

Patient ID SA00148221	Patient Name TESTINGRNA, ATLAS	Birth Date 1989-01-09	Gender F	Age 32
Order Number SA00148221	Client Order Number SA00148221	Ordering Physician CLIENT, CLIENT	Report Notes	
Account Information C7028846 DLMP Rochester		Collected 06 Oct 2021 12:00		

Acute Porphyria Gene Panel

Interpretation

MCR

PPOX, c.454C>T (p.R152C), PATHOGENIC

The heterozygous c.454C>T (p.R152C) missense variant in the PPOX gene (mim:600923) is an established pathogenic variant. Variants in the PPOX gene have been associated with autosomal recessive variegate porphyria. This result is supportive of a diagnosis of variegate porphyria for this individual. Clinical correlation is recommended.

PPOX, c.-185G>T, VARIANT OF UNCERTAIN SIGNIFICANCE

The significance of the c.-185G>T alteration in the PPOX gene is uncertain. Alterations occurring in the 5'UTR (untranslated region) may affect normal gene regulatory function, particularly if they occur in the promoter region of the gene. The overall minor allele frequency for this alteration (rs114493458) is approximately 0.23% with a frequency up to 0.39% in certain Non Finnish European sub-populations (1-2). This alteration has been reported previously in one patient with variegate Porphyria and a luciferase assay demonstrated reduced activity in vitro, but retained transcription (3). Thus, we are currently unable to determine whether this alteration is a polymorphism or disease-causing mutation. It may be helpful to test affected family members to determine if the alteration identified in this individual segregates with disease.

CPOX, c.814A>C, (p.N272H), VARIANT

The c.814A>C (p.N272H) alteration is a polymorphism of the coproporphyrinogen oxidase gene that modifies the effect of mercury on porphyrin metabolism in humans, resulting in the excretion of unexpectedly high levels of atypical porphyrin upon mercury exposure.

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 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.

REFERENCES:

1. gnomAD Browser: gnomad.broadinstitute.org/; Karczewski K, Francioli LC, MacArthur DG, et al. The mutational constraint spectrum quantified from variation in 141,456 humans. Nature. 2020; 581(7809):434-443 (PMID 32461654)
2. dbSNP: www.ncbi.nlm.nih.gov/snp; Sherry ST, Ward M and Sirotkin K. dbSNP-Database for Single Nucleotide Polymorphisms and Other Classes of Minor Genetic Variation. Genome Res. 1999;9:677-679 (PMID 10447503)
3. Fiorentino V, Brancaloni V, Granata F, Graziadei G, Di Piero E. The assessment of noncoding variant of PPOX gene in variegate porphyria reveals post-transcriptional role of the 5' untranslated exon 1. Blood Cells Mol Dis. 2016;61:48-53. doi:10.1016/j.bcmd.2016.08.002(PMID 27667166)

Result Summary

MCR

Pathogenic and Other Variants Detected

Result

MCR

The following heterozygous PATHOGENIC variant was detected:

PPOX (NM_000309.4), p.R152C (p.Arg152Cys), c.454C>T, Chr1(GRCh37):g.161137900

The following heterozygous VARIANT OF UNCERTAIN SIGNIFICANCE was detected: PPOX (NM_000309.4), c.-185G>T, Chr1(GRCh37):g.161136225

The following heterozygous VARIANT was detected: CPOX (NM_000097.5), p.N272H (p.Asn272His), c.814A>C, Chr3(GRCh37):g.98307696

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

Test Description

MCR

Evaluation of 4 genes associated with acute porphyria

Performing Site Legend

Code	Laboratory	Address	Lab Director	CLIA Certificate
MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	William G. Morice M.D. Ph.D	24D0404292

Patient ID SA00148221	Patient Name TESTINGRNV, ATLAS	Birth Date 1989-01-09	Gender F	Age 32
Order Number SA00148221	Client Order Number SA00148221	Ordering Physician CLIENT, CLIENT	Report Notes	
Account Information C7028846 DLMP Rochester		Collected 06 Oct 2021 12:00		

Specimen

MCR

WB Whole Blood

Resources

MCR

Disease specific information, including current therapies may be available at:

1. GeneReviews: <https://www.ncbi.nlm.nih.gov/books/NBK1116/>
2. <https://www.fda.gov/drugs>

Information regarding clinical trials, if available, can be found at the following sites:

1. ClinicalTrials.gov: <http://clinicaltrials.gov/ct2/search/advanced>

Method

MCR

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 select 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 >30X. Sensitivity is estimated at >99% for single nucleotide variants, >94% for indels up to 39 base pairs, >95% for deletions up to 75 base pairs and insertions up to 47 base pairs. NGS and/or a 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 APGP for details regarding genes with regions not routinely covered.

Genes Analyzed

MCR

ALAD, CPOX, HMBS, and PPOX

Disclaimer

1 MCR

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.

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Account Information C7028846 DLMP Rochester		Collected 06 Oct 2021 12:00		

Genes may be added or removed based on updated clinical relevance. Please refer to the Targeted Genes and Methodology Details for the Acute Porphyria 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

APGP 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.

Released By

Devin Oglesbee, Ph.D.

MCR

Received: 07 Oct 2021 16:12

Reported: 15 Oct 2021 10:36

Laboratory Notes

- 1 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.

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Code	Laboratory	Address	Lab Director	CLIA Certificate
MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	William G. Morice M.D. Ph.D	24D0404292



1-800-533-1710
Acute Porphyría Gene Panel

APGP

PATIENT NAME TESTINGRNV, ATLAS				ORDER NUMBER L107000376
PATIENT ID SA00148221	DATE OF BIRTH 01/09/1989	AGE 32 Y	SEX Female	REQUESTED BY CLIENT CLIENT
COLLECTED 10/6/2021, 12:00 PM	RECEIVED 10/7/2021, 4:12 PM	REPORTED 10/15/2021, 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 SA00148221 CLIENT MRN SA00148221

TEST DESCRIPTION

Evaluation of 4 genes associated with acute porphyria

SPECIMEN

WB Whole Blood

RESULT SUMMARY

Pathogenic and Other Variants Detected

RESULT

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CPOX (NM_000097.5), p.N272H (p.Asn272His), c.814A>C, Chr3(GRCh37):g.98307696

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INTERPRETATION

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CPOX, c.814A>C, (p.N272H), VARIANT

PATIENT NAME TESTINGRNV, ATLAS

21-44560



1-800-533-1710
Acute Porphyría Gene Panel

APGP

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PATIENT ID SA00148221	DATE OF BIRTH 01/09/1989	AGE 32 Y	SEX Female	REQUESTED BY CLIENT CLIENT
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RESOURCES

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GENES ANALYZED

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DISCLAIMER

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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 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 Devin Oglesbee, Ph.D.				

Code : MCR Laboratory : Mayo Clinic Laboratories - Rochester Main Campus
Lab Director : WILLIAM G MORICE, II MD, PhD CLIA Certificate : 24D0404292

Address : 200 FIRST STREET SW
ROCHESTER MN 55905