Development of human papillomavirus and its detection methods (Review)

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Abstract. Human papillomavirus (HPV) infection plays an important role in cervical cancer. HPV is classified within the *Papillomaviridae* family and is a non-enveloped, small DNA virus. HPV infection can be classified into two distinct scenarios: i) With or without integration into the host chromosomes. Detection of its infection can be useful in the study of cervical lesions. In the present review, the structural and functional features of HPV, HPV typing, infection and transmission mode, the risk factors for cervical susceptibility to infection and HPV detection methods are described in detail. The development of HPV detection methods may have far-reaching significance in the prevention and treatment of cervical disease. This review summarizes the advantages and limitations of each HPV detection method.

Contents

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1. Introduction

In 1907, papillomavirus was discovered to be responsible for the manifestation of skin warts (1). In 1933, Shope successfully identified papillomavirus in the cotton tail rabbit, marking the first instance of its detection in this species (2). Subsequently, papillomavirus was identified in humans and other animals (3). In 1974, zur Hausen *et al* (4) proposed a close association between human papillomavirus (HPV) infection and the occurrence of atypical hyperplasia of the reproductive epithelium and cervical cancer. At present, HPV infection has been established as the primary instigator of cervical intraepithelial neoplasia and cervical cancer, and this is substantiated by epidemiological and fundamental scientific research (5). The escalating prevalence of condyloma acuminatum, more commonly known as genital warts, within sexually transmitted infections, coupled with the rising rates of cervical cancer and anal cancer, has resulted in increasing attention being paid to HPV infection (6,7). HPV detection has been proposed as a useful tool for the management of HPV-related conditions, such as prompt treatment, symptom relief and the reduction of transmission. Early detection allows for timely intervention, reducing the risk of cancer development and lessening the burden of HPV-related diseases.

2. The structural and functional features of HPV

HPV is classified within the *Papillomaviridae* family and is a non-enveloped small DNA virus. Its external viral capsid is comprised of 72 shell particles, while its internal layer is enveloped by double-stranded closed-loop viral genomic DNA (8). The virus has a diameter of 50-55 nm, and possesses a molecular structure that is double-stranded and icosahedral in shape (9). The viral genome spans ~8,000 bp, encompassing both coding and non-coding regions (10). The coding region is further subdivided into the early (E) and late (L) coding regions, while the non-coding region is

referred to as the upstream regulatory region (URR) or long control region (11-13). The E region spans ~4,500 bp, which contains six open reading frames that encode six functional viral proteins: E1, E2, E4, E5, E6 and E7. Notably, the E1 protein exhibits DNA helicase activity, thereby facilitating the initiation of HPV DNA replication (14). The E2 protein homodimer can bind to the virus control region's specific sequence, thus it can impede the transactivation of viral DNA transcription (15,16). Furthermore, the E2 protein can hinder cell proliferation (17,18). The E4 protein has the ability to impede the entry of Cyclin B1/CDK1 into the nucleus, resulting in cell cycle arrest at the G2 phase (19,20). Additionally, the E4 protein can form a complex with the E1 protein, resulting in the formation of the E1^E4 splicing protein, which acts on the intracellular keratin network and degrades the cytoskeleton (21,22). The E5 protein can activate epidermal growth factor receptors through binding, and can also influence endocytosis and Golgi apparatus acidification, growth factor receptor metabolism and intercellular communication (23,24). E6-AP, a related protein of the E6 protein, has the ability to degrade the p53 protein, leading to the loss of its cancer-suppressing function (25). Additionally, the E6 protein can activate telomerase, resulting in chromosomal abnormalities (26). Notably, the E7 protein can degrade the pRb protein, allowing the transcription factor E2F to enter the nucleus and initiate the S phase (27,28). The L coding region is ~2,500 bp in length and encodes the L1 major capsid protein and the L2 minor capsid protein (29). L1 is highly conserved, while L2 is highly variable, reflecting the polymorphism of the region (30). The non-coding region, also known as the URR, spans ~1,000 bp and is situated between the L1 and E6 genes; this region harbors corresponding sequences that regulate gene expression (31,32).

Each region interacts with specific proteins. For example, specific URR sequences can specifically bind to E1 and E2 proteins, thereby regulating gene transcription. The upregulation of E6 and E7 proteins is attributed to the inactivation of the E2 protein (26,33). Additionally, the E5 protein synergistically interacts with E6 and E7 proteins to promote the degradation of p53 and pRb proteins, thereby facilitating the carcinogenic potential of HPV (34).

3. HPV typing

The primary basis for HPV typing is the comparison of the homology of the L1 gene sequence, which is determined by the conserved nature of the HPV genome. By assessing the homology of the L1 gene with other types, new 'types' are designated if their homology is <90%, 'subtypes' are designated if their homology falls between 90 and 98%, and 'variant strains' are designated if their homology exceeds 98% (35,36). Additionally, HPV is classified based on the structure of the L1 gene and the parent-source relationship within the phylogenetic tree (37,38); the benefit of this approach lies in its facilitation of virus classification. Nevertheless, similar to the first method, virus types sharing comparable biological traits and pathogenicity cannot be entirely categorized into a single class. Consequently, numerous scholarly works classify viruses based on the biological characteristics and pathogenicity of HPV (39).

In a previous study, HPV was segregated into skin and mucosal groups depending upon the distinct tissue sites invaded by HPV (40). Additionally, the skin groups can be further subdivided into low-risk skin type and high-risk skin type based on the variance in lesions caused by HPV infection (41,42). The mucosa group can also be divided into low-risk and high-risk types (43). Notably, >90% of cases of genital warts and cervical low-risk squamous epithelial hyperplasia have been shown to be closely related to infection with low-risk HPV6 and 11, while ~70% of cervical cancer cases were linked to high-risk HPV16 and 18 infections (44,45). Furthermore, the potential of certain HPV types to induce lesions, whether benign or malignant, remains unclear and necessitates further investigation. The differentiation between high-risk and low-risk HPV can be discerned by examining the literature, which suggests that the ability of HPV to infect cells and induce malignant tumors serves as a crucial distinguishing factor (43,46,47). This distinction holds significant potential for guiding future identification of high-risk and low-risk HPV strains.

4. HPV infection

HPV infection can be classified into two distinct scenarios (48,49). The first scenario involves the failure of HPV-infected cells to integrate with the host chromosomes, resulting in the existence of multiple extrachromosomal copies (50). The second scenario involves the integration of HPV DNA with the host chromosomes, resulting in the integration of single or multiple copies into the cell genes (51,52). The current understanding of the receptor for HPV invasion into cells remains unclear, since HPV not only binds to normal squamous epithelial cells but also to various other cell types (53,54). Consequently, the characteristics of HPV keratophilic epithelium appear to be independent of the cell receptor, suggesting that the underlying cells may lack specific receptors for HPV (55).

The first scenario of HPV infection involves a comprehensive HPV life cycle. This entails HPV infecting the basal layer cells of the epidermis through a minor skin or mucosal wound, subsequently entering the host cell via endocytosis (56,57). HPV then gradually eliminates its capsid. Upon entry of the HPV genome into the nucleus, the early region promoter is activated, leading to the expression of various proteins, such as E1, E2, E6 and E7 (58,59). These proteins fulfill their respective roles in facilitating the replication and transcription of the HPV genome. The HPV genome then exhibits a copy number ranging from 20 to 100 in each infected cell, which is transported to daughter cells through cell division (20); this phase is referred to as the proliferative infection stage of the HPV life cycle (60). Subsequently, the infected cells in the basal layer migrate towards the surface, leading to the activation of the promoter in the HPV L region. This activation facilitates the expression of the L coding region L1 and L2 proteins. At this juncture, the necessary components for the assembly of HPV have been prepared, and the encapsulation of the virus genome by the virus shell protein occurs concurrently with its self-assembly (61,62), forming a complete HPV particle (63,64). After the cuticle cells are shed, the next

Table I. Main detection methods for HPV nucleic acid molecules.

Detection methods	Characteristic	Application	(Refs.)
Southern blot	Obtaining high-quality HPV information	Laboratory method of assessment	(100-103)
Northern blot	Obtaining high-quality HPV information	Laboratory method of assessment	(102,103)
Reverse dot blot	Expeditiousness, simplicity, high sensitivity, and robust specificity	Genotyping, gene mutation, and pathogen detection	(100-101,105,106)
in-situ hybridization	A high level of sensitivity and is capable of detecting low abundance mRNA expression	Widely utilized for the detection of HPV nucleic acid molecules in tissues due	(104,107-112)
Hybrid Capture II	High sensitivity, good specificity, repeatability, and objectivity	Most commonly utilized approach for clinical detection	(100-101,113-117)
Polymerase Chain Reaction	Instrumental in assessing HPV DNA expression and ultimately determining clinical HPV infection	Due to the inherent instability of RNA molecules, their utilization in HPV detection is infrequent	(104,118-119)
Microarray technology	Capable of detecting and analyzing a vast number of specimens simultaneously, boasting high sensitivity, minimal sample requirements, rapid detection speed, high throughput, and reduced environmental contamination	The cost of gene chip technology remains relatively elevated	(100-101,121-122)

round of infection is carried out, which forms a complete HPV life cycle.

As for the second scenario of HPV infection, the E2 gene fragment is missing, and the expression of the E6 and E7 genes is also dysregulated. At this point, the L1 shell protein ceases to be expressed (65), frequently leading to the development of invasive cancer.

5. HPV transmission mode and risk factors for cervical susceptibility to infection

The primary modes of HPV transmission include: Firstly, sexual transmission, wherein individuals are susceptible to HPV infection during sexual contact with individuals carrying HPV (66,67). Secondly, vertical transmission between a mother and child may occur; during birth when the baby comes into close contact with the birth canal of the pregnant mother infected with HPV, thereby leading to HPV infection (68-70). Thirdly, close contact with HPV-infected individuals may result in infection. Fourthly, indirect contact, primarily through contact with the daily necessities and clothing of infected individuals, may lead to HPV transmission (68). Finally, infection during medical procedures, which refers to the transmission of HPV between medical personnel and patients due to inadequate protective measures during the course of treatment (20,71).

The risk factors associated with susceptibility to HPV infection in the cervix primarily include: Firstly, sexual activity. Early initiation of sexual intercourse, a high frequency of sexual encounters, multiple sexual partners and a lack of protective measures during sexual intercourse may contribute to the acquisition of HPV infection in the cervix (72,73). Additionally, the relatively young age of individuals, coupled with the immaturity of the human cervical epithelial tissue, renders the cervical epithelium susceptible to repeated HPV infections and other influencing factors. Consequently, the potential for cellular variation arises, which, if left unchecked, may progress to the development of cancer (74). A relatively active sexual life can also increase the susceptibility to HPV infection, if accompanied by the lack of good sexual hygiene habits (54,75,76).

Secondly, individuals with low immune function experience a decline in their ability to clear the virus, leading to persistent infection and an increased occurrence of cervical lesions (77). Thirdly, studies have indicated a correlation between sex hormone level disorders and higher HPV detection rates (78,79), with some research suggesting that the use of sex hormone drugs by menopausal women may also contribute to an increased risk of cervical HPV infection (80-82). Fourthly, genetic factors (9,83). Cervical cancer has been observed to exhibit familial clustering, with a higher susceptibility to HPV infection observed among individuals within particular families (75,84).

Fifthly, age, education level and socioeconomic status all play a role in the susceptibility to HPV infection (85,86). Individuals with higher education levels and socioeconomic status tend to have access to abundant medical and health resources, possess a greater understanding and command of relevant medical and health knowledge, and adhere to regular medical and healthcare measures (72). Consequently, this particular group exhibits a lower susceptibility to HPV infection compared with other groups. Moreover, studies have indicated that over 85% of cervical cancer cases worldwide occur in developing countries, thereby underscoring this phenomenon (87,88). Finally, other risk factors for cervical susceptibility to HPV infection, such as smoking, pregnancy and age, remain to be explored.

