

MICROBIOLOGY COURSE MATERIAL

Semester - III

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CC5: UNIT 4: PART A: VIRUS & CANCER

B.Sc (HONOURS) MICROBIOLOGY (CBCS STRUCTURE)
SEMESTER – III
CC5: UNIT – 4: PART- A
VIRUSES & CANCER

❖ **Oncogenic Viruses**

Viruses are the intracellular pathogens that reproduce only in the living cell and manipulate the cellular machinery to produce more viruses. Viral replications can affect cellular genes of the host in multiple cancerous ways. An oncovirus is a virus that can cause cancer. Viruses account for about 20% of total human cancer cases. Although many viruses can cause various tumors in animals, only seven of them are associated with human cancers and are currently considered oncogenic viruses. During the viral replication process, certain virus's DNA or RNA affects the host cell's genes in ways that may cause it to become cancerous. These viruses are known as oncogenic viruses, meaning viruses that cause or give rise to tumors. Multiple viruses from very different families are already known to be connected with cancer in humans. Studying these cancer causing viruses and discovering new ones, may lead to vaccines and other approaches that prevent or treat certain human cancers in the future. Although it may seem appropriate to lump all cancer causing viruses into one group it would not be accurate. Each virus is a unique type that together represents a variety of virus families with different genomes and replication cycles.

It is important to note that the process from the initial viral infection to tumor formation is slow and inefficient; only a small percentage of viral infections progress to cancer years or decades after the initial infection. Other factors may increase the chance of cancer including immune system complications, cell mutations, exposure

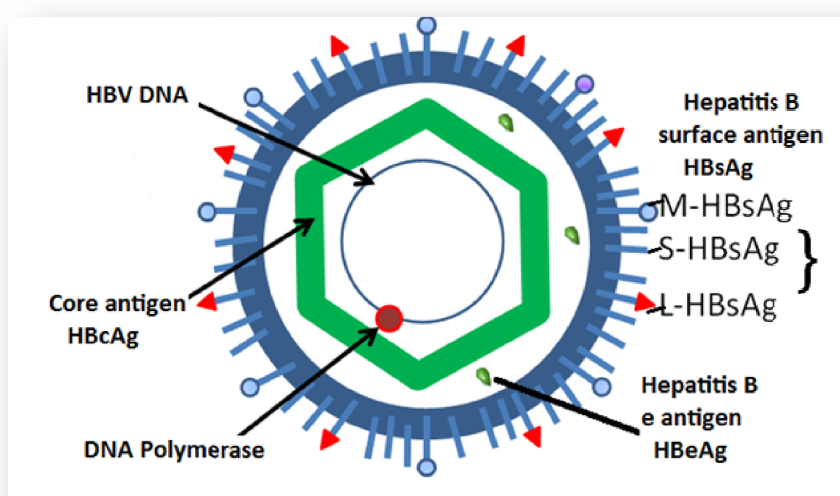
to cancer causing agents and hereditary susceptibility. The viruses now known or suspected of being linked to cancer in humans include:

- ✚ Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Human Papilloma Virus (HPV), Epstein Barr Virus (EBV), Human Herpes Virus 8 (HHV8), Merkel Cell Polyomavirus (MCPyV), and HTLV-1.
- ✚ HBV and HCV cause approximately 80% of Hepatocellular Carcinoma (HCC), the most common cancer of the liver.
- ✚ High-risk HPV strains are the major causes of cervical cancer and other anogenital neoplasms as well as a significant proportion of head and neck tumors.
- ✚ EBV is associated with Nasopharyngeal Carcinoma, Hodgkin's Lymphoma, and Burkitt's Lymphoma.
- ✚ HHV8 (also called Kaposi's Sarcoma-associated Herpes Virus, KSHV) is responsible for Kaposi's sarcoma often found in patients with acquired immunodeficiency syndrome (AIDS).
- ✚ MCPyV causes Merkel Cell Carcinoma and HTLV-1 is the causative agent of adult T-cell Lymphoma.

