HPV-INDUCED OROPHARYNGEAL CARCINOMA: MECHANISMS AND CLINICAL IMPLICATIONS

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Introduction

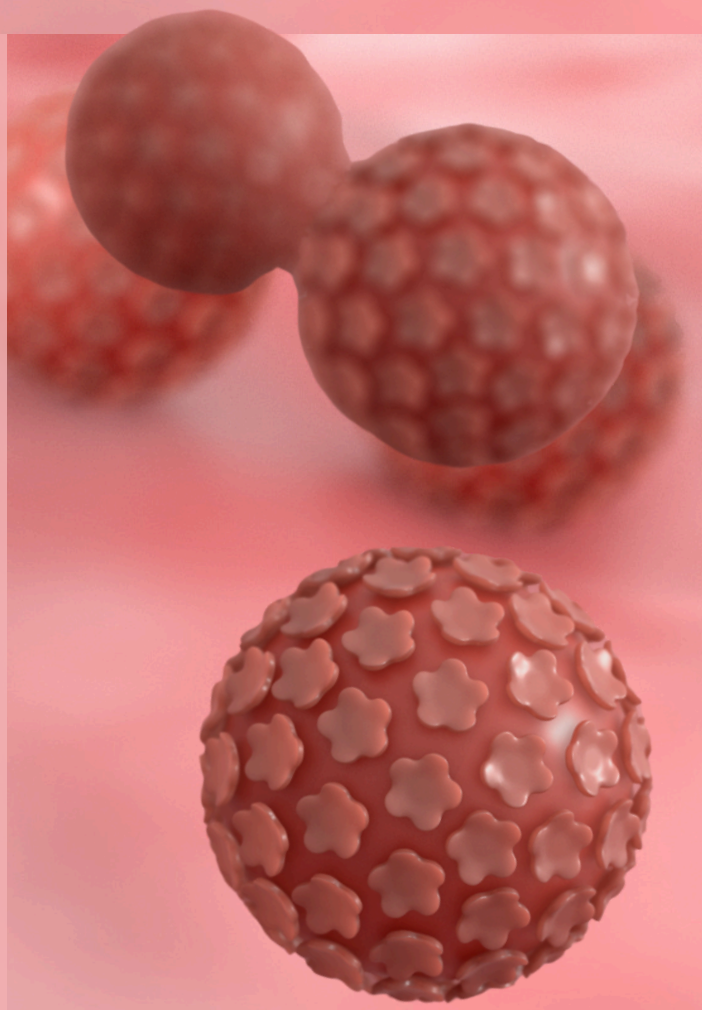
Oropharyngeal Squamous Cell Carcinoma (OPSCC) is a multifactorial health concern with a significant burden on public health systems worldwide. In India, it is one of the leading causes of morbidity.

There exists an intricate interplay between Human papillomavirus (HPV) infection and Oropharyngeal Carcinogenesis. Embracing emerging associations like HPV helps to enhance prevention, early detection, and management strategies on a global scale.

This article explores the incidence of HPV-associated OPSCC, molecular pathways of HPV-associated OPSCC development, and the potential of HPV vaccination in preventing OPSCC.

Epidemiology:

Numerous epidemiological studies indicate a higher prevalence of HPV in OPSCC compared to controls. HPV-positive cancer is presented as a distinct clinical and pathological entity frequently manifesting in younger patients, non-smokers, and non-alcoholics. HPV emerges as a prognostic biomarker, with HPV-positive tumors exhibiting enhanced treatment responsiveness and improved survival outcomes.

