The Human Papilloma Virus and its capacity to cause various Cancers

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Abstract

A brief analysis and assessment has been done in acquiring information and knowledge regarding the Human Papilloma virus and its capacity to cause various cancers. The understanding of HPV and its capacity to cause various cancers has been acknowledged. This article includes HPV Family and Clinical Significance, Pathogenesis and Mode of action, Mode of infection, Molecular diagnosis, and Biological activity of oncoproteins, Capacity of HPV in cancer development, and finally HPV vaccination and prevention. The article mainly focused on the main mechanism of action of HPV in causing cancer in the host.

Keywords: HPV; Squamous intraepithelial cells; Molecular onco-proteins; Neoplasia; Centrosomes

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Key facts

Virtually all cervical cancer cases (99%) are linked to genital infection with HPV

HPV infection causes 72,000 cases of cervical cancer and 34,000 cervical cancer deaths in the Americas each year (2018 data)

As of 2017, the WHO estimates that the Regional prevalence of HPV in women is 16.1%. If current trends continue, cervical cancer is projected to increase in Latin America and the Caribbean by 27% in the number of new cases and by 34% in number of deaths, by 2030

As of 2017, 35 countries and territories in the Americas had introduced HPV vaccination for girls aged 9 to 14 in their national immunization programs

Despite the high prevalence of HPV-related anal lesions in person who live with HIV, these populations are not yet prioritized in HPV immunization programs, and most countries have only a limited capacity for screening, diagnosing, and treating HPV-related lesions

What is Human Papilloma Virus?

Human Papilloma virus (HPV) is a group of viruses that are extremely common worldwide. There are more than 100 types of HPV, of which at least 13 are cancer-causing (also known as high risk type). Papilloma viruses are small, non-enveloped, epitheliotropic, double-stranded DNA viruses that infect mucosal and cutaneous epithelia in a wide variety of higher vertebrates in a species-specific manner and induce cellular proliferation. HPV is mainly transmitted through sexual contact and most people are infected with HPV shortly after the onset of sexual activity.

Pathogenesis and mechanism of infection:

The virus initially attacks the squamous epithelial cells that have the ability to proliferate, and get access to basal cell at the time of trauma. In the basal cells, HPV infection induces the expression of viral genes that favours the replication of virus. The interaction of HPV with the host cells occurs with the help of surface receptors such as heparin sulfate proteoglycans and alpha 6 integrins. The early proteins E1 and E2 are needed for the initiation of replication. The protein E2, which is the transcriptional repressor of E6 and E7, controls the expression of E6 and E7. The way of replication is the rolling circle mechanism during which the virus gets incorporated into the human genome. This incorporation disturbs the E2 gene consequentially resulting in a higher expression of E6 and E7 oncoproteins and leading to cell transformation. After the replication of virus, the L1 and L2 gene products form the virus capsid and the mature virus is produced. Finally, the virus is released with the help of E4 protein.

Mode of Infection:

The factors that can cause HPV can be early onset of sexual activity, multiple sexual partners, and use of oral contraceptives. In addition, low socioeconomic status and smoking habit of individuals have reported to increase the risk of acquiring the infection.

Molecular diagnosis:

Target amplification
Capacity of HPV in cancer development:

Located near the squamo-columnar junctions that form the replication proteins E1 and E2 may play a role in the partitioning where the viral transcription is regulated by E2. A tissue culture and transgenic mouse model systems have been established precursors of cervical cancers. At low passage numbers, however, high-risk HPV immortalized cells are nontumorigenic. They can undergo malignant progression after extended growth in tissue culture or when additional oncogenes such as ras or fos are expressed. The development of cervical cancers in a transgenic mouse model in which HPV-16 E6/E7 is expressed in basal epithelial cells is dependent on long-term exposure to low doses of oestrogen.

Biological activities of HPV Oncoproteins:

The oncogenic activities of high-risk HPV E6 and E7 genes in tissue culture and transgenic mouse model systems have been documented extensively. Expression of high-risk HPV E6 and E7 genes in primary human keratinocytes effectively facilitates their immortalization. When grown under conditions that allow stratification and the formation of skin like structures, high-risk HPV E6/E7 immortalized cells display histo-morphological hallmarks of high-grade squamous intraepithelial lesions, well-established precursors of cervical cancers. At low passage numbers, however, high-risk HPV immortalized cells are non-tumorigenic. They can undergo malignant progression after extended growth in tissue culture or when additional oncogenes such as ras or fos are expressed. The development of cervical cancers in a transgenic mouse model in which HPV-16 E6/E7 is expressed in basal epithelial cells is dependent on long-term exposure to low doses of oestrogen.

Stimulate telomerase (TERT). Telomerase activation is a fundamental stage for the high risk HPV type mediated cell immortalization in vitro [6-8].

HPV Vaccination and Prevention:

The HPV vaccine Gardasil 9 protects against infection with nine HPV types: the two low-risk HPV types that cause most genital warts, plus the seven high-risk HPV types that cause most HPV-related cancers [9-13].

HPV vaccination is recommended by the Centres for Disease Control and Prevention (CDC)’s Advisory Committee on Immunizations Practices (ACIP) to prevent new HPV infections and HPV-associated diseases, including some cancers.

HPV vaccination provides strong protection against new HPV infections, but the vaccine does not cure, and is not used to treat, HPV infections or diseases caused by HPV. HPV vaccination offers the most protection when given before someone is exposed to the virus.

Conclusion:

Biological studies have elucidated in detail many of the molecular mechanisms of E6 and E7 Oncoproteins for altering the regulation of fundamental cellular events, such as cell cycle, apoptosis, differentiation, senescence, cell polarity, and activation of immune-response-related pathways. These studies not only are important for understanding the viral mechanisms but also have significantly contributed to the understanding of cell biology. The epidemiological studies have demonstrated the association of HR HPV types with pre-malignant and malignant cervical lesions worldwide, highlighting the worldwide predominance of HPV16 and 18 and different distribution of the other HR HPV types in different geographical areas. Most importantly, these studies have demonstrated that HR HPV infections are also involved in a subset of other genital cancers, i.e. cancers of the vagina, vulva, penis, and anus, as well as cancer of the oro-pharynx. These research activities have had a great impact on public health, facilitating the establishment of novel screening and prophylactic strategies. The generation of the L1-based prophylactic vaccine has been a remarkable achievement. The vaccine has proven to be highly efficient in preventing HPV infection and the development of pre-malignant cervical lesions. Despite the large effort in HPV research and the achievements attained, many questions remain to be answered.
For instance, very little is known about the natural history of HR HPV infections in sites other than cervix. Very limited information is available on the natural history of HR HPV infections in the oral cavity and viral molecular mechanisms occurring during carcinogenesis of the oro-pharynx. In particular, it is not yet clear whether HR HPV cooperates with environmental risk factors in this anatomical region. In addition, the classification of LR mucosal HPV types as benign viruses needs to be further evaluated. Regarding cutaneous HPV types, only a limited number of biological and epidemiological studies have been performed on beta HPV types. No information is available on the biological properties of the gamma HPV types that are highly prevalent on the skin of normal individuals. Although the initial findings support a possible link between beta HPV types and NMSC, the issue is still under debate. In conclusion, it is obvious that much HPV research still remains to be done and many more findings will come in the future, improving our knowledge of cellular biology and virus-mediated carcinogenesis.

References:

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