❖ Hepatitis B Virus (HBV) & Hepatitis C Virus (HCV)

HBV and HCV can cause a liver infection that can sometimes lead to liver cancer. You pick up these viruses if you share needles used to inject drugs, have unprotected sex, or get a transfusion with contaminated blood. Doctors treat HBV and HCV infections with medicine. You can often get rid of HCV after a few months of treatment. Medication doesn't cure HBV, but it can lower the chance of liver damage and liver cancer.

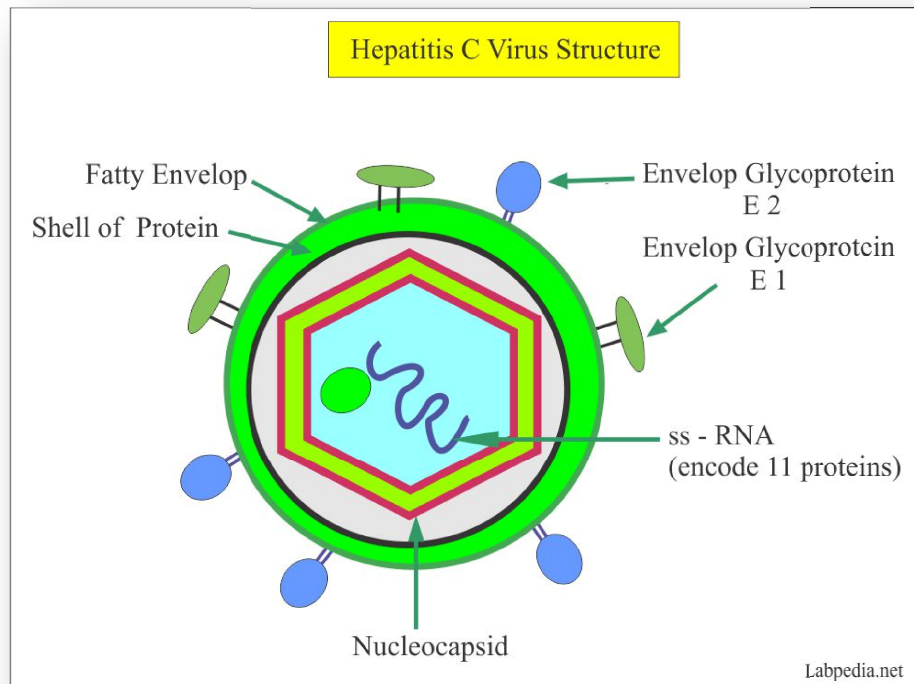
There's a vaccine to prevent HBV, but not HCV. Those with higher chances of getting HBV should get vaccinated. That includes people who have HIV, inject illicit drugs, or are health care workers. HBV and HCV are two types of viruses that cause viral hepatitis, a type of liver infection. Hepatitis A can also cause viral hepatitis but HBV and HCV are known to cause long term infections that increase chances of liver cancer. Worldwide, most liver cancers are caused by HBV or HCV.



Hepatitis B Virus Structure

Hepatitis B virus, is known to cause flu like symptoms and jaundice, or yellowing of the eyes and skin. Most people with HBV infection recover completely and are not chronic carriers of the virus. Hepatitis C infection may not cause any symptoms and is more likely to be chronic, which can lead to liver damage or even cancer.

Antiviral drugs are available to treat people with Hepatitis B and C. There is also a preventative but not therapeutic vaccine available for Hepatitis B, which is most commonly given to people who are at risk of contracting the virus, such as health care workers. There is no vaccine available for the Hepatitis C virus.

