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REVIEW ARTICLE

The Link between Human Papillomavirus and Prostate Cancer: A Narrative Literature Review

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Abstract: Prostate cancer (PCa) remains a leading cause of cancer mortality in men globally. Age, genetic predisposition, and inflammation are the major risk factors. Increasing evidence suggests that oncogenic viruses, HPV types 16/18, could be involved in prostate carcinogenesis. This review critically examines the potential association between HPV infection and prostate cancer, including both molecular mechanisms and epidemiological evidence. We conducted a narrative literature review by systematically searching PubMed, Scopus, and Google Scholar for papers published from 2013 to 2025. We used search terms such as prostate cancer, HPV, oncogenic viruses, and viral carcinogenesis. We reviewed several peer-reviewed papers that involved molecular information, clinical documentation, and meta-analytic data. The evidence reports HPV DNA in 15-36% of PCa tissues, the most common being HPV-16/18. Mechanistically, HPV proteins (E6/E7) inactivate central tumor suppressors (p53, Rb), activate anti-apoptotic proteins (Bcl-2, survivin), and induce changes associated with cancer onset (through N-cadherin/TWIST), as observed in HPV-positive anogenital cancers. Genomic signatures reveal that HPV-positive PCa has characteristic patterns of mutation (e.g., KMT2C/D disruption). Nonetheless, heterogeneity across HPV detection assays and small sample sizes in a few studies call for cautious interpretation.

Today, we have data suggesting that HPV may cause PCa, possibly through inflammation (NF-B) and unstable genes; however, the exact mechanism remains unclear. We require large trials in many centers and additional screens to determine the role of HPV in this. As we can prevent HPV, these findings suggest that HPV vaccines could be of critical importance in preventing PCa. We must find out more.

Keywords: Prostatic Neoplasms, Papillomavirus Infections, Carcinogenesis, Viral, Oncogenic Viruses

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1. Introduction

Prostate cancer (PCa), a neoplasm in the prostate gland, a vital male accessory organ for the production of seminal fluid, is diagnosed most frequently by digital rectal examination or an elevated Prostate-Specific Antigen (PSA) level (levels >4 ng/mL to detect likely disease). PCa is among the world's most frequent cancers in men and ranks as an important public health concern, occurring in about one in six people worldwide. Though having an extremely high incidence rate, PCa is extremely curable if diagnosed at early stages(1). PCa accounted for 1,414,259 new cancer cases and was the second most prevalent cancer in the world in 2020, as per the World Health Organization (WHO). Furthermore, it was the fifth most common cancer-related death in men, with an estimated 375,304 male deaths across all ages worldwide (Global Cancer Statistics 2020)(2). Several risk factors are known to contribute to the development of prostate cancer

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(PCa), including increasing age, obesity, dietary patterns, alcohol consumption, smoking, and family history. According to the National Cancer Institute (NCI), the median age at diagnosis is approximately 60–70 years, with the majority of cases occurring in individuals over the age of 65(3, 4). Oncoviruses, or cancer-causing viruses, are estimated to account for approximately one-ninth of all cancers worldwide. These viral pathogens can induce host cell transformation, leading to uncontrolled cell proliferation and, ultimately, oncogenesis (4). The International Agency for Research on Cancer (IARC) has classified a subset of these viruses as human carcinogens. And these are certain Human Papillomaviruses (HPVs), that is, type 16, as well as Epstein-Barr virus (EBV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), Kaposi's sarcoma-associated herpesvirus (KSHV), and Human T-lymphotropic virus type 1 (HTLV-1). These viruses significantly account for the majority of human cancers(5). Although there are various oncogenic viruses, the focus of this review is particularly directed towards Human Papillomaviruses (HPVs) due to increasing evidence pointing toward their possible involvement in prostate carcinogenesis.

HPV is a common sexually transmitted disease in the world and a significant burden to public health systems. HPV-16 and HPV-18 are high-risk types and established etiologic agents for most human cancers, especially squamous epithelial cell cancers(3, 6, 7). The high-risk types of HPV are closely associated with the etiology of many cancers, such as anogenital and upper gastrointestinal cancer(8, 9). In the last half-century, the epidemiological pattern of cancers of HPV has changed radically, with rising rates among men, who now account for a significant portion of new cancers(10).