6. Methods of HPV detection

Due to its strict tissue and species restrictions, the complete virus cycle and infectivity of HPV are limited to human epithelial tissue, and cannot be cultured *in vitro*. Consequently, the detection of HPV has been primarily reliant on serological, histological and molecular biological methods (89,90). However, the serological test for HPV lacks the ability to differentiate between recent and late infections, and its accuracy is suboptimal (91,92). Regarding the histological identification of HPV, the identification of vacuolated or keratinized cells in the spinous layer serves as the primary indicator of HPV infection (93,94). The conventional Pap smear, which is commonly employed for HPV detection, possesses a high false-negative rate despite its effectiveness in early-stage cervical cancer screening and its role in the significant reduction in the incidence of cervical invasive cancer (95,96). Although thin layer liquid-based cytology has replaced the Pap smear, its specificity and sensitivity remain suboptimal (97,98). Consequently, the accurate diagnosis of HPV relies on molecular biological techniques.

In the molecular biological detection of HPV, HPV nucleic acid molecules (DNA and RNA) and viral proteins are commonly utilized as indicators for detection. The detection methods for HPV virus proteins include immunohistochemistry, electron microscopy, western blotting and others. These methods are not only complex, but also require a significant amount of time (99). Notably, HPV nucleic acid molecular detection methods include Southern blotting, northern blotting, reverse dot blot hybridization, *in-situ* hybridization, hybrid capture (HC)II, polymerase chain reaction (PCR) and microarray technology (100,101) (Table I).

Southern blotting is utilized to detect DNA molecules, while northern blotting detects RNA molecules, with the aim of identifying HPV through gel electrophoresis, which facilitates HPV typing (102,103). Despite the potential for obtaining high-quality HPV information, the utilization of these two methods necessitates a considerable quantity of highly purified nucleic acid molecules, resulting in a time-consuming and cumbersome process. Additionally, hybridization is conducted in the solid phase, necessitating strict preservation conditions for nucleic acid molecules to maintain their ideal state, rendering it unsuitable for clinical detection, and limiting its use to a traditional laboratory method of assessment (15).

The conventional method of dot hybridization involves immobilizing target DNA and subsequently hybridizing it with a labeled probe to facilitate color development (104). Conversely, the reverse dot hybridization approach entails immobilizing a labeled probe and subsequently hybridizing it with the target DNA to achieve color development (105). In comparison to forward dot hybridization and gel electrophoresis, reverse dot hybridization exhibits certain benefits, such as speed, simplicity, high sensitivity and robust specificity, particularly regarding genotyping, and gene mutation and pathogen detection (106).

The application principle of *in-situ* hybridization involves the pairing of radioactive or non-radioactive foreign nucleic acid, referred to as a probe, with the DNA or RNA to be examined on tissues, cells or chromosomes (107). This technique is utilized to determine the presence of HPV infection in the body and to perform HPV typing (108). Notably, fluorescence *in-situ* hybridization enables the mapping of the precise location of HPV DNA in the cell chromosome, which is crucial for predicting the integration of HPV DNA with the host cell chromosomes (109). The detection of HPV nucleic acid molecules through *in-situ* hybridization exhibits a high level of sensitivity and is capable of detecting low abundance mRNA expression. Despite the potential for genotyping errors, this method remains widely utilized for the detection of HPV nucleic acid molecules in tissues due to its high sensitivity and specificity (110-112).

The HC method operates on the fundamental principle of utilizing a sensitive chemiluminescence signal amplification system and an efficient liquid phase technique for the typing and quantitative analysis of HPV DNA (113,114). Currently, there are three hybridization capture methods: HCI, HCII and HCIII (115). The HCII method is the most commonly utilized approach for the clinical detection of HPV due to its high sensitivity, good specificity, repeatability and objectivity (116). By contrast, the HCI method can detect nine high-risk HPV types with limited sensitivity, but strong specificity and positive prediction. HCIII, on the other hand, is incapable of typing HPV DNA (117). Notably, HCII has been approved by the US Food and Drug Administration and offers several advantages, including suitability for automated operation, no requirement for a strict laboratory environment or complex laboratory skills and no gene amplification, thereby eliminating the possibility of cross-contamination (116).

The fundamental concept of PCR involves the amplification of a specific DNA segment to identify HPV. PCR methodologies include conventional PCR, real-time fluorescent quantitative PCR, reverse transcription PCR (RT-PCR) and the amalgamation of PCR and *in-situ* hybridization (104). Despite the heightened sensitivity of conventional PCR detection, the potential for sample or reagent cross-contamination may result in false positives and other problems (118,119). Real-time fluorescent quantitative PCR technology represents an improvement over conventional PCR technology, offering superior sensitivity, accuracy, reduced contamination and quantitative detection capabilities (120). Consequently, the utilization of this technology in HPV detection is gaining traction. RT-PCR is a viable method for detecting HPV RNA, and is instrumental in assessing HPV DNA expression and ultimately identifying clinical HPV infection. However, due to the inherent instability of RNA molecules, they are infrequently used in HPV detection.

Microarray technology involves the immobilization of numerous probe molecules onto a solid phase support, allowing for typing and quantitative detection of HPV DNA samples through nucleic acid molecular hybridization pairing (121,122). In accordance with the principles of Southern and northern blotting, these techniques employ established nucleic acid sequences and complementary target sequences to conduct qualitative and quantitative analyses based on hybridization signals (123). Gene chip technology, on the other hand, is capable of detecting and analyzing a vast number of specimens simultaneously, boasting high sensitivity, minimal sample requirements, rapid detection speed, high throughput

and reduced environmental contamination (124). However, the cost of gene chip technology remains relatively high.

7. Conclusion

HPV infection is a major risk factor for the development of cervical cancer. The clinical surveillance of HPV plays a crucial role in the prevention and diagnosis of cervical cancer. Molecular assays are the gold standard for HPV identification. The aim of the present review and the clinical material available is to determine the optimal method for HPV detection. The present review aims to provide a comprehensive overview of the existing HPV detection methods, including their principles, application environments and clinical value, to provide a reference for the detection of HPV in clinical practice, with the ultimate aim of reducing the incidence and mortality of HPV-related diseases. Further investigation is required to clarify the role of molecular HPV testing in current primary cervical screening programs. With the continued development of detection technology, low-cost methods with high versatility, operability, and improved sensitivity and specificity will be needed for the early diagnosis of cervical HPV infection.

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Competing interests

The authors declare that they have no competing interests.

