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

Physician: Doctor, Example

Patient: Patient, Example

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

Marfan Syndrome (FBN1) Sequencing and Deletion/Duplication

ARUP test code 3004102

Marfan Syndrome (FBN1) Specimen	Whole Blood

Marfan Syndrome (FBN1) Interpretation

Negative

INDICATION FOR TESTING
Not provided.

RESULT
No pathogenic variants were detected in the FBN1 gene.

INTERPRETATION
No pathogenic variants were identified by massively parallel sequencing of the coding regions and exon-intron boundaries of the FBN1 gene. No large exonic deletions and duplications were identified by deletion/duplication analysis. This result decreases the likelihood of, but does not exclude, a diagnosis of Marfan syndrome or other FBN1-related disorders. Please refer to the background information included in this report for the clinical sensitivity and limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and family history. Genetic consultation is recommended. If suspicion remains for a genetic aortopathy, consider testing for other diseases known to affect the aorta (Aortopathy Panel, Sequencing and Deletion/Duplication, ARUP test code 2006540).

COMMENTS
Likely benign and benign variants are not included in this report.

This result has been reviewed and approved by [redacted]

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

BACKGROUND INFORMATION: Marfan Syndrome (FBN1) Sequencing and Deletion/Duplication

CHARACTERISTICS: Marfan syndrome is a connective tissue disorder affecting the ocular, skeletal, and cardiovascular systems with a high degree of clinical variability. Common ocular findings include: myopia, ectopia lentis, retinal detachment, glaucoma, and early cataracts. Skeletal involvement may include: bone overgrowth and joint laxity, disproportionally long extremities, pectus excavatum/carinatum, and scoliosis. Cardiovascular findings include: aortic dilatation/dissection, mitral and/or tricuspid valve prolapse, and enlargement of the proximal pulmonary artery. Cardiovascular disease management is necessary to decrease morbidity and early mortality.

EPIDEMIOLOGY: Prevalence is 1 in 5,000 to 1 in 10,000.

CAUSE: Pathogenic germline variants in the FBN1 gene.

INHERITANCE: Autosomal dominant. De novo pathogenic variants are causative for 25 percent of cases.

PENETRANCE: Complete, but age dependent.

CLINICAL SENSITIVITY: 95-98 percent.

GENE TESTED: FBN1.

METHODOLOGY: 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. Multiplex ligation-dependent probe amplification (MLPA) was used to detect large deletions or duplications.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity of sequencing 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. The analytical sensitivity for MLPA is 99 percent.

LIMITATIONS: A negative result does not exclude a diagnosis of Marfan syndrome or other FBN1-related disorders. This test only detects variants within the coding regions and intron-exon boundaries of the FBN1 gene. Regulatory region variants and deep intronic variants will not be identified and breakpoints of large deletions/duplications will not be determined. Deletions/duplications/insertions of any size may not be detected by massively 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 mosaic or somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Noncoding transcripts were not analyzed.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US 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.

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VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Marfan Syndrome (FBN1) Specimen	21-320-103645	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Marfan Syndrome (FBN1) Interpretation	21-320-103645	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