With the unequivocally proven oncogenic potential of high-risk types of HPV in other human cancers, and the new but sometimes controversial data regarding their presence in the prostate gland tissue, the current review attempts to critically analyze the existing scientific evidence for the potential role of infection with HPV, and more specifically, high-risk types thereof, in the etiology of prostate cancer. We will also discuss the suggested molecular pathways by which HPV may play a role in prostate carcinogenesis. This review will first establish a background context of PCa pathogenesis and known risk factors before considering the high-risk HPV types and their oncogenic proteins. The crux of this review will be a summation of the current studies that have attempted to confirm an association between the presence of HPV and prostate cancer and hence charting the potential mechanisms by which HPV infection would lead to PCa development. The final subsection will discuss research limitations and variability in findings and provide recommendations for future studies on the possible relationship between HPV and prostate cancer.

2. Methodology

For the purpose of this narrative review, we conducted a comprehensive literature search in the major electronic databases PubMed, Scopus, and Google Scholar. The search covered publications from January 2013 through December 2025. A combination of keywords and Medical Subject Headings (MeSH) terms was applied, including "prostate cancer," "prostatic neoplasms," "human papillomavirus," "HPV," "papillomavirus infections," "oncogenic viruses," and "viral carcinogenesis."

The inclusion criteria encompassed peer-reviewed original research articles, review articles, systematic reviews, and meta-analyses that focused on the correlation between HPV infection and prostate cancer. Studies that did not address the central topic of this review were excluded. To ensure comprehensive coverage, we retrieved articles from both subscription-based and open-access databases. We started with 50 possible articles from our exhaustive search. Following a preliminary screening of titles and abstracts to exclude duplicates and irrelevant records, 34 articles were chosen for full-text assessment and eventual use in this research.

To guarantee the quality and rigor of our review, we employed principles outlined in reporting guidelines like PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). Although we did not prepare a full PRISMA flow diagram for this narrative review, we extracted data systematically from included studies. Targeted extraction of information on study design, sample size, detection means for HPV, HPV types found, molecular data (e.g., E6/E7 expression, p53/Rb inactivation), and clinical data with significance to prostate cancer. An independent assessment of each study's quality was performed based on methodological rigor, reliability of findings, and susceptibility to bias, with particular emphasis on sample size and statistical analysis. This rigorous evaluation provided a robust and unbiased foundation for the present review.

2.1. Overview of HPV and Its Oncogenic Potential

HPVs, particularly those belonging to the alpha and beta papillomavirus genera, primarily infect epithelial cells lining mucocutaneous surfaces (such as the oral and anogenital regions) as well as cutaneous surfaces. Persistent infection can lead to the development of proliferative squamous lesions, commonly referred to as warts (11). Curiously, there are some high-risk HPV types possessing a specific genetic composition allowing malignant transformation of these lesions. Based on IARC Monograph classification, the high-risk alpha-papillomavirus types of HPV with definite association with carcinogenesis include type 16, 31, 52, and 58 (clade A9); type 18, 45, and 59 (clade A7); type 51 (clade A5); and type 56

and 66 (clade A6)(5). HPV is primarily transmitted by sexual intercourse but also through fomite transmission or non-sexual transmission. Risk factors that increase the risk of HPV acquisition are early initiation of sex, having multiple sexual partners, men who have sex with men (MSM), and oral contraceptive use. Socioeconomic disadvantage and smoking of tobacco are other cofactors that increase susceptibility to infection(12). Coinocident Sexually Transmitted Infections (STIs) like Neisseria gonorrhoeae, Chlamydia trachomatis, and Human Immunodeficiency Virus (HIV) can enhance the pathogenicity of HPV by greater exposure and prolonged viral persistence. For example, bacterial STIs like chlamydia and gonorrhea have been known to cause inflammation and breach the integrity of mucosal barriers, thereby facilitating entry of HPV into host epithelial cells(13). STIs also compromise host immune surveillance, thereby inhibiting successful clearance of HPV infections(14).

