Test Definition: BRAJ3

BRCA Ashkenazi Jewish 3 Site Panel

Overview

Useful For

Establishing a diagnosis of hereditary breast and ovarian cancer (HBOC) in patients of Ashkenazi Jewish ancestry

Genetics Test Information

This test utilizes targeted next-generation sequencing to detect the 3 Ashkenazi Jewish founder mutations, c.68_69delAG and c.5266dupC in *BRCA1*, and c.5946delT in *BRCA2*. These are also well-known by their previous nomenclature: c.185delAG and c.5385insC in *BRCA1*, and c.6174delT in *BRCA2*. Sanger sequencing may also be performed to confirm detected variants. Analysis is performed for the 3 Ashkenazi Jewish mutations only. This assay does not rule out presence of other mutations within BRCA1 or BRCA2.

Note: Analysis of the area surrounding the three Ashkenazi Jewish variants may be required in the performance of this assay, which could result in identification of additional variants. Contact the laboratory at 800-533-1710 with any questions regarding assay performance.

Highlights

This test offers diagnostic or predictive testing for breast and ovarian cancer risk in a patient of Ashkenazi Jewish ancestry.

This test is appropriate for familial diagnostic or predictive testing for breast and ovarian cancer risk in a patient of Ashkenazi Jewish ancestry with a family member found to have 1 of the Ashkenazi Jewish founder mutations.

Special Instructions

- Molecular Genetics: Inherited Cancer Syndromes Patient Information
- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)

Method Name

Custom Sequence Capture and Targeted Next-Generation Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Specimen Type: Whole blood

Container/Tube:

Preferred: Lavender top (EDTA) or yellow top (ACD)

Acceptable: Any anticoagulant

Specimen Volume: 10 mL

Collection Instructions:

1. Invert several times to mix blood.

2. Send specimen in original tube.

Additional Information:

To ensure minimum volume and concentration of DNA is met, the preferred volume of blood must be submitted. Testing may be canceled if DNA requirements are inadequate.

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

-Informed Consent for Genetic Testing (T576)

-Informed Consent for Genetic Testing-Spanish (T826)

2. Molecular Genetics: Inherited Cancer Syndromes Patient Information in Special Instructions

Specimen Minimum Volume

3 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Frozen		
	Refrigerated		

Clinical and Interpretive

Clinical Information

Hereditary breast and ovarian cancer (HBOC) is an autosomal dominant hereditary cancer syndrome associated with germline mutations in the *BRCA1* or *BRCA2* genes. Mutations within these 2 genes account for the majority of hereditary breast and ovarian cancer families. HBOC is predominantly characterized by young-onset breast cancer and ovarian cancer. However, HBOC is also associated with increased risks for prostate cancer, pancreatic cancer, fallopian tube cancer, and male breast cancer. HBOC is highly penetrant; the risk for developing an invasive breast

cancer is about 60% to 65% and the risk for developing ovarian cancer is about 40% by age 70. Some individuals develop multiple primary or bilateral cancers. The National Comprehensive Cancer Network and the American Cancer Society provide recommendations regarding the medical management of individuals with HBOC.

There are founder mutations in *BRCA1* and *BRCA2* described in several populations including the Dutch, Icelandic, and Ashkenazi Jewish populations. The 3 common founder mutations in the Ashkenazi Jewish population are c.68_69delAG and c.5266dupC in *BRCA1*, and c.5946delT in *BRCA2*. These are listed according to current Human Genome Variation Society guidelines; however, these are also well-known by their previous nomenclature: c.185delAG and c.5385insC in *BRCA1*, and c.6174delT in *BRCA2*. The overall prevalence of the *BRCA1/2* founder mutations in the Ashkenazi Jewish population is 1 in 40. Per the National Comprehensive Cancer Network, women of Ashkenazi Jewish ancestry who have been diagnosed with breast or ovarian cancer should be considered for testing for the 3 common founder mutations (www.nccn.org).

