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

Physician: Doctor, Example

Patient: Patient, Example

DOB	12/31/1752
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Hereditary Paraganglioma-Pheochromocytoma (SDHB) Sequencing and Deletion/Duplication

ARUP test code 2007108

HPGL-PCC (SDHB) Seq, DelDup Specimen	Whole Blood	
HPGL-PCC (SDHB) Seq, DelDup Interp	**Positive**	*

H – high L – low * – abnormal C – critical

TEST PERFORMED - 2007108
TEST DESCRIPTION - Hereditary Paraganglioma-Pheochromocytoma (SDHB) Sequencing and Deletion/Duplication
INDICATION FOR TEST - Confirm Diagnosis

RESULT
One pathogenic variant detected in the SDHB gene.

DNA VARIANT
Pathogenic
Nucleic Acid Change: c.19_41dup23; Heterozygous
Amino Acid Alteration: Frameshift

INTERPRETATION
One pathogenic variant, c.19_41dup23, was detected in the SDHB gene by sequencing. This variant is listed in the dbSNP variant database (rs794728951) with no minor allele frequency reported in general population databases, and reported once as a pathogenic variant in ClinVar (see link). The c.19_41dup23 variant causes a frameshift and is predicted to result in a truncated protein or an absent transcript; therefore, we consider this variant to be pathogenic. This result is consistent with a diagnosis of Hereditary Paraganglioma-Pheochromocytoma Syndrome; clinical manifestations are variable. Each of this individual's offspring have a 50 percent risk of inheriting the pathogenic variant.

No pathogenic variants were detected by deletion/duplication analysis.

RECOMMENDATIONS
Genetic consultation is indicated, including a discussion of medical screening and management. At-risk family members should be offered targeted testing for the identified pathogenic variant (Familial Mutation, Targeted Sequencing, ARUP test code 2001961).

COMMENTS
Reference Sequence: GenBank # NM_003000.2 (SDHB)
Nucleotide numbering begins at the "A" of the ATG initiation codon.
Benign variants are not included on this report but are available upon request.

REFERENCES
Link to ClinVar for c.19_41dup23:
http://www.ncbi.nlm.nih.gov/clinvar/variation/201608/#summary-evidence

This result has been reviewed and approved by Elaine Lyon, Ph.D.

BACKGROUND INFORMATION: Hereditary Paraganglioma-Pheochromocytoma (SDHB) Sequencing and Deletion/Duplication

CHARACTERISTICS: Hereditary paraganglioma-pheochromocytoma (PGL/PCC) syndromes are characterized by paragangliomas (neuroendocrine tumors of the autonomic nervous system) and pheochromocytomas (paragangliomas of the adrenal medulla). Pathogenic germline mutations in a number of genes, including SDHB, predispose to paraganglioma and pheochromocytoma with risk of malignant transformation.
INCIDENCE: About 1 in 300,000 per year.
INHERITANCE: Autosomal dominant.
CAUSE: Pathogenic succinate dehydrogenase, subunits B, C, and D (SDHB, SDHC, and SDHD) gene mutations. Mutations in other genes, including TMEM127, EGLN1, MAX, SDHA, and SDHAF2, may also be causative.
CLINICAL SENSITIVITY: 7-11 percent.
METHODOLOGY: Bidirectional sequencing of all coding regions and intron-exon boundaries of the SDHB gene; Multiplex Ligation-dependent Probe Amplification (MLPA) to detect large SDHB deletions /duplications.
ANALYTICAL SENSITIVITY AND SPECIFICITY: Sequencing: 99 percent. MLPA: 90 and 99 percent, respectively.
LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. Regulatory region mutations and deep intronic mutations will not be detected. The breakpoints of large deletions/duplications will not be determined. Mutations in genes other than SDHB are not evaluated.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
HPGL-PCC (SDHB) Seq, DelDup Specimen	17-017-110742	1/17/2017 1:29:00 PM	1/17/2017 1:30:08 PM	3/8/2017 1:14:27 PM
HPGL-PCC (SDHB) Seq, DelDup Interp	17-017-110742	1/17/2017 1:29:00 PM	1/17/2017 1:30:08 PM	3/8/2017 1:14:27 PM

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