ARUP LABORATORIES
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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	7/28/1978
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Multiple Endocrine Neoplasia Type 2 (MEN2), RET Sequencing

ARUP test code 3004572

MEN2 Specimen	Whole Blood
MEN2 Interp	Negative

RESULT
No pathogenic variants were detected in the RET gene.

INTERPRETATION
No pathogenic variants were detected in the RET gene. This result decreases the likelihood of, but does not exclude, a diagnosis of multiple endocrine neoplasia type 2 (MEN2). Please refer to the background information included in this report for the methodology and limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and family history. If this individual has a family history, determination of a causative familial variant in an affected family member is necessary for optimal interpretation of this negative result. Further testing may be warranted if there is a familial variant that is not detectable by this assay. Genetic consultation is recommended. If suspicion remains for a hereditary cancer syndrome, consideration may be given to ordering the Hereditary Cancer Panel, Sequencing and Deletion/Duplication (ARUP test code 2012032).

COMMENTS
Likely benign and benign variants are not reported.
Variants in the following region(s) may not be detected by NGS with sufficient confidence in this sample due to technical limitations:
NONE

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Multiple Endocrine Neoplasia Type 2 (MEN2), RET Sequencing

CHARACTERISTICS: Multiple endocrine neoplasia type 2 (MEN2) is a hereditary syndrome caused by pathogenic variants in the RET gene. MEN2 is classified into subtypes MEN2A, MEN2B, and familial medullary thyroid cancer (FMTC). All MEN2 subtypes have an increased risk of medullary thyroid cancer (MTC). MEN2A is also associated with benign parathyroid adenomas/hyperplasia and pheochromocytoma (PCC). MEN2B is associated with more aggressive MTC that can occur during childhood, PCC, neuromas, eye anomalies, and distinctive physical features. FMTC is considered a disease variant of MEN2A and is characterized as multiple cases of MTC in a family, typically without the presence of PCC

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

or hyperparathryoidism.

EPIDEMIOLOGY: One in 35,000 individuals are estimated to have MEN2. Approximately 25-30 percent of all individuals with MTC have a germline RET pathogenic variant.

CAUSE: Pathogenic germline variants in the RET gene

INHERITANCE: Autosomal dominant

PENETRANCE: The penetrance of MTC in MEN2A is 95 percent, and in MEN2B and FMTC is 100 percent.

CLINICAL SENSITIVITY: MEN2A: >95 percent; MEN2B: >98 percent; FMTC: >88-95 percent

GENE TESTED: RET (NM_020975)

METHODOLOGY: Probe hybridization-based capture of all coding exons and exon-intron junctions of the targeted genes, followed by massively parallel sequencing. Sanger sequencing was performed as necessary to fill in regions of low coverage and to confirm reported variants that do not meet acceptable quality metrics. Human genome build 19 (Hg 19) was used for data analysis.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions (indels) from 1-10 base pairs in size. Indels greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced. Specificity is greater than 99.9 percent for all variant classes.

LIMITATIONS: A negative result does not exclude a diagnosis of MEN2. This test only detects variants within the coding regions and intron-exon boundaries of the RET gene. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. Regulatory region variants, deep intronic variants, and large deletions/duplications will not be identified. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations caused by the presence of pseudogenes, repetitive, or homologous regions. This test is not intended to detect low-level mosaic or somatic variants, gene conversion events, complex inversions, translocations, mitochondrial DNA (mtDNA) mutations, or repeat expansions. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Noncoding transcripts were not analyzed.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the U.S. 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
MEN2 Specimen	23-242-401134	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
MEN2 Interp	23-242-401134	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