References

1. Kobashi H, Adachi T, Tsubota T, Asano K, Fukai M, Namba J, Izumi K, Hoshijima T, Miura H and Sezaki T: The role of drugs and lymphocytes in granulocyte-macrophage colony formation in patients with drug induced agranulocytosis. Rinsho Ketsueki 30: 282-288, 1989 (In Japanese).
2. Shope RE and Hurst EW: Infectious papillomatosis of rabbits: With a note on the histopathology. J Exp Med 58: 607-624, 1933.
3. Hopfl R, hristensen ND, Angell MG and Kreider JW: Leukocyte proliferation in vitro against cottontail rabbit papillomavirus in rabbits with persisting papillomas/cancer or after regression. Arch Dermatol Res 287: 652-658, 1995.
4. zur Hausen H, Meinhof W, Scheiber W and Bornkamm GW: Attempts to detect virus-secific DNA in human tumors. I. Nucleic acid hybridizations with complementary RNA of human wart virus. Int J Cancer 13: 650-656, 1974.
5. Borgogna JC, Shardell MD, Santori EK, Nelson TM, Rath JM, Glover ED, Ravel J, Gravitt PE, Yeoman CJ and Brotman RM: The vaginal metabolome and microbiota of cervical HPV-positive and HPV-negative women: A cross-sectional analysis. BJOG 127: 182-192, 2020.
6. Purzycka-Bohdan D, Nowicki RJ, Herms F, Casanova JL, Fouere S and Beziat V: The pathogenesis of giant condyloma acuminatum (Buschke-Lowenstein Tumor): An overview. Int J Mol Sci 23: 4547, 2022.
7. Yuan H, Li R, Lv J, Yi G, Sun X, Zhao N, Zhao F, Xu A, Kou Z and Wen H: Epidemiology of human papillomavirus on condyloma acuminatum in Shandong Province, China. Hum Vaccin Immunother 19: 2170662, 2023.
8. Bishop B, Dasgupta J and Chen XS: Structure-based engineering of papillomavirus major capsid l1: Controlling particle assembly. Virol J 4: 3, 2007.
9. McBride AA: Human papillomaviruses: diversity, infection and host interactions. Nature reviews Microbiology 20: 95-108, 2022.
10. de Oliveira CM, Bravo IG, Santiago e Souza NC, Genta ML, Fregnani JH, Tacla M, Carvalho JP, Longatto-Filho A and Levi JE: High-level of viral genomic diversity in cervical cancers: A Brazilian study on human papillomavirus type 16. Infect Genet Evol 34: 44-51, 2015.
11. Morin G, Fradet-Turcotte A, Di Lello P, Bergeron-Labrecque F, Omichinski JG and Archambault J: A conserved amphipathic helix in the N-terminal regulatory region of the papillomavirus E1 helicase is required for efficient viral DNA replication. J Virol 85: 5287-5300, 2011.
12. Chow LT, Reilly SS, Broker TR and Taichman LB: Identification and mapping of human papillomavirus type 1 RNA transcripts recovered from plantar warts and infected epithelial cell cultures. J Virol 61: 1913-1918, 1987.
13. O'Neill FJ and Miller TH: Isolation of a papovavirus with a bipartite genome containing unlinked SV40 and BKV sequences. Virology 143: 75-87, 1985.
14. Doorbar J, Egawa N, Griffin H, Kranjec C and Murakami I: Human papillomavirus molecular biology and disease association. Rev Med Virol 25 (Suppl 1): S2-S23, 2015.
15. Chojnacki M and Melendy T: The HPV E2 transcriptional transactivation protein stimulates cellular DNA polymerase epsilon. Viruses 10: 321, 2018.
16. Jose L, Androphy EJ and DeSmet M: SETD6 Regulates E2-Dependent human papillomavirus transcription. J Virol 96: e0129522, 2022.
17. Demeret C, Garcia-Carranca A and Thierry F: Transcription-independent triggering of the extrinsic pathway of apoptosis by human papillomavirus 18 E2 protein. Oncogene 22: 168-175, 2003.
18. Ren S, Gaykalova DA, Guo T, Favorov AV, Fertig EJ, Tamayo P, Callejas-Valera JL, Allevato M, Gilardi M, Santos J, *et al*: HPV E2, E4, E5 drive alternative carcinogenic pathways in HPV positive cancers. Oncogene 39: 6327-6339, 2020.
19. Sund DT, Brouwer AF, Walline HM, Carey TE, Meza R, Jackson T and Eisenberg MC: Understanding the mechanisms of HPV-related carcinogenesis: Implications for cell cycle dynamics. J Theor Biol 551-552: 111235, 2022.
20. Graham SV: The human papillomavirus replication cycle, and its links to cancer progression: A comprehensive review. Clin Sci (Lond) 131: 2201-2221, 2017.

