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Oncogenic Microbes: Mechanistic Insights into Bacteria and Virus-Induced Tumorigenesis

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ABSTRACT

Microbial pathogens, particularly specific viruses and bacteria, have been increasingly recognized as significant contributors to the development of various human cancers. Oncogenic viruses—including Human Papillomavirus (HPV), Epstein–Barr Virus (EBV), and Hepatitis B and C viruses (HBV, HCV)—as well as bacteria such as Helicobacter pylori, have been implicated in the initiation and progression of malignancies through multiple interrelated mechanisms. These include the induction of chronic inflammation, generation of reactive oxygen species leading to genomic instability, interference with host tumor suppressor pathways, and modulation of immune responses. Viral oncoproteins and bacterial toxins often disrupt cell cycle regulation, inhibit apoptosis, and promote sustained proliferative signaling, all of which contribute to a tumor-permissive microenvironment. Moreover, microbial infections can induce epigenetic modifications and alter the host microbiome, further compounding oncogenic processes. This review comprehensively explores the mechanistic underpinnings of microbe-induced tumorigenesis and underscores the importance of early detection, vaccination, and targeted therapeutic strategies. Advancing our understanding of these interactions will be crucial for developing effective interventions to reduce the global cancer burden attributable to infectious agents.

Keywords: *Oncogenic microbes, tumorigenesis, HPV, EBV, Helicobacter pylori, viral oncoproteins, chronic inflammation, cancer microbiome.*

1. Introduction

Cancer continues to be a leading cause of morbidity and mortality worldwide, accounting for millions of deaths annually. While genetic and environmental factors such as smoking, diet, radiation exposure, and pollutants are well-established contributors to cancer risk, infectious agents also play a crucial, and often underrecognized, role in tumor development [1]. According to estimates by the International Agency for Research on Cancer (IARC), approximately 15–20% of global cancer cases are attributable to microbial infections. This figure is even higher in low- and middle-income countries, where the burden of infection-related cancers is compounded by limited access to healthcare and preventive services. Microbes contribute to carcinogenesis through complex and multifaceted mechanisms. Oncogenic viruses, including Human Papillomavirus (HPV), Epstein–Barr Virus (EBV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Human T-cell Leukemia Virus type 1 (HTLV-1), and Kaposi's Sarcoma-associated Herpesvirus (KSHV), are the most well-documented viral agents linked to cancer [2]. Similarly, certain bacteria—most notably *Helicobacter pylori*—have been conclusively associated with gastric cancer and mucosa-associated lymphoid tissue (MALT) lymphoma, parasitic infections like *Schistosoma haematobium* have been implicated in bladder cancer, highlighting the diversity of microbial oncogenic potential across different pathogens.

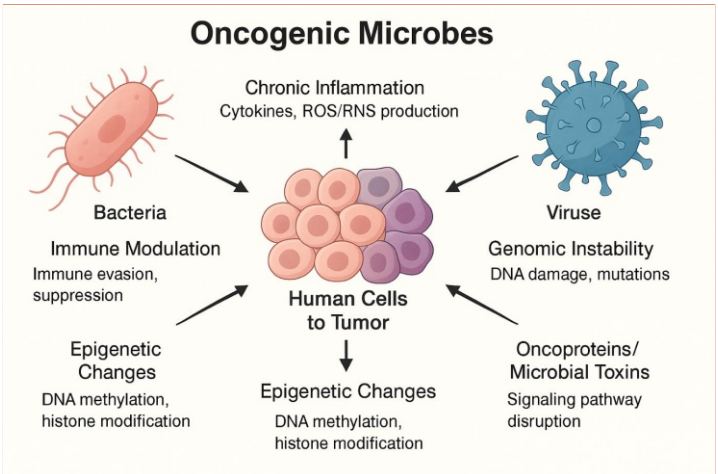

Figure 1: Microbial Mechanisms in Cancer Development

This figure 1 illustrates the multifaceted mechanisms by which oncogenic microbes contribute to tumorigenesis. It highlights key viral and bacterial agents, their molecular targets (e.g., p53, Rb), and the resulting cellular outcomes, such as chronic inflammation, immune evasion, and epigenetic reprogramming that collectively promote cancer progression.