Of all the many different types of HPV, in most cases of cervical cancer, the origin is due to types 16 and 18 primarily, since they code for the oncoproteins E6 and E7. In particular, the viral protein E6 causes the proteasomal degradation of the tumor suppressor p53 via ubiquitination, thus inactivating the p53 tumor suppressor pathway that is crucial(15). Simultaneously, the E7 protein is counteracting the retinoblastoma (Rb) tumor suppressor pathway by triggering Rb protein degradation via a calpain-mediated process in the proteasome. Such dual interference by E6 and E7 constitutes a basic oncogene drive. In addition to their direct interference with cell cycle control, these viral oncoproteins trigger immunosuppression by interfering with interferon signal transduction pathways. This immunomodulatory property enables transformed cells to escape host immune detection and killing. HPV genomic sequence integration into the host genome, insertional mutagenesis, is a landmark in cervical carcinogenesis. This integration results in the sustained and uncontrolled expression of the oncogenic viral proteins E6 and E7, whose production substantially contributes to tumor genesis and metastasis(5). While these fundamental mechanisms of E6/E7 action are well-established, their specific roles and intricate interplay in diverse cancer types, particularly prostate cancer, are subjects of ongoing investigation, revealing unique nuances.

2.2. HPV-Related Malignancies Beyond the Cervix

Anal cancer represents a significant global health concern, with the majority of cases attributable to HPV infections of the anal canal. Notably, high-risk HPV-16 has been implicated in more than 90% of anal squamous cell carcinomas (SCC). Over the past two decades, age-standardized incidence rates of anal cancer have been rising in both men and women worldwide. A particularly high prevalence of anal HPV infection has been documented among HIV-positive men who have sex with men (MSM), likely explained in part by self-inoculation (16).

Several factors are associated with an elevated risk of anal cancer, including being unmarried, smoking, a history of anogenital warts, engaging in anal intercourse, co-infection with other genital viruses, and having multiple sexual partners (12). Importantly, HPV transmission in the anal region is not limited to anal intercourse; it may also occur through direct and indirect contact, such as perianal wiping (17).

Evidence indicates a substantially increased risk of anal cancer in specific high-risk groups, including individuals with HIV, MSM, organ transplant recipients, women with HPV-associated anogenital intraepithelial neoplasia or cancer, and those with autoimmune diseases (18).

Penile cancer, a disabling neoplasm, is most typically linked with HPV infection, which manifests as masses or lesions of the penis. HPV is most often seen in specific histological subtypes, including warty and basaloid carcinomas, whereas its relationship with other penile squamous cell carcinomas may be variable. Certain specific high-risk types of HPV, including HPV-16, 18, 31, 33, 45, 56, and 65, are identified as cofactors in penile carcinogenesis(19). HPV infection of the penis is also common and most common in young adults, with the highest rates in those aged in their twenties. The prevalence is significantly rising, especially in the MSM group(12). In a 2021 meta-analysis of 107 global studies of 36,773 MSM, the prevalence of genital HPV infection was 36.2%(20). This confirms a strong association between genital HPV prevalence and risk of anogenital malignancy in this population.

There were an estimated 700,000 cases of head and neck cancer (HNC) and 360,000 deaths globally in 2020. The majority of these cases were seen in Western nations. In the past three decades, several Western countries witnessed an increase in HPV-related oropharyngeal cancer, which has now become the most common HPV-related cancer, surpassing that of cervical cancer. The rate of HNC incidence caused by HPV has decreased over the years in high-income countries and is now estimated to be about 70% of HPV-driven HNC incidence, and the majority are men(21-23). Research indicates that about 85% of HPV-caused high-risk HNC incidence is from HPV-16 and HPV-18, and 15% from other types of HPV. Evidence indicates that Epstein-Barr virus (EBV) could synergize with the high-risk subtypes of HPV in HNC initiation and progression(24).

