



CENTER FOR  
PRECISION DIAGNOSTICS

## BRCA1 & BRCA2 Ashkenazi Jewish Mutation Panel

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BRCA1	BRCA2								

### Indication

This panel analyzes BRCA1 and BRCA2 genes, that code for proteins that help repair DNA damage. Inherited mutations in BRCA1 or BRCA2 are associated with autosomal dominant hereditary breast and ovarian cancer (HBOC) syndrome (OMIM ID: 604370) which is characterized by increased lifetime risk for developing breast, ovarian and other types of cancer. Mutations in BRCA1 and BRCA2 are responsible for approximately 20 to 25% of hereditary breast cancers and about 5 to 10% of all breast cancers. In addition, mutations in BRCA1 and BRCA2 cause around 15% of ovarian cancers. Specific cancer risks are different between BRCA1 and BRCA2. BRCA1 pathogenic mutations are associated with increased lifetime risk for breast cancer (40-87%), ovarian cancer (16-54%), male breast cancer (1-2%), prostate cancer (up to 20%), and pancreatic cancer (1-3%). BRCA2 pathogenic mutations are associated with increased lifetime risk for breast cancer (up to 84%), ovarian cancer (up to 27%), male breast cancer (6%), prostate cancer (up to 20%), pancreatic cancer (2-7%), and melanoma. Updated NCCN guidelines for familial cancer risk assessment and clinical managements of individuals with HBOC syndrome are available at [www.NCCN.org](http://www.NCCN.org).

Members of certain ethnic groups, such as individuals of Ashkenazi Jewish ancestry, have an increased risk for carrying specific types of pathogenic mutations in BRCA1 or BRCA2, known as founder mutations. Per NCCN guidelines, any woman of Ashkenazi Jewish ancestry who has been diagnosed with breast or ovarian cancer meets criteria for BRCA founder variant testing that includes three known founder mutations: BRCA1 c.68\_69delAG, BRCA1 c.5266dupC, and BRCA2 c.5946delT. Clues that a hereditary cancer syndrome may be present include the following:

- Breast or ovarian cancer and Ashkenazi Jewish ethnicity
- Cancer diagnosed at an unusually young age (<50 year of age for breast cancer)
- Multiple BRCA-associated cancers in the same person
- Bilateral or multiple primary breast cancers
- Family history of ovarian, breast, pancreatic, melanoma, or prostate cancer
- Occurrence of certain types of adult cancer in which the probability of harboring a hereditary cancer syndrome is high: triple negative (ER-/PR-/HER2/neu-) breast cancer; ovarian, tubal or peritoneal cancer; male breast cancer

### Testing method

This test utilizes targeted next-generation sequencing (NGS) to detect three Ashkenazi Jewish founder mutations: BRCA1 c.68\_69delAG (c.185delAG), BRCA1 c.5266dupC (c.5385insC), and BRCA2 c.5946delT (c.6174delT). These small insertions/deletions are detected using a combination of clinically validated computational data analysis methods for sequence variant calling, filtering, and annotation. This

targeted mutation analysis will not detect other pathogenic mutations or deletions/duplications in *BRCA1* and *BRCA2*. A negative test result cannot be used to exclude a diagnosis HBOC. If clinical presentation is suspicious for HBOC diagnosis, a comprehensive *BRCA1* and *BRCA2* panel that includes full gene sequencing and full deletion/duplication analysis of both genes should be considered to assess for mutations and large deletions and duplications outside of the 3 Ashkenazi Jewish founder mutations.

### Turnaround time

5-10 business days

### Sample requirements

3 ml peripheral blood in EDTA (lavender) top tube

Specimen stability: Ambient - 72 hours; Refrigerated - 1 week

### CPT codes

81212, G0452

### References

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Lu KH, Wood ME, Daniels M, Burke C, et al. American Society of Clinical Oncology Expert Statement: collection and use of a cancer family history for oncology providers. *J Clin Oncol* 2014;32:833-840.

Roa BB et al. Ashkenazi Jewish population frequencies for common mutations in *BRCA1* and *BRCA2*. *Nat Genet*. 1996 Oct;14(2):185-7.

King, MC, et al. Breast and ovarian cancer risks due to inherited mutations in *BRCA1* and *BRCA2*. *Science*. 2003; 302(5645):643-6.

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Breast, Cancer, Linkage, Consortium. Cancer risks in *BRCA2* mutation carriers. *J. Natl. Cancer Inst*. 1999; 91(15):1310-6.

#### **Ship Specimens to:**

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