Combined Urine and Plasma Biomarkers are Highly Accurate for Predicting High Grade Prostate Cancer

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Distinguishing between low-grade and high-grade prostate cancer (PCa) as detected by biopsy results is very important, not only for diagnosis, but also for monitoring patients on active surveillance. However, biopsy results may underestimate the actual grade of the PCa when prostatectomy is performed. We previously developed a urine/plasma assay and algorithm to predict high grade prostate cancer and determined it performed better than sPSA alone.

### Participant Characteristics

<table>
<thead>
<tr>
<th>Age (Median, Min-Max)</th>
<th>Male (Sex No.)</th>
<th>Family History</th>
<th>Prior Biopsies</th>
<th>Stage</th>
<th>Gleason</th>
<th>PSA (ng/ml) (Median, Min-Max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>61 (36-77)</td>
<td>414 (22-165)</td>
<td>59 (14.6%)</td>
<td>64 (15%)</td>
<td>3+3</td>
<td>0</td>
<td>10.5 (9.3-13.2)</td>
</tr>
</tbody>
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### Participants

This prospective blinded study was conducted in a community based setting at six different large urology groups.

- Urine and blood samples from 306 patients were collected and tested prior to prostatectomy and at least 2 months after biopsy.
- All recruited patients were treatment naive and without metastases.
- Most patients were Caucasian (80.4%), while 16.3% were African American.
- The majority of patients were staged at T1c or lower (91.7%).

### Objective

To determine whether our previously developed noninvasive test may predict tumor grade as well or better than biopsy, we tested the algorithm using cell-free RNA (cfRNA) levels of UAP1, FOLH1, IMPDH2, HSPD1, PCA3, PSA, TMPRSS2-ERG, AR, PTEN, and ERG genes in both urine and peripheral blood plasma against the results of biopsy and prostatectomy for the presence of high-grade PCa as measured by Gleason Score.

Digital rectal exam was normal in 202 (66%) of patients.

- More than half (41.4%) of patients had no family history of prostate cancer.
- The RNA levels of FOLH1, HSPD1, IMPDH2, PCA3, TMPRSS2, ERG, UAP1, PTEN, AR, GAPDH, and B2M genes were quantified in urine and plasma using qRT-PCR as previously detailed.
- An algorithm incorporating RNA levels with clinical information, previously developed, was used for predicting high-risk, standard-risk, and low-risk advanced prostate cancer (Gleason ≥ 3+4).

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### Results

- The algorithms and urine/plasma test used in this study resulted in predicting the presence of high-grade PCAs with sensitivity (92-97%) and specificity (36-57%).
- Prediction of Gleason ≥ 4+3: Sensitivity 96-99% with specificity 37-59%.
- Diagnosis of Gleason ≥ 3+4 was missed in 0.2% to 1%.
- More than half (61.4%) of patients had no family history of prostate cancer.
- The majority of patients were staged at T1c or lower (91.7%).

### Conclusion

We show that this algorithm is highly reliable in predicting high grade (Gleason ≥ 3+4) PCa based on biopsy results in 306 patients who underwent prostatectomy. Taking advantage of urine/plasma biomarkers, serum PSA, prostate size, and prior history of biopsy, we were able to predict high grade prostate cancer with negative predictive value (NPV) of 97% to 99% for Gleason ≥ 3+4 and 99% to 98% for Gleason ≥ 4+3. Furthermore, this test was further proved to be highly sensitive as confirmed by prostatectomy data.