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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	Unknown
Gender:	Unknown
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Early-Onset Alzheimer's Panel, Sequencing

ARUP test code 3001585

Alzheimer's Specimen	Whole Blood

Alzheimer's Interp	Negative

INDICATION FOR TESTING
Early-onset dementia.

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 genes tested. This result decreases the likelihood of, but does not exclude, a heritable form of early-onset Alzheimers disease. 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, but are available upon request.

This result has been reviewed and approved by Hunter Best, Ph.D.

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

BACKGROUND INFORMATION: Early-Onset Alzheimer's Panel, Sequencing
CHARACTERISTICS: Alzheimer's disease (AD) is characterized by progressive memory loss leading to dementia. Up to 25 percent of AD may be hereditary. Less than 2 percent is the early-onset familial form defined as a diagnosis of AD before age 65, while 15-25 percent is a late-onset familial form. Although symptoms of familial early-onset AD are similar to late-onset (sporadic AD), there is a greatly increased chance of identifying a genetic etiology with early-onset AD. Diagnosis of AD requires autopsy or a molecular genetic confirmation.
EPIDEMIOLOGY: Nearly 6 million individuals in the U. S. are affected with AD; approximately 200,000 are <65 yrs.
CAUSE: Pathogenic germline APP, PSEN1 and PSEN2 gene variants are causative of early-onset AD.
INHERITANCE: Autosomal dominant.
PENETRANCE: PSEN2 has reduced penetrance.
CLINICAL SENSITIVITY: 60-80 percent for familial early-onset AD.
GENES TESTED: APP*, PSEN1, PSEN2
*One or more exons are not covered by sequencing for the indicated gene; see limitations section below.
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 confirm reported variants. Human genome build 19 (Hg 19) was used for data analysis.
ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity of sequencing 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 heritable form of early onset AD. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Regulatory region variants and deep intronic variants 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.

The following region is not sequenced due to technical limitations of the assay:
APP (NM_001136016.3) exon 1

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

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VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Alzheimer's Specimen	19-309-104002	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Alzheimer's Interp	19-309-104002	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