21. Przybylski M, Pruski D, Millert-Kalińska S, Krzyżaniak M, de Mezer M, Frydrychowicz M, Jach R and Żurawski J: Expression of E4 Protein and HPV Major Capsid Protein (L1) as a novel combination in squamous intraepithelial lesions. Biomedicines 11: 225, 2023.
22. Budhathoki S, Diergaarde B, Liu G, Olshan A, Ness A, Waterboer T, Virani S, Basta P, Bender N, Brenner N, *et al*: A risk prediction model for head and neck cancers incorporating lifestyle factors, HPV serology and genetic markers. Int J Cancer 152: 2069-2080, 2023.
23. Chen B, Zhao L, Yang R and Xu T: Advances in molecular mechanism of HPV16 E5 oncoprotein carcinogenesis. Arch Biochem Biophys 745: 109716, 2023.
24. Rodríguez MI, Finbow ME and Alonso A: Binding of human papillomavirus 16 E5 to the 16 kDa subunit c (proteolipid) of the vacuolar H+-ATPase can be dissociated from the E5-mediated epidermal growth factor receptor overactivation. Oncogene 19: 3727-3732, 2000.
25. Templeton CW and Laimins LA: p53-dependent R-loop formation and HPV pathogenesis. Proc Natl Acad Sci USA 120: e2305907120, 2023.
26. Díaz L, Bernadez-Vallejo SV, Vargas-Castro R, Avila E, Gómez-Ceja KA, García-Becerra R, Segovia-Mendoza M, Prado-Garcia H, Lara-Sotelo G, Camacho J, *et al*: The Phytochemical α-Mangostin inhibits cervical cancer cell proliferation and tumor growth by downregulating E6/E7-HPV Oncogenes and KCNH1 gene expression. Int J Mol Sci 24: 3055, 2023.
27. Challagundla N, Chrisophe-Bourdon J and Agrawal-Rajput R: Chlamydia trachomatis infection co-operatively enhances HPV E6-E7 oncogenes mediated tumorigenesis and immunosuppression. Microb Pathog 175: 105929, 2023.
28. Pan W, Wang S, Liu X, Wang M, Han X, Tian X, Lin J, Qiao X and Wang X: KNTC1, regulated by HPV E7, inhibits cervical carcinogenesis partially through Smad2. Exp Cell Res 423: 113458, 2023.
29. Mane A, Patil L, Limaye S, Nirmalkar A and Kulkarni-Kale U: Characterization of major capsid protein (L1) variants of Human papillomavirus type 16 by cervical neoplastic status in Indian women: Phylogenetic and functional analysis. J Med Virol 92: 1303-1308, 2020.
30. DiGiuseppe S, Bienkowska-Haba M, Guion LGM, Keiffer TR and Sapp M: Human papillomavirus major capsid protein L1 remains associated with the incoming viral genome throughout the entry process. J Virol 91: e00537-17, 2017.
31. Rubben A, Spelten B, Albrecht J and Grussendorf-Conen EI: Demonstration of URR-duplication variants of human papillomavirus type 6 in paraffin-embedded tissue sections of one condyloma acuminatum and one Buschke-Loewenstein tumour. J Pathol 174: 7-12, 1994.
32. Arany I, Grattendick KJ, Whitehead WE, Ember IA and Tyring SK: A functional interferon regulatory factor-1 (IRF-1)-binding site in the upstream regulatory region (URR) of human papillomavirus type 16. Virology 310: 280-286, 2003.
33. Jaiswal N, Nandi D, Cheema PS and Nag A: The anaphase-promoting complex/cyclosome co-activator, Cdh1, is a novel target of human papillomavirus 16 E7 oncoprotein in cervical oncogenesis. Carcinogenesis 43: 988-1001, 2022.
34. Li Q, Xie B, Chen X, Lu B, Chen S, Sheng X and Zhao Y: SNORD6 promotes cervical cancer progression by accelerating E6-mediated p53 degradation. Cell Death Discov 9: 192, 2023.
35. Bernard HU, Burk RD, Chen Z, van Doorslaer K, zur Hausen H and de Villiers EM: Classification of papillomaviruses (PVs) based on 189 PV types and proposal of taxonomic amendments. Virology 401: 70-79, 2010.
36. de Villiers EM, Fauquet C, Broker TR, Bernard HU and zur Hausen H: Classification of papillomaviruses. Virology 324: 17-27, 2004.
37. Brendle S, Li JJ, Cladel NM, Shearer DA, Budgeon LR, Balogh KK, Atkins H, Costa-Fujishima M, Lopez P, Christensen ND, *et al*: Mouse Papillomavirus L1 and L2 Are dispensable for viral infection and persistence at both cutaneous and mucosal tissues. Viruses 13: 1824, 2021.
38. Balanda M, Fernandez J, Vergara N, Campano C, Arata L, Martin HS and Ramírez E: Genetic variability of human papillomavirus type 66 L1 gene among women presenting for cervical cancer screening in Chile. Med Microbiol Immunol 208: 757-771, 2019.
39. Markowitz LE and Schiller JT: Human papillomavirus vaccines. J Infect Dis 224 (12 Suppl 2): S367-S378, 2021.
