A BIOPSY-BASED GENOMIC APPROACH TO SELECTING MEN FOR ACTIVE SURVEILLANCE

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Introduction: Conventional tools available at diagnosis do not reliably discriminate aggressive from indolent prostate cancers, resulting in overtreatment. Tumor heterogeneity and sampling error with prostate biopsies pose challenges to accurate risk assessment at the time of diagnosis.
Methods: We used a cohort sampling design including 127 patients with and 374 patients without clinical recurrence treated with radical prostatectomy (RP) for clinical T1/T2 prostate cancer. Quantitative gene expression for 732 candidate genes by RT-PCR was assessed in two spatially distinct tumor specimens from each patient, including the primary and highest Gleason Patterns. 81 informative genes were then evaluated in needle biopsy specimens from a separate patient cohort.
Results: In 441 patients with evaluable tissue, gene expression across multiple biological pathways was associated with clinical recurrence in both primary and highest Gleason patterns. After adjustment for PSA, biopsy Gleason score, and clinical stage, 198 genes were strongly associated with clinical recurrence in both RP and biopsy. Gene groups representative of pathways including stromal response, cellular organization, androgen, and proliferation also predicted high-grade/non-organ-confined disease at RP, biochemical recurrence and prostate cancer-specific survival. Assessment in biopsies from a separate patient cohort confirmed strong association of these genes and gene groups with high-grade, non-organ-confined disease.
Conclusion: Genes in multiple biological pathways enable discrimination between clinically aggressive and indolent disease in the context of tumor heterogeneity and limited sampling with prostate biopsies. These results support the value of a needle biopsy-based genomic assay for predicting clinically aggressive disease that may help select men for active surveillance.