Carnitine Palmitoyltransferase II Deficiency: CPT2 Gene Deletion/Duplication

**Test Code:** EX  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

**Condition Description**
Carnitine palmitoyltransferase II (CPT II) deficiency is a disorder of long-chain fatty-acid oxidation. There are three clinical presentations: a lethal neonatal form, a severe infantile hepatocardiomuscular form, and a myopathic form that is usually mild and can manifest from infancy to adulthood. The former two are severe multisystemic diseases characterized by liver failure with hypoketotic hypoglycemia, cardiomyopathy, seizures, and early death. The myopathic form is characterized by exercise-induced muscle pain and weakness, sometimes associated with myoglobinuria. While the disorder is inherited in an autosomal recessive manner, males are more likely to be affected than females, for currently unknown reasons.

Tandem mass spectrometric measurement of serum/plasma acylcarnitines can be used as an initial screening test. The finding suggestive of a defect in mitochondrial beta-oxidation (and thus suspect for CPT II deficiency) is an elevation of C12 to C18 acylcarnitines, notably of C16 and C18:1. Diagnosis can be made by detection of reduced CPT enzyme activity, however, measured enzyme activity is dependent on assay conditions, which have not been standardized, making comparisons of published data from different laboratories difficult. Molecular genetic testing of **CPT2** (1p32), the only gene known to be associated with CPT II deficiency, provides additional means for noninvasive, rapid, and specific diagnosis. Carriers can be detected by measuring enzyme activity in muscle homogenates; no data regarding the use of MS/MS for carrier detection are available. When causative mutations are known, carrier testing should rely on molecular genetic methods.

Sequencing of the **CPT2** gene is recommended after a biochemical analysis consistent with CPT II, and provides a complementary method to confirm the presence of mutations in a proband, identify carriers among the proband's relatives, and provide prenatal diagnosis in families with known mutations.

**References:**
- GeneReviews Clinical Summary

**Genes**

**CPT2**

**Indications**
This test is indicated for:
- Confirmation of a clinical/biochemical diagnosis of CPT II.
- Carrier testing in adults with a family history of CPT II.

**Methodology**
DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**
Detection is limited to duplications and deletions. Array CGH will not detect point mutations or intronic mutations. Results of molecular analysis must interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**
Submit only 1 of the following specimen types
- * Preferred specimen type: Whole Blood

**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: Saliva

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

Special Instructions

Submit copies of diagnostic biochemical test results with the sample. Contact the laboratory if further information is needed. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

Related Tests

- Acylcarnitine profile (AR).
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by sequencing.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.