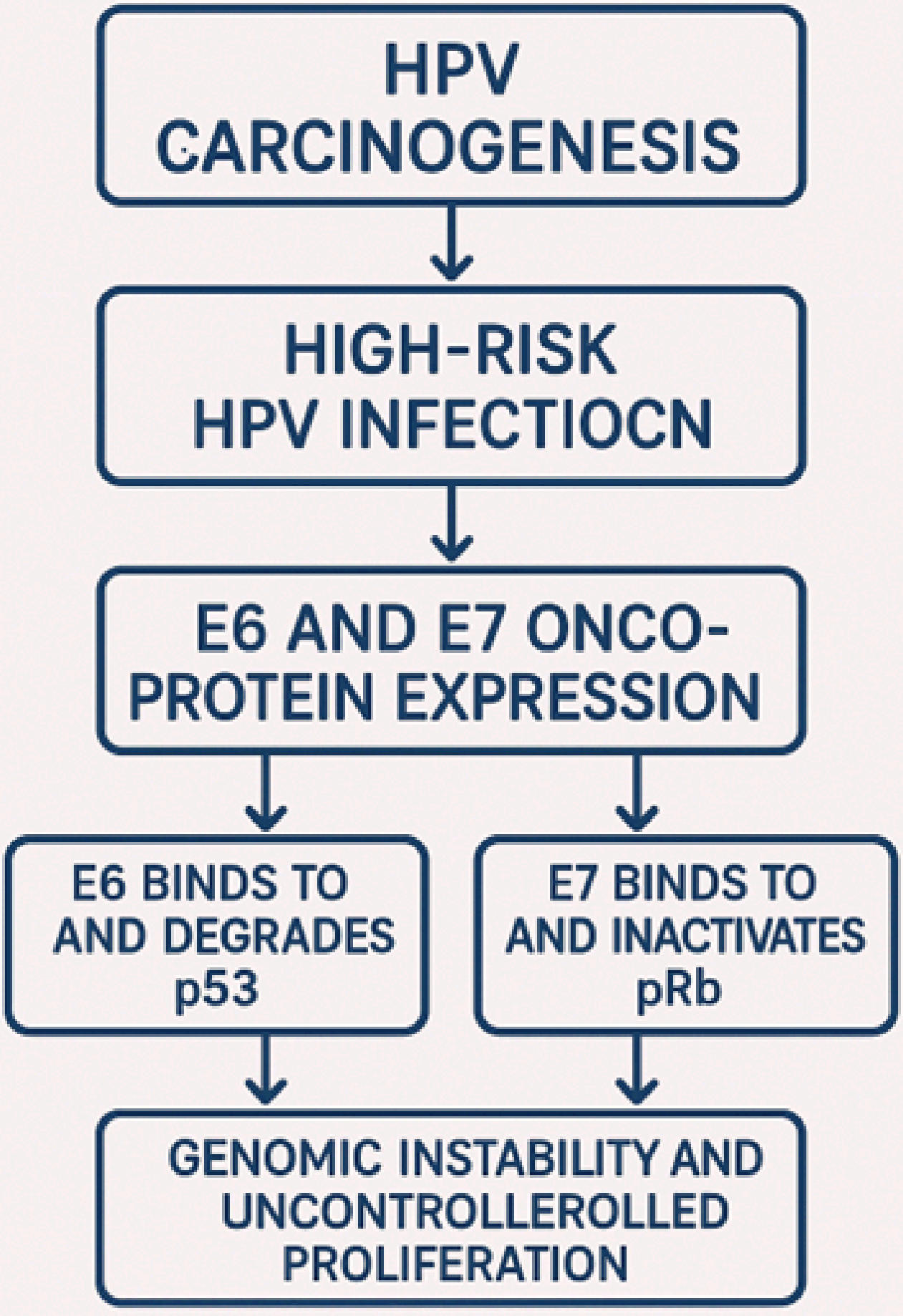


Molecular Pathways:
Further molecular investigations unravel the mechanisms by which HPV promotes Carcinogenesis. The integration of HPV into the host genome disrupts cell growth and division regulation.
HPV oncoproteins notably E6 and E7, have the capability to inhibit tumor suppressor genes such as p53 and pRb, effectively dismantling mechanisms that regulate cell proliferation. Cells infected with HPV experience unhindered growth, division, and survival which creates a positive environment for malignant transformation. HPV has diverse oncogenic potential with specific strains such as HPV16 having greater potential for genomic instability. This provides fertile ground for oncogenesis.

