Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	7/2/2012
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Mitochondrial Disorders Panel (mtDNA and Nuclear Genes)

ARUP test code 3001959

Ordering Physician Name	
Ordering Physician Phone Number	
EER Mito Disorders, mtDNA/Nuclear Genes	See Note Authorized individuals can access the ARUP Enhanced Report using the following link: [redacted]
Mito Disorders, mtDNA and Nuclear Genes	Negative Date Test(s) Started: 6/14/2023 15:51:08 Sample Source: Blood in EDTA Date Collected: 5/21/2023 Date Received: 5/25/2023 Testing Date Started: 6/14/2023 Date Reported: 7/20/2023 Provider Account #: A.R.U.P Laboratories Additional Provider: Test(s) Requested Combined Mito Genome Plus Mito Focused Nuclear Gene Panel/ Sequencing and Deletion Analysis of the Mitochondrial Genome and Sequencing and Deletion/Duplication Analysis of 188 Nuclear Genes Result: Negative No pathogenic, likely pathogenic, or variants of uncertain significance were identified by this analysis. Interpretation This negative result does not exclude a genetic basis for this individual's clinical features and/or family history. It is possible that this patient has a pathogenic variant in a portion of a nuclear gene that is not included in the analysis or in a nuclear gene that is not included in this panel. Furthermore, the percentage of mutant mtDNA (the degree of variant heteroplasmy) varies among tissues so that mtDNA variants may be detected in some tissues, but not others. Therefore it is usually best to test an involved tissue, such as muscle or liver. Recommendation(s) Genetic counseling is recommended to discuss

H=High, L=Low, *=Abnormal, C=Critical

the implications
of these results.
The level of variant heteroplasmy may differ among tissues so that mtDNA
variants may be detected in some tissues, but not others. Therefore it is
usually best to test an involved tissue, such as muscle or liver. If clinically
indicated, full sequence analysis and deletion testing of the mitochondrial
genome can be repeated on a muscle biopsy (approximately 50mg).The MitoXpanded
panel, which includes concurrent patient and parent sequencing of approximately
1800 genes associated with mitochondrial disorders or a similar phenotype is
also available. Whole exome sequencing could also be considered. Please visit
our website for additional information: http: //www.genedx.com.
Resources MyGene2 is a portal through which families with rare genetic
conditions who are interested in sharing their health and genetic information
can connect with other families, clinicians, and researchers. If you are
interested in learning more and/or participating, please visit www.mygene2.org.
GenomeConnect is an NIH initiative created to enable individuals and families
with the same genetic variant or medical history to connect and share
de-identified information. If you are interested in participating, please visit
www.genomeconnect.org.
Additional Comments This individual's haplogroup and a table of observed
variants are also provided.* The observed variants have not been reported to be
associated with a disorder of mitochondrial metabolism when present in
association with this individual's specific haplogroup.
Genes Evaluated AARS2, ABCB7, ACAD9, ACO2, AFG3L2, AGK, AIFM1, ALAS2, APOPT1,
ATP5A1, ATP5E, ATP7B, ATPAF2, AUH, BCS1L, BOLA3, C12ORF65, C19ORF12, C20ORF7,
C8ORF38, CARS2, CLPB, COA6, COASY, COQ2, COQ4, COQ6, COQ7, COQ8A, COQ8B, COQ9,
COX10, COX15, COX20, COX6A1, COX6B1, CYC1, DARS2, DGUOK, DLAT, DLD, DNA2,
DNAJC19, DNM1L, EARS2, ECHS1, ELAC2, ETFA, ETFB, ETFDH, ETHE1, FARS2, FASTKD2,
FBXL4, FDX1L, FH, FLAD1, FOXRED1, GARS, GCDH, GFER, GFM1, GFM2, GLRX5, GTPBP3,
HARS2, HMGCL, HTRA2, IARS2, IBA57, ISCA2, ISCU, LAMP2, LARS, LARS2, LIAS,
LIPT1, LRPPRC, LYRM4, LYRM7, MARS2, MFF, MFN2, MGME1, MICU1, Mitochondrial
Genome, MPC1, MPV17, MRPL3, MRPL44, MRPS16, MRPS22, MTFMT, MTO1, MTPAP, NARS2,
NDUFA1, NDUFA10, NDUFA12, NDUFA2, NDUFA9, NDUFAF1, NDUFAF2, NDUFAF3, NDUFAF4,
NDUFB11, NDUFB3, NDUFS1, NDUFS2, NDUFS3, NDUFS4, NDUFS6, NDUFS7, NDUFS8,
NDUFV1, NDUFV2, NFU1, NR2F1, NUBPL, OPA1, OPA3, OTC, PARS2, PC, PCCA, PCCB,
PDHA1, PDHB, PDHX, PDP1, PDSS1, PDSS2, PET100, PNPT1, POLG, POLG2, PRKAG2,
PUS1, QARS, RARS, RARS2, RMND1, RNASEH1, RRM2B, SARS2, SCO1, SCO2, SDHA,
SDHAF1, SERAC1, SFXN4, SLC19A2, SLC19A3, SLC22A5, SLC25A26, SLC25A3, SLC25A38,
SLC25A4, SLC25A46, SPAST, SPG7, SUCLA2, SUCLG1, SURF1, TACO1,

