

**P-53**  
**BIOINFORMATICS ANALYSIS OF IMMUNE**  
**CHARACTERISTICS IN TUMORS WITH**  
**ALTERNATIVE TUMORIGENESIS PATHWAYS**  
**ASSOCIATED WITH HUMAN PAPILLOMAVIRUSES**

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Human papillomaviruses induce a subset of head and neck squamous cell carcinomas (HNSCC) and anogenital cancers, particularly cervical cancer (CC). The main viral proteins that contribute to tumorigenesis are the E6 and E7 oncoproteins, the expression of which is usually enhanced after the integration of viral DNA into the host genome. Recently, an alternative tumorigenesis pathway has been suggested in about half of HNSCC and CC cases associated with HPV infection (1). This pathway is characterized by extrachromosomal HPV persistence and increased expression of the viral E2, E4, and E5 genes. The E6, E7, E5, and E2 proteins were shown to modify the expression of numerous cellular immune-related genes. The antitumor immune response is a crucial factor in the prognosis of HPV-driven cancers and its characterization can contribute to the prediction and personalization of increasingly used cancer immunotherapy. Therefore, we analyzed immune characteristics of HPV-dependent tumors and their association with types of tumorigenesis. For this analysis, transcriptomic HNSCC and CC datasets from The Cancer Genome Atlas were used. Although patients with tumors with high E2/E4/E5 expression showed better survival, only small differences were found in the composition of tumor-infiltrating immune cells and the expression profiles of immune-related genes. In patients with high E2/E4/E5 expression, a higher age at the time of tumor diagnosis was found for CC and a lower Winter hypoxia score for HNSCC. Unsupervised clustering of both HNSCC and CC samples identified a group of patients with better overall survival, a lower Winter hypoxia score, and lower keratinization of tumors. These characteristics were associated with enhanced infiltration of immune cells and markedly different expression profiles of immune-related genes. Our analysis suggests that while detection of immune reactions against HPV-driven tumors may be a marker of a better prognosis and an important factor in therapy selection, the type of tumorigenesis seems not to play a decisive role in the induction of antitumor immunity.

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REFERENCE

1. Ren S., *et al.*: *Oncogene* 39, 6327 (2020).