Warde Medical Laboratory

LABORATORY REPORT

Example Client, XYZ123
1234 Warde Road
Ann Arbor MI 48108

EXAMPLE, REPORT W
WX0000003827 M 07/08/1978 45 Y

Referral Testing

Collected: 08/31/2023 10:56 Received: 08/31/2023 10:56

Test Name	Result	Flag	Ref-Ranges	Units	Site
BRCA PANEL					
Result	POSITIVE				QCRL
	PATHOGENIC VARIANT IDENTIFIED Test Performed at: Quest Diagnostics Nichols Institute 33608 Ortega Highway San Juan Capistrano, CA 92675-2042 I Maramica MD, PhD, MBA				
VARIANT 1					
Gene	SEE NOTE				QCRL
	BRCA2				
Variant	SEE NOTE				QCRL
	c.3599_3600del (p.Cys1200*)				
Classification	SEE NOTE				QCRL
	PATHOGENIC Test Performed at: Quest Diagnostics Nichols Institute 33608 Ortega Highway San Juan Capistrano, CA 92675-2042 I Maramica MD, PhD, MBA				
VARIANT 2					
Gene 2	.				QCRL
Variant 2	.				QCRL
Classification 2	.				QCRL
VARIANT 3					
Gene 3	.				QCRL
Variant 3	.				QCRL
Classification 3	.				QCRL
VARIANT 4					
Gene 4	.				QCRL

LAB: L - LOW, H - HIGH, AB - ABNORMAL, C - CRITICAL, . - NOT TESTED

F231000022
WX0000003827
Printed D&T: 08/31/23 11:00

Ordered By: KAJAL SITWALA, MD, PhD
WX00000000002365

Kajal V. Sitwala, MD, PhD - Medical Director
Form: MM RL1

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Variant 4	.				QCRL
Classification 4	.				QCRL

VARIANT 5

Gene 5	.				QCRL
Variant 5	.				QCRL
Classification 5	.				QCRL

VUS

VUS(s)	.				QCRL
Gene List	.				QCRL

CLINICAL INTERPRETATION

Clinical Interpretation	POSITIVE				QCRL

A pathogenic variant was identified in one copy of the BRCA2 gene. A pathogenic variant in the BRCA2 gene is consistent with a diagnosis of BRCA-related breast and/or ovarian cancer syndrome. Women with one copy of a BRCA2 pathogenic variant have an elevated risk of breast cancer (up to 69% to age 80) and ovarian cancer (up to 20% to age 70) (PMID: 32676552 (2020), 28632866 (2017), 17416853 (2007), 12677558 (2003)). Emerging data suggest there may be a slightly increased risk for endometrial cancer (PMID: 33710348 (2021)). Men with one copy of a BRCA2 pathogenic variant have an elevated risk of breast cancer (6.8% by age 70) (PMID: 18042939 (2007)) and prostate cancer (20%-34% by age 80) (PMID: 31495749 (2019), 11170890 (2001)). Both men and women with one copy of a BRCA2 pathogenic variant have an elevated risk of pancreatic cancer and melanoma, though the degree of risk is not well defined (PMID: 17301269 (2007), 16141007 (2005), 11170890 (2001)). Reproductive Risk: Offspring of parents who both carry a pathogenic BRCA2 variant are at risk for Fanconi anemia, complementation group D1, a condition characterized by physical abnormalities, bone marrow failure, and elevated risk of cancer (OMIM 605724). There is an additional risk to the patient's offspring if their partner also has a clinically significant variant in the same gene. The patient's reproductive partner may wish to discuss genetic testing with a healthcare provider.

Recommendations regarding cancer treatment, surveillance and/or prevention are available yet may change over time. For examples of medical management resources, please visit QuestHereditaryCancer.com. Blood relatives of this patient are at risk for carrying the same clinically actionable variant(s) and should be advised to discuss genetic testing with a healthcare provider. Genetic counseling is

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recommended for any individual undergoing genetic testing.