TARS2, TAZ, TFAM,
TIMM8A, TK2, TMEM126A, TMEM126B, TMEM70, TPK1, TRIT1, TRMT10C,
TRMU, TRNT1,
TSFM, TTC19, TUFM, TWNK, TYMP, UQCC2, UQCRB, UQCRC2, VARS2,
WDR45, WFS1, YARS2
Methods Genomic DNA was extracted directly from the submitted
specimen or, if
applicable, from cultured fibroblasts. For the nuclear genome,
the DNA was
enriched for the complete coding regions and splice junctions of
the genes on
this panel using a proprietary targeted capture system developed
by GeneDx for
next-generation sequencing with CNV calling (NGS-CNV). The
enriched targets
were simultaneously sequenced with paired-end reads on an
Illumina platform.
Bi-directional sequence reads were assembled and aligned to
reference sequences
based on NCBI RefSeq transcripts and human genome build
GRCh37/UCSC hg19. After
gene specific filtering, data were analyzed to identify sequence
variants and
most deletions and duplications involving coding exons at the
exon-level;
however, technical limitations and inherent sequence properties
effectively
reduce this resolution for some genes. Alternative sequencing or
copy number
detection methods were used to analyze or confirm regions with
inadequate
sequence or copy number data by NGS. Sequence variants are
reported according
to the Human Genome Variation Society (HGVS) guidelines. Copy
number variants
are reported based on the probe coordinates, the coordinates of
the exons
involved, or precise breakpoints when known. The entire
mitochondrial genome
from the submitted sample was amplified and sequenced using
next-generation
sequencing. DNA sequence was assembled and analyzed in
comparison with the
revised Cambridge Reference Sequence (rCRS GeneBank number
NC_012920) and the
reported variants listed in the MITOMAP database (http:
//www.mitomap.org).
Next generation sequencing may not detect large-scale mtDNA
deletions present
at 5% heteroplasmy or lower or mtDNA point variants present at
1.5%
heteroplasmy or lower. Alternative sequencing or other detection
methods may be
used to analyze or confirm mtDNA variants. Reportable variants
in both the
nuclear and mitochondrial genome include pathogenic variants,
likely pathogenic
variants and variants of uncertain significance. Likely benign
and benign
variants, if present, are not routinely reported but are
available upon
request. Available evidence for variant classification may
change over time and
variant(s) in nuclear genes may be reclassified according to the
ACMG/AMP
Standards and Guidelines (PMID: 25741868), while the reported
variant(s) in
mtDNA may be reclassified according to our mitochondrial variant
classification
guidelines aligned with the ACMG/AMP Standards and Guidelines
which may lead to
issuing a revised report. If included in this test, the

following gene specific
information applies. Gene specific exclusions for exon-level deletion/duplication testing for this panel are: SCO2 and SDHA, no copy number
testing; COX6A1, GTPBP3, NDUFAF4, NDUFB3, NR2F1, SLC25A26, TAZ, and TYMP genes,
only whole gene deletions or duplications may be detected.
Disclaimer Genetic testing using the methods applied at GeneDx is expected to
be highly accurate. Normal findings do not rule out the diagnosis of a genetic
disorder since some genetic abnormalities may be undetectable by this test. The
methods used cannot reliably detect deletions of 20bp to 500bp in size, or
insertions of 10bp to 500bp in size. Sequencing cannot detect low-level
mosaicism. The copy number assessment methods used with this test cannot
reliably detect mosaicism and cannot identify balanced chromosome aberrations.
Regions of certain genes have inherent sequence properties (for example:
repeat, homology, or pseudogene regions, high GC content, rare polymorphisms)
that yield suboptimal data, potentially impairing accuracy of the results.
Inaccurate results may occur in the setting of allogeneic bone marrow/stem cell
transplantation, active or chronic hematologic conditions, recent blood
transfusion, suboptimal DNA quality, or in other rare circumstances. Rarely,
incidental findings of large chromosomal rearrangements outside the gene of
interest may be identified. As the ability to detect genetic variants and
naming conventions can differ among laboratories, rare false negative results
may occur when no positive control is provided for testing of a specific
variant identified at another laboratory. In addition, the chance of an
erroneous result due to laboratory errors incurred during any phase of testing
cannot be completely excluded. Interpretations are made with the assumption
that any clinical information provided, including family relationships, are
accurate. Consultation with a genetics professional is recommended for
interpretation of results.
This test was developed and its performance characteristics determined by
GeneDx. This test has not been cleared or approved by the U.S. Food and Drug
Administration. The FDA has determined that such clearance or approval is not
necessary. The test is used for clinical purposes and should not be regarded as
investigational or for research. The laboratory is certified under the Clinical
Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform
high-complexity clinical testing.
References Lek et al. (2016) Nature 536 (7616): 285-91 (PMID: 27535533);Stenson
et al. (2014) Human genetics 133 (1): 1-9 (PMID: 24077912);Landrum et al.
(2016) Nucleic Acids Res. 44 (D1): D862-8 (PMID: 26582918);Lott et al. (2013)
Curr Protoc Bioinformatics 44 : 1.23.1-26 (PMID:

