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Review

# Oncology Meets Virology: Exploring Viral Contributions to Cancer Development and Therapy

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## Abstract

Viruses contribute to a substantial fraction of human cancers globally, with an estimated 12–15% of all cancer cases being linked to viral infections. This review synthesizes the current understanding of oncogenic viruses, their mechanisms of viral carcinogenesis, and the types of cancers associated with different viral pathogens. We explore the evolving therapeutic landscape, including vaccines, immunotherapies, and oncolytic virotherapy, and discuss the latest advances in clinical trials. The review also examines the challenges of viral cancer treatment, such as immune evasion and resistance to therapies, and looks forward to promising future directions in personalised medicine, advanced viral therapies, and drug discovery. The intersection of virology and oncology offers new opportunities for cancer prevention and treatment that could transform patient outcomes globally.

**Keywords:** virotherapy; oncogenic viruses; personalised medicine; immunotherapy; carcinogenesis

## 1. Introduction

The field of viral oncology has evolved dramatically in recent years, shedding light on the substantial role viruses play in the initiation and progression of cancer. Historically, viruses were considered primarily pathogens that caused acute or chronic infections. However, as scientific understanding has progressed, it has become clear that several viruses, both DNA and RNA types, can drive oncogenesis. The relationship between viruses and cancer is complex and multifaceted, ranging from direct genetic integration to modulation of immune responses and cellular signaling pathways [1,2].

The epidemiology of virus-associated cancers highlights the need for global preventive measures. Human papillomavirus (HPV), for example, is responsible for over 99% of cervical cancers, with approximately 311,000 deaths globally in 2020 [1,3]. Hepatitis B virus (HBV) and hepatitis C virus (HCV) contribute to a significant proportion of liver cancer cases, with liver cancer being the second-leading cause of cancer-related deaths worldwide [4,5]. As viruses play such a central role in the etiology of cancer, the study of viral mechanisms offers crucial insights into cancer biology, paving the way for innovative treatments and preventive strategies.

Viral oncogenesis is an area of active research, with advances in molecular biology, immunology, and clinical therapeutics driving much of the recent progress. This review focuses on understanding how viruses contribute to cancer, detailing the mechanisms of viral carcinogenesis, the types of cancers associated with specific viruses, current therapeutic approaches, and the challenges and future directions in the field of viral oncology.

## 2. How Viruses Contribute to Cancer

Oncogenic viruses exploit various mechanisms to induce cancer, including genomic instability, immune evasion, chronic inflammation, and epigenetic alterations. Viruses often integrate their genetic material into the host genome or express oncoproteins that directly interfere with the cell cycle, DNA repair, or apoptosis pathways [1,2,6].

### *Genomic Integration and Oncogene Expression*

For DNA viruses like HPV and HBV, integration into the host genome is a common mechanism of viral oncogenesis. In HPV-associated cancers, particularly cervical cancer, the viral oncoproteins E6 and E7 are key drivers of tumorigenesis. E6 binds to and promotes the degradation of the tumor suppressor protein p53, while E7 binds to the retinoblastoma (Rb) protein, preventing it from inhibiting the E2F transcription factor. This disruption of the cell cycle regulatory machinery results in uncontrolled cell proliferation [7,8]. In the case of HBV, the HBx protein interferes with cellular pathways involved in DNA repair, apoptosis, and cell growth, leading to increased mutagenesis and genomic instability, which can eventually result in liver cancer [6,9].

### *Chronic Inflammation and Immunosuppression*

Chronic inflammation is a hallmark of many viral infections and plays a central role in virus-induced carcinogenesis. HCV and HBV are prime examples, where chronic infection leads to persistent liver inflammation, fibrosis, and cirrhosis. Over time, these changes foster an environment conducive to tumor formation. The inflammatory response leads to the production of reactive oxygen and nitrogen species, which cause DNA damage and mutagenesis, promoting the initiation of cancer [5,10].

Furthermore, viruses have evolved sophisticated mechanisms to evade the immune system. Epstein-Barr virus (EBV) and Kaposi sarcoma-associated herpesvirus (KSHV) both exploit immune evasion strategies to establish persistent infections and promote oncogenesis. EBV, for instance, can downregulate major histocompatibility complex (MHC) molecules, impairing antigen presentation and allowing the virus to persist undetected by the immune system [11,12].

