

Specimen Collected: 01-Jul-22 12:17

HR Heredit Breast Cancer by NGS, |Received: 01-Jul-22 12:19

Report/Verified: 01-Jul-22 12:26

DelDup

Procedure	Result	Units	Reference Interval
BCHR Interp	Negative <sup>i1</sup>		
Spcm BCHR	Whole Blood		

**Test Information**

i1: BCHR Interp

BACKGROUND INFORMATION: Hereditary Breast Cancer High-Risk Panel, Sequencing and Deletion/Duplication

CHARACTERISTICS: Pathogenic germline variants in multiple genes have been implicated in hereditary breast cancer. Risk-reducing options have been recommended for high-risk hereditary breast cancer genes. These genes include: BRCA1, BRCA2, CDH1, PALB2, PTEN, and TP53.

EPIDEMIOLOGY: Approximately 5-10 percent of breast cancer is associated with a hereditary cause.

CAUSE: Pathogenic germline variants in genes associated with a high lifetime risk of hereditary breast cancer.

INHERITANCE: Autosomal dominant. Additionally, some genes are also associated with autosomal recessive childhood cancer predisposition or other syndromes.

GENES TESTED: BRCA1\*; BRCA2; CDH1\*; PALB2; PTEN\*; TP53

\*One or more exons are not covered by sequencing and/or deletion/duplication analysis for the indicated gene; see limitations section below.

METHODOLOGY: Probe hybridization-based capture of all coding exons and exon-intron junctions of the targeted genes, (including selected PTEN promoter variants), followed by massively parallel sequencing. Sanger sequencing was performed as necessary to fill in regions of low coverage and to confirm reported variants that do not meet acceptable quality metrics. A proprietary bioinformatic algorithm was used to detect large (single exon-level or larger) deletions or duplications in the indicated genes. Large deletions/duplications confirmed using an orthogonal exon-level microarray. Human genome build 19 (Hg 19) was used for data analysis. Testing of selected exons (and exon/intron boundaries) of PTEN was performed by bidirectional Sanger sequencing.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions (indels) from 1-10 base pairs in size. Indels greater than 10 base pairs may be detected, but the analytical sensitivity may be

\*=Abnormal, #=Corrected, C=Critical, f=Result Footnote, H-High, i-Test Information, L-Low, t-Interpretive Text, @=Performing lab

Unless otherwise indicated, testing performed at:

ARUP Laboratories

500 Chipeta Way, Salt Lake City, UT 84108

Laboratory Director: Jonathan R. Genzen, MD, PhD

ARUP Accession: 22-182-900090

Report Request ID: 16422886

Printed: 20-Sep-22 12:21

Page 1 of 2

**Test Information**

i1: BCHR Interp

reduced. Deletions of 2 exons or larger are detected with sensitivity greater than 97 percent; single exon deletions are detected with 62 percent sensitivity. Duplications of 3 exons or larger are detected at greater than 83 percent sensitivity. Specificity is greater than 99.9 percent for all variant classes.

LIMITATIONS: A negative result does not exclude a heritable form of breast cancer. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. Regulatory region variants and deep intronic variants will not be identified. Precise breakpoints for large deletions or duplications are not determined in this assay and single exon deletions/duplications may not be detected based on the breakpoints of the rearrangement. The actual breakpoints for the deletion or duplication may extend beyond or be within the exon(s) reported. This test is not intended to detect duplications of 2 or fewer exons in size, though these may be identified. Single exon deletions are reported but called at a lower sensitivity. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations caused by the presence of pseudogenes, repetitive, or homologous regions. This test is not intended to detect low-level mosaic or somatic variants, gene conversion events, complex inversions, translocations, mitochondrial DNA (mtDNA) variants, or repeat expansions. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Noncoding transcripts were not analyzed.

The following regions are not sequenced due to technical limitations of the assay:  
BRCA1 (NM\_007300) exon 13

Deletions/duplications will not be called for the following exons:  
BRCA1 (NM\_007294, NM\_007299, NM\_007300) 2; BRCA1 (NM\_007298) 1; CDH1 (NM\_001317185) 10; PTEN (NM\_000314, NM\_001304718) 9; PTEN (NM\_001304717) 1,10

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the U.S. Food and Drug Administration. This test was performed in a CLIA-certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.

\*=Abnormal, #=Corrected, C=Critical, f=Result Footnote, H-High, i-Test Information, L-Low, t-Interpretive Text, @=Performing lab

**Unless otherwise indicated, testing performed at:**

**ARUP Laboratories**

500 Chipeta Way, Salt Lake City, UT 84108

Laboratory Director: Jonathan R. Genzen, MD, PhD

**ARUP Accession:** 22-182-900090

**Report Request ID:** 16422886

**Printed:** 20-Sep-22 12:21

Page 2 of 2