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Tracy I. George, MD, Chief Medical Officer

Client: ARUP Example Report Only
500 Chipeta Way
Salt Lake City, UT 84108
UNITED STATES

Physician: arup, arup

Patient: Genomics, Notch3 2

DOB	
Sex:	Female
Patient Identifiers:	36439
Visit Number (FIN):	36758
Collection Date:	2/23/2022 10:18

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 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 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 a list of the genes analyzed and 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 included in this report.

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.

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

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.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
CADASIL (NOTCH3) Specimen	22-054-102900	2/23/2022 10:18:00 AM	2/23/2022 10:18:25 AM	2/23/2022 12:15:00 PM
CADASIL (NOTCH3) Interp	22-054-102900	2/23/2022 10:18:00 AM	2/23/2022 10:18:25 AM	2/23/2022 12:15:00 PM

END OF CHART

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