Tuberous Sclerosis: Sequencing Panel

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.

Genes

TSC1, TSC2

Indications

The test is indicated for:
- Individuals with a clinical or suspected diagnosis of tuberous sclerosis.

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**

- Tuberous Sclerosis: Deletion/Duplication Panel.