

## Ashkenazi Jewish: *BRCA* Targeted Mutation Panel

**Test Code:** MSAJ3

**Turnaround time:** 2 weeks

**CPT Codes:** 81212 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.

The three mutations included in this panel are:

- *BRCA1*: Ex2:c.68\_69delAG (aka 185 delAG/187delAG)
- *BRCA1*: Ex19:c.5266dupC (aka c.5266dupC/5382insC/5385insC)
- *BRCA2*: Ex11:c.5946delT (aka: c.6174delT)

These specific mutations in *BRCA1* and *BRCA2* are more common in the Ashkenazi Jewish (AJ) population and are found in 1 out of every 40 people of AJ descent, compared to only 1 in 500 people of non-AJ descent. Testing for these 3 mutations alone will detect approximately 99% of all *BRCA1* or *BRCA2* mutations in someone of AJ descent.

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 (eg. Ashkenazi Jewish)

This *BRCA1/BRCA2* mutation panel should only be offered to those of Ashkenazi Jewish descent. Individuals with mixed ethnicities or non-Ashkenazi Jewish background should consider other *BRCA1/BRCA2* testing options.

References:

- Ford et al. (1998), *Am J Hum Genet*, 62:676-689.
- Shannon and Chittenden (2012), *The Cancer Journal*, 18(4):310-319.
- Janavicius (2010) *EPMA J*, 1(3):397-412.

### Genes

[BRCA1](#), [BRCA2](#)

### Indications

This test is indicated for:

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

### Methodology

PCR amplification of 3 specific mutations contained in the *BRCA1* and *BRCA2* genes is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

## Detection

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 will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%

## Specimen Requirements

**Submit only 1 of the following specimen types**

### Type: DNA, Isolated

#### Specimen Requirements:

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ 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: Saliva

#### Specimen Requirements:

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used 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.

### 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 72 hours of collection. Do not freeze.

## Related Tests

- Hereditary Breast and Ovarian Cancer Syndrome: *BRCA1/BRCA2* Deletion/Duplication Panel
- Hereditary Breast and Ovarian Cancer Syndrome: *BRCA1/BRCA2* Gene Sequencing Panel
- Hereditary Breast and Ovarian Cancer Syndrome: *BRCA1/BRCA2* Gene Sequencing and Deletion/Duplication Panel