Hereditary Prostate Cancer
Genetic Testing

Brooke Overstreet, MS, CGC
Causes of Cancer

- **70-80% sporadic**
- **5-10% hereditary**
- **10-20% familial**

**Sporadic Cancer**
- Happens in one person or possibly two distantly related family members at older ages

**Familial Cancer**
- A clustering of cancer in a family that may be due to genes and/or other shared factors, such as environment and lifestyle

**Hereditary Cancer**
- A clustering of cancer in a family due to inherited gene changes (mutations), which can be passed from parent to child
Introduction to Genetics

Cell

Chromosome

Gene

DNA Base

DNA

(Deoxyribonucleic Acid)
Hereditary Breast and Ovarian Cancer Syndrome
Lifetime Cancer Risks (%)

- Breast Cancer: 12% (General Population), 45-87% (BRCA1/2 Positive)
- Ovarian Cancer: 2% (General Population), 11-40% (BRCA1/2 Positive)
- Male Breast Cancer: 0.1% (General Population), 5-10% (BRCA1/2 Positive)
- Prostate Cancer: 14% (General Population), 15-20% (BRCA1/2 Positive)
- Pancreatic Cancer: Increased Risk, 1.5% (BRCA1/2 Positive)
## Who is an Appropriate Candidate for Genetic Testing?

### Personal History
- Prostate cancer at or before age 50
- Metastatic prostate cancer
- Prostate cancer Gleeson 7 or higher
- More than one primary cancer diagnosis
- Prostate cancer plus a family history of cancer

### Family History
- 3 or more prostate or other cancers on the same side of the family
- Prostate, breast, colorectal or uterine cancer before age 50 in a relative
- Male breast or ovarian cancer in a relative

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Ambry Genetics®
BRCA-Related Cancer Panel Results: Males vs. Females

Females with Personal History of Breast Cancer (N>100,000)
- Positive: 7.9%
- No Mutation: 92.1%

Males with Personal History of Prostate Cancer (N=360)
- Positive: 14.2%
- No Mutation: 85.8%

Bowling et al. ASCO 2016, Chicago IL
Mutations in Various Genes in Prostate Cancer Cohort

- BRCA: 39.2%
- ATM: 17.7%
- CHEK2: 13.7%
- LYNCH: 11.8%
- PALB2: 3.9%
- TP53: 3.9%
- Other Genes: 14.2%

Over 90% of mutations found in genes with published medical management guidelines

Bowling et al. ASCO 2016, Chicago IL
How Will Genetic Testing Benefit Patients?

• **BRCA1/2** Prostate-Specific Early Detection
  – **BRCA2**: Recommend prostate cancer screening beginning at age 45
  – **BRCA1**: Consider prostate cancer screening beginning at age 45

• Prostate Cancer: Risk-Appropriate Management
  – Given the aggressive nature of **BRCA1/2**-associated prostate cancer, more aggressive prostate cancer treatment may be considered

  *Lynparza™ (olaparib) granted Breakthrough Therapy designation by US FDA for treatment of BRCA1/2 or ATM gene mutated metastatic Castration Resistant Prostate Cancer*
How Will Genetic Testing Benefit Patients?

• Beneficial for Family Members
  – Relatives (e.g. daughters, sisters, brothers) can be tested to determine if they inherited the mutation and get appropriate medical management

• Other Cancers: Risk-Appropriate Management
  – Male breast cancer: Annual clinical breast exam and self-breast exam training beginning age 35
  – Pancreatic: Consider referral to GI specialist to discuss pancreatic surveillance protocols (especially if pancreatic cancer in family)
  – Melanoma: Consider annual full-body skin and eye exam (ocular melanoma)
Summary

Prostate cancer can be an indicator for hereditary cancer susceptibility

Identification of a hereditary mutation has **prognostic**, **therapeutic**, and **familial** implications

Talk to your provider about genetic testing
Overall Benefits of Genetic Testing

Improved management of men with prostate cancer

• Consider more aggressive management of men with non-metastatic prostate cancer

Identification of men at high risk for prostate cancer

• Recommend increased surveillance to detect early prostate cancer
• Recommend surveillance and possible prevention options for other cancers

Benefits to family members

• Relatives may be tested to learn more about their cancer risks
• Personalized surveillance and prevention options available to family members

Thank You
Introduction to Genetics

1. **Inside our cells, we have genes**

2. **Genes are like “recipes” that tell our bodies how to make proteins**

3. **These proteins help our bodies work properly**

4. **Mutations in our genes can change these proteins, which can affect any part of our bodies**

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*Ambry Genetics*
Myth Busters:
Hereditary Cancer Impacts Both Men and Women
And yet... who is being tested?

BRCA-Related Hereditary Cancer Panels (N>100,000)

- Males: 96%
- Females: 4%

Bowling et al. ASCO 2016, Chicago IL
ProstateNext – 14 gene panel test

<table>
<thead>
<tr>
<th>GENE(S)</th>
<th>ASSOCIATED CANCERS AND RISKS</th>
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<tbody>
<tr>
<td>BRCA1</td>
<td>Female breast (57-87%), ovarian (39-40%), pancreatic, melanoma, prostate, male breast</td>
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<tr>
<td>BRCA2</td>
<td>Female breast (45-84%), ovarian (11-18%), pancreatic, melanoma, prostate (15%), male breast (&gt;6%)</td>
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<tr>
<td>EPCAM</td>
<td>Colorectal (52-82%), uterine (12-55%), possibly prostate, other</td>
</tr>
<tr>
<td>MLH1</td>
<td>Colorectal (52-82%), uterine (25-60%), stomach (6-13%), ovarian (4-12%), prostate (2 fold), other</td>
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<tr>
<td>MSH2</td>
<td>Colorectal (52-82%), uterine (25-60%), stomach (6-13%), ovarian (4-12%), prostate (2 fold), other</td>
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<tr>
<td>MSH6</td>
<td>Colorectal (20-44%), uterine (up to 44%), prostate (2 fold), other</td>
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<tr>
<td>PMS2</td>
<td>Colorectal (15-20%), uterine (15%), possibly prostate, other</td>
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<tr>
<td>ATM</td>
<td>Breast (2-4 fold), pancreatic, prostate</td>
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<tr>
<td>CHEK2</td>
<td>Breast (2 fold), colorectal, prostate, other</td>
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<tr>
<td>HOXB13</td>
<td>Prostate</td>
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<tr>
<td>NBN</td>
<td>Breast, possibly ovarian, brain, prostate</td>
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<tr>
<td>PALB2</td>
<td>Breast (33-58%), pancreatic, ovarian, possibly prostate, male breast</td>
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<tr>
<td>RAD51D</td>
<td>Ovarian (10-12%), breast, prostate</td>
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<tr>
<td>TP53</td>
<td>Breast, sarcoma, brain, adrenocortical, leukemia, other</td>
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