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Differential mutation spectrum and immune landscape in African Americans *versus* Whites: A possible determinant to health disparity in head and neck cancer

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ABSTRACT

African Americans (AA) with Head and Neck Squamous Cell Carcinoma (HNSCC) have a worse disease prognosis than White patients despite adjusting for socio-economic factors, suggesting the potential biological contribution. Therefore, we investigated the genomic and immunological components that drive the differential tumor biology among race. We utilized the cancer genome atlas and cancer digital archive of HNSCC patients (1992–2013) for our study. We found that AA patients with HNSCC had a higher frequency of mutation compared to Whites in the key driver genes—*P53*, *FAT1*, *CASP8* and *HRAS*. AA tumors also exhibited lower intratumoral infiltration of effector immune cells ($CD8^+$, γδT, resting memory $CD4^+$ and activated memory $CD4^+$ T cells) with shorter survival than Whites. Unsupervised hierarchical clustering of differentially expressed genes demonstrated distinct gene clusters between AA and White patients with unique signaling pathway enrichments. Connectivity map analysis identified drugs (Neratinib and Selumetinib) that target aberrant PI3K/RAS/MEK signaling and may reduce racial disparity in therapy response.

1. Introduction

Epidemiological evidence indicates the potential influence of race and ethnic disparities in differential cancer incidence and mortality rates. Like many other cancers [1–3], African American (AA) patients with Head and Neck Squamous Cell Carcinoma (HNSCC) have a disproportionally increased tumor burden and a five-year survival lower (29.3–31.0%) than Whites (54.7–59.0%) [4–7]. The survival disadvantage is attributed to late disease presentation [6], while a recent retrospective study also revealed decreased survival of AA with localized HNSCC tumors [8]. The racial disparity is caused by a complex interplay between lifestyle, environment and genetic factors of patients [9]. Other factors associated with HNSCC disparity include treatment inequalities, lifestyle, socioeconomic status (SES) and environmental factors [10]. However, after adjusting for these extrinsic factors [11–13], the survival inconsistencies persisted among races and thus suggest the potential role of inherent biological factors in driving disparate racial outcomes [10]. The SEER 18 data (Surveillance, Epidemiology, and End Results

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