

**UCLA DIAGNOSTIC MOLECULAR PATHOLOGY LABORATORY**  
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**BRCA 1 / 2 Ashkenazi Jewish Mutations**

**↑CPT**

83890; 83898 (x3); 83904 (x3); 83912

**↑Synonyms**

Ashkenazi Jewish; Breast or Ovarian Cancer

**↑Test Includes**

Detection of three Ashkenazi Jewish BRCA1&2 mutations – 185delAG (BRCA1, exon 2), 5382insC (BRCA1, exon 20), and 6174delT (BRCA2).

**↑Laboratory**

Molecular Pathology

**↑Availability**

Monday-Friday, 0700-1700

**↑Turnaround Time**

3-28 days

**↑Special Instructions**

Pretest counseling and informed consent is required for this test.

**↑Specimen**

Whole blood

**↑Volume**

4 mL

### ↑ **Minimum Volume**

3 mL

### ↑ **Container**

Lavender top (EDTA) tube

### ↑ **Storage Instructions**

All specimens should be sent to the Laboratory immediately after collection, preferably by overnight delivery. Specimens should be kept at room temperature or refrigerated but not frozen.

### ↑ **Causes for Rejection**

Blood samples frozen and thawed will yield low quality DNA; specimens inadequately identified; specimen from individuals of non-Ashkenazi Jewish descent or from individuals <18 years of age

### ↑ **Reference Range**

No mutations detected

### ↑ **Use**

Female carriers of germline BRCA1 mutations have a lifetime risk of breast cancer of 50% to 85% and risk of ovarian cancer of 25% to 45%. Carriers of BRCA2 mutations have a similar risk of breast cancer and a more moderately increased risk of ovarian cancer. Male carriers show a 7% lifetime risk of breast cancer. BRCA1 and BRCA2, located on the long arms of chromosomes 17 and 13, respectively, are thought to be tumor suppressor genes, inhibiting tumor development when functioning normally. Both are large genes, distributed over approximately 100,000 base pairs of genomic DNA, encoding large negatively charged proteins. Inactivating mutations identified to date are distributed throughout both genes, with an increased frequency of two distinct BRCA1 mutations and one BRCA2 mutation in individuals of Ashkenazi Jewish descent. Given the high lifetime penetrance of germline BRCA1 and BRCA2 mutations and the early age of onset in many carriers, detection of a mutation may indicate more frequent and earlier mammography screening and/or preventative measures such as prophylactic mastectomy, oophorectomy, or anti-hormonal therapy. A positive result explains the genetic etiology of cancers in the family, and provides the opportunity for other at-risk relatives to be tested.

## ↑ Limitations

The test procedure performed in the Laboratory is designed to detect only the three Ashkenazi Jewish BRCA1/2 mutations; it will not detect the hundreds of other possible mutations in these genes. For testing on non-Jewish individuals whose familial mutation is not known, complete DNA sequencing of both genes in a specialized reference lab is required.

## ↑ Methodology

Sanger sequencing is performed to detect the three Ashkenazi Jewish BRCA1/2 mutations – 185delAG (BRCA1, exon 2), 5382insC (BRCA1, exon 20), and 6174delT (BRCA2).

## ↑ Additional Information

In the Ashkenazi Jewish population, three recurrent germline mutations have been identified in the breast carcinoma susceptibility genes BRCA1 and BRCA2: 185delAG (BRCA1, exon 2), 5382insC (BRCA1, exon 20), and 6174delT (BRCA2). The aggregate frequency of these mutations in the general Ashkenazi population approaches 2.5%.

BRCA testing in the UCLA Clinical Laboratories is only available, subcontracted with the gene patent holder, for the three Ashkenazi-Jewish founder mutations common in individuals of that ethnic group. This test is not appropriate for individuals of other ethnic groups, who must instead be tested by full gene sequencing of BRCA1 and BRCA2. That test is available only at Myriad Genetics Laboratories in Salt Lake City. Referring physicians must contact that facility directly for instructions on sending samples and required pre-test counseling, informed consent, and payment procedures. Alternatively, the patient can be referred to the UCLA Medical Genetics Clinic (x66581) where all of these procedures can be arranged.

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