Carnitine deficiency, systemic primary (CDSP), secondary to *SLC22A5* mutations

Disorder: Carnitine deficiency (CDSP), also known as carnitine uptake deficiency (CUD), is a disorder of fatty acid oxidation caused by biallelic mutations in the *SLC22A5* gene (5q31.1) and inherited in an autosomal recessive manner. The physical presentations of CDSP, typically manifested under conditions of fasting or illness, may include failure to thrive, encephalopathy, cardiomyopathy, respiratory insufficiency, vomiting, skeletal muscle weakness, and hypoglycemia. CDSP shows variability amongst individuals, even those with the same genotype. Symptoms may present from infancy through adulthood.

Indications:

- Confirmation of diagnosis in a symptomatic individual
- Abnormal newborn screen or acylcarnitine profile suggesting CDSP/CUD
- Presymptomatic testing of at-risk siblings
- Prenatal diagnosis of an at-risk fetus, after confirmation of biallelic mutations in the parents (by prior arrangement only)
- Carrier testing in relative of a patient with CDSP/CUD

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.

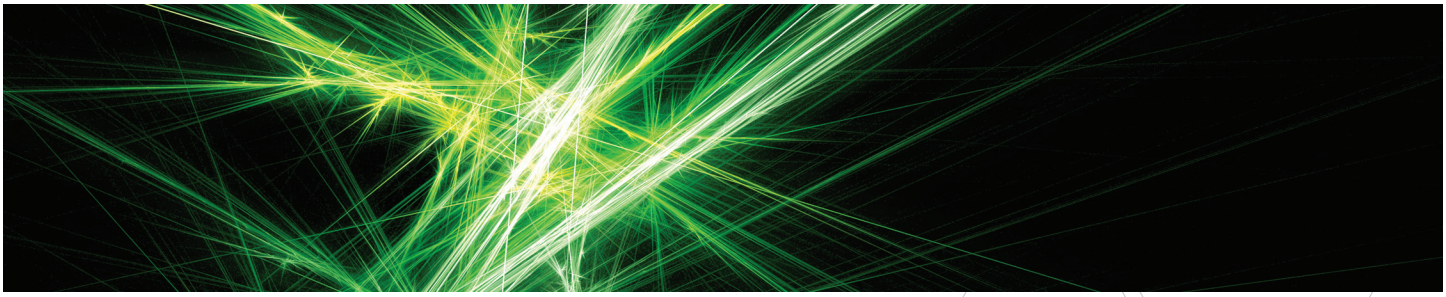
Place samples in styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday

Ship to:

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

Cincinnati Children's®
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 10 exons and exon/intron boundaries of the *SLC22A5* gene.

Test Sensitivity: PCR-based sequencing of all 10 exons and exon/intron boundaries of the *SLC22A5* gene detects approximately 93% of patients with *SLC22A5* 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. *SLC22A5* is the only gene associated with CDSP.

MetaboSeq® fatty acid oxidation defects panel detects mutations in *SLC22A5* 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:

- *SLC22A5* full gene sequence analysis: 81405
- *SLC22A5* 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:

El-Hattab, A. W. (2012). Systemic Primary Carnitine Deficiency. GeneReviews. R. A. Pagon, T. D. Bird, C. R. Dolan, K. Stephens and M. P. Adam. Seattle (WA).

El-Hattab, A. W., F. Y. Li, et al. (2010). Maternal systemic primary carnitine deficiency uncovered by newborn screening: clinical, biochemical, and molecular aspects. Genet Med 12(1): 19-24.

Lee, N. C., N. L. Tang, et al. (2010). Diagnoses of newborns and mothers with carnitine uptake defects through newborn screening. Mol Genet Metab 100(1): 46-50.

Li, F. Y., A. W. El-Hattab, et al. (2010). Molecular spectrum of SLC22A5 (OCTN2) gene mutations detected in 143 subjects evaluated for systemic carnitine deficiency. Hum Mutat 31(8): E1632-1651.

Schimmenti, L. A., E. A. Crombez, et al. (2007). Expanded newborn screening identifies maternal primary carnitine deficiency. Mol Genet Metab 90(4): 441-445.