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

Physician: Doctor, Example

Patient: Patient, Example

DOB	Unknown
Gender:	Unknown
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Charcot-Marie-Tooth Type 1A (CMT1A)/Hereditary Neuropathy with Liability to Pressure Palsies (HNPP), PMP22 Deletion/Duplication

ARUP test code 2012160

Charcot-Marie-Tooth/HNPP DelDup Specimen	Whole Blood
Charcot-Marie-Tooth/HNPP DelDup Interp	Positive

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

Charcot-Marie-Tooth Type 1A/HNPP DelDup

TEST PERFORMED - 2012160
TEST DESCRIPTION - Charcot-Marie-Tooth Type 1A (CMT1A)/Hereditary Neuropathy with Liability to Pressure Palsies (HNPP), PMP22 Deletion/Duplication
INDICATION FOR TESTING - Validation

RESULT
One pathogenic variant detected in the PMP22 gene.

DNA VARIANT(S)
Classification: Pathogenic
Gene: PMP22
Nucleic Acid Change: Deletion of exons 1-5 (whole gene deletion); Heterozygous

INTERPRETATION
One pathogenic variant, deletion of the entire PMP22 gene, was detected by deletion/duplication analysis. This result is consistent with a diagnosis of hereditary neuropathy with liability to pressure palsies (HNPP), an autosomal dominant neurological disorder characterized by repeated focal pressure neuropathies and peripheral neuropathy. Offspring of this individual have a 50 percent chance of inheriting the causative variant.

Evidence for variant classification: The PMP22 whole gene deletion is reported in the literature in individuals with HNPP (3) and loss of function is a disease mechanism for HNPP (1). Considering available information, this deletion is classified as pathogenic.

Pathogenic (2)

RECOMMENDATIONS
Genetic consultation is indicated, including a discussion of medical screening and management. At-risk adult relatives and symptomatic family members may be offered targeted testing for the identified deletion (Charcot-Marie-Tooth 1A (CMT1A)/Hereditary Neuropathy with Liability to Pressure Palsies (HNPP), PMP22 Deletion/Duplication; ARUP test code 2012160).

COMMENTS
Reference Sequence: GenBank # NM_000304.3

REFERENCES
1: Li J, Parker B, Martyn C et al, The PMP22 gene and its related diseases. Mol Neurobiol 2013. PMID:23224996
2: Makar AB, McMartin KE, Palese M et al, Formate assay in body fluids: application in methanol poisoning. Biochem Med 1975. PMID:1
3: Zhang F, Seeman P, Liu P et al, Mechanisms for nonrecurrent genomic rearrangements associated with CMT1A or HNPP: rare CNVs as a cause for missing heritability. Am J Hum Genet 2010. PMID:20493460

This result has been reviewed and approved by [redacted]

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

BACKGROUND INFORMATION: Charcot-Marie-Tooth 1A (CMT1A)/ Hereditary Neuropathy with Liability to Pressure Palsies (HNPP), PMP22 Deletion/Duplication

CHARACTERISTICS: Charcot-Marie-Tooth disease, type 1A (CMT1A) is a subtype of CMT1, a hereditary neuropathy characterized by demyelinating progressive distal motor and sensory neuropathy, muscle weakness and atrophy, pes cavus foot deformity, and other findings. CMT1A is caused by duplication of the PMP22 gene. Hereditary neuropathy with liability to pressure palsies (HNPP) is a neurological disorder characterized by repeated focal pressure neuropathies and peripheral neuropathy caused by deletion of the PMP22 gene.

INCIDENCE: CMT1A- 1/10,000; HNPP 1/20,000-1/50,000.

INHERITANCE: Autosomal dominant; 10-20 percent of PMP22 duplications are de novo.

CAUSE: CMT1A is caused by a 1.5 Mb duplication at 17p11.2 including the PMP22 gene, while HNPP is caused by the reciprocal deletion of the same region.

CLINICAL SENSITIVITY: 70-80 percent for CMT1; 80 percent for HNPP.

METHODOLOGY: Multiplex ligation-dependent probe amplification (MLPA) of the PMP22 gene.

ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.

LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. Single base pair substitutions, small deletions/duplications, regulatory region mutations, and deep intronic mutations are not detected. The breakpoints of large deletions/duplications are not determined.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Charcot-Marie-Tooth/HNPP DelDup Specimen	22-152-101137	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Charcot-Marie-Tooth/HNPP DelDup Interp	22-152-101137	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