40. Al-Eitan LN, Tarkhan AH, Alghamdi MA, Al-Qarqaz FA and Al-Kofahi HS: Transcriptome analysis of HPV-induced warts and healthy skin in humans. BMC Med Genomics 13: 35, 2020.
41. Redzic N, Pereira AR, Menon S, Bogers J, Coppens A, Kehoe K and Vanden Broeck D: Characterization of type-specific HPV prevalence in a population of persistent cutaneous warts in Flanders, Belgium. Sci Rep 13: 17492, 2023.
42. Reusser NM, Downing C, Guidry J and Tyring SK: HPV carcinomas in immunocompromised patients. J Clin Med 4: 260-281, 2015.
43. Sudarshan SR, Schlegel R and Liu X: Two conserved amino acids differentiate the biology of high-risk and low-risk HPV E5 proteins. J Med Virol 94: 4565-4575, 2022.
44. Bzhalava D, Eklund C and Dillner J: International standardization and classification of human papillomavirus types. Virology 476: 341-344, 2015.
45. Rahmat F, Kuan JY, Hajiman Z, Mohamed Shakrin NNS, Che Roos NA, Mustapa M, Ahmad Zaidi NA and Ahmad A: Human Papillomavirus (HPV) Prevalence and Type Distribution in Urban Areas of Malaysia. Asian Pac J Cancer Prev 22: 2969-2976, 2021.
46. Dalstein V, Riethmuller D, Prétet JL, Le Bail Carval K, Sautière JL, Carbillet JP, Kantelip B, Schaal JP and Mougin C: Persistence and load of high-risk HPV are predictors for development of high-grade cervical lesions: A longitudinal French cohort study. Int J Cancer 106: 396-403, 2003.
47. Hatterschide J, Bohidar AE, Grace M, Nulton TJ, Kim HW, Windle B, Morgan IM, Munger K and White EA: PTPN14 degradation by high-risk human papillomavirus E7 limits keratinocyte differentiation and contributes to HPV-mediated oncogenesis. Proc Natl Acad Sci USA 116: 7033-7042, 2019.
48. Pett M and Coleman N: Integration of high-risk human papillomavirus: A key event in cervical carcinogenesis? J Pathol 212: 356-367, 2007.
49. Kalantari M, Calleja-Macias IE, Tewari D, Hagmar B, Lie K, Barrera-Saldana HA, Wiley DJ and Bernard HU: Conserved methylation patterns of human papillomavirus type 16 DNA in asymptomatic infection and cervical neoplasia. J Virol 78: 12762-12772, 2004.
50. Jackson R, Rosa BA, Lameiras S, Cuninghame S, Bernard J, Floriano WB, Lambert PF, Nicolas A and Zehbe I: Functional variants of human papillomavirus type 16 demonstrate host genome integration and transcriptional alterations corresponding to their unique cancer epidemiology. BMC Genomics 17: 851, 2016.
51. Sivars L, Palsdottir K, Crona Guterstam Y, Falconer H, Hellman K and Tham E: The current status of cell-free human papillomavirus DNA as a biomarker in cervical cancer and other HPV-associated tumors: A review. Int J Cancer 152: 2232-2242, 2023.
52. Yu L, Majerciak V, Lobanov A, Mirza S, Band V, Liu H, Cam M, Hughes SH, Lowy DR and Zheng Z-M: HPV oncogenes expressed from only one of multiple integrated HPV DNA copies drive clonal cell expansion in cervical cancer. mBio 15: e0072924, 2024.
53. Doorbar J: Molecular biology of human papillomavirus infection and cervical cancer. Clin Sci (Lond) 110: 525-541, 2006.
54. Okunade KS: Human papillomavirus and cervical cancer. J Obstet Gynaecol 40: 602-608, 2020.
55. Yousefi Z, Aria H, Ghaedrahmati F, Bakhtiari T, Azizi M, Bastan R, Hosseini R and Eskandari N: An update on human papilloma virus vaccines: History, types, protection, and efficacy. Front Immunol 12: 805695, 2022.
56. Horvath CA, Boulet GA, Renoux VM, Delvenne PO and Bogers JP: Mechanisms of cell entry by human papillomaviruses: An overview. Virol J 7: 11, 2010.
57. Graßel L, Fast LA, Scheffer KD, Boukhallouk F, Spoden GA, Tenzer S, Boller K, Bago R, Rajesh S, Overduin M, *et al*: The CD63-Syntenin-1 complex controls post-endocytic trafficking of oncogenic human papillomaviruses. Sci Rep 6: 32337, 2016.
58. Braunstein TH, Madsen BS, Gavnholt B, Rosenstierne MW, Koefoed Johnsen C and Norrild B: Identification of a new promoter in the early region of the human papillomavirus type 16 genome. J Gen Virol 80 (Pt 12): 3241-3250, 1999.
59. Bhattacharjee R, Das SS, Biswal SS, Nath A, Das D, Basu A, Malik S, Kumar L, Kar S, Singh SK, *et al*: Mechanistic role of HPV-associated early proteins in cervical cancer: Molecular pathways and targeted therapeutic strategies. Crit Rev Oncol Hematol 174: 103675, 2022.

