A non-invasive urine exosome gene expression assay (ExoIntelliScore™ *Prostate*) accurately predicts pathologic stage and grade in the prostatectomy specimen

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Introduction

Over 2 million prostate biopsies are performed in the United States and Europe each year, with the majority for an elevated PSA . With over-diagnosis and over-treatment of indolent prostate cancer, non-invasive screening tools that add predictive value for identifying high-grade, Gleason score (GS) ≥7 should result in a reduction of biopsies performed each year. We have developed standardized processes to isolate exosomal-RNA from first-catch, non DRE, urine specimens and have validated a three gene signature (ExoIntelliScore *Prostate*) that reliably differentiates GS7+ from GS6 and benign disease at the time of an initial biopsy.

A critical next step in this analysis was to equate the gene signature with the objective clinical features present in the prostatectomy specimen including Gleason score, pathologic stage and volume of cancer.

Methods:

- Pre-Radical Prostatectomy (RP) urine specimens from 5 Urology practices (academic / community); First-catch, non DRE, 4C storage for up to two weeks and then shipped (on ice) to a clinical grade CLIA laboratory for processing.
- Exosomes were isolated and RNA extraction performed.
- RT-qPCR RNA CT values of ERG and PCA3 were normalized to SPDEF to produce an ExoIntelliScore Test result.
- Spearman and Pearson correlation along with AUC was used to evaluate performance.

Results

- 430 post-RP patients with 16% GS6, 45% GS7 (3+4), 39% >/= GS 4+3; 85% PSA <10 ng/mL; 13%, T2a, 70% with T2b-c; 17% >/=T3; 50% upgrading. 359 patients with complete clinical data and ExoIntelliScore *Prostate* results were evaluated.
- There was significant correlation of ExoIntelliScore *Prostate* with RP Gleason grade (Figure 1, p value=0.025), RP pathologic stage (Figure 2, p value=0.002), and RP tumor volume (Figure 3, p value=0.002).
- Utilizing only those patients with a biopsy Gleason score of 6, (Figure 4) the distribution of ExoIntelliScore *Prostate* discriminated adverse RP pathology (3+4 vs 4+3, red line) and predicted an RP Gleason >3+4, AUC=0.68 (CI: 0.55-0.80); correlation trended towards significance (p value =0.076).
- We compared the distribution of ERG (absolute) CT values and the association with biopsy and RP Gleason grades. As annotated in red (Figure 5), there is a wide ERG CT distribution in the Gleason 6 group between the biopsy vs RP, supporting observed upgrading in the cohort.

Figure 1. ExoIntelliScore *Prostate* vs. Prostatectomy Gleason Grade

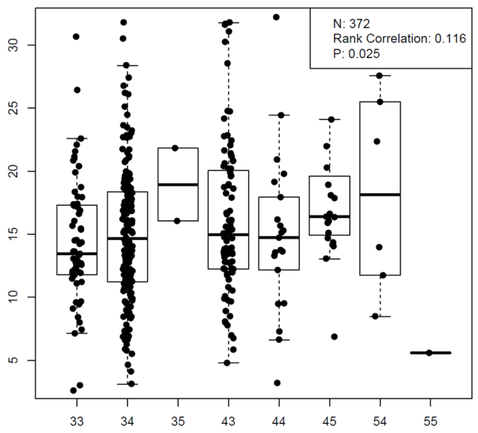


Figure 2. ExoIntelliScore *Prostate* vs. Prostatectomy Stage

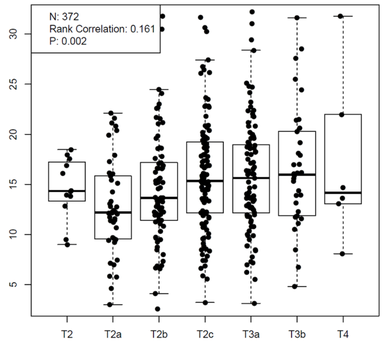


Figure 3. ExoIntelliScore *Prostate* vs Tumor Volume

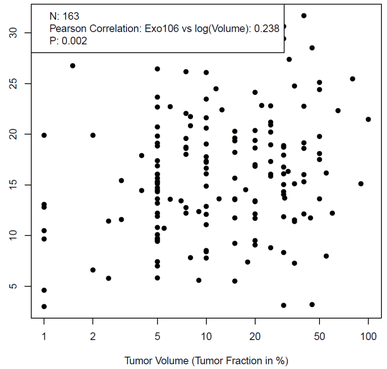


Figure 4. Applying ExoIntelliScore *Prostate* to Biopsy Gleason 6 patients to predict > RP Gleason 3+4

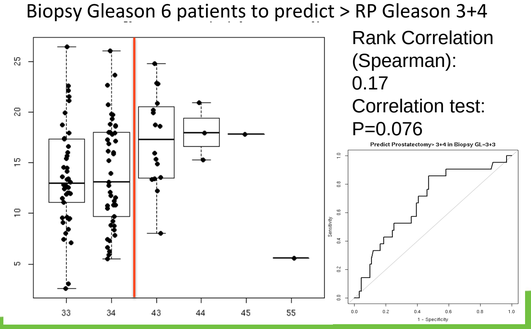
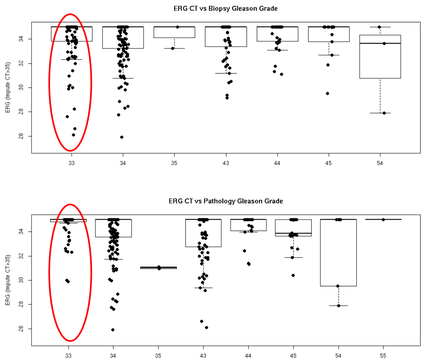


Figure 5. Distribution of ERG, absolute CT values in Biopsy vs. Prostatectomy Gleason grades



Conclusions

- ExoIntelliScore *Prostate* significantly correlated with the RP Gleason score (p=0.025); RP tumor volume and stage (p=0.002).
- Improved discrimination of RP 4+3 adverse pathology suggests role in sequential monitoring of patients enrolled in active surveillance.
- Distribution of ERG is reflective of upgrading in RP specimens.

References

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