ARUP LABORATORIES
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Tracy I. George, MD, Chief Medical Officer

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

Physician: Doctor, Example

Patient: Patient, Example

DOB	12/31/1752
Gender:	Unknown
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Primary Carnitine Deficiency (SLC22A5) Sequencing and Deletion/Duplication

ARUP test code 2004203

PCD FGA Specimen	Whole Blood	
Primary Carnitine Deficiency Interpretat	**Positive**	*

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

TEST PERFORMED - 2004203
TEST DESCRIPTION - Primary Carnitine Deficiency (SLC22A5) Sequencing and Deletion/Duplication
INDICATION FOR TEST - Not Provided

RESULT
Two copies of a pathogenic variant were detected in the SLC22A5 gene.

DNA VARIANT
Classification: Pathogenic
Gene: SLC22A5
Nucleic Acid Change: c.41G>A; Homozygous
Amino Acid Alteration: p.Trp14Ter

INTERPRETATION
Two copies of a pathogenic variant, c.41G>A; p.Trp14Ter, were detected in the SLC22A5 gene by sequencing; no pathogenic variants were detected by deletion/duplication analysis. This result is consistent with a diagnosis of primary carnitine deficiency.

Evidence for variant classification: The SLC22A5 c.41G>A; p.Trp14Ter variant, to our knowledge, is not reported in the medical literature or gene specific databases. This variant is also absent from general population databases (Exome Variant Server, Genome Aggregation Database), indicating it is not a common polymorphism. This variant induces an early termination codon and is predicted to result in a truncated protein or mRNA subject to nonsense-mediated decay. Premature truncating variants occurring in the downstream part of the protein have been associated with carnitine deficiency (Frigeni 2017, Li 2010, Roussel 2016). Based on available information, this variant is considered to be pathogenic.

RECOMMENDATIONS
Dietary carnitine supplementation should be considered. At-risk relatives should be offered targeted testing for the identified pathogenic variant (Familial Mutation, Targeted Sequencing, ARUP test code 2001961). This individual's reproductive partner should be offered carrier testing for pathogenic SLC22A5 variants. Genetic consultation is recommended.

COMMENTS
Reference Sequence: GenBank # NM_003060.3 (SLC22A5)
Nucleotide numbering begins at the "A" of the ATG initiation codon.
Likely benign and benign variants are not included in this report.

REFERENCES
Frigeni M et al. Functional and molecular studies in primary carnitine deficiency. Hum Mutat. 2017 38:1684-1699.
Li FY et al. Molecular spectrum of SLC22A5 (OCTN2) gene mutations detected in 143 subjects evaluated for systemic carnitine deficiency. Hum Mutat. 2010 31:E1632-1651.
Roussel J et al. Carnitine deficiency induces a short QT syndrome. Heart Rhythm. 2016 13:165-174.

This result has been reviewed and approved by [redacted]

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BACKGROUND INFORMATION: Primary Carnitine Deficiency (SLC22A5) Sequencing and Deletion/Duplication

CHARACTERISTICS: Hypoketotic hypoglycemia during periods of fasting, hepatomegaly, Reye syndrome, sudden infant death, developmental delay, cardiac and/or skeletal myopathy, hypotonia and enlarged heart.
INCIDENCE: 1 in 40,000 for European Caucasian and Japanese, lower in other populations.
INHERITENCE: Autosomal recessive.
CAUSE: Pathogenic SLC22A5 gene mutations.
CLINICAL SENSITIVITY: May be as high as 95 percent.
METHODS: Bidirectional sequencing of the entire coding region and intron-exon boundaries of SLC22A5 gene; Multiplex Ligation-dependent Probe Amplification (MLPA) to detect large SLC22A5 coding region deletions/duplications.
ANALYTICAL SENSITIVITY: Greater than 99 percent.
LIMITATIONS: Mutations in genes other than SLC22A5 will not be detected; deletion/duplication breakpoints will not be determined; deep intronic mutations and promoter mutations in the SLC22A5 gene will not be detected. Mutations within the primer/probe regions could affect the analytical sensitivity of this assay. Diagnostic errors can occur due to rare sequence variations.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
PCD FGA Specimen	20-056-112504	2/25/2020 1:10:00 PM	2/25/2020 1:18:12 PM	2/28/2020 10:47:00 AM
Primary Carnitine Deficiency Interpretat	20-056-112504	2/25/2020 1:10:00 PM	2/25/2020 1:18:12 PM	2/28/2020 10:47:00 AM

END OF CHART

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