60. Du J, Ährlund-Richter A, Näsman A and Dalianis T: Human papilloma virus (HPV) prevalence upon HPV vaccination in Swedish youth: A review based on our findings 2008-2018, and perspectives on cancer prevention. Arch Gynecol Obstet 303: 329-335, 2021.
61. Rosmeita CN, Budiarti S, Mustopa AZ, Novianti E, Swasthikawati S, Chairunnisa S, Hertati A, Nurfatwa M, Ekawati N and Hasan N: Expression, purification, and characterization of self-assembly virus-like particles of capsid protein L1 HPV 52 in Pichia pastoris GS115. J Genet Eng Biotechnol 21: 126, 2023.
62. Zhao G, Chandrudu S, Skwarczynski M and Toth I: The application of self-assembled nanostructures in peptide-based subunit vaccine development. Eur Polym J 93: 670-681, 2017.
63. Chen XS, Casini G, Harrison SC and Garcea RL: Papillomavirus capsid protein expression in Escherichia coli: Purification and assembly of HPV11 and HPV16 L1. J Mol Biol 307: 173-182, 2001.
64. Casini GL, Graham D, Heine D, Garcea RL and Wu DT: In vitro papillomavirus capsid assembly analyzed by light scattering. Virology 325: 320-327, 2004.
65. Bugnon Valdano M, Massimi P, Broniarczyk J, Pim D, Myers M, Gardiol D and Banks L: Human Papillomavirus infection requires the CCT Chaperonin Complex. J Virol 95: e01943-20, 2021.
66. Liu Z, Rashid T and Nyitray AG: Penises not required: A systematic review of the potential for human papillomavirus horizontal transmission that is non-sexual or does not include penile penetration. Sex Health 13: 10-21, 2016.
67. American College of Obstetricians and Gynecologists: ACOG Practice Bulletin. clinical management guidelines for obstetrician-gynecologists. Number 61, April 2005. Human papillomavirus. Obstet Gynecol 105: 905-918, 2005.
68. Burchell AN, Winer RL, de Sanjosé S and Franco EL: Chapter 6: Epidemiology and transmission dynamics of genital HPV infection. Vaccine 24 (Suppl 3): S3/52-61, 2006.
69. Tumban E: A current update on human papillomavirus-associated head and neck cancers. Viruses 11: 922, 2019.
70. Smith EM, Parker MA, Rubenstein LM, Haugen TH, Hamsikova E and Turek LP: Evidence for vertical transmission of HPV from mothers to infants. Infect Dis Obstet Gynecol 2010: 326369, 2010.
71. Pattyn J, Van Keer S, Tjalma W, Matheeussen V, Van Damme P and Vorsters A: Infection and vaccine-induced HPV-specific antibodies in cervicovaginal secretions. A review of the literature. Papillomavirus Res 8: 100185, 2019.
72. Kombe Kombe AJ, Li B, Zahid A, Mengist HM, Bounda GA, Zhou Y and Jin T: Epidemiology and Burden of human papillomavirus and related diseases, molecular pathogenesis, and vaccine evaluation. Front Public Health 8: 552028, 2020.
73. Yuan Y, Cai X, Shen F and Ma F: HPV post-infection microenvironment and cervical cancer. Cancer Lett 497: 243-254, 2021.
74. Bowden SJ, Doulgeraki T, Bouras E, Markozannes G, Athanasiou A, Grout-Smith H, Kechagias KS, Ellis LB, Zuber V, Chadeau-Hyam M, *et al*: Risk factors for human papillomavirus infection, cervical intraepithelial neoplasia and cervical cancer: An umbrella review and follow-up Mendelian randomisation studies. BMC Med 21: 274, 2023.
75. Oyouni AAA: Human papillomavirus in cancer: Infection, disease transmission, and progress in vaccines. J Infect Public Health 16: 626-631, 2023.
76. Kero K and Rautava J: HPV infections in heterosexual couples: Mechanisms and covariates of virus transmission. Acta Cytol 63: 143-147, 2019.
77. Goulenok T, Ferré VM, Mageau A, Papo T and Sacré K: Risk factors for high-risk human papillomavirus cervical infection and clearance in patients with systemic lupus erythematosus. Eur J Intern Med 116: 149-151, 2023.
78. Scott-Wittenborn N and Fakhry C: Epidemiology of HPV related malignancies. Semin Radiat Oncol 31: 286-296, 2021.
79. Kyrgiou M and Moscicki AB: Vaginal microbiome and cervical cancer. Semin Cancer Biol 86 (Pt 3): 189-198, 2022.
80. Bruno MT, Coco A, Di Pasqua S and Bonanno G: Management of ASC-US/HPV positive post-menopausal woman. Virol J 16: 39, 2019.
81. Salazar EL, Mercado E, Sojo I and Salcedo M: Relationship between estradiol 16 alpha-hydroxylation and human papillomavirus infection in cervical cell transformation. Gynecol Endocrinol 15: 335-340, 2001.
82. Kedzia W, Goździcka-Józefiak A, Kwaśniewska A, Schmidt M, Miturski R and Spaczyński M: Relationship between HPV infection of the cervix and blood serum levels of steroid hormones among pre- and postmenopausal women. Eur J Gynaecol Oncol 21: 177-179, 2000.
83. Melo BAC, Vilar LG, Oliveira NR, Lima PO, Pinheiro MB, Domingueti CP and Pereira MC: Human papillomavirus infection and oral squamous cell carcinoma-a systematic review. Braz J Otorhinolaryngol 87: 346-352, 2021.
84. Stanley M: Pathology and epidemiology of HPV infection in females. Gynecol Oncol 117 (2 Suppl): S5-S10, 2010.
85. Terada M, Shimazu T, Saito J, Odawara M, Otsuki A, Yaguchi-Saito A, Miyawaki R, Kuchiba A, Ishikawa H, Fujimori M, *et al*: Age, gender and socioeconomic disparities in human papillomavirus (HPV) awareness and knowledge among Japanese adults after a 7-year suspension of proactive recommendation for the HPV vaccine: A nationally representative cross-sectional survey. Vaccine 41: 7147-7158, 2023.
86. Bean MB, Switchenko JM, Steuer CE, Patel M, Higgins K, McDonald M, Chen GZ, Beitler JJ, Shin DM, Gillespie T and Saba NF: Demographic and socioeconomic factors associated with metastases at presentation in HPV-Related squamous cell carcinoma of the head and neck: An NCDB analysis. JCO Oncol Pract 16: e476-e487, 2020.
87. Cohen PA, Jhingran A, Oaknin A and Denny L: Cervical cancer. Lancet 393: 169-182, 2019.
88. Pimple S and Mishra G: Cancer cervix: Epidemiology and disease burden. CytoJournal 19: 21, 2022.
89. Leung E, Han K, Zou J, Zhao Z, Zheng Y, Wang TT, Rostami A, Siu LL, Pugh TJ and Bratman SV: HPV sequencing facilitates ultrasensitive detection of HPV circulating tumor DNA. Clin Cancer Res 27: 5857-5868, 2021.
90. Wu L, Wang W, Zhang J, Wu X, Chen Y, Gu X, Shao H, Li H and Liu W: Detection of five types of HPV genotypes causing anogenital warts (Condyloma Acuminatum) Using PCR-Tm analysis technology. Front Microbiol 13: 857410, 2022.
91. McMullen C, Chung CH and Hernandez-Prera JC: Evolving role of human papillomavirus as a clinically significant biomarker in head and neck squamous cell carcinoma. Expert Rev Mol Diagn 19: 63-70, 2019.
92. Krasniqi E, Barba M, Venuti A, Pizzuti L, Cappuzzo F, Landi L, Carpano S, Marchetti P, Villa A, Vizza E, *et al*: Circulating HPV DNA in the management of oropharyngeal and cervical cancers: Current knowledge and future perspectives. J Clin Med 10: 1525, 2021.
93. Bragulla HH and Homberger DG: Structure and functions of keratin proteins in simple, stratified, keratinized and cornified epithelia. J Anat 214: 516-559, 2009.
94. Aloi F, Tomasini C and Pippione M: HPV-related follicular cysts. Am J Dermatopathol 14: 37-41, 1992.
95. Burmeister CA, Khan SF, Schafer G, Mbatani N, Adams T, Moodley J and Prince S: Cervical cancer therapies: Current challenges and future perspectives. Tumour Virus Res 13: 200238, 2022.
96. Mahmoodi P, Rezayi M, Rasouli E, Avan A, Gholami M, Ghayour Mobarhan M, Karimi E and Alias Y: Early-stage cervical cancer diagnosis based on an ultra-sensitive electrochemical DNA nanobiosensor for HPV-18 detection in real samples. J Nanobiotechnology 18: 11, 2020.
97. Depuydt CE, Vereecken AJ, Salembier GM, Vanbrabant AS, Boels LA, van Herck E, Arbyn M, Segers K and Bogers JJ: Thin-layer liquid-based cervical cytology and PCR for detecting and typing human papillomavirus DNA in Flemish women. Br J Cancer 88: 560-566, 2003.
98. Sherman ME, Mendoza M, Lee KR, Ashfaq R, Birdsong GG, Corkill ME, McIntosh KM, Inhorn SL, Zahniser DJ, Baber G, *et al*: Performance of liquid-based, thin-layer cervical cytology: Correlation with reference diagnoses and human papillomavirus testing. Mod Pathol 11: 837-843, 1998.
99. Dom-Chima N, Ajang YA, Dom-Chima CI, Biswas-Fiss E, Aminu M and Biswas SB: Human papillomavirus spectrum of HPV-infected women in Nigeria: An analysis by next-generation sequencing and type-specific PCR. Virol J 20: 144, 2023.
100. Brink AA, Snijders PJ and Meijer CJ: HPV detection methods. Dis Markers 23: 273-281, 2007.
101. Westra WH: Detection of human papillomavirus (HPV) in clinical samples: Evolving methods and strategies for the accurate determination of HPV status of head and neck carcinomas. Oral Oncol 50: 771-779, 2014.

