

Quantitative gene expression in primary and highest Gleason pattern cancer specimens identifies genes associated with clinical recurrence and prostate cancer-specific survival after radical prostatectomy.

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Background: Prostate biopsy may not adequately sample small, secondary or tertiary Gleason pattern tumors which can drive clinical outcome. We conducted a study to determine whether tumor-derived gene expression profiling could identify a distinct underlying biology associated with clinical recurrence (cR) after radical prostatectomy (RP) across both the primary and highest Gleason pattern (GP) samples. **Methods:** All patients (pts) with clinical stage T1/T2 prostate cancer treated with RP at Cleveland Clinic from 1987 to 2004 were identified (n~2,600). A cohort sampling design was used to select 127 patients with cR and 374 patients without cR after RP. Each patient had two spatially distinct tumor specimens sampled that included the primary GP (PGP) and the highest GP (HGP). Surgical GS and clinical data were centrally reviewed. RNA was extracted from 6 manually dissected 10 μ m fixed paraffin embedded tissue sections obtained from the RP tumor specimens and expression of 732 cancer-related and reference genes was quantified using RT-PCR. Clinical recurrence-free interval (cRFI) and prostate cancer-specific survival (PCSS) were analyzed using Cox PH regression. **Results:** Blocks from 441 patients were evaluable. Median F/U was 5.8 years. Pts were mostly Caucasian (83%), clinical stage T1 (66%), had baseline PSA <10 ng/mL (82%), and surgical GS \leq 7 (87%). We identified 235 genes associated with cRFI in both the PGP and HGP samples, well in excess of the number expected by chance. 75% of these genes were also associated with PCSS. Many genes remained significantly associated with cRFI in multivariate analyses adjusted for pathologic T-stage, GS, AUA risk group and CAPRA score (221, 99, 244, and 271 genes respectively). **Conclusions:** Gene expression analysis using quantitative RT-PCR identified a large number of genes, and underlying biology, that are strongly associated with clinical recurrence in both the primary and the highest Gleason pattern that adds prognostic value beyond clinical and pathology covariates.