Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	7/17/1988
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

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

ARUP test code 3004480

SDH Specimen: Whole Blood

SDH Interp: Negative

RESULT
No pathogenic variants were detected in any of the genes tested.

INTERPRETATION
No pathogenic variants were detected in any of the genes tested. This result decreases the likelihood of, but does not exclude, a diagnosis of Hereditary Paraganglioma-Pheochromocytoma syndrome. Please refer to the background information included in this report for a list of the genes analyzed, methodology, and limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and family history. If this individual has a family history, determination of a causative familial variant in an affected family member is necessary for optimal interpretation of this negative result. Further testing may be warranted if there is a familial variant that is not detectable by this assay. Genetic consultation is recommended. If suspicion remains for a hereditary cancer syndrome, consideration should be given to ordering the Hereditary Cancer Panel, Sequencing and Deletion/Duplication (ARUP test code 2012032).

COMMENTS
Likely benign and benign variants are not reported.
Variants in the following region(s) may not be detected by NGS with sufficient confidence in this sample due to technical limitations: None

This result has been reviewed and approved by [redacted]

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 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.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
SDH Specimen	23-278-104787	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
SDH Interp	23-278-104787	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical