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
SA00088610	REPORTVALIDATION, MITON		1985-02-28	F	32
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00088610	SA00088610	CLIENT, CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		07 Apr 2017 00:00			

Result Summary

Pathogenic Variant Identified

Result

MCR

Gene	Amino Acid Change	DNA Change	Genomic Position	Zygosity	Classification
TYMP	p.T88IfsX35 (Thr88IlefsX35)	c.263_264delCC	Chr22: 50967718_50967719	Homozygous	**PATHOGENIC**

The following homozygous PATHOGENIC alteration was identified: TYMP, p.T88IfsX35 (Thr88IlefsX35), c.263_264delCC, Chr22: 50967718_50967719

Interpretation

1 MCR

The c.263_264delCC (p.T88IfsX35) alteration in TYMP is a known pathogenic mutation. Alterations in the TYMP gene have been associated with autosomal recessive mitochondrial DNA depletion syndrome, MNGIE type (Mitochondrial Neurogastrointestinal Encephalomyopathy). The c.263_264delCC variant is predicted to cause protein truncation and is expected to be an inactivating (loss of function) mutation. This variant is absent in large population-based cohorts, suggesting it is not a common benign polymorphism. This variant has also been reported in patients with clinical and biochemical features of MNGIE syndrome (1). This result is, therefore, consistent with a diagnosis of mitochondrial DNA depletion syndrome for this individual.

Since mutations have been identified, genetic testing of at risk family members could be considered. Mutation specific testing is available at Mayo Medical Laboratories by ordering FMTT / Familial Mutation, Targeted Testing. Please contact the Genomics Laboratory at 1–800–533–1710 with questions about this test.

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,

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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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 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.

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Additional Information

MCR

Mutation nomenclature is based on the following GenBank Accession number(s) (build GRCh37 (h19)): TYMP NM_001953.

REFERENCES

1. Brain. 2011 Nov;134(Pt 11):3326–32 (PMID 21933806)

Specimen

MCR

WB Whole Blood

Released By

MCR

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

Received: 07 Apr 2017 13:12 **Reported:** 12 Apr 2017 14:27

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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