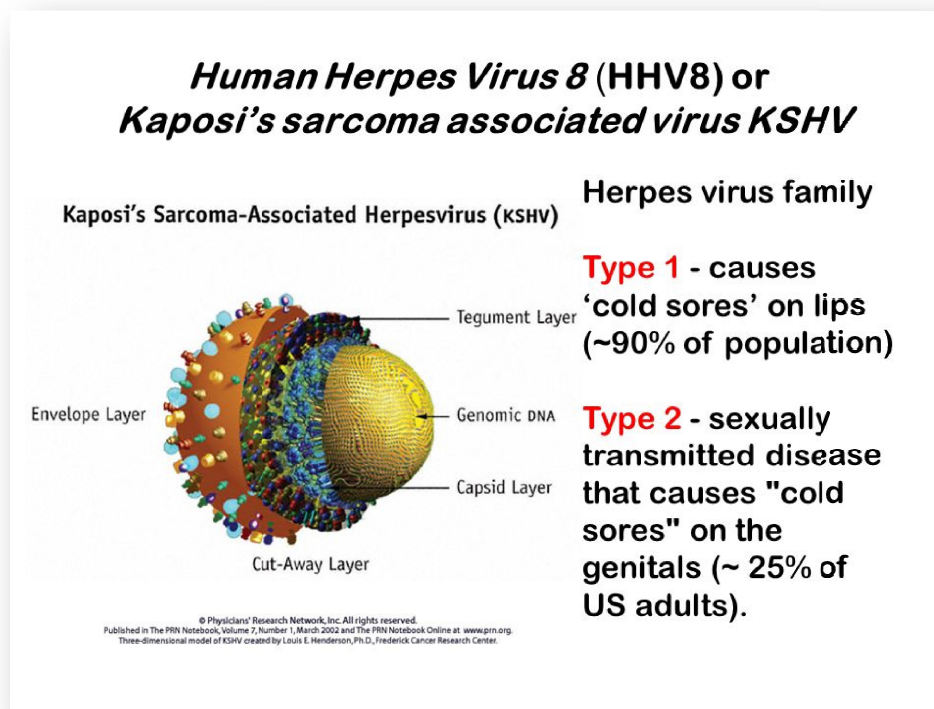


❖ Kaposi Sarcoma Associated Herpes Virus (KSHV)

KSHV is a Herpes Virus that can cause Kaposi sarcoma, a cancer of the blood vessels, as well as two types of lymphoma. You're more likely to get cancer from KSHV if you have a weakened immune system because you had an organ transplant, get chemotherapy, or have AIDS. The virus can be spread during sex, and also through blood and saliva.

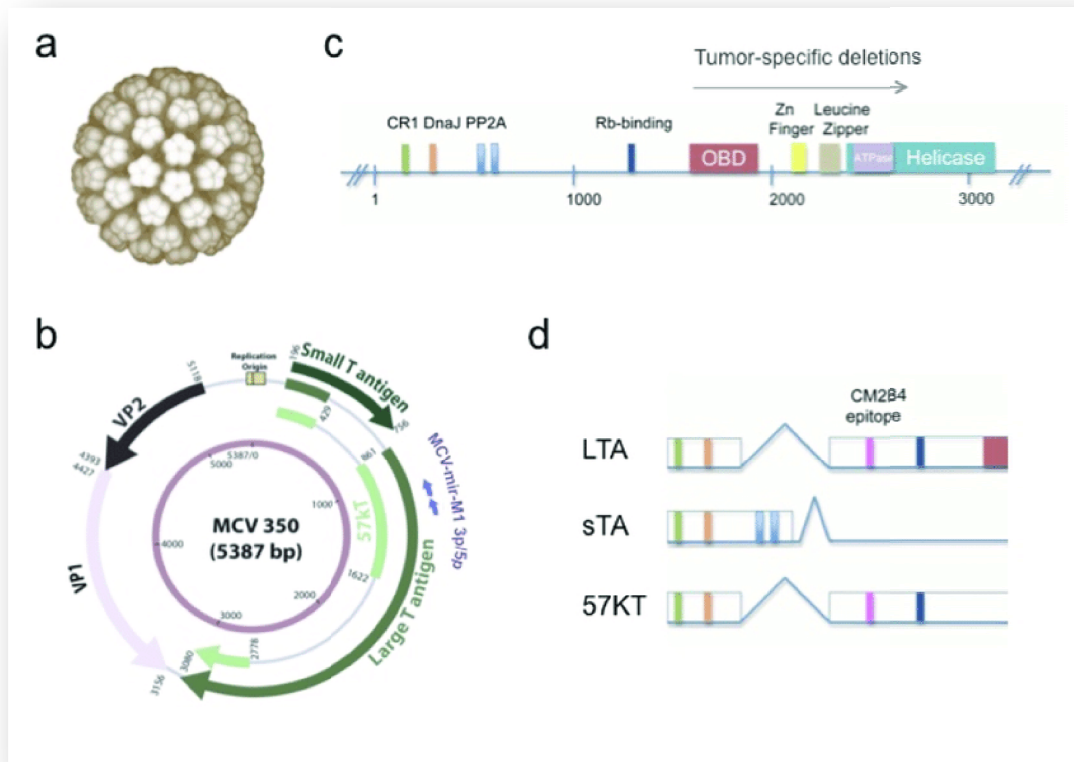
The Human Herpes Virus 8 is also known as Kaposi Sarcoma (KS) associated Herpes Virus (KSHV) and has been found in rare slow growing cancerous tumors that appear as reddish-purple or blue-brown underneath the skin known as KS. This virus is transmitted sexually and is present in about 10% of the US population, but the HHV-8 virus does not appear to cause disease in most healthy individuals. People who develop KS usually have a weakened immune system from the Human Immunodeficiency Virus (HIV) or are taking immune suppression medication. Like

