

Client: ARUP Example Report Only
500 Chipeta Way
Salt Lake City, UT 84108
UNITED STATES

Physician: ARUP, ARUP

Patient: PAH PANEL, NEGATIVE EXAMPLE

DOB

Sex: Female

Patient Identifiers: 41725

Visit Number (FIN): 42050

Collection Date: 8/17/2022 09:44

Pulmonary Arterial Hypertension (PAH) Panel, Sequencing and Deletion/Duplication

ARUP test code 2009345

PAH Pan. Seq/DelDup, Specimen	whole Blood
PAH Pan. Seq/DelDup, Interp	<p>Negative</p> <p>INDICATION FOR TESTING Not provided</p> <p>RESULT No pathogenic variants detected in any of the genes tested</p> <p>INTERPRETATION No pathogenic variants were identified by massively parallel sequencing of the coding regions and exon-intron boundaries of the genes tested. No large exonic deletions and duplications were identified in the genes tested. This result decreases the likelihood of, but does not exclude, a heritable form of pulmonary arterial hypertension. Please refer to the background information included in this report for a list of the genes analyzed and limitations of this test.</p> <p>RECOMMENDATIONS Medical screening and management of this individual should rely on clinical findings and family history. Genetic consultation is recommended.</p> <p>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; reportable variants are confirmed by Sanger sequencing: None</p> <p>This result has been reviewed and approved by [REDACTED]</p> <p>BACKGROUND INFORMATION: Pulmonary Arterial Hypertension (PAH) Panel, Sequencing and Deletion/Duplication</p> <p>CHARACTERISTICS: Pulmonary arterial hypertension (PAH) is caused by widespread occlusion or destruction of the smallest pulmonary arteries, leading to increased blood flow resistance, right ventricular hypertrophy, and heart failure. Approximately 80 percent of PAH is idiopathic and 20 percent is heritable.</p> <p>EPIDEMIOLOGY: The incidence is 1-2 in 1,000,000.</p> <p>INHERITANCE: Autosomal dominant (ACVRL1, BMPR2, CAV1, ENG, KCNA5, KCNK3, GDF2, and SMAD9); autosomal recessive (EIF2AK4, TBX4)</p>

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

Unless otherwise indicated, testing performed at:

ARUP LABORATORIES | 800-522-2787 | aruplab.com
500 Chipeta Way, Salt Lake City, UT 84108-1221
Jonathan R. Genzen, MD, PhD, Laboratory Director

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CLINICAL SENSITIVITY: 75-80 percent for familial cases, approximately 25 percent for simplex cases.

GENES TESTED: ACVRL1, BMPR2, CAV1, EIF2AK4, ENG,* KCNA5, KCNK3, GDF2, SMAD9, and TBX4

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

METHODOLOGY: Probe hybridization-based capture of all coding exons and exon-intron junctions of the targeted genes (including the 5' UTR of ENG, and a region of ACVRL1 intron 9 encompassing the CT-rich variant hotspot region), 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 greater than 10 base pairs may be detected but the analytical sensitivity may be 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 PAH. 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.

Single exon deletions/duplications may not be called in the following exons: ENG (NM_001114753) 1

This test was developed and its performance characteristics determined by ARUP Laboratories. The U.S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use. The results are not intended to be used as the sole means for clinical diagnosis or patient management decisions.

Counseling and informed consent are recommended for genetic

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testing. Consent forms are available online.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
PAH Pan. Seq/DelDup, Specimen	22-229-102534	8/17/2022 9:44:00 AM	8/17/2022 9:45:03 AM	8/17/2022 9:46:00 AM
PAH Pan. Seq/DelDup, Interp	22-229-102534	8/17/2022 9:44:00 AM	8/17/2022 9:45:03 AM	8/17/2022 9:46:00 AM

END OF CHART

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