MICROBIAL TRIGGERS OF CARCINOGENESIS THE INTERSECTION OF INFECTION, HISTOPATHOLOGY, AND TUMOR BIOLOGY

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Abstract:

Cancer is conventionally seen as a hereditary disorder; nonetheless, a substantial proportion of human malignancies originate from microbial infections, especially viruses. Oncogenic viruses cause persistent infection, change cellular genomes, disrupt cell-cycle regulation, and encourage unchecked growth. Infectious agents include human papillomavirus (HPV), Epstein-Barr virus (EBV), hepatitis B and C viruses (HBV, HCV), human T-cell leukemia virus type 1 (HTLV-1), Kaposi's sarcoma-associated herpesvirus (KSHV), and Merkel cell polyomavirus (MCV) are responsible for around 15–20% of all cancer cases worldwide. Comprehending their mechanisms facilitates the development of vaccines and antiviral therapies and offers profound insights into tumor biology. The microbiological and molecular mechanisms by which these viruses contribute to oncogenesis are examined in this review.

Overview:

Oncovirology is the study of how microbes have a role in the development of cancer. It is a science that combines microbiology and oncology. Carcinogenesis is traditionally linked to mutations induced by chemicals or radiation; nevertheless, specific pathogenic pathogens can also trigger analogous molecular disturbances. These pathogens stay in the host, add their own DNA, and change the way cells work to make sure they can survive and reproduce, often at the expense of regular cell control. Preventive vaccinations like the HPV and HBV vaccines, which lower the incidence of liver and cervical cancers, respectively, were made possible by the realization that certain viruses can cause cancer.

1. Mechanisms of Viral Oncogenesis

Oncogenic viruses facilitate cancer by one or more of the following mechanisms:

1. Insertional Mutagenesis: Viral DNA becomes part of the host genome and which can turn off tumor suppressor genes or turn on proto-oncogenes.

HPV integration adjacent to the E6 and E7 genes in cervical epithelium facilitates the degradation of p53 and Rb proteins, hence abolishing cell-cycle regulation.

2. Viral Oncoprotein Expression: Viral genes directly encode proteins that disrupt host regulatory mechanisms.

EBV's LMP1 functions as a constitutively active receptor, perpetually transmitting growth impulses to B-cells.

3. Chronic Inflammation and Immune Evasion — Long-term infections cause oxidative damage to DNA, cell regeneration, and a weakened immune system.

Chronic HBV/HCV infection causes persistent hepatocyte turnover, resulting in fibrosis and the accumulation of mutations.

4. Inhibition of Apoptosis: A lot of viruses prevent programmed cell death in order to keep infected cells alive, which permits the development of carcinogenic mutations.

KSHV encodes vBcl-2, a viral homolog that inhibits apoptosis in endothelial cells.

2. Major Oncogenic Viruses and Associated Cancers

2.1 Human Papillomavirus (HPV)

• Type: DNA virus (Papillomaviridae family)

• How it spreads: sexual contact and skin-to-skin contact

• Cancers linked to it: cervical carcinoma, anal cancer, oropharyngeal carcinoma, and penile cancer

• Mechanism: The viral oncoproteins E6 and E7 deactivate p53 and Rb, which makes the genome unstable.

• Prevention: Vaccination against HPV (bivalent, quadrivalent, and nonavalent vaccinations) is a big success in the fight against cancer around the world.

2.2 Epstein–Barr Virus (EBV)

• Type: DNA virus (Herpesviridae family)

• Transmission: Saliva (“kissing disease”)

• Related cancers: Burkitt's lymphoma, Hodgkin's lymphoma, nasopharyngeal carcinoma, post-transplant lymphoproliferative disease.

• Mechanism: Latent membrane protein 1 (LMP1) mimics tumor necrosis factor receptor signaling, boosting proliferation and blocking apoptosis.

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

• Type: HBV is a DNA virus, whereas HCV is an RNA virus.

• How it spreads: by blood, sexual contact, and vertical transmission.

• Related cancers: Hepatocellular carcinoma (HCC)

• Mechanism: persistent inflammation, oxidative stress, and direct incorporation (HBV DNA). HCV facilitates carcinogenesis through the core protein and NS5A, impairing apoptosis and lipid metabolism.

• To avoid getting HCC, get vaccinated against HBV and take antiviral drugs (such sofosbuvir for HCV).

2.4 Human T-cell Leukemia Virus Type 1 (HTLV-1)

• Type: RNA virus (Retroviridae family)

• Transmission: Sexual, blood, lactation

• Associated cancers: Adult T-cell leukemia/lymphoma (ATLL)

• Mechanism: Tax and HBZ viral proteins turn on NF-κB signaling and stop DNA repair, which makes the genome unstable.

2.5 Kaposi's Sarcoma-associated Herpesvirus (KSHV / HHV-8)

• Type: DNA virus

• How it spreads: sexual contact, saliva, organ donation

• Cancers it is linked to: Kaposi's sarcoma, primary effusion lymphoma, and multicentric Castleman's illness

• Mechanism: Viral proteins such as vGPCR and vBcl-2 facilitate angiogenesis and cellular viability.

• Clinical feature: Predominantly observed in immunocompromised individuals (e.g., AIDS).

2.6 Merkel Cell Polyomavirus (MCV)

• Type: DNA virus

• How it spreads: likely by skin contact

• Cancer it is linked to: Merkel cell carcinoma (a rare skin cancer)

• How it works: The viral big T-antigen breaks down the tumor suppressors p53 and Rb, which makes cells divide uncontrollably.

3. Diagnostic Techniques in Oncovirology

Histology, molecular biology, and immunology are all used in modern diagnostic tools:

• Polymerase Chain Reaction (PCR): Finds viral DNA/RNA in tissues, like HPV DNA testing for cervical screening.

• Immunohistochemistry (IHC): Finds viral antigens, like LMP1 in malignancies related to EBV.

• In Situ Hybridization (ISH): Finds viral nucleic acids in cancer cells. • Serology: checks for antibodies, like anti-HBs for immunity to HBV.

• Next-Generation Sequencing (NGS): Finds viral genomes that are integrated and mutational profiles.

4. Ways to Prevent and Treat

1. **Vaccination**:

• HPV vaccines stop people from getting infected with high-risk strains (types 16 and 18).

• The HBV vaccine greatly lowers the number of cases of liver cancer.

2. **Antiviral Therapy:**

• Interferon-based medicines and direct-acting antivirals (DAAs) stop viruses from making copies of themselves (for example, HCV).

1. **Screening and Early Detection:**

• Regular Pap smears, HBV/HCV testing, and EBV serology improve prognosis. 4. **Immunotherapy:**

• Immune checkpoint drugs (such PD-1/PD-L1 blockers) look like they could work against cancers caused by viruses.

5. New Trends in Oncovirology

• Scientists are looking at using CRISPR-Cas gene editing to cut out viral genomes from cells that are already infected.

• AI-based histopathology can find little viral patterns in the shape of tumors.
• Researchers are looking at how bacteria and viruses interact with each other, which could make viral oncogenesis worse.

• Oncolytic viruses are being made to treat tumors by specifically killing tumor cells.

Conclusion

The microbiological approach of cancer enhances our comprehension beyond genes and mutations. Viruses, even though they are little and simple, can change the machinery of cells in ways that can lead to cancer. After years of research, these findings have turned into public health wins, such immunizations that stop millions of tumors every year. Combining molecular precision, immunologic knowledge, and preventative medicine is the best way to get rid of all malignancies caused by infections in the future of oncovirology.

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