other herpes viruses that cause cold sores or chicken pox, HHV-8 infections never go away. Researchers are still trying to determine how HHV-8 contributes to the development of Kaposi sarcoma.



❖ Merkel Cell Polyomavirus (MCV)

MCV is a common virus that infects the skin. It usually doesn't cause symptoms or lead to cancer. But in some people, MCV causes a rare skin cancer called Merkel Cell Carcinoma.



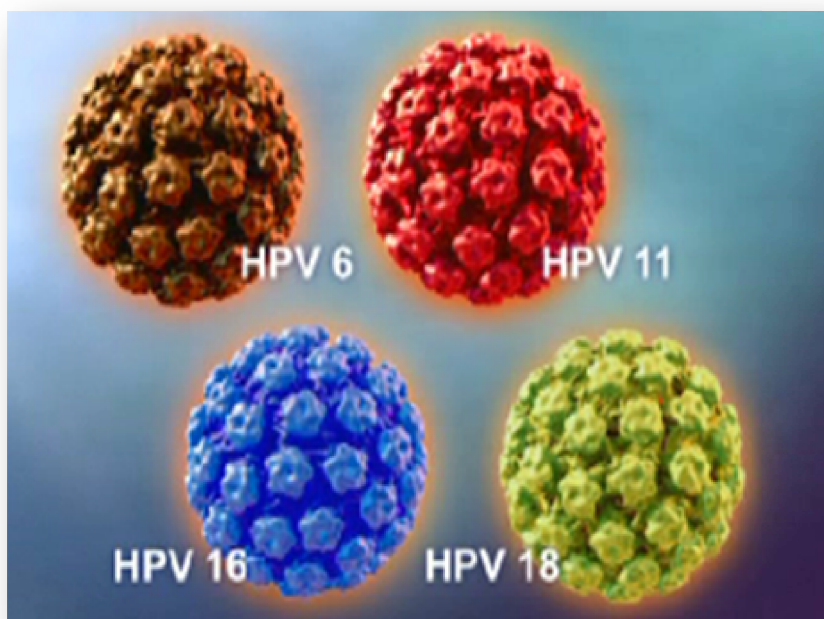
Structure of Merkel Cell Polyomavirus

❖ Human Papilloma Virus (HPV)

HPV is a group of more than 200 viruses, and at least a dozen of them can cause cancer. HPV spreads during vaginal or anal sex. HPV often goes away on its own and doesn't cause any health problems. Some people stay infected, though. If they have the HPV that causes cancer, it can lead to cancers of the cervix, vulva, vagina, penis, anus, tonsils, or tongue. HPV vaccines can keep you from getting infected with the virus. Specific Human Papilloma Viruses are known to cause cervical cancer, which is the second most common cancer among women worldwide. In the United States, cervical cancer has decreased because of the availability of the Pap test. The test is performed to check for pre-cancerous cells of the cervix that

could be caused by an HPV infection. If abnormal cells are seen, they can be removed to keep cancer from developing.

HPV is estimated to be the cause of 5% of cancers worldwide according to the National Cancer Institute. An oral HPV infection may also cause cancers of the oropharynx (the middle part of the throat including the soft palate, the base of the tongue and the tonsils). Two vaccines, Gardasil and Cervarix, are available to be used against the types of HPV that cause cancer. The vaccines have been shown to help protect against infection from the two main cancer causing HPV types. Further research is currently being conducted to study these vaccines and others like them.