Microbial-induced carcinogenesis can occur through both direct and indirect mechanisms. In the direct mode, microbial gene products (e.g., viral oncoproteins) interfere with host cell

cycle regulation, DNA repair mechanisms, and apoptotic pathways, leading to uncontrolled cell proliferation and accumulation of genetic mutations. In the case of HPV, for instance, the viral E6 and E7 proteins target tumor suppressor proteins p53 and Rb, respectively, facilitating malignant transformation of infected epithelial cells [3]. Similarly, HBV and HCV promote hepatocellular carcinoma via chronic hepatocyte turnover, inflammation, and viral protein-mediated interference with host cellular pathways.Indirect mechanisms of oncogenesis primarily involve chronic inflammation, oxidative stress, and immune modulation. Persistent infections often result in prolonged immune activation and tissue damage, creating a microenvironment rich in cytokines, chemokines, and reactive oxygen and nitrogen species (ROS and RNS). This inflammatory milieu promotes cellular proliferation, angiogenesis, and DNA damage, all of which contribute to tumor initiation and progression. For example, *Helicobacter pylori* infection induces gastritis and the production of inflammatory mediators that can lead to atrophic gastritis and gastric cancer over time. Another critical aspect of microbial carcinogenesis is immune evasion. Many oncogenic pathogens have evolved sophisticated strategies to subvert host immune responses, enabling them to establish long-term persistence [4]. This immune dysregulation may impair the host's ability to recognize and eliminate pre-malignant cells, thereby facilitating cancer development. EBV, for instance, establishes latency within B cells and manipulates host signaling to prevent immune clearance, contributing to lymphoproliferative disorders and various lymphomas, recent advances in microbiome research suggest that dysbiosis—the disruption of the normal microbial community in the human body—may influence carcinogenesis. Alterations in the gut microbiota composition have been associated with colorectal cancer and other malignancies, potentially through mechanisms involving microbial metabolites, modulation of host immunity, and interaction with dietary factors. Understanding these microbe–host interactions at the systems level may offer new insights into cancer etiology and therapeutic interventions, microbial infections represent a significant, and in many cases preventable, cause of cancer [5]. The molecular interplay between pathogenic microbes and host cells reveals potential targets for therapeutic and prophylactic strategies, such as vaccines, antiviral drugs, and microbiome modulation. As the global cancer burden continues to rise, particularly in regions where infectious diseases are endemic, a deeper understanding of the role of microbes in cancer pathogenesis is essential [6]. This review aims to provide a comprehensive examination of the major oncogenic microbes, their mechanisms of action, and the current state of research into preventing and treating microbe-associated cancers.

Table 1. Major Oncogenic Viruses and Their Mechanisms of Action

Virus	Associated Cancers	Important Oncoproteins	Mechanisms of Carcinogenesis
Human Papillomavirus (HPV)	Cervical, oropharyngeal, anal, penile	E6, E7	Inactivation of p53 and pRb; evasion of apoptosis
Epstein–Barr Virus (EBV)	Burkitt lymphoma, Hodgkin lymphoma, NPC	LMP1, EBNA1–6	NF-κB activation, immune evasion, promotion of proliferation
Hepatitis B Virus (HBV)	Hepatocellular carcinoma	HBx	DNA damage, oxidative stress, immune modulation
Hepatitis C Virus (HCV)	Hepatocellular carcinoma	Core proteins	ROS generation, epigenetic changes, chronic inflammation
HTLV-1	Adult T-cell leukemia/lymphoma	Tax	Cell cycle dysregulation, NF-κB activation

