Hereditary Cancer Testing

Breast9
Hereditary Cancer Gene Panel

**including:** sequencing and high resolution deletion/duplication analysis

**PANEL DESCRIPTION:**
Using sequencing and high resolution deletion/duplication analysis, the Hereditary Breast9 Cancer Panel analyzes **nine genes** for genetic variants that predispose a person to breast cancer and, in some cases, other cancers or noncancerous conditions. Identifying causative genetic variants in any of the genes included in this panel provides medically actionable results (treatment and/or risk reduction) and allows for targeted familial screening. Up to 10% of women affected by breast cancer have an inherited genetic syndrome.¹

**TEST DETAILS:**
- This panel includes both sequencing and high resolution deletion/duplication analysis of the genes specified when performed on a blood specimen.
  - **Sequencing** is performed using a customized next generation sequencing library. Analysis includes the coding exons of all genes in the panel plus ten bases into the introns and untranslated regions (5’ and 3’). Sanger sequencing is performed to confirm variants classified as pathogenic or suspected pathogenic.
  - **Deletion/duplication analysis** is performed using a high resolution, custom microarray platform designed to target the genes of interest at the exon level.
    - In addition, deletion/duplication analysis of **CHEK2** will be performed using Multiplex Ligation-dependent Probe Amplification (MLPA) because of the presence of highly homologous pseudogenes. However, MLPA cannot be performed on a buccal specimen.
- Detection rates are limited to the genes specified; this test does not provide whole genome analysis.
- Gene panels are a more cost-effective approach than single gene testing to confirm or establish a diagnosis. However, if single gene testing is desired for the patient or family members of an individual with a known mutation, that must be ordered separately.

**INDICATIONS FOR TESTING:**
- Breast cancer diagnosed ≤ age 45
- Breast cancer diagnosed ≤ age 50 and a close relative with breast cancer at any age
- Breast cancer diagnosed ≤ age 50 with limited or unknown family history
- Bilateral breast cancer or two separate breast primary cancers with the first ≤ age 50
- Breast cancer diagnosed ≤ age 60 with triple negative pathology
- Male breast cancer diagnosed at any age
- Ovarian, fallopian tube, or primary peritoneal cancer diagnosed at any age
- Pancreatic cancer or aggressive prostate cancer in someone who also has a family history of breast, ovarian, pancreatic or aggressive prostate cancer
- Family history of the above indications (typically when affected family members are unavailable for testing or deceased) or limited family history
- Ashkenazi Jewish ancestry and breast or ovarian cancer
- Personal and/or family history raising concern for the syndromes included in this panel
  - Li-Fraumeni syndrome **GeneReviews**² http://www.ncbi.nlm.nih.gov/books/NBK1311/
• Known familial variant in any of the genes included in this panel (targeted analysis)

SPECIMEN COLLECTION & TRANSPORT:
Complimentary test kits are available upon request, but are not required.

SAMPLE TYPE and REQUIREMENTS:
• **blood:** 3 - 5 ml whole blood in an EDTA tube (purple top)
• **buccal mucosa swab:** 5 swabs
  ^ Deletion/duplication and rearrangement analyses cannot be performed for indicated genes on a buccal specimen.
• **extracted DNA (from blood or buccal):** 5 µg in a DNA microcentrifuge tube

SHIPPING:
• Maintain and ship samples at room temperature.
• Coordinate transport for sample to be received in our laboratory within 24-48 hours of collection.
  o **LOCAL:** Call 402-559-5070 (option 1)
  o **OUT OF AREA:** Prior to shipment, please fax the completed test request form to 402-559-7248, including the FedEx® airbill tracking number.
    ▪ Saturday delivery MUST be checked when sending FedEx® on Friday.
    ▪ Please include Internal Billing Reference # 3155070600 on the FedEx® airbill.
    ▪ **Ship To:** Human Genetics Laboratory – Zip 5440
      UNMC Shipping & Receiving Dock
      601 S. Saddle Creek Road
      Omaha, NE 68106

FORMS FOR TESTING: The following forms can be downloaded via our website.
• **Required:** Hereditary Cancer Test Request Form
• **Optional:** Informed Consent for Hereditary Cancer Genetic Testing

POTENTIAL TEST RESULTS:
• **Positive for a Pathogenic Variant** – This designation is reported when a pathogenic change is identified in a gene and the change is known to increase the risk for certain cancers.
• **Negative** – This designation is reported when no harmful or uncertain changes are found in any of the genes tested.
• **A Variant of Uncertain Clinical Significance (UCS)** – This designation is reported when an inconclusive change in a gene is found; the change may increase the risk for cancer or be harmless. Variants of uncertain clinical significance may also be classified as “Likely Pathogenic” or “Likely Benign” based on the ACMG recommendations for variant classification.\(^2\)

TURNAROUND TIME: For all sample types, results are available in under 14 days. In special circumstances a 7 day turnaround time is available. Please contact our laboratory regarding this STAT option.

BILLING: Our laboratory offers patient/self-pay, insurance (including Medicare/Medicaid), and client/institution billing options. Verifying coverage requirements or obtaining preauthorization PRIOR TO OR AT THE TIME OF SPECIMEN COLLECTION is often necessary. We provide preauthorization services upon request by calling 402-559-5070 (option 3); the following form is helpful for obtaining the information required by insurance providers and can be downloaded via our website.
• **Insurance Preauthorization Request**

In some circumstances, a test may be warranted even though insurance coverage is denied or not guaranteed. For these situations, we request the following form be signed by the patient and submitted with the sample. This helps inform patients of their potential financial responsibility, should the costs of genetic testing not be paid by their insurance provider.
• **Advanced Beneficiary Notice of Noncoverage (ABN) –** required when billing Medicare
CPT CODE: 81162

PRICING: For current costs contact the laboratory billing staff at 402-559-5070 (option 3).

GENE LIST:

<table>
<thead>
<tr>
<th>ATM</th>
<th>BRCA1</th>
<th>BRCA2</th>
<th>CDH1</th>
<th>CHEK2*</th>
<th>PALB2</th>
<th>PTEN</th>
<th>STK11</th>
<th>TP53</th>
</tr>
</thead>
</table>

* Deletion/duplication and rearrangement analyses cannot be performed for indicated genes on a buccal specimen.

RESOURCES: The following resource can be downloaded via our website, or you may request brochures for your clinic by contacting our marketing specialist at 402-559-6935 | humangenetics@unmc.edu.

- PATIENT BROCHURE: Breast9 English, Breast9 Spanish

REFERENCES:


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