MAYO CLINIC

1-800-533-1710

aHUS/TMA/C3G Gene Panel

AHUGP

PATIENT NAME				ORDER NUMBER
TESTINGRNV, AHUGP				**M008000177**
PATIENT ID SA00153588	DATE OF BIRTH 09/01/1994	AGE 27 Y	SEX Female	REQUESTED BY CLIENT CLIENT
COLLECTED 7/8/2022, 7:00 AM	RECEIVED 7/8/2022, 11:06 AM	REPORTED 7/14/2022, 11:22 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 SA00153588 CLIENT MRN SA00153588

TEST DESCRIPTION

Evaluation of 15 genes associated with complement-mediated thrombotic microangiopathy/atypical hemolytic uremic syndrome (CM-TMA/aHUS) and complement 3 glomerulopathy (C3G), including targeted assessment of haplotypes and risk alleles in the CFH, CD46, and C5 genes.

SPECIMEN

WB Whole Blood

RESULT SUMMARY

Negative

RESULT

No reportable variants were detected.

INTERPRETATION

This result decreases the likelihood but does not rule out the involvement of the genes evaluated in this panel.

Individuals may have a pathogenic variant in one of the interrogated genes that is not detectable by the methods utilized. Additionally, the clinical phenotype that is observed in this individual and/or family may be due to a pathogenic variant or variants in another gene not targeted by this test.

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

A genetic consultation may be of benefit.

ADDITIONAL RESULTS

CFH-H3 RISK HAPLOTYPE-NEGATIVE
This individual is negative for the extended CFH-H3 risk haplotype. Clinical correlation with other genetic and laboratory findings is recommended. See Method for details. See www.mayocliniclabs.com (Test code AHUGP) for additional information regarding this result.

MCP/CD46 RISK HAPLOTYPE-NEGATIVE
This individual is negative for the MCP/CD46 risk haplotype. Clinical correlation with other genetic and laboratory findings is recommended. See Method for details. See www.mayocliniclabs.com (Test code AHUGP) for additional information regarding this result.

C5 GENOTYPE-NEGATIVE
This individual is negative for the p.Arg885His and p.Arg885Cys variants in the C5 gene that are associated with poor

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response to eculizumab and potentially ravulizumab. Clinical correlation with other genetic and laboratory findings is recommended. See Method for details. See www.mayocliniclabs.com (Test code AHUGP) for additional information regarding this result.

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.
Reporting of the CD46 (NM_002389.4) (also known as the MCP gene) risk haplotype is based on the presence of the following variants: c.989-78G>A (rs1962149); c.-652A>G (rs2796267); c.-366A>G (rs2796268); c.1127+638G>A (rs859705); c.897T>C (rsID not available).

Reporting of the CFH(H3) (NM_000186.3) risk haplotype is based on the presence of the following variants: CFH (NM_000186.3) gene: c.-331C>T (rs3753394); c.1204C>T (rs1061170) ; c.2016A>G (rs3753396); c.2808G>T (rs1065489).

In addition, reporting of the CFH(H3) NM_000186.3 risk haplotype is based on the absence of the following variants: CFH (NM_000186.3) gene: c.184G>A (rs800292); c.2237-543G>A (rs1410996).

Reporting of C5 (NM_001735.2) variants associated with complement inhibitor resistance is based on the presence of the following variants: c.2653C>T, p.Arg885Cys (rs373359894); c.2654G>A, p.Arg885His (rs56040400).
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 AHUGP) for details regarding genes with regions not routinely covered.

GENES ANALYZED

ADAMTS13, C3, C5 (Chr9(GRCh37):g.123759950-123759973 only), CD46 (MCP), CFB, CFH, CFHR1, CFHR2, CFHR3, CFHR4, CFHR5, CFI, DGKE, MMACHC and THBD

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

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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 aHUS/TMA/C3G 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 AHUGP) 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 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

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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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