

Carnitine Palmitoyltransferase CPT2 Deficiency (CPT2 Deficiency)

Disorder: **CPT2 deficiency** is a disorder of long-chain fatty acid oxidation (FAOD) which may result in either of two distinct presentations based upon the affected individual's age and body systems affected. **The infantile / neonatal (hepatocardiomyopathic) form** typically presents before one year of age with hypoketotic hypoglycemia, acute liver failure, cardiomyopathy, and/or sudden death, triggered by fasting or fever. A more severe **neonatal form** of CPT2 deficiency, including dysmorphic features, brain dysplasia, respiratory distress, hypoglycemia, cardiomegaly, heart rhythm disorders, cystic renal dysplasia, hepatomegaly, and neonatal death, has also been described.

The **adult (myopathic) form** typically presents in young adults as episodes of muscle pain, weakness, and rhabdomyolysis triggered by prolonged exercise, or occasionally by illness or fasting. Complications which may arise from the rhabdomyolysis are acute renal failure, respiratory insufficiency, and paroxysmal arrhythmias. In the intervals between episodes, individuals with the classical adult CPT2 deficiency appear healthy. Males are more likely to be affected than females. CPT2 deficiency is inherited in an autosomal recessive manner.

Indications:

- Confirmation of diagnosis in a symptomatic individual
- Abnormal newborn screen or acylcarnitine profile suggesting CPT2 deficiency
- Presymptomatic testing of at-risk siblings
- Carrier identification in individuals with a family history of CPT2 deficiency
- Prenatal diagnosis of an at-risk fetus, after confirmation of biallelic mutations in the parents (by prior arrangement only)

Additional information and test requisitions are available at: www.cchmc.org/molecular-genetics

Shipping Instructions

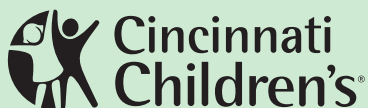
Please enclose **test requisition** with sample.

All information must be completed before sample can be processed.

Place samples in styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday

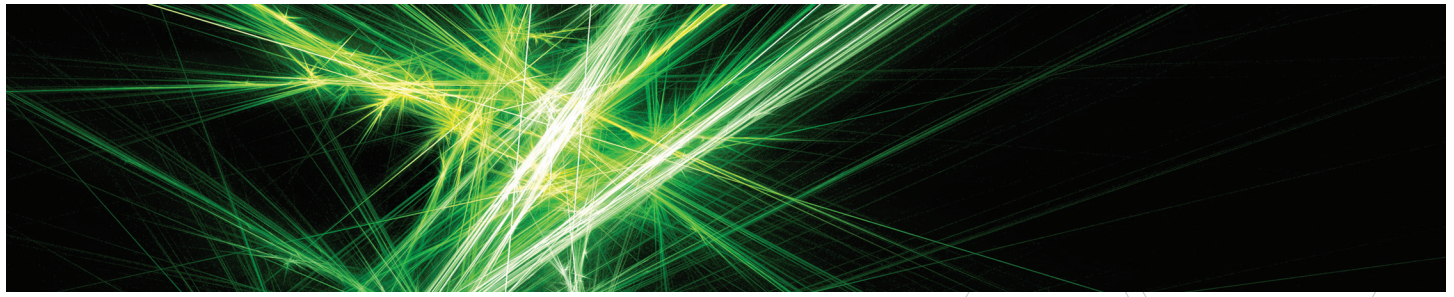
Ship to:

Cytogenetics and Molecular Genetics Laboratories
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474



Human Genetics

Molecular Genetics Laboratory
CLIA#: 36D0656333
Phone: (513) 636-4474
Fax: (513) 636-4373
Email: moleculargenetics@cchmc.org



Specimen: At least 3 mLs of whole blood in purple/lavender top (EDTA) tube. Label tube with patient's name, birth date, and date of collection. Phlebotomist must initial tube to verify patient's identity.

Testing Methodology: Testing is performed by PCR-based sequencing of all 5 exons and exon/intron boundaries of the *CPT2* gene.

Test Sensitivity: PCR-based sequencing of all 5 exons and exon/intron boundaries of the *CPT2* gene detects >95% of patients with *CPT2* deficiency. The sensitivity of DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed. Mutations in regulatory regions or other untranslated regions are not detected by this test. Large deletions involving entire single exons or multiple exons, large insertions and genetic recombinational events may not be identified using these methods. Rare primer site variants may lead to erroneous results. *CPT2* is the only gene associated with *CPT2* deficiency.

MetaboSeq® fatty acid oxidation defects panel detects mutations in *CPT2* as well as 18 other genes involved with FAOD. Please see our website for details.

Turn-Around Time: 28 days

Cost: Please call 1-866-450-4198 for current pricing, assistance with precertification or with any billing questions.

CPT Codes:

- *CPT2* full gene sequence analysis: 81404
- *CPT2* family-specific mutation analysis: 81403

Results: Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.

References:

- Bonnefont, J. P., F. Djouadi, et al. (2004). Carnitine palmitoyltransferases 1 and 2: biochemical, molecular and medical aspects. *Mol Aspects Med* 25(5-6): 495-520.
- Bonnefont, J. P., F. Taroni, et al. (1996). Molecular analysis of carnitine palmitoyltransferase II deficiency with hepatocardiomyopathy. *Am J Hum Genet* 58(5): 971-978.
- Illsinger, S., T. Lucke, et al. (2008). Carnitine-palmitoyltransferase 2 deficiency: novel mutations and relevance of newborn screening. *Am J Med Genet A* 146A(22): 2925-2928.
- Orngreen, M. C., M. Duno, et al. (2005). Fuel utilization in subjects with carnitine palmitoyltransferase 2 gene mutations. *Ann Neurol* 57(1): 60-66.
- Spiekerkoetter, U. (2010). Mitochondrial fatty acid oxidation disorders: clinical presentation of long-chain fatty acid oxidation defects before and after newborn screening. *J Inher Metab Dis* 33(5): 527-532.
- Taroni, F., E. Verderio, et al. (1993). Identification of a common mutation in the carnitine palmitoyltransferase II gene in familial recurrent myoglobinuria patients. *Nat Genet* 4(3): 314-320.
- Wieser, T. (2004; updated 2011). Carnitine Palmitoyltransferase II Deficiency. *GeneReviews*. R. A. Pagon, T. D. Bird, C. R. Dolan, K. Stephens and M. P. Adam. Seattle (WA).