

Specimen ID:

Acct #:

Phone:

Control ID:

Lab Case ID:

## REPORT, SAMPLE

Patient Details	Specimen Details	Physician Details
<b>DOB:</b> <b>Age(y/m/d):</b> <b>Gender:</b> F <b>Patient ID:</b>	<b>Date collected:</b> <b>Date received:</b> <b>Date entered:</b> <b>Date reported:</b>	<b>Ordering:</b> <b>Referring:</b> <b>ID:</b> <b>NPI:</b>

**Specimen Type:** Whole Blood**Clinical Indication:** Testing for familial cancer risk variant(s): *BRCA1* c.135-1G>T (also known as IVS4-1G>T)**RESULTS****POSITIVE FOR TARGETED VARIANT(S)**At least one clinically significant variant was detected in the *BRCA1* gene.

No variants of uncertain significance were identified.

GENE	VARIANT
<i>BRCA1</i>	<b>POSITIVE</b> Heterozygous for c.135-1G>T (Pathogenic)

**INTERPRETATION**

This result increases this individual's risk for cancer.

**Variant details**

The *BRCA1* c.135-1G>T targeted variant is associated with HBOC (Hereditary Breast and Ovarian Cancer Syndrome). This variant is also known as IVS4-1G>T. This splice-site variant is predicted to affect normal gene splicing. It has been reported in ClinVar and in the literature. Functional studies suggest this variant may disrupt normal gene function. Based on LabCorp's in-house variant classification protocol and in accord with the American College of Medical Genetics' guidelines, this variant has been classified as pathogenic and is associated with an increased risk for hereditary breast and ovarian cancer.

**Gene summary**

*BRCA1* (OMIM 113705) and *BRCA2* (OMIM 600185) are tumor suppressor genes that play a critical role in normal DNA repair, cell cycle control, and genomic stability. Pathogenic variants in these genes are associated with familial cancers, including breast, ovarian, pancreatic, prostate, and melanoma.

**Electronically released under the direction of W. Christine Spence, PhD, FACMG**

Testing Performed at Laboratory Corporation of America Holdings, 1912 T.W. Alexander Drive, RTP, NC 27709-0150, 1-800-345-4363, Medical Director: Anjen Chenn, M.D., Ph.D.

Date Reported: 10/27/2023 18:14 ET

**FINAL REPORT**

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## ADDITIONAL CLINICAL INFORMATION

### Cancer risks applicable to this individual

A positive *BRCA1* result is associated with the following cancer risks:

Lifetime high risk	Breast >60%; Ovarian 39-58%
Lifetime increased risk	Pancreatic <5%; Prostate 7-26%

### NCCN Guidelines

When BRCA1 and BRCA2 results are negative, additional testing may be helpful for some patients. Guidelines from the National Comprehensive Cancer Network® (NCCN®) recommend considering germline genetic testing for additional breast, ovarian, prostate, and/or pancreatic cancer susceptibility genes in patients meeting any of the criteria in the table below. To discuss comprehensive genetic testing, a Labcorp Genetic Coordinator is available at 800-345-4363.

Breast cancer diagnosed $\leq$ age 50
Ovarian cancer, pancreatic cancer, male breast cancer, or metastatic/high-risk prostate cancer at any age
Breast cancer diagnosed at any age and one of the following: <ul style="list-style-type: none"> <li>To aid in PARP inhibitor or olaparib treatment</li> <li>Triple negative breast cancer</li> <li>Multiple primary breast cancers</li> <li><math>\geq</math> 3 total diagnoses of breast cancer in patient and/or close blood relatives</li> </ul>
Breast or prostate cancer diagnosed at any age and one of the following: <ul style="list-style-type: none"> <li><math>\geq</math> 1 close relative with breast cancer <math>\leq</math> age 50 or with triple negative breast cancer at any age</li> <li><math>\geq</math> 1 close relative with ovarian, pancreatic, male breast, or metastatic/high-risk prostate cancer</li> <li><math>\geq</math> 2 close relatives with breast or prostate cancer at any age</li> <li>Ashkenazi Jewish ancestry</li> </ul>
Patients with a first or second degree relative meeting certain criteria in this table may consider germline genetic testing as well. Complete criteria may be found at NCCN.org.

