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

Physician: Doctor, Example

Patient: Patient, Example

DOB	2/12/1971
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Vascular Malformations Panel, Sequencing and Deletion/Duplication

ARUP test code 2007384

Vascular Malformations Panel Specimen: Whole Blood

Vascular Malformations Panel Interp: Negative

INDICATION FOR TESTING
Personal history of spinal and cutaneous arteriovenous malformations and lymphangiomas of the abdomen.

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 a vascular malformation disorder. 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 of this individual should rely on clinical findings and family history. Genetic consultation is recommended.

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

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Vascular Malformations Panel, Sequencing and Deletion/Duplication

CHARACTERISTICS: Defects of either blood or lymphatic vessels. This panel focuses on disorders associated with structural defects of blood vessels.

EPIDEMIOLOGY: The prevalence of hereditary hemorrhagic telangiectasia (HHT) is 1 in 10,000; familial cerebral cavernous malformation (CCM) is 1 in 2,000 to 10,000; RASA1-related disorders (CM-AVM, Parkes Weber) is approximately 1 in 100,000; Pulmonary Arterial Hypertension (PAH) is 1-2/100,000; PTEN-related Proteus syndrome (PS)/Proteus-like syndrome (PLS) is estimated at less than 1 in 1,000,000; and Juvenile polyposis/hereditary hemorrhagic telangiectasia (JP/HHT) syndrome is approximately 1 in 100,000.

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

INHERITANCE: Autosomal dominant.

PENETRANCE: All exhibit age-related penetrance. 90 percent or greater for HHT, JP/HHT, RASA1-related disorders, VMCM and GVM. 50-75 percent for CCM. 1-20 percent for PAH, depending on gene. Unknown for PTEN-related PS/PLS.

GENES TESTED: ACVRL1, AKT1**, BMPR2, CAV1, CCBE1, CCM2, EIF2AK4**, ELMO2**, ENG, EPHB4**, FAT4**, FLT4, FOXC2, GATA2**, GDF2, GJC2, GLMN, KCNK3, KRIT1, PDCD10, PIEZO1**, PIK3CA***, PTEN, RASA1, SMAD4, SMAD9**, SOX18***, STAMBP**, TEK, VEGFC**

** - Deletion/duplication detection is not available for this gene.
*** - One or more exons are not covered by sequencing, and deletion/duplication detection is not available for this gene; see limitations section below.

METHODOLOGY: Targeted capture of all coding exons and exon-intron junctions of the targeted genes, including the PTEN promoter region, followed by massively parallel sequencing. The 5' untranslated region of ENG and a region of ACVRL1 intron 9 encompassing the CT-rich variant hotspot region were sequenced. 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 a vascular malformation disorder. 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.

The following regions are not sequenced due to technical limitations of the assay:
PIK3CA(NM_006218) exon(s) 10,11,12,13,14
SOX18(NM_018419) exon(s) 1

Single exon deletions/duplications will not be called for the following exons:
FLT4(NM_002020) 30;FLT4(NM_182925) 20,22;GLMN(NM_053274) 11;PTEN(NM_000314) 8,9;PTEN(NM_001304717) 1;TEK(NM_000459) 1

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

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VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Vascular Malformations Panel Specimen	19-304-402198	10/28/2019 11:58:00 AM	11/1/2019 12:38:00 PM	11/26/2019 10:15:00 PM
Vascular Malformations Panel Interp	19-304-402198	10/28/2019 11:58:00 AM	11/1/2019 12:38:00 PM	11/26/2019 10:15:00 PM

END OF CHART

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