Hereditary Hemorrhagic Telangiectasia: Sequencing Panel

Test Code: MM390  
Turnaround time: 6 weeks  
CPT Codes: 81406 x1, 81479 x1

Condition Description

Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant genetic disorder that leads to abnormal blood vessel formation in the skin, mucous membranes, and often in organs such as the lungs, liver, and brain. Of the five types of HHT identified, three have been linked to specific genes. More than 80% of all cases of HHT are due to mutations in either ENG or ACVRL1. SMAD4 mutations, which cause colonic polyposis in addition to HHT, comprise about 2% of disease-causing mutations.

Reference:

Genes

ACVRL1, ENG, GDF2, RASA1, SMAD4

Indications

The test is indicated for:
- Individuals with a clinical or suspected diagnosis of hereditary hemorrhagic telangiectasia.

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**

Specimen Requirements:

- In EDTA (purple top) tube:
  - Infants (2 years): 3-5 ml
  - Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:

- In microtainer: 60 ug
  - Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

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

Related Tests
- Hereditary Hemorrhagic Telangiectasia: Deletion/Duplication Panel