## RECOMMENDATIONS

NCCN Guidelines provide clinical management recommendations. The most current guidelines may be found at NCCN.org. Modification of surveillance, including initiation of earlier and/or more frequent screening, may be based on guidelines and a patient's personal and/or family history for specific associated cancers.

Genetic counseling is recommended to discuss the potential clinical and/or reproductive implications of these results, as well as recommendations for testing family members. There is a 50% chance (1 in 2) of a first-degree relative having this variant. To access Labcorp Genetic Counselors please visit <https://womenshealth.labcorp.com/genetic-counseling> or call (855) GC-CALLS (855-422-2557). To discuss targeted analysis for other family members with a Labcorp Genetic Coordinator please call 800-345-4363.

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## METHODS AND LIMITATIONS

**Next-generation sequencing:** Genomic regions of interest are selected using a custom capture reagent for target enrichment and sequenced via the Illumina(R) next generation sequencing platform. Regions of interest include all exons and intron/exon junctions (+/-20 nucleotides) of the *BRCA1* (NM\_007294.3) and *BRCA2* (NM\_000059.3) genes. Regions of interest may be extended to include intronic sequences known to harbor pathogenic/likely pathogenic variants. Sequencing reads are aligned with the human genome reference GRCh37/hg19 build. Minimum mean coverage is 40X. Any segment failing minimum read depth coverage is rescued by bi-directional Sanger sequencing to complete sequence analysis. Variants, including SNVs and CNVs, are identified using a custom bioinformatics pipeline.

**Reported variants:** Pathogenic and likely pathogenic variants and variants of uncertain significance (VUS) are reported. Non-deletion variants are specified using the numbering and nomenclature recommended by the Human Genome Variation Society (HGVS, <http://www.hgvs.org/>). Benign variants are not reported. Variant classification and confirmation are consistent with ACMG standards and guidelines (Richards, PMID:25741868; Rehm, PMID:23887774). Detailed variant classification information is available upon request. A variant of uncertain significance (VUS) should not be used in clinical decision making; a VUS is classified based on inadequate or conflicting evidence regarding its pathogenicity or clinical relevance.

**Limitations:** Technologies used do not detect germline mosaicism and do not rule out the presence of large chromosomal aberrations, including rearrangements, gene fusions, or variants in regions or genes not included in this test, or possible inter/ intragenic interactions between variants. Variant classification and/or interpretation may change over time if more information becomes available. False positive or false negative results may occur for reasons that include: genetic variants, pseudogene interference, technical handling, blood transfusions, bone marrow transplantation, mislabeling of samples, or erroneous representation of family relationships. For heterozygous variants in the same gene the assay cannot determine whether they are on the same or different chromosome; to determine phase and clinical significance, rarely, parental testing may be required. Exact breakpoints of exon-level deletions/duplications are not determined. The presence of an inherited cancer syndrome due to a different genetic cause cannot be ruled out. Any interpretation should be clinically correlated with information about the patient's presentation and relevant family history.

## REFERENCES

1. NCCN Genetic/Familial High Risk Assessment: Breast, Ovarian, and Pancreatic. Version 2.2023.
2. Petrucelli, et al. *BRCA1*- and *BRCA2*-Associated Hereditary Breast and Ovarian Cancer. GeneReviews, updated 2022. PMID: 20301425.

This test was developed and its performance characteristics determined by Labcorp. It has not been cleared or approved by the Food and Drug Administration.

## PERFORMING LABS

Component Type	Performed At	Laboratory Director
Technical component, processing	Laboratory Corporation of America, 1912 TW Alexander Drive, RTP, NC, 27709-0150	Anjen Chenn, MD, PhD
Technical component, analysis	Laboratory Corporation of America, 1912 TW Alexander Drive, RTP, NC, 27709-0150	Anjen Chenn, MD, PhD
Professional component	Laboratory Corporation of America, 43957 Championship Place, Ashburn, VA, 20147	W. Christine Spence, PhD, FACMG

For inquiries, the physician may contact the lab at 800-345-4363

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