Argininosuccinate Lyase Deficiency: ASL Gene Deletion/Duplication

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, 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.

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

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) 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**

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 Emory Genetics Laboratory, 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.