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

Physician: Doctor, Example

Patient: Patient, Example

DOB	9/3/1970
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Loeys-Dietz Syndrome Core Panel, Sequencing

ARUP test code 3003947

Spcm LDS	Whole Blood
LDS 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 Loeys-Dietz 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 the risk for a genetic aortopathy remains high, consideration should be given to ordering the Aortopathy Panel, Sequencing and Deletion/Duplication (ARUP test code 2006540).

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]

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

BACKGROUND INFORMATION: Loeys-Dietz Syndrome Core Panel, Sequencing

CHARACTERISTICS: Cardiovascular findings (aortic dissection, arterial aneurysms, arterial tortuosity, MVP), skeletal abnormalities (arachnodactyly, talipes equinovarus, joint laxity, cervical spine malformations and instability, pectus excavatum and carinatum), craniofacial features (hypertelorism, retrognathia, craniosynostosis, and bifid uvula), cutaneous findings (translucent velvety skin, visible veins in chest, widened poorly-formed scars, and easy bruising), allergy and gastrointestinal disease (asthma, allergic rhinitis, food allergy, eosinophilic gastrointestinal disease) and spontaneous rupture of spleen, bowel, and uterus during pregnancy).

EPIDEMIOLOGY: Unknown.

CAUSE: Pathogenic germline variants in SMAD2, SMAD3, TGFB2, TGFB3, TGFBR1, and TGFBR2.

INHERITANCE: Autosomal dominant; 75 percent of cases are caused by a de novo variant.

PENETRANCE: High

CLINICAL SENSITIVITY: Approximately 75-85 percent.

GENES TESTED: TGFBR1, TGFBR2.

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.

ANALYTICAL SENSITIVITY/SPECIFICITY: 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 diagnosis of Loeys-Dietz syndrome. This test only detects variants within the coding regions and intron-exon boundaries of the TGFBR1 and TGFBR2 genes. Variants in other genes, causing LDS (SMAD2, SMAD3, TGFB2, TGFB3) are not analyzed by this core panel. Regulatory region variants and deep intronic variants will not be identified. 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.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Spcm LDS	23-056-400299	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
LDS Interp	23-056-400299	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