Patient ID	Patient Name		Birth Date	Gender	Age
SA00149305	TESTINGRNV, ATLAS		1989-01-16	F	32
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00149305	SA00149305	CLIENT,CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		04 Nov 2021 08:00			

Congenital Lactic Acidosis Panel

Interpretation

MCR

PC, c.1892G>A (p.R631Q), PATHOGENIC
The homozygous c.1892G>A (p.R631Q) variant in the PC gene (mim: 608786) is an established pathogenic variant. Variants in the PC gene have been associated with autosomal recessive pyruvate carboxylase deficiency. This result is supportive of a diagnosis of autosomal recessive pyruvate carboxylase deficiency. 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 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.

Result Summary

MCR

Pathogenic Variants Detected

Result

MCR

The following homozygous PATHOGENIC variant was detected:
PC (NM_000920.3), p.R631Q (p.Arg631Gln), c.1892G>A, Chr11(GRCh37):g.66619351

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 28 nuclear genes associated with congenital lactic acidosis and the mitochondrial genome.

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.

NGS was also performed to test for the presence of variants within the mitochondrial genome (mtDNA) and to determine the mitochondrial haplogroup. Gel electrophoresis and NGS were performed to detect mtDNA deletions.

The haplogroup is only reported when clinically relevant and is computed using the software package HaploGrep (Hum Mutat 2011 Jan;32:25–32) and PhyloTree (Hum Mutat 2009 30(2):E386-E394). www.phylotree.org

There may be regions of genes that cannot be effectively evaluated for sequencing or deletion and duplication analysis as

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	Patient Name		Birth Date	Gender	Age
SA00149305	TESTINGRNV, ATLAS		1989-01-16	F	32
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00149305	SA00149305	CLIENT,CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		04 Nov 2021 08:00			

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 CLADP for details regarding genes with regions not routinely covered.

Genes Analyzed

MCR

ACAD9, AGK, DLD, ECHS1, FBXL4, FLAD1, FOXRED1, GFER, HADHA, HADHB, HLCS, MRPL3, MRPS22, NDUFB11, NDUFS4, OGDH, PC, PDHA1, PDHX, PDP1, SLC25A19, SUCLG1, TMEM70, UQCRC2, VARS2, TPK1, SLC19A2, SLC19A3 and mitochondrial genome.

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.

Genes may be added or removed based on updated clinical relevance. Please refer to the Targeted Genes and Methodology Details for the Congenital Lactic Acidosis 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 CLADP 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

MCR

Devin Oglesbee, Ph.D.

Received: 05 Nov 2021 08:48 **Reported:** 12 Nov 2021 10:28

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

MAYO CLINIC LABORATORIES

Patient ID	Patient Name		Birth Date	Gender	Age
SA00149305	TESTINGRNV, ATLAS		1989-01-16	F	32
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00149305	SA00149305	CLIENT,CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		04 Nov 2021 08:00			

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.

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

MAYO CLINIC

1-800-533-1710

Congenital Lactic Acidosis Panel

CLADP

PATIENT NAME				ORDER NUMBER
TESTINGRNV, ATLAS				**L205000090**
PATIENT ID SA00149305	DATE OF BIRTH 01/16/1989	AGE 32 Y	SEX Female	REQUESTED BY CLIENT CLIENT
COLLECTED 11/4/2021, 8:00 AM	RECEIVED 11/5/2021, 8:48 AM	REPORTED 11/12/2021, 10:28 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 SA00149305 CLIENT MRN SA00149305

TEST DESCRIPTION

Evaluation of 28 nuclear genes associated with congenital lactic acidosis and the mitochondrial genome.

SPECIMEN

WB Whole Blood

RESULT SUMMARY

Pathogenic Variants Detected

RESULT

The following homozygous PATHOGENIC variant was detected:
PC (NM_000920.3), p.R631Q (p.Arg631Gln), c.1892G>A, Chr11(GRCh37):g.66619351

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INTERPRETATION

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PATIENT NAME				ORDER NUMBER
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7028846
MCL RochesterCampus
Rochester MN 55901

CLIENT ORDER NUMBER
SA00149305

CLIENT MRN
SA00149305

METHOD

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GENES ANALYZED

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DISCLAIMER

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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.

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TEST CLASSIFICATION
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RELEASED BY

Devin Oglesbee, Ph.D.

Code : MCR Laboratory : Mayo Clinic Laboratories - Rochester Main Campus Address : 200 FIRST STREET SW
Lab Director : WILLIAM G MORICE, II MD, PhD CLIA Certificate : 24D0404292 ROCHESTER MN 55905