MAYO CLINIC LABORATORIES

1-800-533-1710

MITON

Mitochondrial Nuclear Gene Panel by Next-Generation Sequencing (NGS), Varies

Patient ID	Patient Name		Birth Date	Gender	Age
SA00088609	REPORTVALIDATION, MITON		1985-02-28	F	32
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00088609	SA00088609	CLIENT, CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		07 Apr 2017 00:00			

Result Summary

Negative

Result

MCR

No reportable variants were identified.

Interpretation

1 MCR

This result decreases the likelihood but does not rule out involvement of the genes evaluated in this panel. We predict that there are individuals with mitochondrial disease who have pathogenic mutations in the genes analyzed that are not detectable by the method described (e.g. large deletions/duplications, promoter mutations, or deep intronic mutations). Additionally, the clinical phenotype that is observed in this individual and/or family may be due to disease-causing mutations in other nuclear genes or in the mitochondrial genome.

This result should be interpreted in the context of clinical findings, family history, and other laboratory testing (e.g. mitochondrial genome analysis (MITOP / Mitochondrial Full Genome Analysis), plasma lactate, and electron transport chain studies).

A genetic consultation may be of benefit.

ADDITIONAL INFORMATION

Next generation sequencing and/or Sanger sequencing (build GRCh37 (hg19)) was performed to test for the presence of a mutation in all coding regions and intron/exon boundaries, and to test for the presence of large deletions and duplications in the AARS2, AASS, ABAT, ABCB7, ACACA, ACAD9, ACO2, AFG3L2, AGK, AIFM1 ALDH3A2, AMPD1, APOPT1, APTX, ATP5A1, ATP5E, ATP5G3, ATPAF2, AUH, BCS1L, BOLA3, C12orf65, CA5A, CHAT, CLPP, COA5, COA6, COQ2, COQ4, COQ6, COQ8A (ADCK3), COQ8B (ADCK4), COQ9, COX10, COX14, COX15, COX20, COX4I2, COX6B1, COX7B, CYC1, D2HGDH, DARS2, DGUOK, DLAT, DLD, DNA2, DNAJC19, DNM1L, EARS2, ELAC2, ETFA, ETFB, ETFDH, ETHE1, FARS2, FASTKD2, FBXL4, FH, FOXRED1, FXN, GAMT, GARS, GCDH, GFER, GFM1, HARS2, HIBCH, IARS2, IBA57, IDH2, ISCU, L2HGDH, LARS2, LIAS, LRPPRC, LYRM4, LYRM7, MARS2, MGME1, MICU1, MPC1, MPV17, MRPL3, MRPL44, MRPS16, MRPS22, MTFMT, MTO1, MTPAP, NDUFA1, NDUFA10, NDUFA11, NDUFA12, NDUFA2, NDUFA9, NDUFAF1, NDUFAF2, NDUFAF3, NDUFAF4, NDUFAF5, NDUFAF6, NDUFB3, NDUFB9, NDUFS1, NDUFS2, NDUFS3, NDUFS4, NDUFS6, NDUFS7, NDUFS8, NDUFV1, NDUFV2, NFU1, NUBPL, OGDH, OPA1, OPA3, OXCT1, PANK2, PC, PCK2, PDHA1, PDHB, PDHX, PDP1, PDSS1, PDSS2, PNKD, PNPT1, POLG, POLG2, PUS1, RARS2, RMND1, RRM2B, SACS, SARS2, SCO1, SCO2, SDHAF1, SERAC1, SFXN4, SLC19A3, SLC25A1, SLC25A12, SLC25A19, SLC25A3, SLC25A4, SLC52A2, SUCLA2, SUCLG1, SUGCT, SURF1, TACO1, TARS2, TAZ, TIMM44, TIMM8A, TK2, TMEM126A, TMEM70, TPK1, TRAP1, TRMU, TSFM, TTC19, TUFM, TWNK (C10orf2), TYMP, UQCRB, UQCRC2, UQCRQ, VARS2, XPNPEP3, and YARS2 genes.

Region(s) in the following gene(s) could not be amplified and sequenced due to technical limitations of the assay: COX10, COX20, NDUFV2, and TSFM.

Region(s) in the following gene(s) could not be effectively analyzed for the presence of large deletions and/or duplications as a result of technical limitations of the assay: AFG3L2, COX10, CYC1, GFER, NDUFV2, NUBPL, PDSS1, PNPT1, SERAC1, SLC25A1, SUGCT, SURF1, TIMM44, TRAP1, TSFM, TTC19 and TYMP.

Regions of homology, high GC-rich content, and repetitive sequences may not provide accurate sequence. All reportable alterations will be confirmed by Quantitative PCR(qPCR), PCR, and/or Sanger sequencing analysis based on laboratory developed criteria. However, this does not rule out the possibility

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

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of a false negative result in these regions.

See www.mayocliniclabs.com (Test ID MITON) for additional information about this test.

CAUTIONS:

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.

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.

If testing was performed because of a family history of mitochondrial disease, it is often useful to first test an affected family member. Identification of a specific gene mutation in this family would lead to more informative testing of at risk individuals.

TECHNICAL LIMITATIONS

Due to the limitations of Next Generation Sequencing, small deletions and insertions may not be detected by this test. If a diagnosis of one of the syndromes on this panel is still suspected, contact a molecular genetic counselor in the Genomics Laboratory at 1–800–533–1710 for more information regarding follow-up testing options.

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

Bone marrow transplants from allogenic donors will interfere with testing. Call Mayo Clinic Laboratories 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.

Unless reported or predicted to cause disease alterations that do not result in an amino acid substitution are not reported.

RECLASSIFICATION OF VARIANTS - POLICY

All detected alterations are evaluated according to ACMG recommendations (Genet Med. 2015 May;17(5):405–24). 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 re-review LIKELY PATHOGENIC alterations or VARIANTS OF UNCERTAIN SIGNIFICANCE that have been previously detected and reported. The laboratory encourages health care providers to contact the laboratory at any time to learn how the classification and interpretation of a particular variant may have changed over time.

Specimen MCR

WB Whole Blood

Released By MCR

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

Received: 07 Apr 2017 13:11 **Reported:** 12 Apr 2017 14:26

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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