102. Lindh E, Chua KL, Kataoka A, Bistoletti P, Groff D and Hjerpe A: Detection of human papillomavirus (HPV) using dot blot and Southern blot, hybridizing with a mixture of seven probes. APMIS 100: 301-308, 1992.
103. Schiffman MH, Bauer HM, Lorincz AT, Manos MM, Byrne JC, Glass AG, Cadell DM and Howley PM: Comparison of Southern blot hybridization and polymerase chain reaction methods for the detection of human papillomavirus DNA. J Clin Microbiol 29: 573-577, 1991.
104. Hubbard RA: Human papillomavirus testing methods. Arch Pathol Lab Med 127: 940-945, 2003.
105. Liao Y, Zhou Y, Guo Q, Xie X, Luo E, Li J and Li Q: Simultaneous detection, genotyping, and quantification of human papillomaviruses by multicolor real-time PCR and melting curve analysis. J Clin Microbiol 51: 429-435, 2013.
106. Mahmoodi P, Fani M, Rezayi M, Avan A, Pasdar Z, Karimi E, Amiri IS and Ghayour-Mobarhan M: Early detection of cervical cancer based on high-risk HPV DNA-based genosensors: A systematic review. BioFactors 45: 101-117, 2019.
107. Suresh K, Shah PV, Coates S, Alexiev BA and Samant S: In situ hybridization for high risk HPV E6/E7 mRNA in oropharyngeal squamous cell carcinoma. Am J Otolaryngol 42: 102782, 2021.
108. Coppock JD, Willis BC, Stoler MH and Mills AM: HPV RNA in situ hybridization can inform cervical cytology-histology correlation. Cancer Cytopathol 126: 533-540, 2018.
109. Lewandowski G, Delgado G, Holloway RW, Farrell M, Jenson AB and Lancaster WD: The use of in situ hybridization to show human papillomavirus deoxyribonucleic acid in metastatic cancer cells within lymph nodes. Am J Obstet Gynecol 163 (4 Pt 1): 1333-1337, 1990.
110. Begum S, Gillison ML, Ansari-Lari MA, Shah K and Westra WH: Detection of human papillomavirus in cervical lymph nodes: A highly effective strategy for localizing site of tumor origin. Clin Cancer Res 9: 6469-6475, 2003.
111. Fauzi FH, Hamzan NI, Rahman NA, Suraiya S and Mohamad S: Detection of human papillomavirus in oropharyngeal squamous cell carcinoma. J Zhejiang Univ Sci B 21: 961-976, 2020.
112. Cherif S, Amine A, Thies S, Taube ET, Braicu EI, Sehouli J and Kaufmann AM: Prevalence of human papillomavirus detection in ovarian cancer: A meta-analysis. Eur J Clin Microbiol Infect Dis 40: 1791-1802, 2021.
113. Serour Y, Bendahmane M, Abbou Baker F, Medles M, Moueddene B and Kraiba R: HPV test by Hybrid Capture II for the diagnosis of HR-HPV persistent infection. Med Mal Infect 47: 484-489, 2017.
114. Nazarenko I, Kobayashi L, Giles J, Fishman C, Chen G and Lorincz A: A novel method of HPV genotyping using Hybrid Capture sample preparation method combined with GP5+/6+ PCR and multiplex detection on Luminex XMAP. J Virol Methods 154: 76-81, 2008.
115. Ikenberg H: Laboratory diagnosis of human papillomavirus infection. Curr Probl Dermatol 45: 166-174, 2014.
116. Baleriola C, Millar D, Melki J, Coulston N, Altman P, Rismanto N and Rawlinson W: Comparison of a novel HPV test with the Hybrid Capture II (hcII) and a reference PCR method shows high specificity and positive predictive value for 13 high-risk human papillomavirus infections. J Clin Virol 42: 22-26, 2008.
117. He H, Pan Q, Pan J, Chen Y and Cao L: Study on the correlation between hTREC and HPV load and cervical CINI/II/III lesions and cervical cancer. J Clin Lab Anal 34: e23257, 2020.
118. Santos FLSG, Invencao MCV, Araujo ED, Barros GS and Batista MVA: Comparative analysis of different PCR-based strategies for HPV detection and genotyping from cervical samples. J Med Virol 93: 6347-6354, 2021.
119. Mattox AK, D'Souza G, Khan Z, Allen H, Henson S, Seiwert TY, Koch W, Pardoll DM and Fakhry C: Comparison of next generation sequencing, droplet digital PCR, and quantitative real-time PCR for the earlier detection and quantification of HPV in HPV-positive oropharyngeal cancer. Oral Oncol 128: 105805, 2022.
120. VanGuilder HD, Vrana KE and Freeman WM: Twenty-five years of quantitative PCR for gene expression analysis. Biotechniques 44: 619-626, 2008.
121. Grover S, Seckar T, Gao L, Bhatia R, Lin X, Zetola N, Ramogola-Masire D and Robertson E: Characterization of HPV subtypes in invasive cervical cancer in Botswana patients using a pan-pathogen microarray technology. Tumour Virus Res 15: 200262, 2023.
122. Kim SM, Kwon IJ, Myoung H, Lee JH and Lee SK: Identification of human papillomavirus (HPV) subtype in oral cancer patients through microarray technology. Eur Arch Otorhinolaryngol 275: 535-543, 2018.
123. Kroczek RA: Southern and northern analysis. J Chromatogr 618: 133-145, 1993.
124. Chen WG, Yang CM, Xu LH, Zhang N, Liu XY, Ma YG, Huo XL, Han YS, Tian DA and Zheng Y: Gene chip technology used in the detection of HPV infection in esophageal cancer of Kazakh Chinese in Xinjiang Province. J Huazhong Univ Sci Technolog Med Sci 34: 343-347, 2014.