Very Long-Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD): ACADVL Gene Deletion/Duplication

Test Code: HN
Turnaround time: 2 weeks
CPT Codes: 81228 x1

Condition Description

Very Long-Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD) is an autosomal recessive disorder of mitochondrial fatty acid beta-oxidation [1]. Three heterogeneous phenotypes of the disorder have been described ranging from a severe onset with cardiac failure in infancy, an intermediate childhood form with hypoketotic hypoglycemia, to an adult onset myopathic form with exertional rhabdomyolysis, primarily affecting skeletal muscle. The severe neonatal form is the most common type [2] and presents with cardiomyopathy, hepatopathy, and skeletal myopathy. The intermediate form is mainly characterized by episodes of hypoketotic hypoglycemia in infancy and cardiomyopathy occurs very rarely in this type [3]. The adult form is characterized by isolated skeletal myopathy, usually triggered by exercise or fasting [4]. Biochemical analysis of VLCADD patients reveals impairment of palmitoyl-CoA oxidation, with reduced or deficient very long-chain acyl-CoA dehydrogenase (VLCAD) activity and VLCAD protein in fibroblasts [5]. The molecular analysis of the ACADVL gene (17p13) in these patients depicts a heterogeneous mutational spectrum, including missense mutations, single amino acid deletions, and splicing defects, with most patients being compound heterozygotes [6]. Few phenotype-genotype correlations are well understood [7]. Gene sequencing is available to test for mutations in the ACADVL gene (HK). For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array (HN).

References:

Genes
ACADVL

Indications

This test is indicated for:
- Confirmation of a clinical/biochemical diagnosis of VLCADD.
- Carrier testing in adults with a family history of VLCAD.

Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region. Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

Detection

Detection is limited to duplications and deletions. Array CGH will not detect point mutations or intronic mutations.

Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Specimen Requirements

Submit only 1 of the following specimen types
- Preferred specimen type: Whole Blood
**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Submit copies of diagnostic biochemical test results with the sample. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- **Urine Organic Acids (OA)** and **Plasma Acylcarnitine Profile (AR)** are used in the diagnosis of a patient with VLCADD.
- Sequence analysis of the **ACADVL** gene is available and is required before deletion/duplication analysis.
- 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.