Hereditary Breast and Ovarian Cancer Syndrome: BRCA1/BRCA2 Gene Sequencing Panel

Test Code: MM071
Turnaround time: 3 weeks
CPT Codes: 81163 x1

**Condition Description**

Mutations in the genes BRCA1 and BRCA2 cause hereditary breast and ovarian cancer syndrome (HBOC), an autosomal dominant cancer predisposition syndrome. Mutations in these genes are rare and account for only a small percentage of cancers; about 5-10% of all breast cancers and 10-15% of ovarian cancers are due to mutations in the BRCA1 or BRCA2 genes. Individuals with mutations in these genes, however, are at a significantly increased risk for developing breast, ovarian, and other cancers than those in the general population.

In families with HBOC syndrome, there is typically a pattern of early onset breast cancer (before the age of 50 or premenopausal). Additionally, the family history may show more than one primary breast cancer in an individual, breast cancer in two or more generations, breast cancer in a male relative, and ovarian cancer, with or without a breast cancer diagnosis. Females with a BRCA1 mutation have a 50-85% risk of developing breast cancer and up to a 44% risk of developing ovarian cancer. Females with a BRCA2 mutation have a 40-70% risk of developing breast cancer and up to a 27% risk of developing ovarian cancer. Males with a BRCA1 or BRCA2 mutation can have up to a 5-10% lifetime risk for male breast cancer and an elevated risk of prostate cancer. Additionally, both males and females with BRCA1 or BRCA2 mutations may be at elevated risks for other cancers. Individuals with a mutation in the BRCA1 or BRCA2 gene have a 50% risk of passing on the mutation to their children.

According to the National Comprehensive Cancer Network (NCCN) recommendations, BRCA1 and BRCA2 testing is suggested for individuals with a personal or family history of any of the following:

- Early-onset breast cancer (<50 years of age), bilateral breast cancer or triple negative (PR/ER/HER2 negative) breast cancer (<60 years of age)
- Two primary breast cancers or a diagnosis of both breast and ovarian cancer in one individual
- Personal or family history of male breast cancer
- Ovarian cancer at any age
- Ethnicity with a higher mutation frequency (e.g., Ashkenazi Jewish)

EGL offers the following for BRCA1 and BRCA2 testing:

- BRCA1/BRCA2 Full Gene Sequencing and Deletion/Duplication Panel
- BRCA1/BRCA2 Full Gene Sequencing Panel
- BRCA1/BRCA2 Deletion/Duplication Panel

This test is for the BRCA1/BRCA2 Full Gene Sequencing Panel.


References:


**Genes**

BRCA1, BRCA2

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of HBOC syndrome.
- Carrier testing in adults with a family history of HBOC syndrome.

**Methodology**

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

**Detection**

**Next Generation Sequencing:** Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

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Analytical Sensitivity: ~99%.

## Specimen Requirements

### Submit only 1 of the following specimen types

#### Type: DNA, Isolated

**Specimen Requirements:**
- Microtainer
- 15µg
- Isolation using the Perkin Elmer™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**
- Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

#### Type: Whole Blood (EDTA)

**Specimen Requirements:**
- EDTA (Purple Top)
  - Infants and Young Children (2 years of age to 10 years old): 3-5 ml
  - Older Children & Adults: 5-10 ml
  - Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**
- Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

#### Type: Saliva

**Specimen Requirements:**
- Orangene™ Saliva Collection Kit
  - Use according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**
- Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

## Related Tests

- **BRCA1/BRCA2** Full Gene Sequencing and Deletion/Duplication Panel
- **BRCA1/BRCA2** Deletion/Duplication Panel
- Sequencing and deletion/duplication analysis is also available for other breast/ovarian cancer syndromes, including: TP53, PTEN, STK11, MLH1, PMS2, MSH6, and MSH2.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.