A guide to genetic testing for hereditary cancers

The benefit of knowing
Hereditary cancer genetic testing can play a critical role in managing health

Cancer touches millions of Americans each year. Many people wonder about their own risk of developing cancer. For some patients, genetic testing plays an important role in clarifying that risk. It’s important to choose the right test for the right patient at the right time. This guide highlights important points to consider when choosing a genetic test.
Why consider genetic testing

The decision to pursue genetic testing is a personal one. A patient's current medical status, personal experiences with cancer, and general readiness for genetic information all influence this process.

For some patients, genetic testing can provide the information needed to tailor their screening regimen and open the door to risk-reduction options. However, genetic testing also has the potential for less clear-cut results or variants of unknown clinical significance (VUS) which may not inform medical management. Having an open dialogue with your patients about these topics can assist with shared decision-making.
Ovarian cancer can be caused by many genes

One type of cancer can be caused by several cancer genes, and one gene can cause several different types of cancers. Here is an example highlighting the connection between various hereditary cancers and genes.

Ovarian cancer can be caused by many genes

The MLH1 gene can cause a variety of cancers
Choosing the right patient

Do any of the following apply to your patient?

Current or past diagnosis of cancer

- □ Cancer diagnosed under age 50
- □ Bilateral or multiple primary cancers
- □ Rare cancer (e.g., male breast cancer, ovarian cancer, triple-negative breast cancer)
- □ Cancer diagnosed at any age and significant family history
- □ Ashkenazi Jewish ancestry

Yes

No

Discuss genetic testing: patient possibly high risk

Manage based on family history

Family history of cancer

- □ ≥ 3 relatives with a related cancer on the same side of the family
- □ ≥ 2 relatives with a related cancer, 1 diagnosed under age 50
- □ Relative with a known familial mutation
- □ Ashkenazi Jewish ancestry

Yes

No

Discuss genetic testing: patient possibly high risk

Manage based on family history
## Choosing the right test

Discuss benefits and limitations of genetic testing with patient or refer for genetic counseling

### High-risk personal and/or family history

<table>
<thead>
<tr>
<th>Condition</th>
<th>Panel Description</th>
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</table>
| History consistent with multiple cancer syndromes or history not explained by previous genetic testing | **Comprehensive cancer panel**
  - High-, moderate-, and emerging-risk genes: includes the focused panel and single syndromes, as well as genes that may lack specific risk information and management recommendations. These may be further defined over time. |
| History consistent with single cancer syndrome                              | **Focused panel**
  - High- and moderate-risk genes: most have well-established cancer risks and management guidelines are established. Some cancer risks may not be as well-characterized. |
| Patient has a relative with positive genetic testing                        | **Single syndrome**
  - High-risk genes: cancer risks and management guidelines are established. |
| Patient has a relative with positive genetic testing                        | **Known familial mutation**
  - A pathogenic (disease-causing) or likely pathogenic genetic change previously found in a relative. |

### Additional considerations/actions:

- Begin genetic testing with an affected individual whenever possible
- Threshold for testing may be lower for certain ethnicities or family situations (adoption, small families)
- Guidelines strongly recommend genetic counseling
- Refer to the National Comprehensive Cancer Network (NCCN) guidelines for more detailed selection criteria
- Revisit genetic testing options regularly
34 high-risk, moderate-risk, and emerging-risk genes associated with a broad spectrum of hereditary cancers

13 high-risk genes predominantly associated with gastrointestinal cancers

2 high-risk genes (BRCA1, BRCA2) predominantly associated with breast, ovarian, prostate, melanoma, and pancreatic cancer

5 high-risk genes predominantly associated with colon, endometrial, ovarian, and gastric cancer

**MYvantage™**
Hereditary Comprehensive Cancer Panel

**Glvantage™**
Hereditary Colorectal Cancer Panel

**BRCAvantage™**
Comprehensive

2 high-risk genes (BRCA1, BRCA2) predominantly associated with breast, ovarian, prostate, melanoma, and pancreatic cancer

**Lynch Syndrome Panel**

5 high-risk genes predominantly associated with colon, endometrial, ovarian, and gastric cancer

VUS Rate by Test Type

More genes tested, higher chance for a VUS

Fewer genes tested, lower chance for a VUS

Comprehensive cancer panel

Focused panel

Single syndrome

Known familial mutation

*Available through one of our parent companies, Quest Diagnostics.*
## What the results mean

<table>
<thead>
<tr>
<th>Types of results</th>
<th>Insights</th>
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<tbody>
<tr>
<td><strong>Pathogenic/likely pathogenic variant</strong></td>
<td>- Lifetime cancer risk <strong>elevated</strong></td>
</tr>
<tr>
<td></td>
<td>- Increased cancer risk(s) gene-specific</td>
</tr>
<tr>
<td><strong>Negative</strong></td>
<td>- Patient previously diagnosed with cancer</td>
</tr>
<tr>
<td>No clinically significant variants identified</td>
<td>- Cancer risk based on personal and family history</td>
</tr>
<tr>
<td></td>
<td>- Patient with a family history of cancer only</td>
</tr>
<tr>
<td></td>
<td>- When possible, testing an affected family member is recommended for a more informative risk assessment</td>
</tr>
<tr>
<td></td>
<td>- Cancer risk based on personal and family history</td>
</tr>
<tr>
<td><strong>Variant(s) of unknown clinical significance (VUS)</strong></td>
<td>- A genetic change that is not well-characterized. May or may not be associated with increased cancer risk. A VUS may be further defined over time.</td>
</tr>
</tbody>
</table>
# What steps to consider