Variant Interpretation — SEE NOTE — QCRL

This test has identified one copy of the c.3599_3600del (p.Cys1200*) variant in the BRCA2 gene. This frameshift variant causes the premature termination of BRCA2 protein synthesis. In the published literature, this variant has been reported in symptomatic individuals with breast and/or ovarian cancer and a boy with a phenotype of Fanconi Anemia in the published literature (PMIDs: 22798144 (2012), 24259538 (2014), 24728189 (2014), 26287763 (2015), 29348823 (2017), 30309222 (2019), and 30702160 (2019)). ClinVar contains an entry for this variant (URL: www.ncbi.nlm.nih.gov/clinvar, Variation ID: 51493). Based on the available information, this variant is classified as pathogenic.
Test Performed at:
Quest Diagnostics Nichols Institute
33608 Ortega Highway
San Juan Capistrano, CA 92675-2042 I Maramica MD, PhD, MBA

COMMENTS

Reviewer — SEE NOTE — QCRL

Laboratory results and submitted clinical information reviewed by Chris Antolik, Ph.D., FACMG, CGMBS.

Resources — SEE NOTE — QCRL

Visit QuestHereditaryCancer.com for physician information, patient materials, FAQs, and testing resources. Call 1-866-GENE-INFO (1-866-436-3463) for genetic counseling consultations, pre-authorization services, and help finding patient genetic counseling services.

Methods and Limitations — SEE NOTE — QCRL

Methods: In this assay, enzymatically sheared DNA fragments representing the entire coding region and the splice junction sites of the interrogated genes are selectively enriched through exon capture using DNA baits, and then subjected to nucleotide sequence analysis on a massively parallel sequencing platform. Both genes, BRCA1 and BRCA2, are examined for single nucleotide variants (SNVs), insertions and deletions (InDels), and copy number variants (CNVs) involving deletions and/or duplications of one or more exons, including those

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that affect the entire genes. CNVs are assessed by bioinformatic analysis of sequencing reads and, when indicated, confirmed by an orthogonal method.

The following NCBI reference transcript sequences were utilized for analysis: BRCA1 (NM 007294.3), BRCA2 (NM 000059.3). Reference genome: hg19 (build37).

Limitations: This assay cannot detect variants affecting unexamined gene regions (e.g. deep intronic), nor variants in other unlisted genes. In addition, the effect of rare or novel variants on mRNA splicing, protein synthesis, and/or protein function may remain unclear. Variants due to mosaicism, somatic variants from pre-malignant or malignant cells, false positive, or false negative results may rarely occur. While this assay detects copy number variants (CNVs) spanning a region of interest (ROI) 100bp or more in size with a high level of sensitivity, CNV detection in smaller ROIs, which are clinically rare, is reduced. Results should be interpreted in the context of clinical findings, relevant history, and other laboratory data. This assay does not analyze all genes associated with hereditary cancer. In some situations, additional genetic testing may be appropriate.

Additional Information	SEE NOTE				QCRL

Benign and likely benign variants with no known clinical significance are reported only by request. If a variant is reclassified with clinical implications, Quest Diagnostics will endeavor to contact the ordering provider.

Providers may contact Quest Genomics Client Services at 1-866-GENEINFO (1-866-436-3463) for assistance with result interpretation, questions about variant classification, or to discuss additional testing.

The classification and interpretation of the variant(s) identified reflect the current state of Quest Diagnostics' understanding at the time of this report. Variant classification and interpretation are subject to professional judgment, and may change for a variety of reasons, including but not limited to, updates in classification guidelines and availability of additional scientific and clinical information. This test result should be used in conjunction with the health care provider's clinical evaluation. Inquiry regarding potential changes to the classification of the variant is strongly recommended prior to making any future clinical decision. For questions regarding variant classification updates, please call Quest Diagnostics at 866-GENEINFO (436-3463) to speak to a genetic counselor or laboratory director, or visit http://questdiagnostics.com/variantiq.

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For patients who are interested in sharing de-identified genetic and health information to improve understanding of genetics and health, please visit https://GenomeConnect.org. GenomeConnect is a third party online registry designed by the Clinical Genome Resource (ClinGen) and is not affiliated with Quest Diagnostics in any way.

This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics Nichols Institute San Juan Capistrano. It has not been cleared or approved by FDA. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

Test Performed at:
Quest Diagnostics Nichols Institute
33608 Ortega Highway
San Juan Capistrano, CA 92675-2042 I Maramica MD, PhD, MBA

Performing Site:
QCRL: QUEST DIAGNOSTICS REFERENCE LAB CAPISTRANO 33608 Ortega Highway San Juan Capistrano CA 92675

Reported Date: 2023.08.31 10:59 BRCAP