HPV-associated OPSCC exhibits distinct genetic alterations compared to non-HPV counterparts. These genetic fingerprints provide insights into the unique molecular landscape that is shaped by HPV infection. Traditional risk factors such as smoking and alcohol consumption, along with co-factors like immunocompromised states [e.g., Human Immunodeficiency Virus (HIV) infection], can act synergistically with HPV to facilitate carcinogenesis in OPSCC. They may act independently or synergistically with HPV.

This mechanism is established in high-risk types like HPV 16. Unraveling these complex molecular intricacies helps us understand the disease and development of targeted therapeutic interventions and preventive strategies for improved prognosis.

Prognosis:
The prognostic implications of HPV in OPSCC have garnered attention in medical research. The evidence suggests the potential of HPV as a prognostic biomarker thereby influencing treatment and patient management.
Through numerous studies, a consistent trend of HPV-positive cancers exhibiting improved overall survival and disease-free survival rates compared to their HPV-negative counterparts is established. The mechanisms of HPV provide a more pronounced immune response and enhanced sensitivity to radiation therapy as well as chemotherapy, further enhancing favorable prognosis. The intricate interactions between HPV oncoproteins and cellular regulatory pathways render these tumors susceptible to treatment-induced cell death. Physicians can utilize this information for personalized treatment plans.


HPV CARCINOGENESIS
HIGH-RISK HPV INFECTIOCN
E6 AND E7 ONCO-PROTEIN EXPRESSION
E6 BINDS TO AND DEGRADES p53
E7 BINDS TO AND INACTIVATES pRb
GENOMIC INSTABILITY AND UNCONTROLLEROLLED PROLIFERATION

Vaccination:
While HPV vaccines are proven beneficial in cervical and other anogenital cancers their efficacy in OPSCC is still being studied. Targeted therapies that specifically inhibit molecular pathways involved in HPV-induced tumorigenesis, such as inhibitors of E6 and E7 oncoproteins have shown promise in preclinical and early-phase clinical trials. While substantial progress has been made in understanding the association between HPV and OPSCC, long-term data on Oral Squamous Cell Carcinoma is still emerging.
Future research should focus on identifying high-risk populations and developing targeted therapeutic approaches. HPV vaccination has the potential to serve as a preventive strategy to reduce the incidence of HPV-related cancer.

Acknowledging the limitations of this review, which include the inherent biases of the included studies and the evolving nature of the field, it serves as a comprehensive synthesis of the current evidence on the association between HPV and OPSCC.

References

1.Katirachi SK, Gronlund MP, Jakobsen KK, Gronhoi C, von Buchwald C. The Prevalence of HPV in Oral Cavity Squamous Cell Carcinoma. Viruses. 2023; 15(2):451.
2.Sabatini, M.E., Chiocca, S. Human papillomavirus as a driver of head and neck cancers. Br J Cancer 122, 306–314 (2020).
3.D'Souza G, Westra WH, Wang SJ, et al. Differences in the prevalence of human papillomavirus (HPV) in head and neck squamous cell cancers by sex, race, anatomic tumor site, and HPV detection method. JAMA Oncol. 2017;3(12):1697-1706.
4.Dahlstrom KR, Garden AS, William WN Jr, Lim MY, Sturgis EM. Proposed staging system for patients with HPV-related oropharyngeal cancer based on nasopharyngeal cancer N categories. J Clin Oncol. 2016;34(16):1848-1854.
5. Chaturvedi AK, Engels EA, Pfeiffer RM, et al. Human papillomavirus and rising oropharyngeal cancer incidence in the United States. J Clin Oncol. 2011;29(32):4294-4301.
6.Ang KK, Harris J, Wheeler R, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med. 2010;363(1):24-35.
7.Fakhry C, Westra WH, Li S, et al. Improved survival of patients with human papillomavirus-positive head and neck squamous cell carcinoma in a prospective clinical trial. J Natl Cancer Inst. 2008;100(4):261-269.