

## Congenital Disorder of Glycosylation Ir: *DDOST* Gene Sequencing

**Test Code:** SDDOS

**Turnaround time:** 4 weeks

**CPT Codes:** 81479 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.

Jones et al. (2012) identified two mutations in the *DDOST* gene (1p36.1) in an individual with features of CDG but who had tested negative for 25 genes known to be associated with CDG.

References:

- Jones et al. (2012) Am J Hum Genet, 90:363-368.
- [OMIM #602202](#): *DDOST* gene
- [OMIM #614507](#): CDG Ir

### Genes

[DDOST](#)

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of congenital disorder of glycosylation type Ir.
- Carrier testing in adults with a family history of congenital disorder of glycosylation type Ir.

### Methodology

PCR amplification of 11 exons contained in the *DDOST* gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are 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, and does not detect large deletions.

### 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 clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%

### Specimen Requirements

**Submit only 1 of the following specimen types**

**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: 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: 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**

Special Instructions: Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

**Related Tests**

- Individual full gene sequencing and deletion duplication analysis are available for many CDG-associated genes.
- CDG Next Generation sequencing panels are available and are organized by comprehensive, multiple glycosylation, N-Glycosylation and Type I.
- N-Glycan Structural Analysis and Carbohydrate Deficient Transferrin are available as individual tests and as a panel.
- Individual deletion/duplication analysis is available for other CDG-associated genes, as well as deletion/duplication panels.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- 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.