

ROLE OF TGF β 3 IN PROSTATE CANCER IN AFRICAN-AMERICAN MEN

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Abstract: African American (AA) men are disproportionately affected by prostate cancer (PCa) and display an increased risk of suffering and death from this disease compared to men of other ancestral backgrounds. Epidemiological studies show that AA men are more likely to be diagnosed, diagnosed at an earlier age with more advanced and aggressive prostate cancer compared to any other race/ethnic group, specifically Caucasian (CA) men in the US. Previous reports suggest that in addition to environmental and dietary factors that may influence the severity of PCa, there are specific differences in genes that are expressed in the prostate tissue of AA men, thereby resulting in an increased susceptibility to the development of more aggressive PCa. Previous studies have linked TGF β signaling pathway, specifically the overexpression of TGF- β 1 in health disparities in hypertension, diabetes, and renal failure found in AA, but not CA. Studies have also linked TGF β signaling, specifically TGF- β 3's role in cancer metastases and have shown that this specific isoform, and not TGF- β 1 is involved in more metastatic cancers and is responsible for its effect on the migratory and invasive behavior in breast, endometrial, head/neck, and prostate cancer; however, these studies have not examined TGF- β 3's role in prostate cancer in African American men. In this study, we investigated and determined the circulating levels of TGF- β 3 in AA and CA men diagnosed with prostate cancer. We analyzed serum samples from both AA and CA prostate cancer patients and samples from each ethnic group with no evidence of prostate disease to be used as controls. These samples were analyzed via ELISA to examine TGF- β 3 protein levels and to further determine whether higher levels of TGF- β 3 correlated with advanced degree of disease and whether it is associated with increased incident and advance disease at earlier ages in African American men. In our data we have shown that AA prostate cancer patients had higher levels of TGF- β 3 protein compared to Caucasian patients, in fact, TGF- β 3 protein levels on serum were higher in African American men without prostate cancer compared to Caucasian population, which may correlate with the aggressive cancer metastases seen in African American men. Our further examination of TGF β 's role in AA derived prostate cancer cell lines revealed that TGF- β 3 protein levels were higher compared to Caucasian derived prostate cancer cell lines and in addition, TGF β induced cell migratory and invasive behavior in AA cells with TGF- β 3 having a greater effect. Based on our results, we have demonstrated that AA prostate cancer patients and normal AA men have higher levels of TGF- β 3 protein compared to Caucasian men; and TGF- β 3 induces the migratory and invasive properties in AA derived prostate cancer cell lines which may be the leading causes of metastases in prostate cancer seen in AA men.

Key Words: Transforming growth factor- β 3, prostate cancer metastases, African American men, health disparity

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