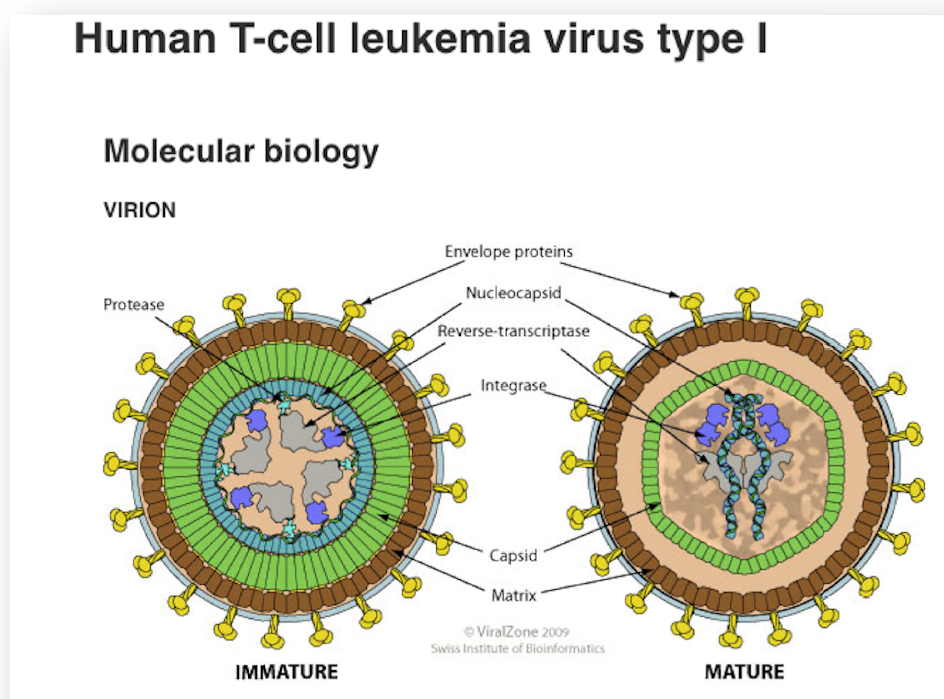


❖ Human T-Cell Lymphotropic Virus Type-1 (HTLV-1)

HTLV-1 infects T cells, which are a type of white blood cell. It can cause leukemia and lymphoma. HTLV-1 spreads in several ways, including:

1. From mother to child during birth,
2. through breastfeeding,
3. sharing needles with infected people,
4. organ transplant,
5. unsafe sex, etc.

About 2% to 5% of people who have the virus get adult T-cell leukemia or other health conditions. It's not clear why some people get leukemia and others don't. Symptoms and how it develops are different for each person. There isn't a cure or treatment for HTLV-1. It's a lifelong condition. But regular checkups can lower your chances of cancer.



HTLV-1 is a type of retrovirus that uses RNA (instead of DNA) for its genetic code. During the replication process, the virus uses an enzyme called reverse transcriptase, which allows the virus to change its RNA genes into DNA. This allows the virus genes to become integrated into the genes of the host cell and can cause a mutation in the host cell genes that controls how the cell divides. This change can sometimes lead to

cancer. HTLV-1 has been linked to a type of lymphocytic leukemia and non-Hodgkin lymphoma called adult T-cell leukemia/lymphoma (ATL). It is most common in populations of southern Japan, Caribbean, Central Africa, and some areas in the United States. Once infected, a person may live 20 years or more with no symptoms. There is about a 5% chance that the infection will lead to cancer.

