

PreventionGenetics

Disease Prevention through Genetic Testing

A FAX to: _____

FAX Number: _____

Cerebral Cavernous Malformation 2 (CCM2) MGC4607 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. Two loci (of 3 identified so far) for autosomal dominant CCM (*CCM1* and *CCM2*) map to chromosome region 7q21-q22 and to 7p15-p13 respectively. 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. More recently the second gene detected that can cause CCMs was identified as MGC4607 (Am J Hum Genet. 73:1459-1464, 2003). MGC4607, similar to the KRIT1 binding partner ICAP1 α , encodes a protein with a PTB (phospho-tyrosine binding) domain. This protein may be part of the complex pathway of integrin signaling, that when perturbed, causes abnormal vascular morphogenesis in the brain leading to CCM formation.

Mutations in the *CCM1* gene, *KRIT1* may account for up to 40% of familial CCM cases. Other CCM kindreds harbor other mutations in other CCM associated genes with mutations in the *CCM2* gene accounting for perhaps an additional 20% of familial cases and mutations in the still to be defined *CCM3* gene and perhaps other still unidentified genes accounting for the remaining 40% of cases. Identification of these other mutations has potential clinical significance for presymptomatic diagnosis of CCM in this population and their families. The identification of a *CCM2* associated mutation entails extraction of genomic DNA from blood, PCR amplification of 10 separate exons of the *MGC4607* gene, sequencing and electrophoretic separation of product, and comparison of this patient specific sequence with "typical" sequence..

SPECIMEN REQUIREMENTS

Collect a minimum of 1 to 10 ml of whole blood in EDTA (purple top tube) or ACD (yellow top tube). Whole blood collected in Na Heparin is acceptable but not preferred.

Ship whole blood specimens at ambient temperature. Do not freeze blood tube.

During hot summer months, include a frozen ice pack in the shipping container. Do not allow the ice pack to come in direct contact with the specimen tubes. In Winter, 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

<i>CCM2</i> Mutation Test DNA Seq		\$980.00
Molec Diag, Ascertainment	83890	
Molec Diag, Isolation	83891	
Molecular Diag, Amplif x10	83898	
Mutat Id By Seq, Single Seg x10	83904	
Molecular Diag, Separation	83894	
Interpretation And Report	83912	

CLIA Certificate of Accreditation Info.

CLIA ID number: **Pending** (LAP#: 7185561 AU ID: 1407125) Effective: 12/28/03

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