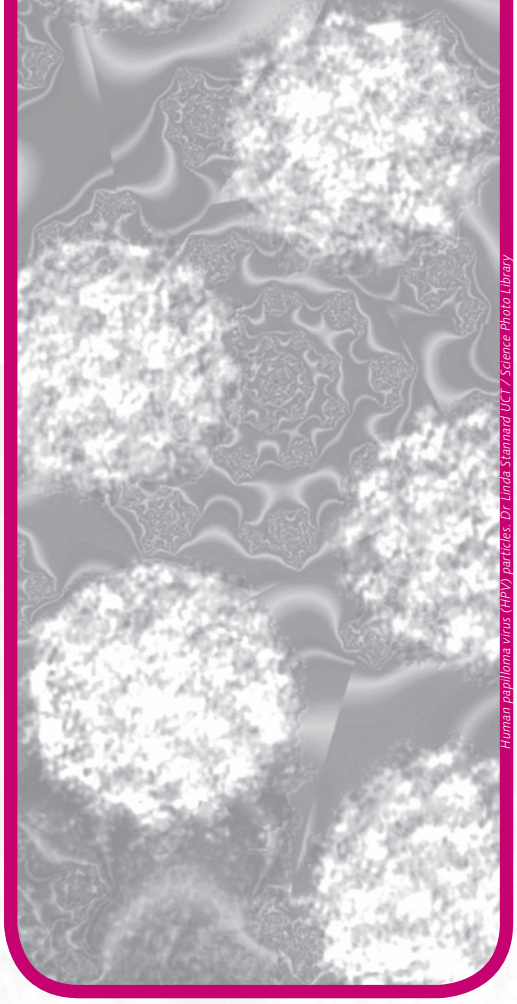
VIRUSES AND CANCER

- Worldwide, viruses are associated with the development of around 15% of cancers.
- In 2010, viruses were found to be linked to around 9,750 (3%) cancer cases in the UK, with human papillomavirus (HPV) responsible for around half of these.
- Cancer develops in only a small proportion of individuals infected with cancer-linked viruses, usually many years after initial infection.



Human papilloma virus (HPV) particles. Dr Linda Stannard UCT / Science Photo Library

OVERVIEW

Cancer develops when cells start to divide uncontrollably because the 'cell cycle machinery' that regulates this process stops working properly. These cancer cells can then invade other tissues. Cancer development is a complex process involving a series of genetic changes that disrupt the cell cycle machinery, interfering with cellular functions such as cell growth.

Some infectious agents, especially viruses, play a key role in the development of certain cancers by contributing to these genetic changes, although cancer itself is not an infectious disease. These viruses are known as tumour viruses or oncogenic viruses. Other genetic, lifestyle and environmental factors also contribute to cancer development.

Seven human viruses have been linked to specific cancers (see Table 1). The involvement of these viruses in human cancer development means that the frequency of these cancers can be reduced either prophylactically by vaccinating against the viruses, or therapeutically by treating the infections.

WHICH VIRUSES ARE LINKED TO CANCERS?

Table 1. The seven human tumour viruses are each genetically and molecularly distinct.

Virus	Examples of notable cancers	No. of virus-associated cases worldwide/year	Vaccine	Tumour virus first identified
Epstein–Barr virus (EBV)	Most Burkitt's lymphoma; some Hodgkin's lymphoma, post-transplant lymphoma, nasopharyngeal carcinoma	113,000	No	1964
Hepatitis B virus (HBV)	Liver cancer	340,000	Yes	1965
Hepatitis C virus (HCV)	Liver cancer	195,000	No	1989
Human papillomavirus (HPV)	Cervical cancer	490,000	Yes	1983
Kaposi's sarcoma herpesvirus (KSHV)	Kaposi's sarcoma, primary effusion lymphoma	66,000	No	1994
Human T-lymphotropic virus-1 (HTLV-1)	Adult T-cell leukaemia	3,000	No	1980
Merkel cell polyomavirus (MCV)	Merkel cell carcinoma	No data	No	2008

HOW VIRUSES CONTRIBUTE TO CANCERS

Viral infection is just one step in the process of cancer development. While this infection is necessary for certain cancers to develop, e.g. HPV in cervical cancer (see Table 1), the vast majority of these infected individuals will not develop cancer. Tumour viruses can therefore be described as risk factors for certain cancers.

Viruses are parasites that require a host cell to replicate. Once inside a host cell, viruses hijack the cell's replication machinery to make copies of themselves. The new virus particles can then spread to other cells in the same host or spread to a different host. Some viruses can persist in host cells without fully replicating for long periods of time, a process known as 'latent' infection.

During latent infection, tumour viruses can cause genetic disruption to the host cell cycle machinery. Usually this disruption means activating genes that drive cell division forwards (oncogenes), or suppressing genes that restrict cell division (tumour suppressor genes). Together, these genetic disruptions act to drive host cell division forwards, predisposing the cell to further genetic mutations and increasing the likelihood of cancer development. These events occur by accident, as a result of the biological make-up of the virus.

Some viruses are indirect tumour viruses. They do not genetically disrupt the host cell cycle machinery themselves. Instead, they set up an environment within the body that makes disruption from other sources more likely. For example, human immunodeficiency virus (HIV) depletes an individual's immune system, making that person more susceptible to cancer caused by direct tumour viruses, e.g. KSHV (see Table 1).

LINKING VIRUSES TO CANCERS

Establishing a link between a virus and a certain cancer is difficult due to the long delay between infection and tumour development. This delay occurs because of the complex genetic changes that are needed for cancer to develop. For a particular virus to be considered responsible for a cancer developing, one or more of the following criteria must be fulfilled:

- All patients with the same cancer have been infected with the same virus
- The virus is present in the tumour cells
- The viral genes are able to promote cancerous growth in the laboratory

VACCINES

Vaccines have been developed against two oncogenic viruses: HBV and HPV.

HBV is endemic in South-east Asia and sub-Saharan Africa where it is transmitted mostly around birth or in early childhood through infected blood or bodily fluids. In 1981, the first vaccine against HBV was approved in the US. As of 2008, 177 countries had incorporated HBV vaccination into their national infant immunization programmes. Evidence shows the incidence of liver cancer in these countries has fallen significantly with the implementation of the HBV vaccine. In the UK, HBV vaccination is provided only to individuals at high risk for contracting the virus.

HPV is common throughout the world and is a sexually transmitted infection. Since 2008, girls aged 12–13 in the UK have been immunized against HPV to protect them against cervical cancer before they are likely to be exposed to HPV. A 'catch-up' campaign also started in 2008 to vaccinate older girls. The current vaccine protects against the two viral strains most commonly associated with cervical cancer: HPV-16 and HPV-18. From September 2012, additional strains of HPV will be included. In June 2011, an Australian study showed the first evidence for the effectiveness of HPV vaccination: rates of abnormal cervical cells that frequently develop into cancer cells had significantly decreased among girls under 18 in the 3 years since the immunization programme had started.

USING VIRUSES TO TARGET CANCER

While the viruses described in Table 1 can cause cancer, other types of virus are being studied for their ability to treat cancer. For example, some viruses can be genetically modified to target cancer cells, inside which they multiply rapidly, resulting in cell death and tumour shrinkage. Others might be used to indirectly kill tumours, either by increasing immune responses against tumour cells or by forcing them to become sensitive to anti-cancer drugs.

SGM BRIEFINGS

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