Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase (LCHAD) Deficiency

Secondary to *HADHA* E510Q Mutation

Disorder: LCHAD deficiency is a disorder of long-chain fatty acid oxidation (FAOD) which may result in variable and potentially lethal outcomes. Some patients present early in life with severe symptoms including cardiomyopathy, cardiac arrhythmias, and hepatic encephalopathy, as well as hypoketotic hypoglycemia induced by metabolic stress, while other patients experience milder, and later-onset symptoms including myopathy and episodic rhabdomyolysis, also induced by metabolic stress.

Women heterozygous for the E510Q *HADHA* mutation and carrying fetuses with LCHAD deficiency may be at risk for acute fatty liver of pregnancy (AFLP) or HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. The most frequent cause of LCHAD deficiency is a homozygous 1528 G>C (E510Q) missense mutation in *HADHA* (2p23); thus LCHAD deficiency is inherited in an autosomal recessive manner.

Indications:

- Confirmation of diagnosis in a symptomatic individual
- Abnormal newborn screen or acylcarnitine profile suggesting LCHAD deficiency
- 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 LCHAD deficiency
- Mothers of fetuses with LCHAD deficiency at risk for acute fatty liver of pregnancy (AFLP) or HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome

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.

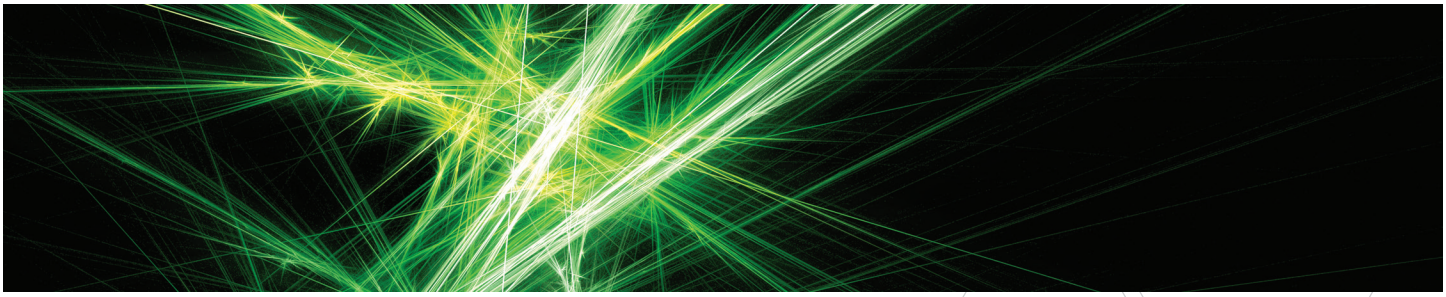
Place samples in styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday

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: Genotype analysis for the E510Q mutation in *HADHA*.

Test Sensitivity: Genotype analysis for the E510Q mutation in *HADHA* detects 75-87% of patients with LCHAD deficiency. LCHAD deficiency may also be caused by compound heterozygosity of E510Q with other mutations in *HADHA*, which are not detected by this test.

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

Turn-Around Time: Two business days

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

CPT Codes:

HADHA 1528 G>C (E510Q) genotype 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:

den Boer, M. E., R. J. Wanders, et al. (2002). Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency: clinical presentation and follow-up of 50 patients. Pediatrics 109(1): 99-104.

Ibdah, J. A., M. J. Bennett, et al. (1999). A fetal fatty-acid oxidation disorder as a cause of liver disease in pregnant women. N Engl J Med 340(22): 1723-1731.

Shekhawat, P. S., D. Matern, et al. (2005). Fetal fatty acid oxidation disorders, their effect on maternal health and neonatal outcome: impact of expanded newborn screening on their diagnosis and management. Pediatr Res 57(5 Pt 2): 78R-86R.

Sperk, A., M. Mueller, et al. (2010). Outcome in six patients with mitochondrial trifunctional protein disorders identified by newborn screening. Mol Genet Metab 101(2-3): 205-207.

Spiekerkoetter, U., Z. Khuchua, et al. (2004). General mitochondrial trifunctional protein (TFP) deficiency as a result of either alpha- or beta-subunit mutations exhibits similar phenotypes because mutations in either subunit alter TFP complex expression and subunit turnover. Pediatr Res 55(2): 190-196.