Very-long-chain acyl-CoA dehydrogenase (VLCAD) deficiency

Disorder: VLCAD deficiency is a disorder of fatty acid metabolism with an incidence of 1 in 40,000 to 1 in 120,000 newborns. VLCAD deficiency is an autosomal recessive disorder of fatty acid oxidation (FAOD). This enzyme deficiency results in the inability to catabolize C10-C18 or longer straight-chain fatty acids for energy utilization. VLCAD deficiency may present in the first two years of life after illness or fasting. This inability to break down long chain fatty acids may result in hypoglycemia, lethargy, muscle weakness, cardiomyopathy, and liver disease especially in infants often leading to death. A milder, late-onset form that occurs in older children or adults may present with muscle soreness and exercise-induced rhabdomyolysis.

Indications:

- Cardiomyopathy, pericardial effusion and/or arrhythmia
- Hypoglycemia
- Rhabdomyolysis/skeletal myopathy
- Abnormal newborn screen suggesting VLCAD deficiency
- Abnormal acylcarnitine profile consistent with VLCAD 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 VLCAD deficiency

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.

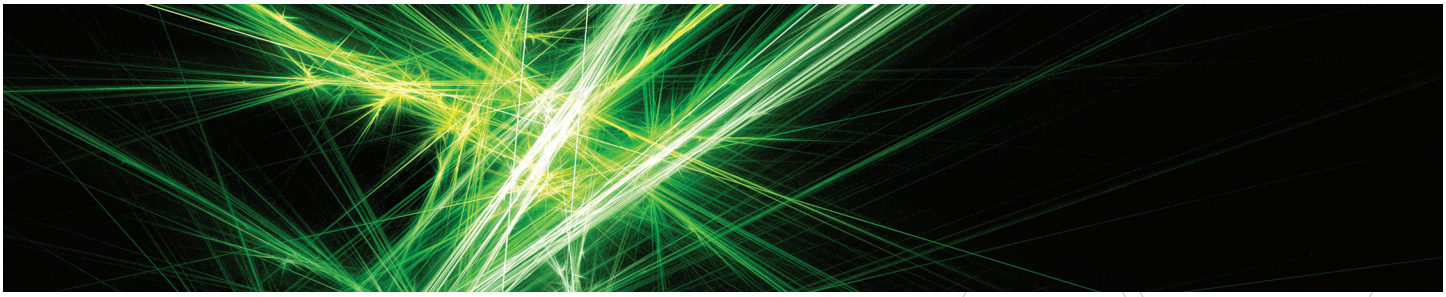
Place samples in styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday

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. Phlebotomist must label tube/flasks with patient's name, birth date, and date of collection.

Testing Methodology: PCR-based sequencing of all 20 exons and exon/intron boundaries of the *ACADVL* gene.

Test Sensitivity: PCR-based sequencing of all 20 exons and exon/intron boundaries of the *ACADVL* gene detects >95% of patients with VLCAD deficiency. The sensitivity of DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed. *ACADVL* is the only gene associated with VLCAD deficiency.

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.

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

- *ACADVL* full gene sequence analysis: 81406
- *ACADVL* family specific mutation analysis: 81403

Results: Each test report includes a detailed interpretation of the genetic or biochemical test results, 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:

Andresen, B. S., S. Olpin, et al. (1999). Clear correlation of genotype with disease phenotype in very-long-chain acyl-CoA dehydrogenase deficiency. Am J Hum Genet 64(2): 479-494.

Boneh, A., B. S. Andresen, et al. (2006). VLCAD deficiency: pitfalls in newborn screening and confirmation of diagnosis by mutation analysis. Mol Genet Metab 88(2): 166-170.

Laforet, P., C. Acquaviva-Bourdain, et al. (2009). Diagnostic assessment and long-term follow-up of 13 patients with Very Long-Chain Acyl-Coenzyme A dehydrogenase (VLCAD) deficiency. Neuromuscul Disord 19(5): 324-329.

Leslie, N. D., B. T. Tinkle, et al. (2009; updated 2011). Very Long-Chain Acyl-Coenzyme A Dehydrogenase Deficiency. GeneReviews. R. A. Pagon, T. D. Bird, C. R. Dolan, K. Stephens and M. P. Adam. Seattle (WA).

Mathur, A., H. F. Sims, et al. (1999). Molecular heterogeneity in very-long-chain acyl-CoA dehydrogenase deficiency causing pediatric cardiomyopathy and sudden death. Circulation 99(10): 1337-1343.