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Patient Report

Patient Age/Sex: 1 day Male

Specimen Collected: 22-Nov-21 09:31

SDH Panel by NGS, DelDup **|Received: 22-Nov-21 09:31** **Report/Verified: 22-Nov-21 09:41**

Procedure	Result	Units	Reference Interval
SDH Specimen	Whole Blood		
SDH Interp	See Note [i1]		

Test Information

i1: SDH Interp

BACKGROUND INFORMATION: Hereditary Paraganglioma-Pheochromocytoma (SDHA, SDHB, SDHC, and SDHD) Panel, Sequencing and Deletion/Duplication

CHARACTERISTICS: Hereditary paraganglioma-pheochromocytoma (PGL/PCC) syndromes are familial cancer syndromes characterized by neuroendocrine tumors: paragangliomas (neuroendocrine tumors of the autonomic nervous system) and pheochromocytomas (paragangliomas of the adrenal medulla). Pathogenic germline variants in SDHA, SDHB, SDHC, and SDHD, among several other genes, predispose individuals to paraganglioma and pheochromocytoma with an increased risk for malignancy.

CAUSE: Pathogenic germline variants in succinate dehydrogenase, subunits A, B, C, and D (SDHA, SDHB, SDHC, and SDHD), and other genes

INHERITANCE: Autosomal dominant; parent-of-origin effect for SDHD

PENETRANCE: Variable and age dependent

CLINICAL SENSITIVITY: 22-45 percent

GENES TESTED: SDHA* (NM_004168), SDHB (NM_003000), SDHC (NM_003001), SDHD (NM_003002)
* - One or more exons are not covered by sequencing, and deletion/duplication detection is not available for this gene; see limitations section below.

METHODOLOGY: Probe hybridization-based capture of all coding exons and exon-intron junctions of the targeted genes 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. Human genome build 19 (Hg 19) was used for data analysis. Multiplex ligation-dependent probe amplification (MLPA) of the targeted genes.

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

Test Information

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reduced. Specificity is greater than 99.9 percent for all variant classes. The analytical sensitivity for MLPA is greater than 99 percent.

LIMITATIONS: A negative result does not exclude a diagnosis of hereditary paraganglioma-pheochromocytoma. This test only detects variants within the coding regions and intron-exon boundaries of the SDHA, SDHB, SDHC, and SDHD 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. 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) mutations, 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: SDHA(NM_004168) exon 14

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.