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

Physician: Doctor, Example

Patient: Patient, Example

DOB	1/2/1995
Sex:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Familial Hypercholesterolemia Panel, Sequencing

ARUP test code 3002110

Familial Hypercholesterolemia Specimen	Whole Blood
Familial Hypercholesterolemia Interp	Negative

RESULT
No pathogenic variants were detected in any of the genes tested.

INTERPRETATION
No pathogenic variants were identified by massively parallel sequencing of the coding regions and exon-intron boundaries of the APOB, LDLR, LDLRAP1, or PCSK9 genes. This result decreases the likelihood of, but does not exclude, a diagnosis of familial hypercholesterolemia (FH). Please refer to the background information included in this report for the limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and family history. Genetic consultation is recommended. If clinical suspicion of FH remains, consideration may be given to LDLR deletion/duplication analysis. LDLR large deletions account for approximately 5 percent of causative variants in many populations.

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; reportable variants are confirmed by Sanger sequencing:
APOB(NM_000384.3) exon 1

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Familial Hypercholesterolemia Panel, Sequencing
CHARACTERISTICS: Familial hypercholesterolemia (FH) is the most common inherited cardiovascular disease. It is characterized by markedly elevated low-density lipoprotein cholesterol (LDL-C) and premature atherosclerotic cardiovascular disease (ASCVD). Manifestations include coronary artery disease (CAD), cardiovascular disease (CVD), angina, myocardial infarction, xanthomas, and corneal arcus. Homozygous FH (HoFH) is a less common disorder, resulting from biallelic variants in a dominant FH-associated gene. HoFH is characterized by severe early-onset CAD, aortic stenosis, and high rate of coronary bypass surgery or death by teenage years.

EPIDEMIOLOGY: FH 1/250, HoFH 1/200,000 in the general population.

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

CAUSE: Pathogenic germline variants in genes associated with FH.

INHERITANCE: Autosomal dominant for LDLR, APOB and PCSK9-associated FH. Autosomal recessive for LDLRAP1-associated FH. HoFH results from biallelic variants in an autosomal dominant FH gene.

PENETRANCE: Estimated at 73-90 percent in individuals with molecularly confirmed FH; influenced by gene, variant, and non-genetic factors.

CLINICAL SENSITIVITY: Up to 85 percent for FH.

GENES TESTED: APOB, LDLR, LDLRAP1, PCSK9.

METHODOLOGY: 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. Human genome build 19 (Hg 19) was used for data analysis.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity of this test is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions from 1-10 base pairs in size. Variants greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced.

LIMITATIONS: A negative result does not exclude a diagnosis of FH. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Regulatory region variants, deep intronic variants, and large deletions/duplications/inversions will not be identified. Deletions/duplications/insertions of any size may not be detected by massive parallel sequencing. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions. This assay may not detect low-level mosaic or somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Non-coding 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 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
Familial Hypercholesterolemia Specimen	22-132-106810	5/12/2022 9:56 00 AM	5/12/2022 8:18:18 PM	5/21/2022 8:23:00 PM
Familial Hypercholesterolemia Interp	22-132-106810	5/12/2022 9:56 00 AM	5/12/2022 8:18:18 PM	5/21/2022 8:23:00 PM

END OF CHART

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