Table 2. Oncogenic Bacteria and Tumorigenic Pathways

Bacterium	Associated Cancer	Important Virulence Factors	Mechanisms of Carcinogenesis
Helicobacter pylori	Gastric carcinoma	CagA, VacA	Chronic gastritis, EMT, ROS-induced DNA damage
Fusobacterium nucleatum	Colorectal cancer	FadA adhesin	β-catenin activation, immune modulation, chronic inflammation

Table 3. Shared Mechanisms of Microbial Carcinogenesis

Mechanism	Description	Examples of Involvement
Chronic Inflammation	Long-term immune activation causing ROS, DNA damage, and cytokine release	H. pylori, HBV, HCV
Immune Evasion	Inhibition of host immune recognition and response	HPV (MHC downregulation), EBV (latency)
Epigenetic Alterations	DNA methylation, histone modifications, and miRNA deregulation	EBV, H. pylori, HCV
Microbiome Dysbiosis	Imbalanced microbial communities influencing tumorigenic pathways	Gut dysbiosis in colorectal cancer

Table 4. Clinical Applications and Preventive Strategies

Strategy	Application	Current Examples
Vaccination	Prevention of oncogenic viral infection	HPV, HBV vaccines
Targeted Therapy	Disruption of microbial oncoprotein function	Antiviral agents (e.g., interferon therapy)
Microbial Biomarkers	Diagnostic and prognostic tools	EBV DNA in nasopharyngeal cancer screening
Microbiota Modulation	Probiotics, antibiotics, FMT for cancer prevention/treatment	Experimental in CRC and immunotherapy support

2. Oncogenic Viruses and Mechanisms of Carcinogenesis

Oncogenic viruses contribute significantly to the global cancer burden, accounting for a substantial portion of infection-associated malignancies. These viruses typically induce cellular transformation through persistent infection, integration into the host genome, and expression of viral oncoproteins that interfere with normal cellular regulatory mechanisms [7]. The following section outlines the principal oncogenic viruses and their mechanisms of carcinogenesis.

2.1 Human Papillomavirus (HPV)

Human Papillomavirus (HPV) is a non-enveloped, double-stranded DNA virus of the Papillomaviridae family. It is one of the most extensively studied oncogenic viruses and is causally linked to nearly all cases of cervical cancer, as well as a significant proportion of anogenital (e.g., vulvar, vaginal, penile, anal) and oropharyngeal cancers. Among over 200 identified HPV genotypes, high-risk types—especially HPV-16 and HPV-18—are most closely associated with malignancy [8]. The oncogenic potential of HPV is primarily mediated through the expression of its early genes E6 and E7. The E6 protein binds to and promotes the degradation of the tumor suppressor protein p53, thereby impairing apoptosis and DNA damage response pathways. Meanwhile, E7 binds to the retinoblastoma protein (pRb), displacing E2F transcription factors and driving unscheduled cell cycle progression. This dual interference with key regulatory pathways leads to genomic instability, accumulation of mutations, and eventual malignant transformation. Persistent infection with high-risk HPV is a critical prerequisite for oncogenesis, underscoring the value of HPV vaccines in cancer prevention.

2.2 Epstein–Barr Virus (EBV)

Epstein–Barr Virus (EBV), a member of the herpesvirus family, infects over 90% of the global population and establishes lifelong latency in B cells. EBV is etiologically linked to a spectrum of malignancies, including Burkitt lymphoma, Hodgkin lymphoma, nasopharyngeal carcinoma, and certain gastric cancers [9]. EBV-induced oncogenesis involves the expression of latent viral proteins such as latent membrane proteins (LMP1, LMP2) and Epstein–Barr nuclear antigens (EBNA1–6). LMP1 mimics a constitutively active receptor in the TNF receptor family, leading to chronic activation of NF-κB, MAPK, and JAK/STAT signaling pathways, all of which promote cell proliferation, survival, and inflammation. LMP2 aids in maintaining latency and confers resistance to apoptosis. The EBNA proteins, particularly EBNA1, are essential for viral genome maintenance and replication within host cells and are also implicated in epigenetic reprogramming. Together, these factors facilitate cellular immortalization and tumor development, particularly in immunocompromised individuals.

