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

Physician: Doctor, Example

Patient: Patient, Example

DOB	2/18/1959
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy, CADASIL (NOTCH3), Sequencing

ARUP test code 3004383

CADASIL (NOTCH3) Specimen	Whole Blood

CADASIL (NOTCH3) Interp	Negative

RESULT
No pathogenic variants were detected in the NOTCH3 gene.

INTERPRETATION
No pathogenic variants were detected by massively parallel sequencing of the coding regions and exon-intron boundaries of the gene tested. This result decreases the likelihood of, but does not exclude, a diagnosis of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). 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.

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]

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

BACKGROUND INFORMATION: Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy, CADASIL (NOTCH3), Sequencing

CHARACTERISTICS: CADASIL is a condition characterized predominantly by subcortical ischemic events, including transient ischemic attacks (TIAs) and strokes. Other features of this condition include cognitive defects, dementia, migraines, psychiatric and mood disorders, and epilepsy. Age of onset and clinical presentation are highly variable.

PREVALENCE: 2-4 in 100,000; penetrance may be variable.

INHERITANCE: Autosomal dominant.

CAUSE: Pathogenic variants in the NOTCH3 gene.

CLINICAL SENSITIVITY: 95 percent.

GENE TESTED: NOTCH3 (NM_000435)
Exon 1 is not covered by sequencing.

METHODOLOGY: Capture of all coding exons and exon-intron junctions of the targeted gene, followed by massively parallel sequencing. Sanger sequencing performed as necessary to fill in regions of low coverage and confirm reported variants.

ANALYTICAL SENSITIVITY: 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 by massively parallel sequencing, but the analytical sensitivity may be reduced.

LIMITATIONS: A negative result does not exclude a diagnosis of CADASIL. This test only detects variants within the coding regions and intron-exon boundaries of the specific gene. Regulatory region variants and deep intronic variants will not be identified. Deletions/duplications/insertions of any size may not be detected by massively 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. Noncoding transcripts were not analyzed.

The following regions are not sequenced due to technical limitations of the assay:
NOTCH3 (NM_000435) exon(s) 1

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.

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
CADASIL (NOTCH3) Specimen	23-292-153768	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
CADASIL (NOTCH3) Interp	23-292-153768	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