Leigh Disease: Mitochondrial Deletions/Duplications and Targeted Mutation Analysis

Test Code: QD
Turnaround time: 4 weeks
CPT Codes: 81401 x1

Condition Description

Leigh syndrome is a necrotizing encephalomyelopathy characterized by progressive neurological disease resulting in developmental delay, brainstem degeneration with or without basal ganglia disease, lactic acidosis and hypertrophic cardiomyopathy. Patients may display complex symptoms including variable combinations of neurodegeneration, hypotonia, elevated in CSF lactate, hepatic dysfunction, cardiomyopathy, or renal dysfunction. It is often fatal within the first 2-3 years of life from respiratory or cardiac failure. The clinical symptoms are thought to be the results of defects in mitochondrial energy production.

Leigh syndrome can be inherited in an autosomal recessive, X-linked recessive, or mitochondrial manner. The prevalence of mitochondrial associated Leigh syndrome is estimated to be 1 in 150,000 to 1 in 200,000. The level of heteroplasmy (meaning the presence of both normal and rearranged mitochondrial DNA molecules) as well as the tissue affected influences the severity of disease.

The 8993T>G and 8993T>C mtDNA mutations account for 10 to 20% of Leigh syndrome mutations. Other mtDNA mutations (including 3243A>G / 9176T>C / 14459G>A and mtDNA deletions and duplications) account for an additional small percentage of Leigh syndrome mutations. Both heteroplasmy and homoplasmy of mitochondrial point mutations have been reported in patients with Leigh syndrome. Heteroplasmic mitochondrial deletions and duplications have also been observed. MitDNA mutations may occasionally not be detectable in blood cells due to uneven replicative segregation (uneven tissue distribution of mitochondrial molecules). For patients with a clinical diagnosis of Leigh syndrome, testing for mtDNA mutations in muscle tissue may be indicated when mutations are not detected in mtDNA isolated from a blood sample.

Indications

- Patients with a confirmed or suspected diagnosis of Leigh disease.
- Family members of an affected patient who are at risk for Leigh disease.

Methodology

Presence or absence of the mutations (3243A>G / 8993T>G,C / 9176T>C / 14459G>A) are detected by pyrosequencing analysis. For Mitochondrial DNA deletions and duplications, Southern blot testing is utilized.

Detection

Approximately 10-30% of individuals with Leigh syndrome have mitochondrial DNA mutations included in this panel. Mitochondrial deletions and duplications account for a small number of Leigh syndrome cases. The 3243A>G mutation can be detected at approximately 10% heteroplasmy. All other mutations will be detected at approximately 15-20% heteroplasmy.

Reference Range

Qualitative assay.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Whole Blood

Specimen Requirements:

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

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

Type: Muscle Biopsy

Specimen Requirements:

- 1-2 mm in length or > 100 mg is acceptable.
- Flash freeze sample upon collection using liquid nitrogen. If storage is required, store sample at -80°C or colder.

Specimen Collection and Shipping: Ship frozen sample on dry ice with overnight delivery.

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Related Tests

Retinitis Pigmentosa and Ataxia (NARP) (QK)