ARUP LABORATORIES
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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

Cerebral Cavernous Malformation Panel, Sequencing and Deletion/Duplication

ARUP test code 3002286

Cerebral Cavernous Malformation Specimen	DNA
Cerebral Cavernous Malformation Interp	Negative

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

BACKGROUND INFORMATION: Cerebral Cavernous Malformation Panel, Sequencing and Deletion/Duplication

CHARACTERISTICS: Cerebral cavernous malformations (CCMs) are vascular malformations occurring in the brain or other CNS locations, which involve closely clustered, enlarged capillary channels without normal intervening brain parenchyma. CCMs do not always cause clinical symptoms, but may result in intracranial hemorrhage, seizures, headaches, or focal neurological deficits without intracranial bleed. Familial CCM (FCCM) is defined by the presence of multiple CCMs, a single CCM and at least one family member with one or more CCM, or a pathogenic heterozygous variant in one of the associated genes (KRIT1, CCM2, or PDCD10).

EPIDEMIOLOGY: CCMs occur in approximately 0.4-0.5 percent of the general population. FCCM is estimated to occur in 1:2,000 to 1:10,000 individuals. Up to 20 percent of all CCMs are familial.

CAUSE: Pathogenic germline variants in CCM2, KRIT1 (CCM1), or PDCD10 (CCM3).

INHERITANCE: Autosomal dominant with reduced penetrance.

PENETRANCE: Up to 50 percent of individuals with a molecular diagnosis of FCCM remain clinically asymptomatic.

CLINICAL SENSITIVITY: 85-95 percent for FCCM.

GENES TESTED: CCM2, KRIT1, PDCD10.

METHODOLOGY: Targeted 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. A custom tiled comparative genomic hybridization array (aCGH) was used to detect large deletions or duplications in the indicated subset of genes. 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 FCCM. 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 and breakpoints of large deletions/duplications will not be determined. Single exon deletions/duplications or deletions/duplications less than 1kb may not be detected. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. Diagnostic errors can occur due to rare sequence variations. 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.

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Cerebral Cavernous Malformation Specimen	20-329-112583	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Cerebral Cavernous Malformation Interp	20-329-112583	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