Oncogenic viruses (Human cancer viruses)

Viruses are etiologic factors in the development of several types of human tumors, including two of great significance worldwide cervical cancer and liver cancer.

At least 15..20% of all human tumors worldwide have a viral cause. The viruses that have been strongly associated with human cancers.

They include **human papillomaviruses** (HPVs), **Epstein-Barr virus** (EBV), **human herpesvirus 8**, **hepatitis B virus**, **hepatitis C virus**, and two **human retroviruses** plus several **candidate human cancer** viruses. Many viruses can cause tumors in animals, either as a consequence of natural infection or afte r experimental inoculation.

A virus that is able to cause cancer is known as an **oncogenic virus**. Evidence that a virus is oncogenic includes the regular presence in the tumour cells of virus DNA, which might be all or a part of the virus is possible that the virus is just one of a number of carcinogenic factors that can give rise to these cancers.

Oncogenic DNA Viruses		
Virus	**Disease**	**Cancer**
Papovaviridae *Papillomavirus* (some)	Warts, including STD genital warts	Uterine (cervical) cancer
Herpesviridae *Lymphocry ptovirus*	Infectious mononucleosis	Burkitt's lymphoma Nasopharyngeal carcinoma

(Epstein-Barr virus)		Hodgkin's disease
Hepadnavirus Hepatitis B virus(HBV)	Hepatitis B (infectious hepatitis)	Liver cancer
Adenoviridae	Acute respiratory disease; Common cold	Adenocarcinomas (cancer of glandular epithelial tissues)
Poxviridae	Smallpox; cowpox	Miscellaneous

Oncogenic RNA Viruses of the Family Retroviridae	
Virus	**Cancer**
Human T-cell leukemia virus (HTLV-1; HTLV-2)	Adult T-cell leukemia Lymphoma
Sarcoma viruses of cats, chickens, rodents	Sarcomas (cancer of connective tissues)
Mammary tumor virus of mice	Mammary gland tumors
Feline leukemia virus (FeLV)	Feline leukemia

General Features of Viral Carcinogenesis

1. Viruses can cause cancer in animals and humans.

2. Tumor viruses frequently establish persistent infections in natural hosts.

3. Host factors are important determinants of virus-induced tumorigenesis.

4. Viruses are seldom complete carcinogens.

5. Virus infections are more common than virus-related tumor formation.

6. Long latent periods usually elapse between initial virus infection and tumor appearance.

7. Viral strains may differ in oncogenic potential.

8. Viruses may be either direct- or indirect-acting carcinogenic agents.

9. Oncogenic viruses modulate growth control pathways in cells.

10. Animal models may reveal mechanisms of viral carcinogenesis.

11. Viral markers are usually present in tumor cells.

12. One virus may be associated with more than one type of tumor.

How do viruses cause cancer?

Most virus-induced cancers develop after a long period of persistent infection with an oncogenic virus; for adult T cell leukaemia this period is exceptionally long (around 60 years). The virus infections persist in their hosts in spite of immune responses, such as the production of virus-specific antibodies.

As cancer develops in only small percentages of virus-infected hosts it is clear that the virus infections alone do not cause cancer. Other factors are involved and these include exposure to particular environmental factors, host genetic factors and immunodeficiency.

Mechanisms of Action by Human Cancer Viruses

Tumor viruses mediate changes in cell behavior by means of a limited amount of genetic information. There are two general patterns by which this is accomplished: The tumor virus introduces a new "**transforming gene**" into the cell (**direct-acting**), or the virus alters the expression of a preexisting cellular gene or genes **(indirect-acting).** In either case, the cell loses control of normal regulation of growth processes. DNA repair

pathways are frequently affected, leading to genetic instability and a mutagenic phenotype.

Cellular transformation may be defined as a stable, heritable change in the growth control of cells in culture. No set of characteristics invariably distinguishes transformed cells from their normal. Transformation to a malignant phenotype is recognized by tumor formation when transformed cells are injected into appropriate test animals.

Papillomavirus-linked cancers

Cervical carcinoma is the third most common cancer in women, with approximately half a million new cases and 280 000 deaths in the world each year. Most, if not all, of these cancers result from infection with a papillomavirus.

The papillomaviruses are small DNA viruses of mammals and birds .

They enter the body through small abrasions and infect keratin-making cells (keratinocytes) in skin or a mucous membrane. Each HPV type infects a preferred site, such as the hands or the genitals, and infection may result in a benign wart (papilloma) or a carcinoma.

Most papillomavirus infections do not become persistent, but in a minority of hosts the infection is not cleared by the host's immune response. In individuals who harbour a persistent infection there is a small risk of cancer developing. This risk is associated with about 15 of the HPV types; these 'high-risk' types include HPV-16 and 18. Infection with other HPV types that infect the genitals carries little or no risk of cancer; these 'low-risk' HPV types include HPV-6 and 11

Human Retroviruses

The human T-lymphotropic (HTLV) group of retroviruses has probably existed in humans for thousands of years. HTLV-1 has been established as the causative agent of adult T cell leukemia-lymphomas (ATL) as well as a nervous system degenerative disorder called tropical spastic paraparesis. It does not carry an oncogene. A related

human virus, HTLV-2, has been isolated but has not been conclusively associated with a specific disease.

Transmission of HTLV-1 seems to involve cell-associated virus. Mother-to-child transmission via breast feeding is an important mode. Such early-life infections are associated with the greatest risk of ATL. Blood transfusion is an effective means of transmission, as are sharing blood-contaminated needles (drug abusers) and sexual intercourse.

Damage to immune defences

Interactions between cell proteins and proteins produced by oncogenic viruses can lead to breakdown of immune defences that may allow the development of a cancer. Papillomavirus proteins interfere with apoptosis, and hence prevent the death of virus-infected cells.