25489354);Richards et al.
(2015) Genetics In Medicine: 17 (5): 405-24 (PMID: 25741868);
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MTDNA BENIGN/LIKELY BENIGN VARIANTS '> Functional Location
Variant Change
Amino Acid Change Frequency (Gen. Pop)
MT-DLOOP m.73 A>G non-coding 37469/49135
MT-DLOOP m.146 T>C non-coding 9497/49135
MT-DLOOP m.242 C>T non-coding 191/49135
MT-DLOOP m.263 A>G non-coding 46799/49135
MT-DLOOP m.295 C>T non-coding 2287/49135
MT-DLOOP m.462 C>T non-coding 1660/49135
MT-DLOOP m.489 T>C non-coding 12687/49135
MT-RNR1 m.750 A>G rRNA 48276/49135
MT-RNR1 m.1438 A>G rRNA 46721/49135
MT-RNR2 m.2158 T>C rRNA 197/49135
MT-RNR2 m.2352 T>C rRNA 1281/49135
MT-RNR2 m.2706 A>G rRNA 38981/49135
MT-RNR2 m.3010 G>A rRNA 7061/49135
MT-RNR2 m.3106del In Frame common
MT-ND1 m.4216 T>C Missense 4862/49135
MT-ND2 m.4769 A>G Synonymous 55528/56895
MT-ND2 m.5460 G>A Missense 3179/49135
MT-CO1 m.7028 C>T Synonymous 39824/49135
MT-CO2 m.8269 G>A Extended Protein 622/49135
MT-ATP6 m.8557 G>A Missense 286/49135
MT-ATP8 m.8557 G>A Synonymous 286/49135
MT-ATP6 m.8860 A>G Missense 48479/49135
MT-ND3 m.10398 A>G Missense 21770/49135
MT-ND4 m.11251 A>G Synonymous 4574/49135
MT-ND4 m.11719 G>A Synonymous 38205/49135
MT-ND4 m.12007 G>A Synonymous 3088/49135
MT-ND5 m.12612 A>G Synonymous 2475/49135
MT-ND5 m.13708 G>A Missense 3506/49135
MT-ND5 m.13879 T>C Missense 362/49135
MT-CYB m.14766 C>T Missense 37907/49135
MT-CYB m.15326 A>G Missense 48493/49135
MT-CYB m.15452 C>A Missense 4577/49135
MT-DLOOP m.16069 C>T non-coding 2413/49135
MT-DLOOP m.16126 T>C non-coding 5522/49135
MT-DLOOP m.16145 G>A non-coding 1412/49135
MT-DLOOP m.16172 T>C non-coding 3696/49135
MT-DLOOP m.16222 C>T non-coding 388/49135
MT-DLOOP m.16261 C>T non-coding 3689/49135
MT-DLOOP m.16311 T>C non-coding 9611/49135
Haplogroup (HG): J1b1a1
Report electronically signed by: Renkui Bai M.D., Ph.D., FACMG
Performed by: GeneDx
207 Perry Parkway
Gaithersburg, MD 20877

Anne Maddalena, Ph.D.,FACMG,

H=High, L=Low, *=Abnormal, C=Critical

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Ordering Physician Name	23-141-400260	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Ordering Physician Phone Number	23-141-400260	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
EER Mito Disorders, mtDNA/Nuclear Genes	23-141-400260	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Mito Disorders, mtDNA and Nuclear Genes	23-141-400260	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical