

Argininosuccinate Lyase Deficiency: *ASL* Gene Sequencing

Test Code: JB

Turnaround time: 4 weeks

CPT Codes: 81479 x1

Condition Description

Argininosuccinate lyase deficiency (ASL deficiency) is an autosomal recessive disorder of the urea cycle caused by mutations in the *ASL* gene (7cen-q11.2). Urea cycle disorders are characterized by hyperammonemia, encephalopathy, and respiratory alkalosis. Five disorders involving different defects in the biosynthesis of the enzymes of the urea cycle have been described: ornithine transcarbamylase deficiency, carbamyl phosphate synthetase deficiency, argininosuccinate synthetase deficiency, or citrullinemia, ASL deficiency, and arginase deficiency.

Two forms of ASL deficiency have been recognized: an early-onset, or malignant, type and a late-onset type. Onset of symptoms of early-onset argininosuccinic aciduria occurs in the first weeks of life. Features include mental and physical retardation, convulsions, episodic unconsciousness, liver enlargement, skin lesions, and dry and brittle hair showing trichorrhexis nodosa microscopically and fluorescing red. The late-onset type of ASL deficiency is characterized by residual enzyme activity as measured by the incorporation of C-14-citrulline into proteins. Symptoms include relatively mild clinical symptoms, variable age of onset, marked argininosuccinic aciduria, and severe, but not complete, deficiency of argininosuccinate lyase. Early treatment of partial argininosuccinate lyase deficiency with arginine supplementation can result in normal intellectual and psychomotor development.

Sequencing of the *ASL* gene is recommended after a biochemical analysis consistent with ASL deficiency, and provides a complementary method to confirm the presence of mutations in a proband, identify carriers among the proband's relatives, and provide prenatal diagnosis in families with known mutations.

For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array (JC).

[Click here](#) for the OMIM summary on this condition.

Genes

[ASL](#)

Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of ASL deficiency.
- Carrier testing in adults with a family history of ASL deficiency.

Methodology

PCR amplification of 16 exons contained in the *ASL* 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

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: ~99%

Specimen Requirements

Submit only 1 of the following specimen types

Type: DNA, Isolated

Specimen Requirements:

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Type: Whole Blood (EDTA)

Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old: 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: Saliva**Specimen Requirements:**

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Special Instructions

Submit copies of diagnostic biochemical test results with the sample. Contact the laboratory if further information is needed. 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

Plasma amino acid (AA) analysis.

Urine organic acids (OA) analysis.

Ornithine transcarbamylase deficiency gene sequencing (HU).

Citrullinemia gene sequencing (JG).

[Custom diagnostic mutation analysis \(KM\)](#) is available to family members if mutations are identified by sequencing.

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.