2.3. HPV and Prostate Cancer: Emerging Evidence and Mechanisms

Of note was a study of the relationship between prostate cancer (PCa) and prior infection with HPV that reported HPV-infected patients were 2.321-fold more likely to have PCa than HPV-naïve patients. Additionally, prostatitis at the time

of diagnosis was a predictive indicator of later diagnosis of PCa, in alignment with observations seen. The current study lends strong epidemiological evidence in favor of a connection between PCa and HPV infection, reinforcing the evidence piling up that indicates a possible association between these two clinical entities(25). NF-B signal transduction pathway, an essential cell regulatory element, is a central mediator which bridges inflammation and oncogenic generation. This pathway can be activated by numerous stimuli, regulating gene transcription of carcinogenesis more often than not. NF-B is induced by most oncogenic viruses such as HPV, human herpes viruses, and Epstein-Barr virus (EBV). A mouse model showed NF-B blockade to reduce inflammation and inhibit tumor growth, establishing its pivotal position. Pathogens have been shown to trigger inflammation, resulting in host cell DNA damage, maybe lead to malignant transformation. Furthermore, epidemiological data pointing towards anti-inflammatory drugs like aspirin reducing cancer risk further support the interface between inflammation, NF-B activation, and carcinogenesis(26).

The expression levels of viral oncogenes (E2, E6, and E7) and cellular markers, including tumor suppressor proteins (Rb and p53), anti-apoptotic proteins (Bcl-2 and survivin), and factors involved in inflammation and angiogenesis, have been examined. HPV DNA was detected in 29 of 58 (32.7%) PCa cases and 5 of 32 (15.6%) normal prostate tissues, although there was no initial statistically significant association between the overall presence of HPV sequences and PCa diagnosis. Among HPV-positive prostate cells, HPV-16 and HPV-18 types were detected in 47.4% and 31.6% of cases, respectively. Expression levels of tumor suppressor proteins (Rb and p53) were significantly decreased in HPV-positive cells compared to HPV-negative cells. Conversely, expression of anti-apoptotic proteins (Bcl-2 and survivin) and pro-angiogenic/inflammatory markers was significantly increased in the HPV-positive cancer group compared to both HPV-negative cancer and normal prostate tissue groups(27, 28). These findings offer crucial insights into how HPV oncoproteins might specifically manipulate cellular pathways in prostate cells, going beyond their generalized effects observed in other cancers.

In a recent investigation, the interaction of HPV oncogenes (i.e., E2, E6, E7) with important cellular genes, including survivin, Bcl-2, tumour suppressors (i.e., Rb, p53), and cell adhesion and metastasis-associated genes such as E-cadherin, N-cadherin, Twist, PTPN13, and SLUG, was also investigated. HPV was detected in 36.1% of prostate cancer samples and 15.9% of control samples, demonstrating an evident link between the presence of HPV and prostate cancer.HPV-16 and -18 were the major HPV types in both prostate cancer and control cohorts. Further analysis showed that HPV-positive PCa had significantly lower expression of the tumor suppressor genes Rb and p53.In contrast, expression of the anti-apoptotic genes Bcl-2 and survivin was significantly higher. Moreover, compared to HPV-negative samples, expression of N-cadherin, SLUG, and TWIST was increased in the HPV-positive samples, whereas expression of PTPN13 and E-cadherin was decreased. These results indicate that HPV may promote prostate cancer progression by affecting the activity of important genes that control cell adhesion and apoptosis(28, 29).

A study further investigated the differential expression of certain miRNAs, including miR-19a, miR-21, miR-23b, miR-34a, and their target genes such as P53 and Rb, in prostate cancer tissues vis-à-vis the HPV oncogene expression. HPV was detected in 17.94% of the normal samples and 28.7% of prostate cancer samples from a cohort of 39 healthy individuals and 112 PCa patients. Nevertheless, this particular analysis could not establish a definite statistical association between HPV and prostate cancer. The study, though, found an increased expression of miR-19a and miR-21 in cancer tissues versus normal samples, while miR-23b and miR-34a experienced downregulation, thus confirming that HPV-associated prostate cancer carries different miRNA expression patterns from HPV-unassociated prostate cancer(28, 30).

Mutations with very similar mutational features were compared between the HPV-positive and HPV-negative PCa according to HPV infection status. HR-HPV was detected in 16.9% of the study cohort, with HPV-16 being the most detected type. HPV-positive PCa had an average mutation rate of 2.68 mutations per Mb, while the rate among HPV-negative tumors was 2.58 mutations per Mb. The mutation spectrum of HPV-negative tumors was typical of PCa, with mutations in SPOP, FOXA1, and MED12 genes being recurrently observed in both groups. HPV-positive cancers, on the other hand, showed an increased frequency of mutations in KMT2C, KMT2D, and ERCC2. The number of copy number alterations per sample was basically the same in both groups, but the genomic regions targeted by these alterations were not. For example, HPV-negative cancers commonly showed losses of major tumor suppressor genes such as CCNC and RB1 and gains in oncogenes such as FCGR2B and CCND1. On the other hand, HPV-positive tumors had losses of a different group of tumor suppressor genes, such as NTRK1 and JAK1(31).

