Patient ID	Patient Name		Birth Date	Gender	Age
SA00004307	TESTINGRNV, REPORTS		1880-01-01	U	135
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00004307	SA00004307	CLIENT, CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		01 Nov 2015 01:00			

Mitochondrial Full Genome Analysis

Result Summary

MCR

NEGATIVE

Result

MCR

No reportable alterations were identified.

Interpretation

1 MCR

This result decreases the likelihood but does not rule out the diagnosis of a mitochondrial DNA (mtDNA) disease. Some individuals who have mitochondrial genome involvement may have a mutation that is not identified by the methods performed (e.g. mutations present at a low heteroplasmy level or confined to tissues that were not tested). This assay also does not rule out mitochondrial disease due to mtDNA depletion or the presence of mutations in nuclear genes associated with mitochondrial disease.

This result should be interpreted in the context of clinical findings, family history, and other laboratory testing. If testing was performed due to a family history of mitochondrial disease, genetic testing of an affected individual should be considered. Identification of the mutations in this family would allow for more accurate risk assessment of at risk individuals.

A genetic consultation may be of benefit.

ADDITIONAL INFORMATION

PCR amplification and Illumina Next Generation Sequencing (NGS) is used to test for the presence of mutations within the entire mitochondrial genome (including 13 protein coding genes, 22 tRNA genes and 2 rRNA genes) (NC_012920). Reported sequence variants are confirmed by an Ion Torrent NGS method. Large deletions within the mitochondrial genome are identified by gel electrophoresis and deletion breakpoints are determined from Illumina NGS data.

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. http://www.phylotree.org).

See www.mayomedicallaboratories.com for additional information about this test.

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.

Test results should be interpreted in context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

Clinical associations that are unrelated to mitochondrial disease will not be reported.

TECHNICAL LIMITATIONS

In some cases, DNA variants of undetermined significance may be identified.

Due to the limitations of next generation sequencing, small deletions and insertions greater than 50 nucleotides in length will not be detected by this test. If a mitochondrial genome mutation is still suspected, consider full genome sequencing using traditional Sanger methods.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

A negative (wild type) result does not rule out the presence of a mutation that may be present but below the limits of detection of this assay (<10% heteroplasmy for point mutations and <20% heteroplasmy for deletions). Of note, the sensitivity of this assay may be lower in blood samples than in muscle biopsy samples.

A previous bone marrow transplant from an allogenic donor will interfere with testing. Call Mayo Clinic Laboratories (800–533–

Performing Site Legend

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MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	William G. Morice M.D. Ph.D	24D0404292

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1710) for instructions for testing patients who have received a bone marrow transplant.

EVALUATION TOOLS

Multiple in-silico evaluation tools were used to assist in the interpretation of these results. These tools are updated regularly; therefore changes to these algorithms may result in different predictions for a given alteration. Additionally, the predictability of these tools for the determination of pathogenicity is currently unvalidated.

Alterations that are predicted or known to be benign will not be reported.

RECLASSIFICATION OF VARIANTS-POLICY

All detected alterations are evaluated according to American College of Medical Genetics and Genomics recommendations (Genet Med 2015:17(5):405–424). Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. At this time, it is not standard practice for the laboratory to systematically review likely pathogenic alterations or variants of uncertain significance that are detected and reported. The laboratory encourages health care providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time.

Specimen

MCR

WB Whole Blood

Released By

MCR

W. Edward Highsmith, Jr., Ph.D.

Received: 04 Nov 2015 08:52 **Reported:** 01 Dec 2015 17:24

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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