<table>
<thead>
<tr>
<th>Testing outcomes</th>
<th>Actions</th>
</tr>
</thead>
</table>
| Positive test result for high-/moderate-risk gene    | • Review medical management guidelines  
- Includes surveillance, chemoprevention, and/or risk-reducing surgery  
• Refer to specialty oncology center  
• Genetic counseling and DNA testing for at-risk family members is recommended |
| Positive for emerging-risk gene                       | • Medical management based on personal and family history  
• Revisit literature for developing guidelines regularly |
| Variant(s) of unknown clinical significance           | • Should not influence medical management decisions  
• Medical management based on personal and family history  
• Reclassified variants will be communicated to the ordering provider. Inquiries about variant status can be made to 866.GENE.INFO |
| Negative test results                                 | • Additional genetic testing may be appropriate for patient or affected relative if a high suspicion of inherited cancer remains  
• Medical management based on personal and family history |
| Patient declines testing                              | • Discuss medical management options  
- Tools to assist in this assessment include NCCN, Gail model, Tyrer-Cusick, Claus tables  
• Refer to specialty oncology center  
• Genetic counseling for family members is advised  
• Revisit genetic testing options regularly  
• Update personal and family histories regularly |

*A result is only as good as the action it inspires.*

Call Quest Genomics Client Services* at 866.GENE.INFO to speak with a genetic counselor.

*Available through one of our parent companies, Quest Diagnostics.*
Sonora Quest Laboratories offers a large test menu, giving the flexibility to select the right test for your patient at the right time.

<table>
<thead>
<tr>
<th>Test Offering</th>
<th>Code</th>
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<tbody>
<tr>
<td><strong>BRCAvantage® Ashkenazi Jewish Screen</strong></td>
<td>906366</td>
</tr>
<tr>
<td>Common founder mutations BRCA1 c.68_69delAG, BRCA1 c.5266dupC, BRCA2 c.5946delT</td>
<td></td>
</tr>
<tr>
<td><strong>BRCAvantage®, Ashkenazi Jewish Screen with Reflex to BRCAvantage® Comprehensive</strong></td>
<td>906474</td>
</tr>
<tr>
<td>Ashkenazi Jewish Screen, if negative reflex to BRCAvantage Comprehensive</td>
<td></td>
</tr>
<tr>
<td><strong>BRCAvantage® Comprehensive</strong></td>
<td>906369</td>
</tr>
<tr>
<td>BRCA1, BRCA2</td>
<td></td>
</tr>
<tr>
<td><strong>BRCAvantage®, Rearrangements</strong></td>
<td>906367</td>
</tr>
<tr>
<td>Large rearrangements of BRCA1 and BRCA2</td>
<td></td>
</tr>
<tr>
<td><strong>Glvantage™ Hereditary Colorectal Cancer Panel</strong></td>
<td>906840</td>
</tr>
<tr>
<td>APC, BMPR1A, CDH1, EPCAM, MLH1, MSH2, MSH6, MUTYH (MYH), PMS2, PTEN, SMAD4, STK11, TP53</td>
<td></td>
</tr>
<tr>
<td><strong>Lynch Syndrome Panel</strong></td>
<td>906541</td>
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<tr>
<td>MLH1, MSH2 (incl. EPCAM), MSH6, PMS2</td>
<td></td>
</tr>
<tr>
<td><strong>MYvantage™ Hereditary Comprehensive Cancer Panel</strong></td>
<td>906745</td>
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<tr>
<td>APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A (p16, p14), CHEK2, EPCAM, MEN1, MLH1, MSH2, MSH6, MUTYH (MYH), NBN, NF1, PALB2, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, RET, SDHB, SDHC, SDHD, SMAD4, STK11, TP53, VHL</td>
<td></td>
</tr>
</tbody>
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Coordinating testing for your patient

☐ Testing ordered from Sonora Quest Laboratories
   Name of test ordered: ________________________________
   Where to go for blood draw: __________________________
   Date of blood draw: ________________________________

☐ No testing ordered
   Update personal and family histories regularly
   Revisit genetic testing options regularly
   Next appointment is: ________________________________
   Call with questions: ________________________________

Helpful information resources

National Comprehensive Cancer Network (NCCN): NCCN.org

National Society of Genetic Counselors (NSGC): NSGC.org

Facing Our Risk of Cancer Empowered (FORCE): Facingourrisk.org

Bright Pink: Brightpink.org

American Cancer Society: Cancer.org
For more information please contact your Sonora Quest Laboratories Account Manager or visit Sonoraquest.com