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

Physician: Doctor, Example

Patient: Patient, Example

DOB	1/4/1949
Sex:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Mitochondrial Disorders (mtDNA) Sequencing and Deletion Analysis by NGS

ARUP test code 3001965

Ordering Physician Name	[redacted]
Ordering Physician Phone Number	[redacted]
EER Mito Disorders, mtDNA, Seq/Del	See Note Access ARUP Enhanced Report using the link below: -Direct access:
Mito Disorders, mtDNA, Seq/Del	NEGATIVE Date Test(s) Started: 9/21/2021 20:01:52 Sample Source: Blood in EDTA Date Collected: 9/14/2021 Date Received: 9/18/2021 Testing Date Started: 9/21/2021 Date Reported: 10/11/2021 Provider Account #: [redacted] ARUP LABORATORIES Additional Provider: Test(s) Requested Mitochondrial Disorders / Sequence Analysis and Deletion Testing of the Mitochondrial Genome Result(s): NEGATIVE No pathogenic variant known to be associated with a disorder of mitochondrial metabolism was identified by this analysis of the entire mitochondrial genome in this patient. Interpretation No pathogenic variant associated with a disorder of mitochondrial metabolism was identified by this analysis of the entire mitochondrial genome; therefore, we cannot confirm a diagnosis of a mitochondrial disorder in this individual. The combination of full sequence analysis plus deletion testing is expected to identify a mitochondrial DNA pathogenic variant in approximately 40% of adults and 10-20% of pediatric patients with a primary mitochondrial disorder (Chinnery et al, 2014; Koenig et al, 2008; Zeviani et al., 2004). This test does not exclude the possibility of a mitochondrial disorder in this individual. Variants in nuclear genes important for normal mitochondrial function would not be detected by this analysis. Furthermore, the percentage of

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

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) Clinical correlation and genetic counseling are recommendedThe 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 Mitochondrial Genome
Methods Genomic DNA was extracted from the submitted specimen, and the entire
mitochondrial genome 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 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

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classification may change over time and the reported variant(s) may be
re-classified according to our mitochondrial variant classification aligned
with the AMP/ACMG guidelines for variant classification (Richards et al. 2015),
which may lead to re-issuing a revised report.
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 with this test.
The methods used may not detect mtDNA sequence variants with a heteroplasmy
lower than 1.5%. For mtDNA large deletions, levels of heteroplasmy of 5% or
lower may not be detected and the standard deviation for heteroplasmy of
large-scale deletions is estimated to be 5%. False negative results may also
occur in the setting of bone marrow transplantation, recent blood transfusion,
or suboptimal DNA quality. 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. The chance of a false positive or false
negative 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 Chinnery PF. Mitochondrial Disorders Overview. 2000 Jun 8 [Updated
2014 Aug 14]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews
[Internet]. Seattle (WA): University of Washington, Seattle; 1993-2021.
Available from: https: //www.ncbi.nlm.nih.gov/books/NBK1224/; Koenig MK. (2008)
Pediatr Neurol 38 (5): 305-13 (PMID: 18410845); Zeviani M and Di Donato S.
(2004) Brain 127 (Pt 10): 2153-72 (PMID: 15358637)
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S S S
MTDNA BENIGN/LIKELY BENIGN VARIANTS " style="cursor: pointer;"
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Functional Location Variant Change Amino Acid Change Frequency (Gen. Pop)

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

MT-DLOOP m.55 T>C non-coding 105/49135
MT-DLOOP m.57 T>C non-coding 137/49135
MT-DLOOP m.61 C>T non-coding 73/50175
MT-DLOOP m.146 T>C non-coding 9497/49135
MT-DLOOP m.263 A>G non-coding 46799/49135
MT-RNR1 m.750 A>G rRNA 48276/49135
MT-RNR1 m.1438 A>G rRNA 46721/49135
MT-RNR2 m.3106 C>- rRNA common
MT-ND2 m.4769 A>G Synonymous 48004/49135
MT-CO1 m.6253 T>C Missense 519/49135
MT-ATP6 m.8860 A>G Missense 48479/49135
MT-ND4 m.11410 T>C Synonymous 98/49135
MT-ND4 m.11914 G>A Synonymous 5367/49135
MT-CYB m.14953 C>T Synonymous 89/49135
MT-CYB m.15326 A>G Missense 48493/49135
MT-DLOOP m.16129 G>A non-coding 6405/49135
MT-DLOOP m.16184 C>T non-coding 374/49135
Haplogroup (HG): H15a1b
Report electronically signed by: Hong Cui PhD, FACMG
Performed by: GeneDx
207 Perry Parkway
Gaithersburg, MD 20877

Anne Maddalena, Ph.D.,FACMG,

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Ordering Physician Name	21-257-120611	9/14/2021 12:05:00 PM	9/17/2021 1:26:58 PM	10/12/2021 8:09:00 AM
Ordering Physician Phone Number	21-257-120611	9/14/2021 12:05:00 PM	9/17/2021 1:26:58 PM	10/12/2021 8:09:00 AM
EER Mito Disorders, mtDNA, Seq/Del	21-257-120611	9/14/2021 12:05:00 PM	9/17/2021 1:26:58 PM	10/12/2021 8:09:00 AM
Mito Disorders, mtDNA, Seq/Del	21-257-120611	9/14/2021 12:05:00 PM	9/17/2021 1:26:58 PM	10/11/2021 12:08:00 PM

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