Whereas the role of persistent HPV infection in PCa pathogenesis is still inconclusive due to the various study results on the prevalence of high-risk HPV (HR-HPV) in PCa, HPV-35 was found to be the most prevalent type in one study. The detection rates of HR-HPVs were found to increase in abnormal prostate tissues like adenocarcinoma or chronic prostatitis as compared to the benign ones. Immunohistochemical analysis (IHC) showed that prostatic cells co-localized viral DNA and HPV E7 protein (Figure 1), hence, the presence of HPV in

prostatic tissue might be correlated with the initiation of at least some subtypes of PCa(32).

Despite methodological heterogeneity in HPV detection assays for PCa, HPV remains a plausible risk factor for such cancer. The discernible association that exists between HPV and PCa is highlighted by the significant prevalence of HPV in various tissue types of prostate cancer. This stresses the need for comprehensive further investigation into this potential etiological link, especially to clarify how exactly HPV can affect PCa progression(33).

The complex and labile process of HPV transmission and carcinogenesis, together with confounding factors such as time of exposure, dose of exposure, and experimental conditions, hinders the ability to reach solid conclusions. HR-HPV may participate in prostate carcinogenesis either by promoting pro-oncogenic inflammation at an early or late stage of tumor development or by causing direct genomic damage to host DNA. Nevertheless, additional well-conducted research is recommended to establish standardized practices and detection techniques. Although some data suggest that HPV may play a role in the etiology of PCa, there is still insufficient evidence to confirm causality without definitive supportive data (34).

3. Conclusion

The role of long-term high-risk Human Papillomavirus (HR-HPV) infections, especially types 16 and 18, in the pathogenesis of prostate cancer (PCa) is of potential significance, but definitive proof is challenging to achieve. Mechanistic investigations have shown that viral proteins E6 and E7 may cause carcinogenesis in prostate cells via interference with tumor suppressor functions (e.g., p53 and Rb), induction of anti-apoptotic mechanisms (e.g., Bcl-2 and Survivin), and alterations in cellular morphology (e.g., N-cadherin and TWIST).

Despite heterogeneity in findings of separate studies, cumulative reviews demonstrate a strong association between the presence of HPV in PCa cells and particular genetic alterations in HPV-positive cases. These include exact mutational patterns in KMT2C/D genes and specific gene losses (e.g., NTRK1 and JAK1) not observed in HPV-negative counterparts. However, to provide strong causal evidence is difficult due to methodological heterogeneity in study designs, small sample sizes, and the presence of confounding factors (e.g., HIV co-infection).

The NF-B signaling pathway, which is involved in inflammation and virus-induced genetic alteration, could be a key mediator between HPV infection and prostate cancer development. To eliminate existing uncertainties, future research must adhere to standardized protocols, involve multi-center study designs, have stringent checkpoints, conduct longitudinal analysis, and rigorously assess the role of HPV in altering prostate cells. Specifically, future studies will be needed to address existing methodological disparities and inconsistencies to determine causality and delineate the precise nature of mechanistic involvement.

Presently, founded on the proven ability of HPV vaccines to reduce the incidence of other cancers, and pending a more elucidation of its role in PCa, HPV vaccination may be a viable preventive strategy for PCa control in high-risk populations.

Although this review distills important findings on the possible association of HPV with prostate cancer, one must recognize its limitations. Being a narrative review, our approach, while exhaustive in its search plan in top databases from 2013 to 2025, does not adhere to the stringent pre-established systematic review guidelines such as PRISMA with complete quantitative meta-analysis. This approach, while yielding a broad overview of the data, is potentially susceptible to selection bias in article interpretation and cannot, with confidence, measure associations. Large, multi-center prospective studies with consistent HPV detection methods need to be conducted in future research to overcome current methodological heterogeneity. Longitudinal studies also need to establish an established causal connection and properly define the multifaceted molecular mechanisms by which HPV might cause prostate carcinogenesis. These limitations will be important to address in solidifying our knowledge and guiding future preventive interventions.

4. Appendix

4.1. Acknowledgment

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4.2. Conflict of Interest Statement

The authors declare that there is no conflict of interest regarding the publication of this paper.

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4.4. Authors contributions

The principal author of this work is Dorna Rafighi, the data analyst is Ali Khodadadeh Jigheh Hasti Samenezhad, and Fatemeh Khodadadeh Jigheh, and the Corresponding Author is Sina Samenezhad.

References

Rebello RJ, Oing C, Knudsen KE, Loeb S, Johnson DC, Reiter RE, et al. Prostate cancer. Nature Reviews Disease

Primers. 2021;7(1):9.
2. Belkahla S, Nahvi I, Biswas S, Nahvi I, Ben Amor N. Advances and development of prostate cancer, treatment, and strategies: A systemic review. Frontiers in Cell and Developmental Biology. 2022;10:991330.
3. de Martel C, Georges D, Bray F, Ferlay J, Clifford GM. Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. The Lancet global health. 2020;8(2):e180-e90.
4. Perdana NR, Mochtar CA, Umbas R, Hamid ARA. The risk factors of prostate cancer and its prevention: a literature review. Acta medica indonesiana. 2016;48(3):228-38.
5. Hatano Y, Ideta T, Hirata A, Hatano K, Tomita H, Okada H, et al. Virus-driven carcinogenesis. Cancers. 2021;13(11):2625.
6. Ghaffarzadeh A, Roshdi Maleki M, Rafighi D, Nikbakht Z, Taghinejad J. Genomic detection of HPV Genotypes 16 and 18 in Cervical Lesions in West Azerbaijan province. Journal of Obstetrics, Gynecology and Cancer Research. 2024;10(2):121-6.
7. Satterwhite CL, Torrone E, Meites E, Dunne EF, Mahajan R, Ocfemia MCB, et al. Sexually transmitted infections among US women and men: prevalence and incidence estimates, 2008. Sexually transmitted diseases. 2013;40(3):187-93.
8. Ozaydin-Yavuz G, Bilgili S, Guducuoglu H, Yavuz I, Elibuyuk-Aksac S, Karadag A. Determinants of hgh-risk human papillomavirus infection in anogenital warts. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii. 2019;36(1):76-81.
9. Patra S, Ghosal S, Shand H, Mondal R, Rath A, Jana SK, et al. Function of gamma delta () T cell in cancer with special emphasis on cervical cancer. Human Immunology. 2023;84(12):110724.
10. Dunne EF, Markowitz LE, Saraiya M, Stokley S, Middleman A, Unger ER, et al. CDC grand rounds: reducing the burden of HPV-associated cancer and disease. MMWR Morb Mortal Wkly Rep. 2014;63(4):69-72.
11. Betz SJ. HPV-related papillary lesions of the oral mucosa: a review. Head and neck pathology. 2019;13(1):80-90.
12. Patra S, Shand H, Ghosal S, Ghorai S. HPV and male cancer: pathogenesis, prevention and impact. Journal of the Oman Medical Association. 2025;2(1):4.
13. Peterman TA, Newman DR, Maddox L, Schmitt K, Shiver S. Risk for HIV following a diagnosis of syphilis, gonorrhoea or chlamydia: 328,456 women in Florida, 2000–2011. International journal of STD & AIDS. 2015;26(2):113-9.
14. Kops NL, Bessel M, Horvath JDC, Domingues C, de Souza FMA, Benzaken AS, et al. Factors associated with HPV and other self-reported STI coinfections among sexually active Brazilian young adults: cross-sectional nationwide study. BMJ open. 2019;9(6):e027438.
15. Travé G, Zanier K. HPV-mediated inactivation of tumor suppressor p53. Cell Cycle. 2016;15(17):2231-2.
16. Albuquerque A, Cappello C, Stirrup O, Selinger CP. Anal high-risk human papillomavirus infection, squamous intraepithelial lesions, and anal cancer in patients with inflammatory bowel disease: a systematic review and meta-analysis. Journal of Crohn's and Colitis. 2023;17(8):1228-34.
17. Simpson Jr S, Blomfield P, Cornall A, Tabrizi SN, Blizzard L, Turner R. Front-to-back & dabbing wiping behaviour post-toilet associated with anal neoplasia & HR-HPV carriage in women with previous HPV-mediated gynaecological neoplasia. Cancer Epidemiology. 2016;42:124-32.
18. Clifford GM, Georges D, Shiels MS, Engels EA, Albuquerque A, Poynten IM, et al. A meta-analysis of anal cancer incidence by risk group: toward a unified anal cancer risk scale. International journal of cancer. 2021;148(1):38-47.
19. Spiess PE, Dhillon J, Baumgarten AS, Johnstone PA, Giuliano AR. Pathophysiological basis of human papillomavirus in penile cancer: Key to prevention and delivery of more effective therapies. CA: A Cancer Journal for Clinicians. 2016;66(6):481-95.
20. Farahmand M, Monavari SH, Tavakoli A. Prevalence and genotype distribution of human papillomavirus infection in different anatomical sites among men who have sex with men: a systematic review and meta-analysis. Reviews in medical virology. 2021;31(6):e2219.
21. El Hussein MT, Dhaliwal S. HPV vaccination for prevention of head and neck cancer among men. The Nurse Practitioner. 2023;48(10):25-32.
22. Marra E, Lin C, Clifford GM. Type-specific anal human papillomavirus prevalence among men, according to sexual preference and HIV status: a systematic literature review and meta-analysis. The Journal of infectious diseases. 2019;219(4):590-8.
23. Meites E. Use of a 2-dose schedule for human papillomavirus vaccination—updated recommendations of the Advisory Committee on Immunization Practices. MMWR Morbidity and mortality weekly report. 2016;65.
24. Gutierrez-Xicotencatl L, Pedroza-Saavedra A, Chihu-Amparan L, Salazar-Piña A, Maldonado-Gama M, Esquivel-Guadarrama F. Cellular functions of HPV16 E5 oncoprotein during oncogenic transformation. Molecular Cancer Research. 2021;19(2):167-79.
25. Yin S-H, Chung S-D, Hung S-H, Liu T-C, Lin H-C. Association of prostate cancer with human papillomavirus infections: A case-control study. Prostate Cancer and Prostatic Diseases. 2024;27(4):743-8.
26. Lawson JS, Glenn WK. Multiple pathogens

and prostate cancer. Infectious agents and cancer. 2022;17(1):23.
27. Nahand JS, Esghaei M, Monavari SH, Moghoofei M, Kiani SJ, Mostafaei S, et al. The assessment of a possible link between HPV-mediated inflammation, apoptosis, and angiogenesis in Prostate cancer. International Immunopharmacology. 2020;88:106913.
28. Zolfi E, Khaleghi Mehr F, Emtiazi N, Moradi Y. A review of the carcinogenic potential of human papillomavirus (HPV) in urological cancers. Virology Journal. 2025;22(1):53.
29. Fatemipour M, Nahand JS, Azar MEF, Baghi HB, Taghizadieh M, Sorayyayi S, et al. Human papillomavirus and prostate cancer: the role of viral expressed proteins in the inhibition of anoikis and induction of metastasis. Microbial pathogenesis. 2021;152:104576.
30. Khatami A, Nahand JS, Kiani SJ, Khoshmirsafa M, Moghoofei M, Khanaliha K, et al. Human papilloma virus (HPV) and prostate cancer (PCa): The potential role of HPV gene expression and selected cellular MiRNAs in PCa development. Microbial pathogenesis. 2022;166:105503.
31. Lang B, Cao C, Zhao X, Wang Y, Cao Y, Zhou X, et al. Genomic alterations related to HPV infection status in a cohort of Chinese prostate cancer patients. European Journal of Medical Research. 2023;28(1):239.
32. Ahmed MY, Salman NA, Sandhu S, Cakir MO, Seddon AM, Kuehne C, et al. Detection of high-risk Human Papillomavirus in prostate cancer from a UK based population. Scientific reports. 2023;13(1):7633.
33. Tsydenova IA, Ibragimova MK, Tsyganov MM, Litviakov NV. Human papillomavirus and prostate cancer: systematic review and meta-analysis. Scientific Reports. 2023;13(1):16597.
34. Opeyemi Bello R, Willis-Powell L, James O, Sharma A, Marsh E, Ellis L, et al. Does human papillomavirus play a causative role in prostate cancer? a systematic review using bradford hill's criteria. Cancers. 2023;15(15):3897.

