Mitochondrial Encephalomyopathy: Lactic Acidosis (Stroke-like Episodes/MELAS)

**Test Code:** QA  
**Turnaround time:** 3 weeks  
**CPT Codes:** 81401 x1

### Condition Description

MELAS is characterized by mitochondrial encephalomyopathy, lactic acidosis, stroke-like episodes, often presenting in childhood. Other common symptoms include seizures, muscle weakness, recurrent headaches and vomiting, and exercise intolerance. Sensorineural hearing loss may also occur. Symptoms are highly variable, in part due to the amount of heteroplasmy (i.e., both normal and mutant mitochondrial DNAs are present in the same cell) and tissue distribution of abnormal mitochondria (replicative segregation). Symptoms may worsen during times of stress or illness.

Mutations in the *MTTL1* mitochondrial gene (tRNA-Leu) have been identified in patients with MELAS. Mutations in *MTTL1* can result in impaired mitochondrial respiratory chain complex I and cytochrome C oxidase activity. Reduction in mitochondrial respiratory chain function reduces the amount of ATP produced by the mitochondria.

The most common mutation in *MTTL1*, present in over 80% of patients with typical clinical findings of MELAS, is a 3243A>G transition in *MTTL1*. The *MTTL1* mutations 3,271 T>C, 3,252 A>G, 3,291 T>C, and 3,260 A>G account for an additional 15-20% of all MELAS mutations. Other rare mutations in the *MTTL1* gene have also been observed. Mitochondrial mutations outside the *MTTL1* gene have been described in rare cases. Mutations associated with MELAS may be heteroplasmic with the degree of heteroplasmy varying in different tissues. Based on clinical presentation, either a blood or a tissue sample (muscle biopsy) may be used.

### References:

- GeneReviews Clinical Summary

### Indications

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

### Methodology

The *MTTL1* mitochondrial gene (tRNA-Leu) is PCR amplified and sequenced in both the forward and reverse directions. The 3243A>G mutation is analyzed by a sensitive allele-specific extension assay to reliably detect heteroplasmic mutations. Patient gene sequences are compared to a normal reference sequence. Sequence variations are then classified as previously described mutations, novel mutations, or variations of unknown significance. This assay may detect variants of *MTTL1* that may require further studies.

### Detection

This assay will detect over 90% of mitochondrial mutations associated with MELAS. The 3243A>G mutation can be detected at approximately 10% heteroplasmy. All other mutations can be detected at approximately 15-20% heteroplasmy. Mutations outside the *MTTL1* gene will not be detected.

### 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.

### Related Tests

- MERRF (QH) Testing may be indicated for patients who also show progressive external ophthalmoplegia and ragged red fibers on muscle biopsy.
- KSS/CPEO (QB) Testing may be indicated for patients who also show progressive external ophthalmoplegia.
- Myotonic Dystrophy (MD) may be indicated for patients who show muscle weakness.