, which presents another regulatory obstacle. It is difficult to provide thorough proof of clinical efficacy, safety, and repeatability to regulatory agencies like the FDA or EMA when biomarkers differ so much between people. Ethical issues add another dimension of complication, notably addressing microbiome data privacy and patient rights. Microbiome profiles are extremely individualized so that they might disclose sensitive information about an individual's health, nutrition, or even vulnerability to particular illnesses. Although obtaining patient consent and protecting their privacy is crucial, the rules governing the preservation of microbiome data are still being developed. Thus, it continues to be difficult in clinical practice to balance the potential advantages of microbial biomarkers in customized therapy and the moral need to protect patient autonomy and data security.

Future Directions and Emerging Trends

The integration of next-generation microbiome-based technologies is becoming increasingly important in the future treatment and diagnosis of cancer. The advancement of liquid biopsy methods

and point-of-care applications that use microbial biomarkers for cancer diagnosis is one field that shows promise. By analyzing microbial DNA and metabolites found in physiological fluids like blood or saliva, these instruments provide a sensitive, non-invasive way to screen for cancer early and track the course of the disease. Personalized cancer screening systems use microbial biomarkers to improve specificity and enable individualized treatment plans based on each patient's microbiome. This customized method has the potential to transform early diagnosis by detecting cancer predispositions in high-risk patients before the manifestation of symptoms. Simultaneously, artificial microorganisms and synthetic biology are becoming potent instruments for the diagnosis and treatment of cancer. By releasing therapeutic compounds directly at the tumor site and detecting surroundings unique to the tumor, these modified bacteria potentially reduce side effects and improve treatment success. Furthermore, the possibility of creating microorganisms to alter the immune system and enhance the body's inherent ability to combat cancer is being investigated. When taken as a whole, these developments mark a significant turning point toward more accurate, effective, and customized cancer therapy, opening the door for novel therapies that take advantage of the body's microbiome and biologically designed systems.

Conclusion

The advancement of cancer therapy can be greatly enhanced by incorporating microbial indicators into ordinary clinical oncology practice. These biomarkers, which come from individuals' microbiological makeup, can completely change disease monitoring, therapy tailoring, and early diagnosis. Microbial markers have found widespread use in preventative oncology, where they may be used as screening instruments for high-risk individuals, spotting cancer early on before symptoms appear. Oncologists could improve the accuracy of risk stratification and the identification of precancerous diseases by adding microbial profiles into routine screening programs. However, strong collaborative research activities across various disciplines, including microbiology, oncology, bioinformatics, and clinical trials, are

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necessary to realize the full promise of microbial biomarkers. Large-scale, multi-institutional investigations are required to verify these biomarkers, assuring their reliability and repeatability across varied patient groups. Advances in our comprehension of the microbiome-cancer axis may lead to biomarker-based discoveries and customized treatments that enhance cancer treatment efficiency and patients' quality of life by reducing adverse effects. This future trajectory places microbial biomarkers at the forefront of the next phase of cancer treatment by bringing together innovation, teamwork, and clinical application.

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