2.3 Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV)

Chronic infection with Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) is a major risk factor for hepatocellular carcinoma (HCC), one of the most common cancers globally. HBV is a partially double-stranded DNA virus, while HCV is a single-stranded RNA virus; both target hepatocytes and cause chronic liver disease, which progresses to cirrhosis and cancer over decades [10]. The HBV X protein (HBx) plays a central role in HBV-induced carcinogenesis by modulating multiple signaling pathways, including p53, Wnt/β-catenin, and PI3K/Akt. HBx can inhibit DNA repair, promote oxidative stress, and alter cell cycle progression. Integration of HBV DNA into the host genome can also disrupt host genes and genomic integrity [11]. HCV contributes to carcinogenesis primarily through indirect mechanisms, such as chronic inflammation, oxidative stress, and immune-mediated hepatocyte destruction and regeneration. However, viral proteins such as the HCV core, NS3, and NS5A have also been shown to interfere with host cell signaling, including pathways regulating apoptosis, immune surveillance, and cell cycle control.

2.4 Human T-lymphotropic Virus Type 1 (HTLV-1)

Human T-cell Leukemia Virus Type 1 (HTLV-1) is a retrovirus linked to adult T-cell leukemia/lymphoma (ATLL), an aggressive hematological malignancy. HTLV-1 infection is endemic in certain regions, including Japan, the Caribbean, and parts of Africa and South America [12]. The principal oncogenic driver of HTLV-1 is the Tax protein, a potent transcriptional activator. Tax constitutively activates NF-κB and CREB signaling pathways, leading to aberrant expression of genes involved in cell proliferation, survival, and inflammation. It also impairs DNA repair mechanisms and inactivates tumor suppressor proteins, thereby promoting genomic instability [13]. Another viral protein, HBZ (HTLV-1 bZIP factor), contributes to disease progression by sustaining T-cell proliferation and modulating host immune responses, often working in opposition to Tax to evade immune detection.

3. Oncogenic Bacteria and Tumorigenic Pathways

While viruses are more commonly associated with cancer, certain bacterial species have also been recognized as potent contributors to oncogenesis. These bacteria typically act through persistent infection, chronic inflammation, production of genotoxins, and disruption of host cellular pathways.

3.1 Helicobacter pylori

Helicobacter pylori is a Gram-negative, microaerophilic bacterium that colonizes the human stomach. It is the most well-established bacterial carcinogen, classified as a Group 1 carcinogen by the World Health Organization (WHO), and is a major risk factor for gastric adenocarcinoma and mucosa-associated lymphoid tissue (MALT) lymphoma [14]. *H. pylori* induces chronic gastritis and mucosal damage, creating a carcinogenic environment over time. A key virulence factor is the *cag* pathogenicity island, which encodes a type IV secretion system used to inject the CagA protein into host epithelial cells. Once inside the cell, CagA undergoes phosphorylation and interacts with SHP-2 phosphatase and other signaling molecules, leading to aberrant activation of pathways such as MAPK/ERK, PI3K/Akt, and Wnt/β-catenin [15]. These disruptions promote cell proliferation, migration, and epithelial–mesenchymal transition (EMT)—a critical step in cancer progression. In addition, *H. pylori* generates reactive oxygen species (ROS) and reactive nitrogen species (RNS), causing oxidative DNA damage and contributing to genomic instability. Epigenetic modifications, such as hypermethylation of tumor suppressor gene promoters, further compound its tumorigenic potential.

