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, CPT1 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.

### 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**

**Type: Whole Blood (EDTA)**

**Specimen Requirements:**

EDTA (Purple Top)
- Infants and Young Children (2 years of age to 10 years old): 3-5 ml
- Older Children & Adults: 5-10 ml
- Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

**Type: DNA, Isolated**

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Specimen Requirements:
Microtainer
8µg
Isolation using the Perkin Elmer™Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Type: Saliva

Specimen Requirements:
Oragene™ Saliva Collection Kit
Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

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.