Immune profiling of prostate tumors from a military cohort of African American and Caucasian American patients

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Background: Immunobiological factors may, in part, contribute to racial disparities in prostate cancer (PCa), the second leading cause of cancer-related death for US men. African American (AA) men face a greater risk of developing PCa and having a poorer outcome of this disease, compared to Caucasian American (CA) men. The goal of this study is to identify immune-specific differences influencing PCa health disparity as well as PCa progression.

Methods: *Ex vivo* tumor biopsies were obtained following radical prostatectomy (RP) from 60 treatment-naïve patients (30 AA, 30 CA) under approved IRB protocols. Total RNA from fresh frozen tissue was isolated and amplified by PCR using NanoString multiplexed target enrichment protocols (n=51) as well as dam-PCR techniques to perform T cell receptor sequencing of the alpha and beta chains (n=55). We evaluated differences in resulting transcripts by self-reported race, pathology, and other clinical and pathologic features. Relative abundances of immune cell subsets were determined using computational methods, including previously published deconvolution algorithms, to estimate cellular content. T cell receptor diversity was represented by the D50 scoring method.

Results: We identified differentially expressed genes between AA and CA tumors that are characterized by genes regulating Natural Killer (NK) cell function and Wnt signaling cancer pathways. Gene expression of *DVL2* and *KLRC2* were significantly upregulated in CA tumors and, among the entire cohort, were associated with worse disease progression. No difference in immune cell abundance was observed by self-reported race; however, T cell receptor diversity D50 scores were significantly different and were associated with outcome. Strikingly, among the entire cohort, low abundance of intratumoral mast cells was also associated with worse PCa pathology and poorer BCR-free and metastasis-free survival.

Conclusions: Using a race-matched military cohort, we found that AA and CA tumors differ in the expression levels of Wnt and NK signaling-related pathways, yet cellular estimations of immune abundance did not significantly differ. Remarkably, the level of mast cell abundance within tumors at time of RP may be protective and prolong BCR-free and metastasis-free survival of patients. Although overall immune cell abundances were not different by race, T cell receptor sequencing highlighted differences attributed to race as well as BCR and metastasis status. These types of in-depth immune profiling assessments have the potential to guide precision medicine and treatment decisions in the clinic.

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