3.2 Fusobacterium nucleatum

Fusobacterium nucleatum is an anaerobic, Gram-negative bacterium commonly found in the oral cavity. In recent years, it has emerged as a significant player in colorectal cancer (CRC). Elevated levels of *F. nucleatum* DNA have been detected in tumor

tissues compared to adjacent normal mucosa, and its abundance correlates with poor prognosis and chemoresistance [16]. The bacterium contributes to carcinogenesis through multiple mechanisms. Its FadA adhesin binds to E-cadherin on colorectal epithelial cells, activating β-catenin signaling and upregulating oncogenes such as c-Myc and cyclin D1, leading to increased cell proliferation. *F. nucleatum* also modulates the tumor immune microenvironment by inhibiting natural killer (NK) cell cytotoxicity and promoting tumor-associated macrophages (TAMs) and myeloid-derived suppressor cells (MDSCs), which suppress antitumor immunity. Its lipopolysaccharide (LPS) stimulates inflammatory pathways, notably NF-κB, further fueling a pro-carcinogenic niche.

4. Shared Mechanisms of Microbial Carcinogenesis

Despite their diversity, oncogenic microbes share several converging mechanisms that contribute to tumor initiation, promotion, and progression. These include chronic inflammation, immune evasion, epigenetic reprogramming, and microbiome disruption.

4.1 Chronic Inflammation

One of the most consistent hallmarks of microbe-associated cancer is persistent inflammation. Chronic infection by oncogenic pathogens leads to the sustained production of inflammatory mediators such as interleukins (e.g., IL-6, IL-1β), tumor necrosis factor-alpha (TNF-α), and prostaglandins. These factors activate signaling pathways like STAT3, NF-κB, and COX-2, promoting cell survival, proliferation, angiogenesis, and mutagenesis, immune cells recruited during infection release ROS and RNS, which directly damage host DNA [17]. This ongoing oxidative stress results in base modifications, DNA strand breaks, and mutational signatures commonly observed in tumors. Repeated tissue regeneration due to inflammation-induced injury further increases the likelihood of accumulating oncogenic mutations.

4.2 Immune Evasion

To establish persistent infections, many oncogenic microbes evolve mechanisms to evade immune surveillance. For instance, viruses like HPV and EBV downregulate major histocompatibility complex (MHC) class I molecules, reducing antigen presentation and T-cell recognition. Others, such as HCV and *F. nucleatum*, promote immunosuppressive environments by inducing regulatory T cells (Tregs), secreting IL-10 and TGF-β, or exhausting cytotoxic T cells via PD-1/PD-L1 pathways [18]. This immune suppression facilitates long-term pathogen persistence, allowing time for genetic and epigenetic changes to accumulate in host cells.

4.3 Epigenetic Alterations

Microbial infections can induce profound changes in the host epigenome, which may lead to oncogenesis without altering the DNA sequence. For example, *H. pylori* infection is associated with hypermethylation of CpG islands in tumor suppressor gene promoters such as *CDH1* and *p16INK4a*, resulting in gene silencing. Viruses like HBV and HPV can also influence histone modification patterns and microRNA (miRNA) expression [19]. These epigenetic modifications contribute to altered gene expression profiles that favor cell proliferation, survival, and evasion of growth suppression.

4.4 Microbiome Dysbiosis

Emerging evidence suggests that cancer risk may be influenced not only by individual pathogens but also by overall microbiome composition. Dysbiosis—an imbalance in microbial diversity and function—can disrupt mucosal barrier integrity, impair immune homeostasis, and alter host metabolism. In the gut, for example, reduced levels of protective commensals and increased abundance of pro-inflammatory species such as *F. nucleatum* or *Escherichia coli* producing colibactin (a genotoxin) have been linked to colorectal tumorigenesis. Microbiome dysbiosis also affects the efficacy of cancer immunotherapy and chemotherapy, highlighting its significance in cancer development and treatment response [20].

