Carnitine Palmitoyltransferase 1A Deficiency: *CPT1A* Gene Sequencing

**Test Code:** PX  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81479 x1

### Condition Description

Carnitine palmitoyltransferase 1A (CPT1A) deficiency is an autosomal recessive disorder of long-chain fatty acid oxidation. Onset of symptoms is typically rapid, and occurs during febrile or gastrointestinal illness when energy demands are increased. Between episodes, individuals may appear developmentally and cognitively normal, unless previous metabolic decompensation has resulted in neurological damage. There are three types of CPT1A: hepatic encephalopathy, adult-onset myopathy, and acute fatty liver of pregnancy. In hepatic encephalopathy, children present with hypoketotic hypoglycemia and sudden onset of liver failure. Adult-onset myopathy has been observed in one individual of Inuit ancestry, whose presenting feature was a history of exercise-induced sudden-onset muscle cramping. Acute fatty liver of pregnancy occurs when the fetus has CPT1A deficiency.

Typical laboratory findings are hypoglycemia, absent or low levels of ketones, elevated liver transaminases, elevated serum ammonia concentration, and elevated total serum carnitine. In most affected individuals, CPT I enzyme activity in cultured skin fibroblasts accounts for 1%-5% of control activity. Screening for CPT1A deficiency by detecting an elevated ratio of free-to-total carnitine in serum or plasma on a blood spot is available in some state newborn screening programs. *CPT1A* (11q13) is the only gene associated with CPT1A deficiency.

### References:
- GeneReviews Clinical Summary

### Genes

**CPT1A**

### Indications

This test is indicated for:
- Confirmation of a clinical/biochemical diagnosis of CPT1A deficiency
- Carrier testing in adults with a family history of CPT1A deficiency

### 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

**Clinical Sensitivity:** For individuals with an enzymatically confirmed diagnosis of CPT1A deficiency, the mutation detection rate using sequence analysis is believed to be higher than 90%. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype. **Analytical Sensitivity:** ~99%

### Specimen Requirements

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**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: 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.

**Related Tests**

- 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.

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