

The Relationship Between Squamous Cell Carcinoma and Human Papillomavirus (HPV)

Pavane L. Gorrepati, MD

Squamous cell carcinoma (SCC) accounts for a significant proportion of skin cancer cases globally, with chronic exposure to ultraviolet (UV) radiation as the primary risk factor. Emerging research, however, has highlighted the potential role of human papillomavirus (HPV) in the development of SCC. HPV, a DNA virus known for its role in cervical, anogenital, and oropharyngeal cancers, has also been shown to play a potential role in skin carcinogenesis, particularly in immunosuppressed individuals.

HPV has over 200 subtypes, which are categorized into low-risk and high-risk types based on their ability to cause cancer. High-risk HPV types, such as HPV 16 and HPV 18, are responsible for the majority of HPV-related cancers in mucosal tissues, such as cervical cancer. Cutaneous HPV types are common and typically asymptomatic in immunocompetent individuals. These viruses are part of the normal skin microbiome and do not usually cause disease. However, in individuals with compromised immune systems, their oncogenic potential is more evident.

Immunocompromised populations, such as organ transplant recipients who are on immunosuppressive therapy, are at a significantly increased risk of developing cutaneous SCC. In these populations, persistent HPV infections are more likely to occur, allowing the virus to evade normal immune clearance. HPV DNA has been detected in a significant proportion of SCC lesions, particularly in immunosuppressed individuals. Although this does not mean causation, these findings do highlight a potential role for HPV in the development of SCC.¹

Vaccination against HPV is currently recommended primarily for the prevention of cervical and other mucosal cancers, but this may also have potential benefits in reducing the burden of HPV-associated SCC. Although current HPV vaccines target high-risk mucosal types such as HPV 16 and HPV 18, expanding vaccine coverage to include cutaneous HPV types could be a future strategy for preventing SCC, particularly in high-risk populations. Understanding this relationship more fully could lead to significant advancements in the prevention and management of SCC.

¹ Wang, J., Aldabagh, B., Yu, J., & Arron, S. T. (2014, April). *Role of human papillomavirus in cutaneous squamous cell carcinoma: A meta-analysis*. Journal of the American Academy of Dermatology. <https://pmc.ncbi.nlm.nih.gov/articles/PMC3959664/>