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

Physician: Doctor, Example

Patient: Patient, Example

DOB	[redacted]
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Multiple Endocrine Neoplasia Type 1 (MEN1) Sequencing and Deletion/Duplication

ARUP test code 2005360

MEN Type 1 (MEN1) Seq, Del/Dup Specimen	Whole Blood	
MEN Type 1 (MEN1) Seq, Del/Dup Interp	**Positive**	*

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

TEST PERFORMED - 2005360
TEST DESCRIPTION - Multiple Endocrine Neoplasia Type 1 (MEN1) Sequencing and Deletion/Duplication
INDICATION FOR TEST - Confirm Diagnosis

RESULT
One likely pathogenic variant was detected in the MEN1 gene.

DNA VARIANT
Classification: Likely Pathogenic
Gene: MEN1
Nucleic Acid Change: c.722G>A; Heterozygous
Amino Acid Alteration: p.Cys241Tyr

INTERPRETATION
One copy of a likely pathogenic variant, c.722G>A; p.Cys241Tyr, was detected in the MEN1 gene by sequencing. This result is consistent with a diagnosis of multiple endocrine neoplasia type 1. Clinical manifestations are variable. This individual's offspring have a 50 percent chance of inheriting the causative variant. No pathogenic variants were detected by deletion/duplication analysis.

Evidence for variant classification: The MEN1 c.722G>A; p.Cys241Tyr variant (rs794728624) is reported in the literature in an individual with a clinical diagnosis of MEN1 (Hai 1999), and is reported in the ClinVar database (Variation ID: 200980). This variant is absent from general population databases (Exome Variant Server, Genome Aggregation Database), indicating it is not a common polymorphism. The cysteine at codon 241 is highly conserved, and computational analyses (SIFT, PolyPhen-2) predict that this variant is deleterious. Additionally, two other variants at this codon (Cys241Arg, Cys241Phe) are reported in individuals with MEN1 (Crepin 2003, Ellard 2005, Mutch 1999, see ClinVar Variation ID: 659647). Based on available information, the p.Cys241Tyr variant is considered to be likely pathogenic.

RECOMMENDATIONS
Genetic consultation is indicated, including a discussion of medical screening and management. At-risk family members should be offered targeted testing for the identified variant (Familial Mutation, Targeted Sequencing, ARUP test code 2001961).

COMMENTS
Reference Sequence: GenBank # NM_130799.2 (MEN1)
Nucleotide numbering begins at the "A" of the ATG initiation codon.
Likely benign and benign variants are not reported.

REFERENCES
Crepin M et al. Efficient mutation detection in MEN1 gene using a combination of single-strand conformation polymorphism (MDGA) and heteroduplex analysis. Electrophoresis. 2003 Jan;24(1-2):26-33.

Ellard S et al. Detection of an MEN1 gene mutation depends on clinical features and supports current referral criteria for diagnostic molecular genetic testing. Clin Endocrinol (Oxf). 2005 Feb;62(2):169-75.

Hai N et al. Germline MEN1 mutations in sixteen Japanese families with multiple endocrine neoplasia type 1 (MEN1). Eur J Endocrinol. 1999 Nov;141(5):475-80.

Mutch MG et al. Germline mutations in the multiple endocrine neoplasia type 1 gene: evidence for frequent splicing defects. Hum Mutat. 1999;13(3):175-85.

This result has been reviewed and approved by Steven Steinberg, Ph.D.

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BACKGROUND INFORMATION: Multiple Endocrine Neoplasia Type 1 (MEN1) Sequencing and Deletion/Duplication
CHARACTERISTICS: Multiple Endocrine Neoplasia Type 1 (MEN1) syndrome can include multiple endocrine and non-endocrine tumors. Common MEN1-related endocrine tumors include parathyroid (90-95 percent), pancreatic islets (30-80 percent), and pituitary (15-90 percent). Non-endocrine tumors include facial angiofibroma, collagenoma, lipoma, meningioma, ependymoma, and leiomyoma. Primary hyperparathyroidism is the most common and often the first manifestation of MEN1. High mortality rates occur in persons with gastrinoma and carcinoid tumors.
INCIDENCE: Approximately 1 in 30,000.
INHERITANCE: Autosomal dominant.
PENETRANCE: Approximately 50 percent by age 20 and 95 percent by age 40.
CAUSE: Pathogenic MEN1 gene mutations.
CLINICAL SENSITIVITY: Approaches 94 percent.
METHODOLOGY: Bidirectional sequencing of the entire coding region and intron-exon boundaries of the MEN1 gene. Multiplex ligation-dependent probe amplification (MLPA) to detect large MEN1 coding region deletions/duplications.
ANALYTICAL SENSITIVITY AND SPECIFICITY: Approximately 98 percent.
LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. Regulatory region mutations and deep intronic mutations will not be detected. The breakpoints of large deletions/duplications will not be detected. Mutations in genes other than MEN1 are not evaluated. This assay is not designed to detect somatic variants associated with malignancy. Interpretation of this test result may be impacted if the patient has had an allogeneic stem cell transplantation.

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
MEN Type 1 (MEN1) Seq, Del/Dup Specimen	20-016-400164	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
MEN Type 1 (MEN1) Seq, Del/Dup Interp	20-016-400164	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