❖ **Epstein-Barr Virus (EBV)**

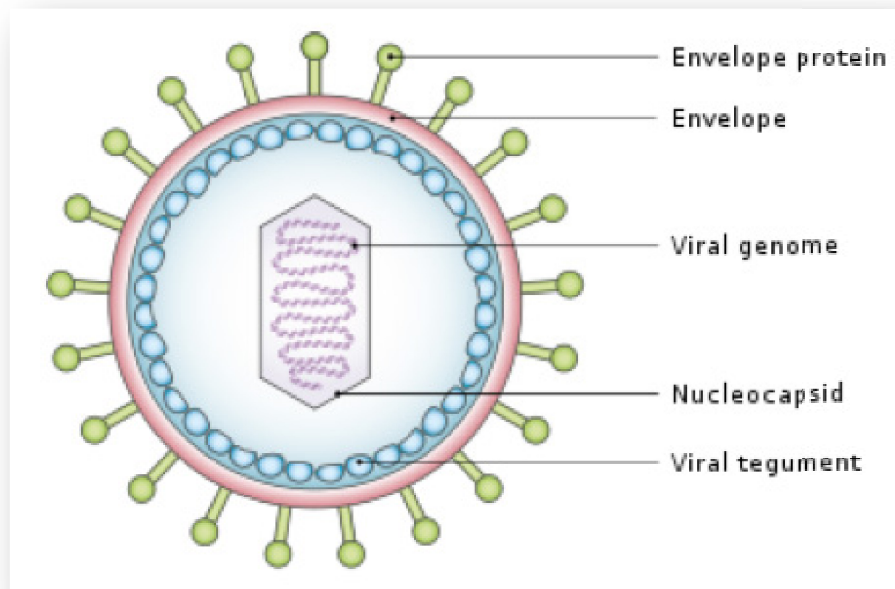
EBV is a common virus. Most people get infected with it at some point in their lives. Most of the time, people with EBV stay healthy and don't have symptoms. For others, EBV can cause mononucleosis and other more serious conditions, from viral meningitis to pneumonia. Several cancers are linked with EBV as well:

- Burkitt's Lymphoma
- Nasopharyngeal Carcinoma (cancer of the upper throat)
- Hodgkin's and non-Hodgkin's Lymphoma
- T-cell Lymphomas
- Post-transplant Lymphoproliferative Disorder (too many white blood cells)
- Leiomyosarcoma (cancer in the soft tissue)

There's no vaccine for EBV, but you can help protect yourself by not kissing or sharing drinks, food, or personal items with someone who has the virus. There's no specific treatment if you have for EVB, but you can ease symptoms if you drink plenty of fluids, get rest, and take medicines for pain and fever.

The Epstein-Bar virus is a type of Herpes Virus and that is best known for causing infectious mononucleosis, better known as "mono" or the "kissing disease". This virus is very common, and it is estimated that about 95% of the US population is infected with the virus, though not everyone shows any symptoms. The virus remains with the person throughout life by infecting epithelial cells and a type of white blood cells

known as B lymphocytes or B cells. However, after a few weeks of initial infection, most people show no symptoms.



Structure of Epstein-Barr Virus

❖ Mechanisms of Viral Oncogenesis

The molecular mechanisms of viral oncogenesis are complex and may involve:

- ✚ Induction of chronic inflammation
- ✚ Disruption of host genetic and epigenetic integrity and homeostasis
- ✚ Interference with cellular DNA repair mechanisms resulting in genome instability
- ✚ Cell cycle dysregulation.

MECHANISM OF ONCOGENECITY

DIRECT ACTING

↓
Introduction of new
'Transforming gene'
into the cell

INDIRECT ACTING

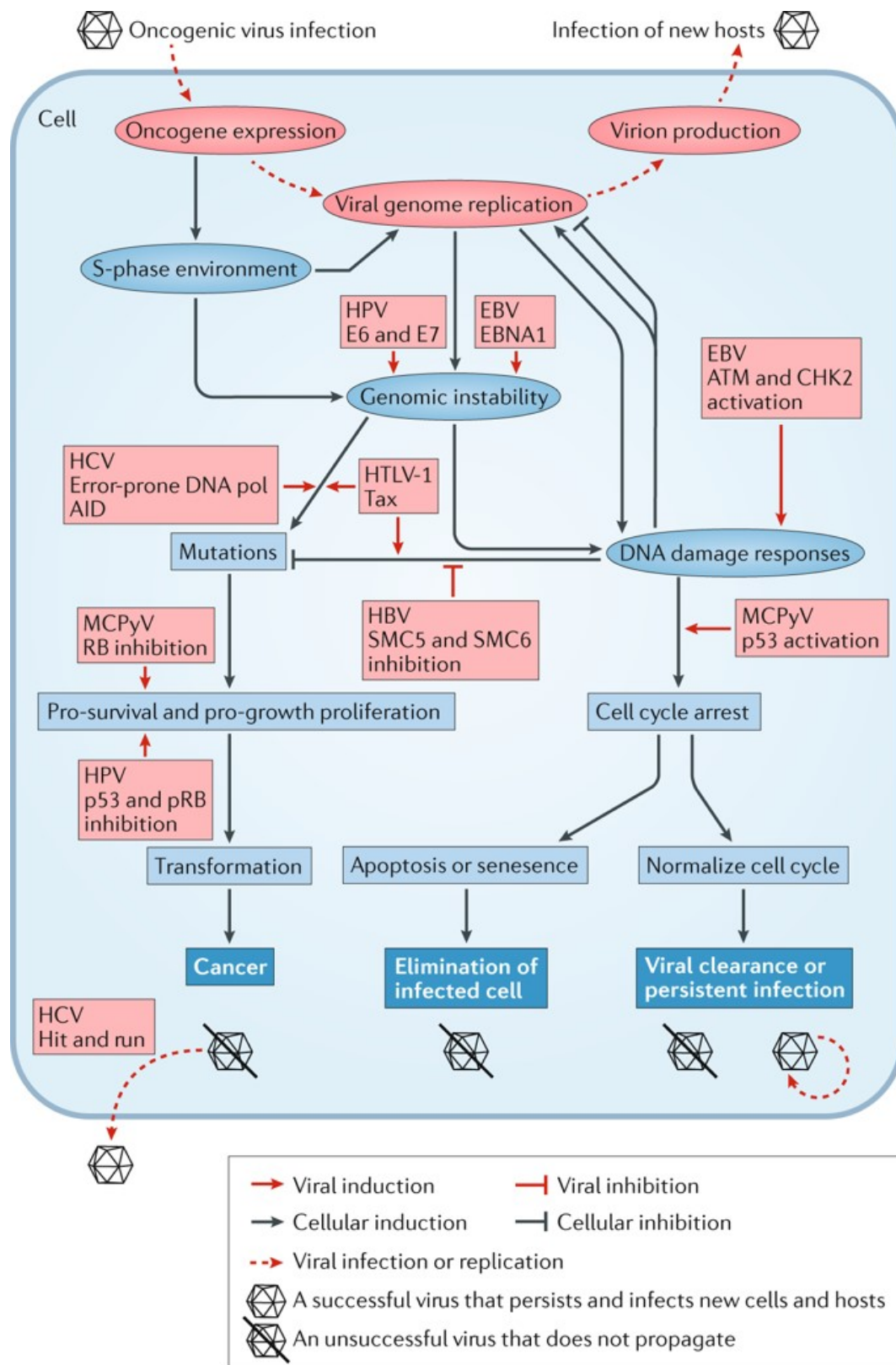
↓
Alteration of expression of
preexisting cellular gene

↘
Loss of normal growth regulation processes
↙
Affection of DNA repair mechanisms
Genetic instability

↓
Mutagenic phenotype

MECHANISM OF VIRAL ONCOGENESIS

- Impairment of the signal transduction pathway
 - Growth factor expression
 - Growth factor receptor activation
 - Cytoplasmic or membrane-bound kinases
 - Transcription factors
- Inactivation of Tumor-suppressor genes
 - Uncontrolled proliferation (Rb gene & P53gene)
 - Inhibition of Apoptosis (P53 gene)



- ✚ Oncogenic DNA viruses can also insert their genomic DNA into cellular chromosomes, resulting in genetic abnormality.
- ✚ Viral ‘oncoproteins’ can activate cellular signaling pathways, alter the expression of cellular genes and microRNAs either transcriptionally or post-transcriptionally, and destabilize or inactivate tumor suppressor proteins and proteins that regulate cell polarity, signal transduction, immune response, and apoptosis.
- ✚ Genetic and epigenetic alterations induced by infection and replication of oncogenic viruses may lead to the appearance and proliferation of cancer stem cells, which are important for the initiation, progression, metastasis, relapse, and chemotherapy resistance of cancers.

The importance and underlying molecular mechanisms of specific cellular genes and signaling pathways in viral oncogenesis are subjects of intense research efforts.