



1-800-533-1710

HHT and Vascular Gene Panel

HHTGG

PATIENT NAME ABNORMAL, HHTGG				ORDER NUMBER M229000193
PATIENT ID SA00154619	DATE OF BIRTH 01/01/1980	AGE 42 Y	SEX Female	REQUESTED BY CLIENT CLIENT
COLLECTED 9/28/2022, 11:00 AM	RECEIVED 9/29/2022, 9:02 AM	REPORTED 9/30/2022, 10:36 AM		
The collected, received, and reported dates and times on the report are in the time zone of the performing location. 7028846 MCL RochesterCampus Rochester MN 55901				CLIENT ORDER NUMBER SA00154619 CLIENT MRN SA00154619

TEST DESCRIPTION

Evaluation of 12 genes associated with hereditary hemorrhagic telangiectasia (HHT), cerebral cavernous malformation (CCM), capillary malformation-arteriovenous malformation syndrome (CM-AVM) and other hereditary vascular malformation syndromes

SPECIMEN

DNA (ul)

RESULT SUMMARY

Pathogenic Variant Detected

RESULT

Gene (Transcript)	Variant	Zygosity	Classification
ACVRL1 (NM_000020.2)	c.1135G>A p.Glu379Lys (p.E379K) Chr12(GRCh37):g.52309906G>A	Heterozygous	Pathogenic

The following heterozygous PATHOGENIC variant was detected: ACVRL1 (NM_000020.2), Chr12 (GRCh37):g.52309906G>A, c.1135G>A, p.Glu379Lys (p.E379K)

No additional reportable variants were detected within all other tested genes. See the Method section for a complete list of genes evaluated by this assay.

INTERPRETATION

ACVRL1 c.1135G>A (p.Glu379Lys): The heterozygous c.1135G>A (p.Glu379Lys) variant in the ACVRL1 gene (MIM: 601284) is classified as pathogenic. The ACVRL1 gene encodes activin receptor-like kinase 1, sometimes termed ALK1, a cell-surface receptor important for the specialization of new blood vessels into arteries or veins. Pathogenic variants in this gene have been associated with autosomal dominant hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu disease. This variant has been previously reported in several individuals with either a diagnosis of, or features of, HHT (1-7). This variant has also been reported in one individual with a diagnosis of idiopathic pulmonary arterial hypertension (8). In addition, functional studies support that this variant impact protein function (9). Taken together, this result is supportive of a diagnosis of hereditary hemorrhagic telangiectasia for this individual. Clinical correlation is recommended.

This result should be interpreted in the context of clinical findings, family history, and other laboratory testing.

Consultation with a genetics professional is recommended for interpretation of this result and to determine whether reproductive risk assessment and familial testing may be of benefit to this family. Genetic testing for family members is available by ordering FMTT / Familial Mutation, Targeted Testing for the specific variant(s) detected. Please contact the laboratory at 1-800-533-1710 or the online test catalog at www.mayocliniclabs.com for information about FMTT.



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ADDITIONAL INFORMATION

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METHOD

Next generation sequencing (NGS) and/or Sanger sequencing was performed to test for the presence of variants in coding regions and intron/exon boundaries of the genes analyzed, as well as some other regions that have known pathogenic variants. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a read depth over 30X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for indels less than 40 base pairs (bp), above 95% for deletions up to 75 bp and insertions up to 47 bp. NGS, and/or a polymerase chain reaction (PCR)-based quantitative method was performed to test for the presence of deletions and duplications in the genes analyzed. See the Genes Analyzed field for a list of genes tested.

There may be regions of genes that cannot be effectively evaluated for sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high GC content, and repetitive sequences. Confirmation of select reportable variants was performed by alternate methodologies based on internal laboratory criteria. See www.mayocliniclabs.com (TEST ID HHTGG) for details regarding genes with regions not routinely covered.

GENES ANALYZED

PATIENT NAME	ABNORMAL, HHTGG	22-39513
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ACVRL1, BMPR2, CCM2, ENG, EPHB4, GDF2, GLMN, KRIT1, PDCD10, RASA1, SMAD4, TEK

DISCLAIMER

Clinical Correlations

An online research opportunity called GenomeConnect (genomeconnect.org), a project of ClinGen, is available for the recipient of this genetic test. This patient registry collects de-identified genetic and health information to advance the knowledge of genetic variants. Mayo Clinic is a collaborator of ClinGen. This may not be applicable for all tests.

If testing was performed because of a clinically significant family history it is often useful to first test an affected family member. Detection of a reportable variant(s) in an affected family member would allow for more informative testing of at risk individuals.

To discuss the availability of further testing options or for assistance in the interpretation of these results, Mayo Clinic Laboratory genetic counselors can be contacted at 1-800-533-1710.

Technical Limitations

Next generation sequencing may not detect all types of genomic variants. In rare cases, false negative or false positive results may occur. The depth of coverage may be variable for some target regions, but assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.

There may be regions of genes that cannot be effectively evaluated for sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high GC content, and repetitive sequences. Confirmation of select reportable variants was performed by alternate methodologies based on internal laboratory criteria.

Additionally, low level mosaic variants may not be detected.

This test is not designed to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.

Genes may be added or removed based on updated clinical relevance. Please refer to the Targeted Genes and Methodology Details for the HHT and Vascular Gene Panel in the Special Instructions section of the Test Catalog for the most up to date list of genes included in this test.

Reclassification of Variants Policy

See www.mayocliniclabs.com (TEST ID HHTGG) for information regarding the laboratory's policy for reclassification of variants.

Variant Evaluation

Variant curation is performed using published ACMG-AMP recommendations as a guideline. Other gene-specific



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guidelines may also be considered. Variants classified as benign or likely benign are not reported.

Results from in silico evaluation tools may change over time and should be interpreted with caution and professional clinical judgment.

TEST CLASSIFICATION

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

RELEASED BY

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