Cerebral Cavernous Malformation: Sequencing Panel

**Test Code:** MM410  
**Turnaround time:** 6 weeks  
**CPT Codes:** 81479 x3

### Condition Description

Cerebral cavernous malformations are collections of small blood vessels in the brain that are enlarged and irregular in structure. This condition is inherited in an autosomal dominant manner, with pathogenic variants in three genes (CCM1, CCM2, and CCM3) accounting for 85-95% of all cases.

While the exact function of these genes is not fully understood, studies show that the proteins produced from these genes are found in the junctions connecting neighboring blood vessel cells. Pathogenic variants in these genes impair the function of the protein complex, resulting in weakened cell-to-cell junctions and increased leakage from vessels as seen in cerebral cavernous malformations.

**Reference:**


### Genes

CCM2, KRIT1, PDCD10

### Indications

The test is indicated for:

- Individuals with a clinical or suspected diagnosis of cerebral cavernous malformation.

### Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

### Detection

**Next Generation Sequencing:** Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

### Specimen Requirements

*Submit only 1 of the following specimen types*

#### Type: Whole Blood (EDTA)

**Specimen Requirements:**  
EDTA (Purple Top)  
Infants and Young Children (2 years of age to 10 years old): 3-5 ml  
Older Children & Adults: 5-10 ml  
Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**  
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

#### Type: DNA, Isolated

**Specimen Requirements:**  
Microtainer  
8µg  
Isolation using the Perkin Elmer™Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Type: Saliva**

**Specimen Requirements:**
Oragene™ Saliva Collection Kit
Orangene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**Related Tests**
- Cerebral Cavernous Malformation: Deletion/Duplication Panel