Androgen Receptor Activity in Prostate Tumors from HIV-infected and HIV-uninfected Men

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Background. Although androgens are required for prostate tumor growth, circulating levels of testosterone are not associated with development of prostate cancer. However, men with low testosterone who develop prostate cancer have tumors that are more aggressive, perhaps because tumors are already partially hormone refractory. Given that men with HIV frequently experience hypogonadism and that studies suggest HIV-infected men may develop more aggressive prostate tumors, we hypothesized that androgen receptor (AR) activity is dysregulated in prostate tumors of men infected with HIV.

Methods. We selected 9 HIV-infected prostate cancer cases and 15 HIV-uninfected cases from among men included in the Uro-Onc Database (UODB) at the University of California, San Francisco for whom whole transcriptome gene expression profiling data was available from biopsy specimens as part of standard care. We evaluated the scores from three published signatures related to androgen receptor activity with respect to HIV status using t-tests.

Results. Differential AR activity as evidenced by the Sharma et al. 16-gene signature, the only signature derived from an analysis of AR binding sites in human prostate tissue, was significantly associated with HIV status (p=0.01). The direction of the association was consistent with HIV-infected men having more aggressive tumors based on previous analyses of the signature with respect to prostate cancer-specific survival in two independent clinical datasets. Mean scores for both of the in vitro-derived signatures, the Kumar et al. signature³ (0.12) and the Faisal et al signature² (p=0.09), were also higher among HIV-infected men compared to HIV-uninfected men.

Conclusions. Our preliminary data suggest that AR activity may be altered in HIV-infected men with prostate cancer. Additional analyses among a larger sample of prostate cancer cases will investigate whether associations are independent of clinical and tumor characteristics, and evaluate the role of circulating steroid hormones as mediating factors. These findings could inform prostate cancer management for HIV-infected men, as well as provide more general insight into the role of testosterone deficiency on prostate tumor development.

Conflict of Interest. No conflicts

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