5. Clinical Implications and Prevention

Understanding the role of oncogenic microbes in tumorigenesis has significantly impacted approaches to cancer prevention, diagnosis, and therapy [21]. By targeting the microbial components of cancer development, it becomes possible to interrupt the carcinogenic process at early stages, improve diagnostic precision, and personalize treatment strategies.

5.1 Vaccination

Vaccination remains the most effective tool for preventing virus-induced cancers. Prophylactic vaccines against Human Papillomavirus (HPV) and Hepatitis B Virus (HBV) have already demonstrated significant public health benefits.

- HPV vaccines (e.g., Gardasil and Cervarix) target high-risk types such as HPV-16 and HPV-18, which are responsible for the majority of cervical, anal, and oropharyngeal cancers. Vaccination programs have led to dramatic declines in HPV infection rates and cervical precancers, particularly in countries with high vaccine coverage.
- HBV vaccines, part of standard infant immunization in many regions, have been instrumental in reducing chronic HBV infection rates and subsequent liver cancer risk, especially in endemic areas such as parts of Asia and Africa.
- Efforts are ongoing to develop vaccines against other oncogenic viruses such as Epstein–Barr Virus (EBV) and Hepatitis C Virus (HCV), although challenges remain due to viral latency and genetic variability [22].

5.2 Targeted Therapy

Insights into the molecular mechanisms of microbial carcinogenesis have opened new avenues for targeted therapies. For instance:

- **Antiviral therapies**: Suppressing viral replication in chronic HBV or HCV infections can significantly reduce the incidence of hepatocellular carcinoma. Nucleos(t)ide analogs (e.g., entecavir, tenofovir) and direct-acting antivirals (DAAs) for HCV have transformed liver cancer prevention strategies [25].
- **Microbiome modulation**: In bacterial-driven cancers, approaches such as antibiotics, probiotics, prebiotics, or fecal microbiota transplantation (FMT) are under investigation to shift the microbiome composition toward a protective profile.
- **Immune checkpoint inhibitors**: Some oncogenic microbes alter the tumor microenvironment to evade immune surveillance. Immunotherapy, particularly immune checkpoint inhibitors (e.g., anti-PD-1, anti-CTLA-4), has shown promise in reversing immune exhaustion in cancers associated with chronic infection and inflammation.

- **Molecular inhibitors**: Targeting microbial proteins or host pathways hijacked by pathogens (e.g., inhibitors of NF-κB or STAT3 in EBV-associated cancers) represents a frontier in precision oncology [23].

5.3 Screening and Diagnostics

Microbial components serve as promising biomarkers for early cancer detection, offering potential for non-invasive, accurate diagnostics:

- **EBV DNA** in plasma is used as a biomarker for early detection and prognosis of **nasopharyngeal carcinoma (NPC)**, particularly in endemic regions like Southeast Asia.
- **Fusobacterium nucleatum** detection in stool samples or tumor tissues is being investigated as a diagnostic marker for **colorectal cancer (CRC)**, especially in early-stage tumors or those with poor prognosis.
- **HPV DNA testing** is now a primary screening tool in many cervical cancer prevention programs, offering higher sensitivity than traditional cytology (Pap smears).
- **H. pylori serology and urea breath tests** are used to identify individuals at risk for **gastric cancer**, particularly in regions with high incidence rates [26]. Eradication of H. pylori has been shown to reduce gastric cancer risk in these populations, integrating microbial biomarkers into screening programs may improve cancer detection at earlier, more treatable stages and enable population-level stratification for preventive interventions [24].

6. Challenges and Future Directions

Despite significant progress in understanding the role of microbes in cancer, several challenges hinder the full translation of this knowledge into clinical practice. Future advancements will rely heavily on interdisciplinary research and the integration of emerging technologies to unravel the complex interplay between hosts and oncogenic microorganisms.

