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

Physician: Doctor, Example

Patient: Patient, Example

DOB	12/9/1980
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Aortopathy Panel, Sequencing and Deletion/Duplication

ARUP test code 2006540

Aortopathy Panel Specimen: Whole Blood

Aortopathy Panel Interpretation: Negative

INDICATION FOR TESTING
Patient referred for testing due to the presence of thoracic aneurysms.

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

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 aortopathy. Please refer to the background information included in this report for a list of the genes analyzed and limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and family history. Genetic consultation is recommended.

COMMENTS
Benign variants are not included in this report, but are available upon request.

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Aortopathy Panel, Sequencing and Deletion/Duplication

CHARACTERISTICS: Life-threatening aortic dilatations, dissections, and/or rupture, including syndromic and familial connective tissue disorders caused by variants identified in multiple genes.

EPIDEMIOLOGY: The prevalence of Marfan syndrome (MFS) is 1 in 5,000 to 1 in 10,000; Homocystinuria due to cystathionine beta-synthase deficiency (HCY) is 1 in 1,800 to 1 in 800,000 depending on the ethnic population; Ehlers-Danlos syndrome, type I/II (EDS I/II) is 1 in 20,000; Ehlers-Danlos syndrome, type IV (EDS IV) is at least 1 in 250,000; thoracic aortic aneurysm and dissection (TAAD) has an incidence of 9-16/100,000 individuals/year and is familial in approximately 20 percent of

cases.

CAUSE: Pathogenic germline variants in genes associated with MFS, HCY, EDS, TAAD, congenital contractural arachnodactyly (CCA), and Loeys-Dietz syndrome (LDS).

INHERITANCE: X-linked for FLNA, autosomal recessive for CBS, EFEMP2, PLOD1, and SLC2A10; autosomal dominant for the other tested genes.

PENETRANCE: Complete for MFS, EDS IV, EDS VI, CCA, and LDS, with rare exceptions; reduced for TAAD and EDS I/ II.

GENES TESTED: ACTA2, CBS, COL3A1, COL5A1, COL5A2, EFEMP2, FBN1, FBN2, FLNA, LOX**, MYH11, MYLK, PLOD1, PRKG1, SKI, SLC2A10, SMAD3, SMAD4, TGFB2, TGFB3, TGFBR1, TGFBR2

** - Deletion/duplication detection is not available for this gene.

METHODOLOGY: Targeted 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 confirm reported variants. A custom tiled comparative genomic hybridization array (aCGH) was used to detect large deletions or duplications in the indicated subset of genes. Human genome build 19 (Hg 19) was used for data analysis.

ANALYTICAL SENSITIVITY: The analytical sensitivity of this test is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions from 1-10 base pairs in size. Variants greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced.

LIMITATIONS: A negative result does not exclude a heritable form of MFS, HCY, EDS, TAAD, CCA, or LDS. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Regulatory region variants and deep intronic variants will not be identified and breakpoints of large deletions/duplications will not be determined. Single exon deletions/duplications or deletions/duplications less than 1kb may not be detected. Deletions/duplications/insertions of any size may not be detected by massive parallel sequencing. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions. This assay may not detect low-level somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Non-coding transcripts were not analyzed.

Single exon deletions/duplications will not be called for the following exons:
COL3A1(NM_000090) 6,7,9,13;COL5A1(NM_000093) 1,16,20;COL5A2(NM_000393) 36;MYH11(NM_001040113) 42;PRKG1(NM_006258) 8,17;TGFBR1(NM_004612) 1

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Aortopathy Panel Specimen	18-344-107914	12/10/2018 12:01:00 PM	12/10/2018 12 02:00 PM	12/10/2018 1:07:00 PM
Aortopathy Panel Interpretation	18-344-107914	12/10/2018 12:01:00 PM	12/10/2018 12 02:00 PM	12/10/2018 1:07:00 PM

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