PreventionGenetics
Disease Prevention Through Genetic Testing

Cerebral Cavernous Malformation *CCM* Known Gene Mutation Detection by Sequencing.

Cerebral cavernous malformations (CCM) are congenital vascular anomalies of the brain that can cause significant neurological disabilities, including intractable seizures and hemorrhagic stroke. Three genes have been identified so far for autosomal dominant CCM, *CCM1* maps to chromosome region 7q21-q22. Using a genomic sequence-based positional cloning strategy, *KRIT1*, encoding a protein that interacts with the Krev-1/rap1a tumor suppressor, has been identified as the *CCM1* gene (Hum. Mol. Gen. 8(12): 2325-2333, 1999). *CCM2* which maps to chromosome region 7p15-p13 and was recently identified as *MGC4607* (Am J Hum Genet.73:1459-1464, 2003). The third gene *CCM3* previously mapped to 3q26-27 was identified in January of 2005 as the programmed cell death 10 (*PDCD10*) (Am J Hum Genet. 76:42-5, 2005).

A single mutation is common to most Mexican-American families with CCM (+/-70%). This C>T transition in exon 10 changes a *GLN* to a premature termination codon. Other Mexican-American and non-Hispanic Caucasian *CCM1* kindreds harbor other mutations in other exons of the *KRIT1* gene. Identification of these other mutations has potential clinical significance for presymptomatic diagnosis of CCM in this population and their families. In general, the identification of any CCM gene mutation entails extraction of genomic DNA from blood, PCR amplification of the separate exons each CCM gene, sequencing and electrophoretic separation of product, and comparison of this patient specific sequence with "typical" sequence.

In patients where a specific mutation has been demonstrated in a family member, testing will focus on sequencing the specific exon where the known mutation has been observed.

Specimen Requirements

- Collect 2-5 ml of whole blood in EDTA (purple top tube) or ACD (yellow top tube). 5 ml is the preferred volume.
- Only one blood tube is required for multiple tests.
- Ship whole blood specimens at room temperature.
- Do not freeze blood.
- During hot weather, include a frozen ice pack in the shipping container. Do not allow the ice pack to come in direct contact with the specimen tube.
- In cold weather, include an unfrozen ice pack to help moderate extremes in temperature. The DNA in whole blood is stable for at least 48 hours at 21°C, 5-7 days at 4°C.

CPT Codes and Cost

CCM Known Mutation Test DNA Seq		**$230.00**
Molec Diag, Ascertainment	83890	
Molec Diag, Isolation	83891	
Molecular Diag, Amplif	83898	
Mutat Id By Seq, Single Seg	83904	
Molecular Diag, Separation	83894	
Interpretation And Report	83912	

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