Tuberous Sclerosis: Sequencing Panel

**Test Code:** MM430
**Turnaround time:** 6 weeks
**CPT Codes:** 81406 x1, 81407 x1

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**Condition Description**

Tuberous sclerosis is inherited in an autosomal dominant pattern and affects 1 in 6,000 people. In approximately one-third of cases, an affected person inherits an altered TSC1 or TSC2 gene from a parent who has the disorder. The remaining two-thirds of cases are due to de novo mutations in the TSC1 or TSC2 gene. TSC1 mutations appear to be more common in familial cases of tuberous sclerosis complex, while mutations in the TSC2 gene occur more frequently in sporadic cases.

The TSC1 and TSC2 genes provide instructions for making the proteins hamartin and tuberin, respectively. Within cells, these two proteins likely work together to help regulate cell growth and size, and also act as tumor suppressors. Affected individuals are born with one mutated copy of the TSC1 or TSC2 gene in each cell. However, enough protein is usually produced from the other, normal copy of the gene to regulate cell growth effectively. For some types of tumors to develop, a second mutation involving the other copy of the TSC1 or TSC2 gene must occur in certain cells.

Tuberous sclerosis complex is characterized by the growth of numerous noncancerous tumors in many parts of the body. These tumors can occur in the skin, brain, eyes, heart, lungs, kidneys, and other organs, in some cases leading to significant health problems. The condition is extremely variable and is associated with seizures, mental retardation, behavior problems, and skin abnormalities (not only tubers, but also lesions).

**Reference:** GeneReviews.

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**Genes**

TSC1, TSC2

**Indications**

The test is indicated for:

- Individuals with a clinical or suspected diagnosis of tuberous sclerosis.

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**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.

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**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:** 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:** 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: Saliva

Specimen Requirements:
Oragene™ Saliva Collection Kit
Oragene™ 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

- Tuberous Sclerosis: Deletion/Duplication Panel.