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STAMBP Analysis for Microcephaly-Capillary Malformation Syndrome

Clinical Features

Microcephaly-Capillary Malformation syndrome [MICCAP, OMIM#614261] is characterized by severe progressive microcephaly, early-onset refractory epilepsy, profound developmental delay, and generalized capillary malformations. The capillary malformations, sometimes referred to as port wine stains, are spread diffusely throughout the body. Other less common features can include hypoplasia of the distal phalanges and of the fingers and toes, mild heart defects, and dysmorphic facies (1, 2).

Molecular Genetics

Mutations of the *STAMBP* [OMIM #606247] gene have been identified in patients with MIC-CAP. McDonnell *et al.,* identified six missense variants, two nonsense mutations, two translational frameshift mutations and three intronic mutations, in a total of 10 patients with MIC-CAP (3). STAMBP is involved with endosomal sorting and trafficking machinery and functions in the regulation of sorting of endosomal sorting complexes required for transport (ESCRTs) machinery and ubiquitinated receptor cargo (3).

Inheritance

MIC-CAP follows an autosomal recessive inheritance pattern. Therefore, parents of an affected child are most likely obligate carriers. Recurrence risk for carrier parents is 25%.

Test methods:

We offer mutation analysis of all coding exons and intron/exon boundaries of *STAMBP* by direct sequencing of amplification products in both the forward and reverse directions. Deletion/duplication analysis is performed by oligonucleotide array-CGH. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by array-CGH. Array-CGH will not detect low-level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of this assay may be reduced when DNA is extracted by an outside laboratory.

STAMBP sequencing

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81405
Turn-around time:	4 weeks

STAMBP deletion/duplication analysis

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81404
Turn-around time:	4 - 6 weeks

Results:

Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

References:

1. Carter MT, Geraghty MT, De La Cruz L et al. A new syndrome with multiple capillary malformations, intractable seizures, and brain and limb anomalies. Am J Med Genet A 2011: 155A: 301-306.
2. Mirzaa GM, Paciorkowski AR, Smyser CD et al. The microcephaly-capillary malformation syndrome. Am J Med Genet A 2011: 155A: 2080-2087.
3. McDonell LM, Mirzaa GM, Alcantara D et al. Mutations in STAMBP, encoding a deubiquitinating enzyme, cause microcephaly-capillary malformation syndrome. Nat Genet 2013: 45: 556-562.

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