False negative results are common during initial and follow-up biopsy procedures. You’re forced to manage false-negative patients in the same manner as those who are negative. What if you could determine the difference between these patients?

Now you can. With the Prostate Core Mitomic Test™ (PCMT™), a molecular test ordered with prostate biopsy pathology, you can confidently stratify and better manage patients.

Learn more about the Prostate Core Mitomic Test
Visit mitomicsinc.com or call 888.763.2644

The cancerization field associated with mitochondrial deletions provides a distinct molecular signature that mtGenomic assessment can detect. Though conventional histology of a biopsy sample might not display evidence of malignancy, if the tissue comes from an area that is within the cancerization field, disease onset will be detectable via this signature. Coupling conventional biopsy methodology with mtGenomic assessment to detect this cancerization field provides vital clinical information.

Parr and Martin: Mitochondrial and nuclear genomics and the emergence of personalized medicine. Human Genomics 2012 6:3.
What is PCMT?
PCMT identifies a large-scale deletion in mitochondrial DNA (mtDNA) that indicates cellular change associated with undiagnosed prostate cancer. By using biopsy tissue samples that have already been collected and stored at the lab, PCMT precludes the need for additional office visits or surgeries. You can order PCMT as a reflex test when you submit a biopsy for evaluation or after the biopsy results are available.

How do you use PCMT?

PCMT outperforms competitors
Because mtDNA has an extended field effect compared to nuclear DNA, PCMT can be used for all negative biopsy patients and delivers the highest sensitivity and negative predictive value of all similar tests.

<table>
<thead>
<tr>
<th>Field effect extent</th>
<th>Clinical utility</th>
<th>Sensitivity</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire prostate</td>
<td>All negative biopsies; requires only 20 microns of tissue</td>
<td>85%</td>
<td>92%</td>
</tr>
</tbody>
</table>

PCMT mtDNA deletion: Stages of discovery and validation
The entire process of discovery and validation involved 396 patients and close to 1,700 prostate core samples. Included were 143 patients with benign histology, and 253 patients with malignant histology. Stage 2 involved an external validation study performed by the National Institute of Standards and Technology under the Early Detection Research Network of the National Cancer Institute (NCI). Stage 3 was conducted within the framework of a clinical trial. The diagram below outlines the flow of work and the study population used in each stage of assay development:

Stage 1: Discovery
- 30/33 (91%) of prostatectomy samples exhibit the 3.4 kb mtDNA deletion

Pilot Studies (2)
- 86 patients: 132 cores
  - 27 benign patients: 43 benign cores
  - 59 malignant patients: 54 malignant cores, 35 PTM cores

Stage 2: Validation
- Internal validation
  - 183 patients: 296 cores
    - 22 benign patients: 98 benign cores
    - 161 malignant patients: 75 malignant cores, 123 PTM cores
- External validation (NIST)
  - Blinded core extracts
    - 46 benign core extracts
    - 25 malignant core extracts
    - 41 PTM core extracts

Stage 3: Clinical Trial
- Initial biopsy
  - 94 patients with benign histology results
  - 553 cores (6 cores per patient; 11 patients with only 5 cores)
- Repeat biopsy within one year
  - 74 patients with benign histology results
  - 20 patients with malignant results

PCMT predicted the outcome of the repeat biopsy with a SEN of 85% and a NPV of 92%.

Gain an advantage in the fight against prostate cancer
- Be more confident in negative results – and provide peace of mind to patients.
- Strive to give patients who are free of the disease from those with undiagnosed prostate cancer.
- Detect undiagnosed prostate cancer early.

Health economic benefits of PCMT

<table>
<thead>
<tr>
<th>Savings category</th>
<th>Range of cost savings (in $US)</th>
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<tbody>
<tr>
<td>Reduce or eliminate unnecessary screening</td>
<td>$3,000 - $15,000</td>
</tr>
<tr>
<td>Reduce the number of unnecessary repeat biopsy procedures</td>
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<td>Eliminate the complications associated with unnecessary repeat biopsy procedures</td>
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Genomic deletions within mitochondria begin to happen long before traditional histology can identify disease. Biochemical signatures can identify genomic deletions associated with a disease and predict its onset much earlier than a pathologist can observe a problem, thus creating a greater window of time for treatment possibilities.

- Parr and Martin: Mitochondrial and nuclear genomics and the emergence of personalized medicine. Human Genomics 2012 6:3.

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Positive biopsy outcome (30%)
- PSA > 4.0 ng/ml
- PSA DT < 3 months
- PSAV > 0.4 ng/ml/year
- Life expectancy > 10 years
- ASAP
- HGPN
- Family history
- African American

Negative biopsy outcome (70%)
- PSA < 4.0 ng/ml
- PSA DT > 3 months
- PSAV < 0.4 ng/ml/year
- Life expectancy < 10 years
- ASAP
- HGPN
- Family history
- African American

Clinical response
- Patient selection
- PCMT negative outcome
  - Patient is at a high risk of undiagnosed prostate cancer
  - A repeat saturation biopsy is recommended with presence of additional risk factors
- PCMT positive outcome
  - Patient is currently at a low risk of undiagnosed prostate cancer
  - Defer repeat biopsy and routine screening by 12 to 14 months.

Addressable market

- Patient selection
- Clinical response

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