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Review

REVIEW

Immunometabolic Alterations by HPV Infection: New Dimensions to Head and Neck Cancer Disparity

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Abstract

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer, with high morbidity and mortality. Racial disparity in HNSCC is observed between African Americans (AAs) and whites, effecting both overall and 5-year survival, with worse prognosis for AAs. In addition to socio-economic status and demographic factors, many epidemiological studies have also identified factors including coexisting human papillomavirus (HPV) infection, primary tumor location, and a variety of somatic mutations that contribute to the prognostic incongruities in HNSCC patients among AAs and whites. Recent research also suggests HPV-induced dysregulation of tumor metabolism and immune microenvironment as the major regulators of HNSCC patient prognosis. Outcomes of several preclinical and clinical studies on targeted therapeutics warrant the need to elucidate the inherent mechanistic and population-based disparities underlying patient responses. This review systematically reports the underlying reasons for inconsistency in disease prognosis and therapy responses among HNSCC patients from different racial populations. The focus of this review is twofold: aside from discussing the causes of racial disparity, we also seek to identify the consequences of such disparity in terms of HPV infection and its associated mutational, metabolic, and immune landscapes. Considering the clinical impact of differential patient outcomes among AA and white populations, understanding the underlying cause of this disparity may pave the way for novel precision therapy for HNSCC.

Head and neck cancer squamous cell carcinoma (HNSCC) is the sixth-most common cancer worldwide, estimated to comprise approximately 3% of all cancers in the United States. In 2018, approximately 51 540 new cases are projected and 10 030 people are expected to die of oral cavity and pharynx cancer in the United States alone (https://seer.cancer.gov/). Despite considerable efforts, the 5-year overall survival (OS) rate of HNSCC patients has not improved substantially in several decades. The median age at diagnosis of the disease is approximately 63 years (1), although initial disease presentation at younger age is on the rise (2). Generally, HNSCC develops in the upper aerodigestive tract of the head and neck, which includes the oral cavity, nasal cavity, larynx, pharynx, and salivary glands. The traditional etiology of HNSCC generally involves tobacco use (either chewing or smoking) and alcohol consumption. Recent epidemiological and laboratory results, however, have implicated human papillomavirus (HPV) as a causative agent for some HNSCC types. HPV generally infects the tonsillar tissue of Waldeyer's ring. This includes the subsites of the base of the tongue and palatine tonsillar region, both components of the oropharynx. Approximately 70% of oropharyngeal cancers (OPC) in the United States are caused by HPV infection, which generally depicts the younger population as having a very distinct prognosis compared with tobacco-and alcohol-induced OPC (3). HNSCC is endemic in Southeast Asian countries, where tobacco and beetle quid chewing is a cultural norm. In the United States,

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