6.1 Limitations in Causal Inference

While the oncogenic potential of certain microbes—such as HPV, EBV, HBV, HCV, and H. pylori—is well established, many other microbe–cancer associations remain correlative rather than causal. Disentangling correlation from causation is complicated by factors such as the diversity of microbial communities, host genetics, environmental exposures, and co-infections. Establishing definitive causal links requires longitudinal cohort studies, animal models, and functional validation using genetic and molecular tools.

6.2 Complexity of Microbiome–Host Interactions

The human microbiome is highly dynamic and context-dependent. Its influence on carcinogenesis is modulated by host immunity, diet, age, medications, and lifestyle factors. This complexity makes it difficult to identify universal microbial signatures of cancer [3]. Additionally, microbial community structure and function, rather than the presence of individual species, may be more relevant to oncogenesis. Integrative approaches combining metagenomics, transcriptomics, proteomics, and metabolomics are essential to capture this multidimensional complexity and identify functionally relevant microbial interactions.

6.3 Microbiome-Based Therapeutics: Opportunities and Risks

Therapeutic manipulation of the microbiome through probiotics, prebiotics, antibiotics, phage therapy, or fecal microbiota transplantation (FMT) holds promise in cancer prevention and treatment [8]. However, these strategies present significant challenges:

- **Lack of standardization**: Formulations, dosing, and delivery routes vary widely across studies, making reproducibility and comparison difficult.
- **Safety concerns**: Altering the microbiome could inadvertently promote the growth of pathogenic strains or disrupt beneficial microbial communities.
- **Regulatory hurdles**: Microbiome-based therapies fall under complex regulatory frameworks and require rigorous testing for safety, efficacy, and long-term outcomes.

Rigorous clinical trials and mechanistic studies are needed to validate the therapeutic potential of these interventions.

6.4 Emerging Technologies and Research Priorities

Advances in single-cell sequencing, CRISPR-based gene editing, spatial transcriptomics, and artificial intelligence (AI)-driven bioinformatics are revolutionizing our ability to study microbial oncogenesis. These tools enable researchers to:

- Precisely map microbial gene expression and interactions in the tumor microenvironment.
- Identify novel oncogenic strains or microbial metabolites involved in tumor promotion.
- Predict host–microbe responses and personalize interventions based on host microbiome profiles.

Future research should prioritize:

- Functional characterization of lesser-known microbial candidates implicated in cancer.
- Exploration of non-gastrointestinal microbiomes (e.g., oral, urogenital, skin) in tumorigenesis.
- Development of multi-omic, spatial, and temporal datasets to understand the dynamics of microbe–host–tumor interactions.

7. Conclusion

Oncogenic microbes, including specific viruses and bacteria, play a significant role in global cancer incidence through a range of molecular and cellular mechanisms. These pathogens promote carcinogenesis by inducing chronic inflammation, interfering with host immune responses, and directly altering host genomic integrity through the action of viral oncoproteins, bacterial toxins, and epigenetic modulators. For example, high-risk strains of Human Papillomavirus (HPV) and Hepatitis B Virus (HBV) have well-characterized mechanisms of inactivating tumor suppressor genes, while bacteria such as *Helicobacter pylori* and *Fusobacterium nucleatum* contribute to gastrointestinal tumorigenesis through inflammation and disruption of cellular signaling. Understanding these complex mechanisms is vital for the development of targeted prevention and treatment strategies. Vaccines against HPV and HBV have already demonstrated tremendous success in reducing infection rates and related cancers. Further, microbial biomarkers are increasingly being used in diagnostics and risk stratification. As microbiome research advances, therapeutic interventions such as microbiota modulation or oncolytic viral therapies hold great promise. Nevertheless, many challenges remain, including establishing causality in emerging microbial–cancer associations and navigating the complexity of host–microbiome interactions. A comprehensive, multidisciplinary approach that incorporates microbiology, immunology, oncology, genomics, and systems biology is essential to unlock the full potential of microbe-targeted cancer prevention and therapy.

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