Congenital Disorder of Glycosylation II: ALG2 Gene Deletion/Duplication

Test Code: DALG2
Turnaround time: 2 weeks
CPT Codes: 81228 x1

Condition Description

Congenital disorders of glycosylation (CDG) are a group of autosomal recessive genetic disorders caused by the alteration in synthesis and structure of protein and lipid glycosylation. In the past decade, over 30 genetic diseases have been identified that alter glycan synthesis, structure and ultimately the function of nearly all organ systems.

CDG type I (CDGI) disorders result from impaired synthesis of the incomplete lipid linked oligosaccharide (LLO) and/or its attachment to the growing polypeptide chain. CDG-Ia is the most common form reported, due to phosphomannomutase deficiency, an enzyme that converts mannose-6-phosphate to mannose-1-phosphate. CDG-Ib (phosphomannose isomerase, MPI deficiency) is the only known treatable form, by giving mannose orally. CDG type II (CDGII) includes defects in processing of N-glycans.

Phenotypes of this disorder are extremely variable. Manifestations range from severe developmental delay and hypotonia with multiple organ system involvement beginning in infancy, to hypoglycemia and protein-losing enteropathy with normal development. Most subtypes have been described in only a few individuals, however, thus understanding of the phenotypes is limited.

The current diagnostic test for CDG is analysis of serum transferrin glycoforms, also called "transferrin isoforms analysis", or "carbohydrate-deficient transferrin analysis." If positive, this testing can be followed by DNA testing to identify mutations in the gene involved.

One patient has been described with CDG II. She was normal at birth but presented within the first year of life with a multisystemic disorder that included mental retardation, seizures, coloboma of the iris, hypomyelination, hepatomegaly, and coagulation abnormalities. She also had unilateral cataract, an irregular nystagmus, and brisk tendon reflexes.

She was found to have two mutations in the ALG2 gene (9q22).

For patients with suspected CDG II, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

References:

Genes

ALG2

Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of CDG II in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of CDG II in whom sequence analysis was negative.

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. The CGH array will not detect point 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:

Oragen™ 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, if appropriate. 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**

- Sequence analysis of the ALG2 gene is available and is required before deletion/duplication analysis.
- Analysis of other CDG genes is also available.
- Biochemical carbohydrate deficient transferrin analysis for CDGs is also available.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.