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

All detected alterations are evaluated according to American College of Medical Genetics and Genomics recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

Clinical Correlations:

This assay will not detect all of the mutations that cause hereditary breast and ovarian cancer (HBOC). Therefore, the absence of a mutation does not eliminate the possibility of a diagnosis of HBOC. For predictive testing, it is important to first document the presence of a *BRCA1* or *BRCA2* gene mutation in an affected family member.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete. We strongly recommend that patients undergoing predictive testing receive genetic counseling both prior to testing and after results are available.

Technical Limitations:

The methodology used for this assay is targeted next-generation sequencing; therefore, analysis of mutations outside of the 3 Ashkenazi Jewish founder mutations is not performed. If a diagnosis is still suspected, consider full gene sequencing using AJADD (BRCA1/BRCA2 Full Gene Add On) to assess for mutations and large deletions outside of the 3 Ashkenazi Jewish founder mutations.

Note: Analysis of the area surrounding the familial variant may be required in the performance of this assay, which could result in identification of additional variants. Call 800-533-1710 with any questions regarding assay performance.

Clinical Reference

1. Richards CS, Nazneen A, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med 2015 May;17(5):405-424

2. Petrucelli N, Daly MB, Feldman GL. Hereditary Breast and Ovarian Cancer due to Mutations in BRCA1 and BRCA2. Genet Med. 2010 May;12(5):245-259

3. BRCA1 and BRCA2 Hereditary Breast and Ovarian Cancer-GeneReviews-NCBI Bookshelf. Accessed 12/14/16. Available at

www.ncbi.nlm.nih.gov/books/NBK1247/

4. Lindor NM, McMaster ML, Lindor CJ, et al: Concise Handbook of Familial Cancer Susceptibility Syndromes. Second Edition. J Natl Cancer Inst Monogr 2008;(38):1-93

5. Saslow D, Boetes C, Burke W, et al: American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. CA Cancer J Clin 2007 Mar-Apr;57(2):75-89

6. Chen S, Parmigiani G: Meta-analysis of BRCA1 and BRCA2 penetrance. J Clin Oncol 2007 Apr 10;25(11):1329-1333

7. Janavivius R. Founder BRCA1/2 Mutations in Europe: implications for hereditary breast-ovarian cancer prevention and control. EPMA J. 2010 Sept;1(3):397-412

Performance

Method Description

Next-generation sequencing is performed to test for the presence of a mutation in the *BRCA1* and *BRCA2* genes.(Pritchard CC, Smith C, Salipante SJ, et al: ColoSeq provides comprehensive Lynch and polyposis syndrome mutational analysis using massively parallel sequencing. J Mol Diagn 2012;14[4]:357-366).Â Bioinformatic metrics are utilized to mask data outside of the targeted reportable regions.Â This assay specifically targets the Ashkenazi Jewish founder mutations, c.68_69delAG and c.5266dupC in *BRCA1*, and c.5946delT in *BRCA2*.Â

Reported variants detected by next generation sequencing will be confirmed by Sanger sequencing.

Note: analysis of the area surrounding the familial variant may be required in the performance of this assay, which could result in identification of additional variants. Contact the laboratory at 800-533-1710 with any questions regarding assay performance.

PDF Report

No

Day(s) and Time(s) Test Performed

Performed weekly; Varies

Analytic Time

3 weeks

Maximum Laboratory Time

4 weeks

Specimen Retention Time

Whole Blood: 2 weeks (if available) Extracted DNA: 3 months

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

81212

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
BRAJ3	BRCA Ashkenazi Jewish 3 Site Panel	50995-0

Result ID	Test Result Name	Result LOINC Value
48417	Result Summary	50397-9
48418	Result	82939-0
48419	Interpretation	69047-9
48420	Additional Information	48767-8
48421	Specimen	31208-2
48422	Source	31208-2
48423	Released By	18771-6