ARUP LABORATORIES | aruplab.com
500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: 801-583-2787, toll free: 800-522-2787
Jonathan R. Genzen, MD, PhD, Chief Medical Officer

PATIENT REPORT

Patient Age/Sex: Female

Specimen Collected: 04-Jun-24 08:36

DNA Extract and Hold	**|Received: 04-Jun-24 08:36**		**Report/Verified: 04-Jun-24 08:40**
Procedure	**Result**	**Units**	**Reference Interval**
DNA Extract and Hold	Complete [i1]		

Early Onset Alzheimer's Sequencing	**|Received: 04-Jun-24 08:36**		**Report/Verified: 04-Jun-24 08:40**
Procedure	**Result**	**Units**	**Reference Interval**
Alzheimer's Specimen	Whole Blood		
Alzheimer's Interp	Negative [i2]		

Test Information

i1: DNA Extract and Hold

INTERPRETIVE INFORMATION: DNA Extract and Hold

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.

i2: Alzheimer's Interp

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

Test Information

i2: Alzheimer's Interp

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

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Counseling and informed consent are recommended for genetic testing. Consent forms are available online.