Look beyond the core

The Mitomic™ Prostate Core Test from MDNA Life Sciences
Enhance your prostate biopsy results for better patient management

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. But what if you could determine the difference between these patients?

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

What is MPCT?

MPCT 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, MPCT precludes the need for additional office visits or surgeries. You can order MPCT as a reflex test when you submit a biopsy for evaluation or after the biopsy results are available.

How do you use MPCT?

<table>
<thead>
<tr>
<th>Addressable market</th>
<th>Clinical response</th>
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</thead>
<tbody>
<tr>
<td>Positive biopsy outcome (30%)</td>
<td><strong>MPCT negative outcome</strong></td>
</tr>
<tr>
<td>PSA &gt; 4.0 ng/ml</td>
<td>Patient is currently at a low risk of undiagnosed prostate cancer. Defer repeat biopsy and routine screening by 12 to 14 months.</td>
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<tr>
<td>PSADT &lt; 3 months</td>
<td></td>
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<tr>
<td>PSAV &gt; 0.4 ng/ml/year</td>
<td></td>
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<tr>
<td>Life expectancy &gt; 10 years</td>
<td></td>
</tr>
<tr>
<td>Negative biopsy outcome (70%)</td>
<td><strong>MPCT positive outcome</strong></td>
</tr>
<tr>
<td>ASAP</td>
<td>Patient is at a high risk of undiagnosed prostate cancer. A repeat saturation biopsy is recommended with presence of additional risk factors.</td>
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<tr>
<td>HGPIN</td>
<td></td>
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<tr>
<td>Family history</td>
<td></td>
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<tr>
<td>African American</td>
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Note: Patient selection and clinical response to a positive or negative MPCT outcome is based on the feedback of an independent panel of leading U.S. urologists and active users of MPCT.
How does MPCT work?

With 85-percent sensitivity, MPCT detects the presence of malignant cells in normal-appearing tissue via a tumor field effect. Studies have indicated the field effect for MPCT is gland-wide. Detect undiagnosed prostate cancer early.

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.

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MPCT outperforms competitors

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

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

Gain an advantage in the fight against prostate cancer

- Be more confident in negative results – and provide peace of mind to patients
- Stratify patients who are free of the disease from those with undiagnosed prostate cancer
- Detect undiagnosed prostate cancer early
- Tailor patient management for improved care
- Avoid causing patients added pain, anxiety, and risk from extra and potentially unnecessary biopsies

Health economic benefits of MPCT

<table>
<thead>
<tr>
<th>Savings category</th>
<th>Range of cost savings (in $US)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduce or eliminate unnecessary screening</td>
<td>$3,800 - $15,000</td>
</tr>
<tr>
<td>Reduce the number of unnecessary repeat biopsy procedures</td>
<td>$9,600</td>
</tr>
<tr>
<td>Eliminate the complications associated with unnecessary repeat biopsy procedures</td>
<td>$2,000</td>
</tr>
<tr>
<td>Total</td>
<td>$15,400 - $26,600</td>
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MPCT 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
- 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

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

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.

Now you can know more from every biopsy

Receive the early insight you need to tailor patient management. Request the Prostate Core Mitomic Test with your next prostate biopsy pathology.

Learn more about this simple and informative test at mdnalifesciences.com
Scientific publications on MPCT

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


Ryan Parr, Jennifer Creed, Brian Reguly, Cortney Powell, Roy Wittock, Daniel Klein, Andrea Maggrah, Kerry Robinson.* Large-scale mitochondrial genome deletion as an aid for negative prostate biopsy uncertainty. Poster presented as part of the Society of Urologic Oncology Annual Meeting, Bethesda, MD, Dec. 8-10, 2010.


John Mills*, Luis Martin, François Guimont, Brian Reguly, Andrew Harbottle, John Pedersen, Jennifer Creed, Ryan Parr. Large-Scale 3.4kb Mitochondrial Genome Deletion is Significantly Associated with a Prostate Cancer Field Effect. *Abstract accepted as part of the American Urological Association Annual Meeting, San Diego, CA, May 4-8, 2013.

Learn more about the Mitomic Prostate Core Test
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