### *Epigenetic Reprogramming*

Viruses can also cause epigenetic alterations that contribute to cancer development. EBV has been shown to modulate host chromatin through its latent proteins, resulting in the silencing of tumor suppressor genes and activation of pro-oncogenic pathways [13]. HPV and KSHV can alter DNA methylation patterns and histone modifications in host cells, destabilizing the genome and favoring oncogenesis [14,15].

The ability of viruses to manipulate both the host's genetic and epigenetic landscape makes them powerful drivers of cancer. These mechanisms not only initiate tumorigenesis but also contribute to the maintenance and progression of cancer by facilitating immune evasion, genomic instability, and uncontrolled cell growth.

## 3. Types of Cancers Caused by Different Viruses

Oncogenic viruses are linked to a variety of cancer types, and understanding the virus-cancer associations is key to developing targeted prevention and therapeutic strategies.

### *Human Papillomavirus (HPV)*

HPV is the most well-known and studied oncogenic virus. High-risk HPV types, especially HPV-16 and HPV-18, are responsible for the majority of cervical cancers and also play a significant role in oropharyngeal, anal, penile, and vulvar cancers [7,8]. The viral oncoproteins E6 and E7 inactivate p53 and Rb, respectively, leading to uncontrolled proliferation and evasion of apoptosis.

### *Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV)*

HBV and HCV are leading causes of hepatocellular carcinoma (HCC). Chronic HBV infection leads to liver inflammation and fibrosis, while HBx induces genomic instability. HCV infection triggers oxidative stress and inflammatory responses, promoting mutagenesis [6,10,16].

### *Epstein-Barr Virus (EBV)*

EBV is implicated in Burkitt lymphoma, Hodgkin lymphoma, nasopharyngeal carcinoma, and some gastric cancers. EBV latent proteins (LMP1, LMP2) promote cell survival and proliferation, facilitating tumor growth [11,12,17].

### *Human T-cell Leukemia Virus Type 1 (HTLV-1)*

HTLV-1 causes adult T-cell leukemia/lymphoma (ATLL), with the viral tax protein driving proliferation and survival of T cells [18].

### *Kaposi Sarcoma-Associated Herpesvirus (KSHV)*

KSHV is associated with Kaposi's sarcoma, primary effusion lymphoma, and multicentric Castleman disease. The viral latency-associated nuclear antigen (LANA) promotes cell survival and modulates immune responses [12,15].

## **4. Current Status of Research and Treatment**

### *Prophylactic Vaccines*

Vaccines have been transformative in viral oncology. HPV vaccines effectively prevent cervical and other HPV-associated cancers, while HBV vaccines reduce liver cancer incidence, particularly in endemic regions [3,9,19]. Development of vaccines for EBV and HCV remains challenging due to viral latency and high mutation rates, though antiviral therapies for HCV are highly effective in preventing progression to HCC [5,20].

### *Oncolytic Virotherapy*

Oncolytic viruses selectively infect and destroy tumor cells. Herpes simplex virus-based therapies (e.g., talimogene laherparepvec, T-VEC) have demonstrated durable responses in melanoma and are being tested in combination with immune checkpoint inhibitors [21,22]. Other engineered viruses deliver immunostimulatory genes or tumor antigens to enhance anti-tumor immunity [21,23].

### *Targeted Therapies and Immunotherapy*

Virus-induced cancers are increasingly targeted with immunotherapies, such as adoptive T-cell therapy or checkpoint inhibitors, particularly in EBV- and HPV-associated malignancies [12,17,23]. Small-molecule inhibitors targeting viral oncoproteins are also being explored, including drugs that inhibit HPV E6/E7 interactions with tumor suppressors [7,14].

## **5. Challenges**

Key challenges in viral oncology include viral immune evasion, tumor heterogeneity, resistance to therapy, and the difficulty of developing vaccines for latent or highly variable viruses [1,11,14]. Additionally, the long latency period of many virus-associated cancers complicates early detection and preventive intervention.

## **6. Future Prospects**

Future directions in viral oncology include the integration of precision medicine with virology, development of combination therapies, novel antiviral vaccines, and oncolytic virus engineering. Epigenetic therapy targeting virus-driven chromatin alterations is also a promising area [13,14]. Advances in genome editing, high-throughput drug screening, and immunotherapy may revolutionise the treatment landscape for virus-associated cancers [23,24,25].

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