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

M. Donovan1, J. Eastham2, V. Patel3, J. McKeeman4, M. Nothlen5, S. Belote6, B. Banitav7, V. O'Neill8

1Icahn School of Medicine at Mt. Sinai, Pathology, New York, City, USA 2Memorial Sloan Kettering Cancer Center, Urology, New York City, USA 3Global Robotics Institute, Urology, Celebration, USA 4Columbia University, Urology, New York City, USA 5Exosome Diagnostics, Product Development, Martinsried, Germany 6Exosome Diagnostics, Clinical, Cambridge, USA

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% >G5 GS 3+4; 85% PSA <10 ng/ml; 13%, T2a, 70% with T2b-c; 17% >G5 T3; 30% 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 >G3+4. (Figure 5) correlation trended towards significance (p value=0.076).
- We compared the distribution of ERG (absolute) CT values in the biopsy Gleason 6 group between the biopsy vs prostatectomy specimen, supporting observed upgrading in the cohort.

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

1. Donovan et al., A molecular signature of PCA3 and ERG exosomal RNA from non-DRE urine is predictive of initial biopsy result. Prostate cancer Prostatic Disease. 2015, Sept 8.