

Specimen Collected: 26-Jul-22 10:02

Retinoblastoma by NGS, DelDup Procedure	Received: 26-Jul-22 10:03	Report/Verified: 03-Aug-22 15:06	
	Result	Units	Reference Interval
RB1 Interp	See Note ¹¹		
Spcm RB1	See Note		

Test Information

11: RB1 Interp

BACKGROUND INFORMATION: Hereditary Retinoblastoma (RB1)

Sequencing and Deletion/Duplication

CHARACTERISTICS: Retinoblastoma is a malignant tumor of the retina that typically occurs in children under 5 years of age. Hereditary retinoblastoma, caused by a single germline pathogenic variant in the RB1 gene, predisposes individuals to retinoblastoma and other nonocular tumors (including pinealoblastoma, osteosarcoma, soft tissue sarcoma, and melanoma).

EPIDEMIOLOGY: Retinoblastoma affects approximately 1:15,000 to 1:20,000 live births. Hereditary retinoblastoma accounts for approximately 10 percent of retinoblastoma cases.

CAUSE: Pathogenic germline variants in the RB1 gene

INHERITANCE: Autosomal dominant

PENETRANCE: Complete penetrance, except for fewer than 10 percent of families that show a low-penetrance phenotype with reduced expressivity

CLINICAL SENSITIVITY: Varies, dependent on phenotype

GENE TESTED: RB1* (NM_000321)

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

METHODOLOGY: Probe hybridization-based capture of all coding exons and exon-intron junctions of the RB1 gene, 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.

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

*=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: 22-207-900035

Report Request ID: 16378800

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Test Information

i1: RB1 Interp
greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced. Deletions of two exons or larger are detected with sensitivity greater than 97 percent; single exon deletions are detected with 62 percent sensitivity. Duplications of three 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 retinoblastoma. This test only detects variants within the coding regions and intron-exon boundaries of the RB1 gene. 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 two 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 exons may have reduced sequencing sensitivity due to technical limitations of the assay:

RB1 (NM_000321) 22

Deletions/duplications will not be called for the following exons:

RB1 (NM_000321) 22

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.

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