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

Physician: Doctor, Example

Patient: Patient, Example

DOB	5/12/1996
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Vascular Malformations Panel, Sequencing and Deletion/Duplication

ARUP test code 2007384

Vascular Malformations Panel Specimen: Whole Blood

Vascular Malformations Panel 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 heritable form of a vascular malformation disorder. 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.

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]
BACKGROUND INFORMATION: Vascular Malformations Panel, Sequencing and Deletion/Duplication
CHARACTERISTICS: Pathogenic variants in vascular malformation genes lead to defects of blood vessels, causing fast-flow or slow-flow lesions, shunting, swelling, or skin findings. For some disorders, this may lead to potentially life-threatening hemorrhage, stroke, or heart failure.

EPIDEMIOLOGY: The prevalence of hereditary hemorrhagic telangiectasia (HHT) is estimated to be 1 in 5,000 to 1 in 10,000; familial cerebral cavernous malformation (CCM) is 1 in 2,000 to 1 in 10,000; RASA1-CM-AVM is approximately 1 in 20,000; EPHB4-CM-AVM is approximately 1 in 12,000; PTEN hamartoma tumor syndrome is 1 in 200,000; and AKT1-related proteus syndrome is less than 1 in 1,000,000.

INHERITANCE: Autosomal dominant and/or autosomal recessive, depending on the causative gene

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

PENETRANCE: All conditions exhibit age-related penetrance.

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

* - One or more exons are not covered by sequencing and/or deletion/duplication analysis for the indicated gene; 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, a region of ACVRL1 intron 9 encompassing the CT-rich variant hotspot region, and selected PTEN promoter variants), 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: 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 vascular malformation disorder. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes, unless otherwise noted in the methodology section above. 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.

The following regions are not sequenced due to technical limitations of the assay:
CCM2(NM_001363458) exon(s) 7
CCM2(NM_001363459) exon(s) 6
FLT4(NM_001354989) exon(s) 30
GJC2(NM_020435) partial exon(s) 2(Chr1:228346380-228346419)
PTEN(NM_000314) exon(s) 9
PTEN(NM_001304717) exon(s) 10
PTEN(NM_001304718) exon(s) 9

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

SOX18(NM_018419) partial exon(s) 1(Chr20:62680707-62680791)
STAMBP(NM_001353969) exon(s) 10
STAMBP(NM_001353970) exon(s) 11
STAMBP(NM_001353976) exon(s) 10

Single exon deletions/duplications will not be called for the following exons:
CCM2(NM_001363458) 7; CCM2(NM_001363459) 6; ENG(NM_001114753) 1; ENG(NM_000118) 1; FLT4(NM_001354989) 30; GLMN(NM_053274) 16; GLMN(NM_001319683) 15; PIEZO1(NM_001142864) 1,25,47; PTEN(NM_000314) 9; PTEN(NM_001304717) 1,10; PTEN(NM_001304718) 9; STAMBP(NM_001353969) 10; STAMBP(NM_001353970) 11; STAMBP(NM_001353976) 10

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
Vascular Malformations Panel Specimen	25-031-125563	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Vascular Malformations Panel Interp	25-031-125563	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