Gene Sequencing

JW

81479 x1

gene located at the 21q22 [8]. About 30 mutations in the

4 weeks

The age of onset is one of the distinguishing factors with HLCS typically presenting between birth and 3 months of age and biotinidase deficiency typically presenting after 3 months. The symptoms in these disorders are similar and clinical differentiation is often difficult. In untreated states, both are usually characterized by seizures, hypotonia, ataxia, developmental delay, vision problems, hearing loss, and cutaneous changes such as alopecia, skin rash, and candidiasis. With age, motor limb weakness, spastic paresis, and decreased visual acuity occur. Both HLCS and biotinidase deficiency are biotin-responsive and early recognition and biotin supplementation result in rapid clinical improvement [4-5]. Newborn screening allows early symptomatic treatment that can prevent neurological deterioration [6].


Reference:

HLCS

Confirmation of a clinical/biochemical diagnosis of HLCS deficiency

Carrier testing in adults with a family history of HLCS deficiency

Methodology

PCR amplification of 14 exons contained in the HLCS gene is performed on patient genomic DNA. Direct sequencing of amplification products is performed in both the forward and reverse directions using automated fluorescence dideoxy sequencing methods. Patient gene sequences are compared to a normal reference sequence. Sequence variations are then classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay
does not interrogate the promoter region, deep intronic regions, or other regulatory elements. Large deletions are not detected by this analysis.

**Detection**

The majority of patients with clinical and biochemical diagnosis of HLCS deficiency will have an abnormal DNA test. Clinical Sensitivity: 18/18 mutations identified in 9 patients [8]; 6/8 mutations identified in 4 patients [10]. Analytical Sensitivity: ~99%.

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) or ACD (yellow 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**

Laboratory, please submit a copy of the sequencing report with the 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 Emory Genetics test requisition.

**Related Tests**

- Urine Organic Acids (OA), and Plasma Acylcarnitine Profile (AR) are used in the diagnoses of a patient with HLCS deficiency
- Biotinidase Assay (BX) may also be used in some instances to aid in diagnosis of HLCS deficiency
- Custom Diagnostic Mutation Analysis (KM) is available to family members if mutations are identified by sequencing.
- Deletion/Duplication Assay is available separately for individuals where mutations are not identified by sequence analysis. Refer to the test requisition or contact the laboratory for more information.
- Prenatal testing is available for known familial mutations only. Please call the Laboratory Genetic Counselor before collecting a fetal sample.