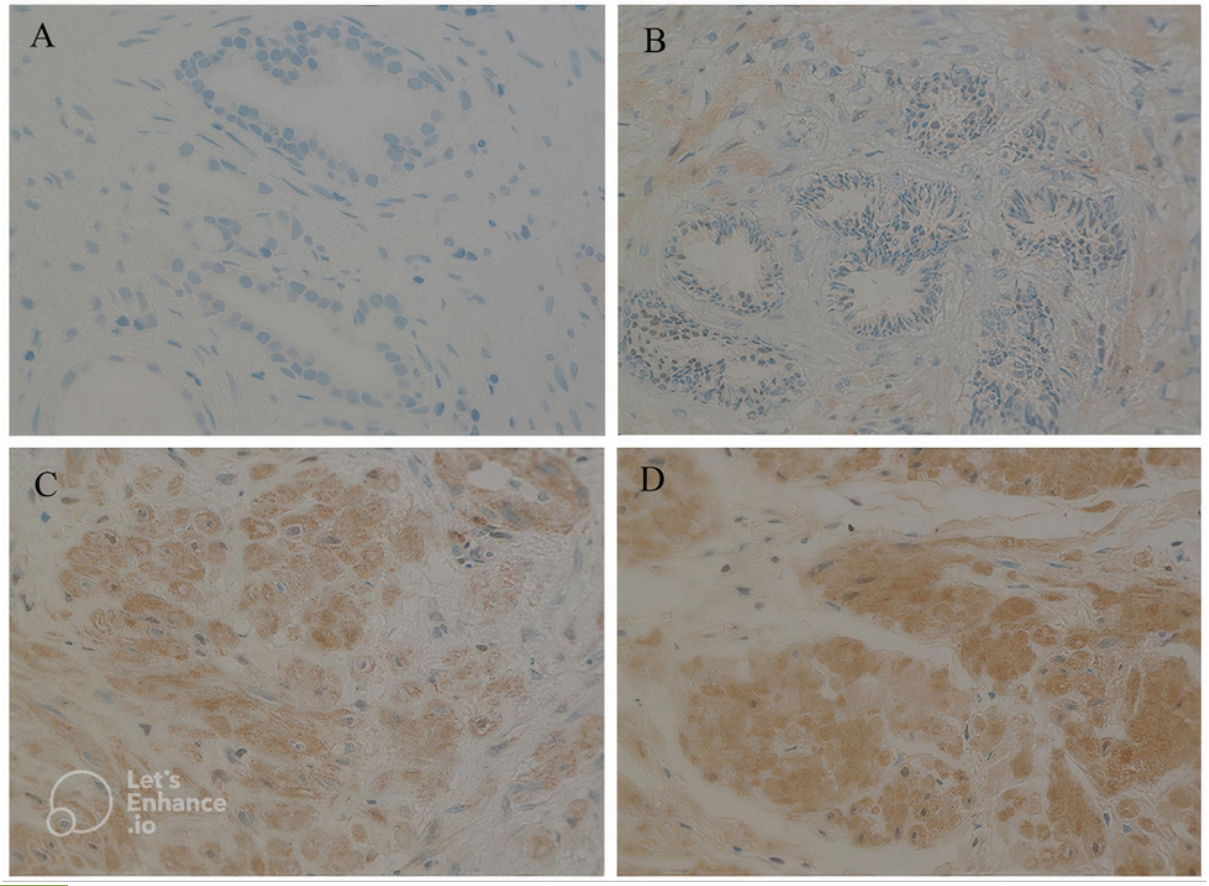

Figure 1: Immunohistochemical visualization of HPV oncoprotein E7. (A) Section of prostate tissue with no HPV positivity. (B, C) Sections from benign and malignant prostate samples showing HPV positivity, respectively, (D) section from prostate tissue showing HPV co-localization and high expression(32).