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

Familial Transthyretin Amyloidosis (TTR) Sequencing

ARUP test code 3004531

TTR Specimen	Whole Blood
TTR Interp	Negative

RESULT
No pathogenic variants were detected in the TTR gene.

INTERPRETATION
No pathogenic variants were identified by massively parallel sequencing of the coding regions and exon-intron boundaries of the TTR gene. This result significantly decreases the likelihood of, but does not exclude, a diagnosis of familial transthyretin amyloidosis. Please refer to the background information included in this report for limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and family history. Genetic consultation is recommended.

COMMENTS
Likely benign and benign variants are not reported.

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Familial Transthyretin Amyloidosis (TTR) Sequencing

CHARACTERISTICS: Familial transthyretin amyloidosis (ATTR) is caused by pathogenic variants of the TTR gene resulting in abnormal amyloid accumulation in various tissues and is generally categorized into three phenotypes: 1) familial amyloid polyneuropathy, a slowly progressive sensorimotor and autonomic neuropathy; 2) familial amyloid cardiomyopathy, a restrictive cardiomyopathy with cardiomegaly, conduction block, angina, congestive heart failure, and aortic dissection/dilatation; and 3) leptomeningeal amyloidosis, primarily affecting the central nervous systems, causing dementia, visual impairment, seizures, ataxia, psychosis, hemorrhage, and hydrocephalus. TTR variants can also be associated with benign familial euthyroid hyperthyroxinemia.

EPIDEMIOLOGY: 1 in 538 individuals from northern Portugal; 1 in 100,000 individuals of northern European descent in the U.S.

CAUSE: Pathogenic germline TTR variants.

INHERITANCE: Autosomal dominant.

PENETRANCE: Incomplete.

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

CLINICAL SENSITIVITY: 99 percent for familial TTR amyloidosis.

GENE TESTED: TTR (NM_000371)

METHODOLOGY: Probe hybridization-based capture of all coding exons and exon-intron junctions of the TTR gene, 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 hereditary amyloidosis. This test only detects variants within the coding regions and intron-exon boundaries of the TTR 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) variants, 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
TTR Specimen	22-136-101061	5/16/2022 8:26:00 AM	5/16/2022 8:27:01 AM	5/16/2022 8:42:00 AM
TTR Interp	22-136-101061	5/16/2022 8:26:00 AM	5/16/2022 8:27:01 AM	5/16/2022 8:42:00 AM

END OF CHART

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