Hereditary Cancer Testing

Ashkenazi Jewish founder mutation
Hereditary Cancer Gene Panel

**including:** Sanger sequencing analysis

**PANEL DESCRIPTION:**
Using Sanger sequencing analysis, the Ashkenazi Jewish founder mutation panel analyzes the BRCA1 and BRCA2 genes for three specific variants (c.68_69delAG in exon 2 and c.5266dupC in exon 19 of BRCA1 (NM_007294.3) and c.5946delT in exon 11 of BRCA2 (NM_000059.3)), which cause hereditary breast and ovarian cancer and are seen at an increased frequency in individuals of Ashkenazi Jewish ancestry. Identifying these three variants provides medically actionable results (treatment and/or risk reduction). Up to 1 in 40 individuals of Ashkenazi Jewish ancestry carry one of these three variants.¹

**TEST DETAILS:**
- This panel provides Sanger sequencing of the regions where the three specific Ashkenazi Jewish founder variants are located.
  - **NOTE:** As this test involves sequencing of small regions around the three founder variants, there is a small chance for an incidental finding, such as a non-founder pathogenic variant or variant of uncertain clinical significance in these regions.
- Detection rates are limited to the three variants specified; a full analysis of BRCA1 and BRCA2 is not performed.

**INDICATIONS FOR TESTING:**
- Ashkenazi Jewish ancestry and a known familial variant in BRCA1 / BRCA2 (targeted analysis)
- Ashkenazi Jewish ancestry and a personal or family history suggestive of hereditary breast and/or ovarian cancer which may include the following features:
  - 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

**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
- **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 one or more of the three Ashkenazi Jewish founder variants is identified.
• **Negative** – This designation is reported when none of the three founder variants are identified.
• **As this test involves sequencing of small regions around the three founder variants, there is a small chance for an incidental finding, such as a non-founder pathogenic variant or variant of uncertain clinical significance in these regions.**
  ▪ A **Variant of Uncertain Clinical Significance (UCS)** may be 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 typically available in 14 days.

**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:** 81212

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

**VARIANT LIST:**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Variant Description</th>
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<tbody>
<tr>
<td>BRCA1</td>
<td>c.68_69delAG in exon 2 and c.5266dupC in exon 19 (NM_007294.3)</td>
</tr>
<tr>
<td>BRCA2</td>
<td>c.5946delT in exon 11 of BRCA2 (NM_000059.3)</td>
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**REFERENCES:**

updated 9-2018