**Commercial gene expression tests for prostate cancer prognosis provide paradoxical estimates of race-specific risk**

**Race-specific risk in prostate panels**

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**Background:** Commercial gene expression signatures of prostate cancer (PCa) prognosis were developed and validated in cohorts of predominantly European American men (EAM), and limited research exists on the value of such signatures in African American men (AAM), who have poorer PCa outcomes [1-5]. We explored differences in gene expression between EAM and AAM for three panels recommended by the National Comprehensive Cancer Network for PCa prognosis.

**Methods:** 232 EAM and 95 AAM patients provided radical prostatectomy specimens. Gene expression was quantified using Nanostring for 60 genes spanning the Oncotype DX Prostate, Prolaris, and Decipher panels. Differential expression and intrapanel co-expression by race were assessed using Mann-Whitney tests and Spearman’s correlations, respectively. A continuous expression-based risk score was approximated for each panel with higher scores indicating worse outcomes. Race-specific risks were compared using Mann-Whitney tests and Spearman’s correlations.

**Results:** Clinical and pathologic features were similar between AAM and EAM. Differential expression by race was observed for 48% of genes measured, though the magnitudes of expression differences were small. Co-expression patterns were more strongly preserved by race group for Oncotype DX and Decipher versus Prolaris (integrative correlations of 0.87, 0.73, and 0.62, respectively) (Figure 1). Paradoxically, poorer prognosis was estimated in EAM versus AAM for Prolaris and Oncotype DX ( for both), whereas worse prognosis was predicted for AAM versus EAM using Decipher ().

**Discussion:** Replication of our findings directly on the commercial panels with long-term follow-up is thus warranted. Due to observed racial differences across three commercial gene expression panels for PCa prognosis, caution is warranted when applying these panels in clinical decision-making in AAM. Given our findings, appropriate usage of these tests for AAM remains unclear.

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Figure 1: Intrapanel gene correlation heatmaps in EAM (left) and AAM (middle) and interative correlations (right) in Prolaris (top), Oncotype (middle) and Deipher (bottom).