

## Congenital Disorder of Glycosylation, *GNE*-related: *GNE* Gene Deletion/Duplication

**Test Code:** DGNEX

**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.

Sialic acid modification of glycoproteins and glycolipids expressed at the cell surface is crucial for their function in many biologic processes, including cell adhesion and signal transduction. Differential sialylation of cell surface molecules is also implicated in the tumorigenicity and metastatic behavior of malignant cells. *GNE* is the rate-limiting enzyme in the sialic acid biosynthetic pathway.

Mutations in the *GNE* gene (9p12-p11) have been identified in individuals with sialuria (autosomal dominant inheritance), autosomal recessive inclusion body myopathy, and Nonaka myopathy (autosomal recessive inheritance).

For patients with suspected *GNE*-related CDG, 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:

- Freeze HH. Congenital disorders of glycosylation: CDG-I, CDG-II, and beyond. *Curr Mol Med* 2007; 7:389-396.
- [GeneTests: Congenital Disorders of Glycosylation Overview](#)
- Jaeken J, Matthijs G. Congenital disorders of glycosylation: A rapidly expanding disease family. *Annu Rev Genomics Hum Genet* 2007; 8:261-278.
- [OMIM: UDP-N-Acetylglucosamine 2-Epimerase/N-Acetylmannosamine kinase](#)

### Genes

[GNE](#)

### Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of *GNE*-related CDG in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of *GNE*-related CDG 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.

### 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**

**Type: DNA, Isolated****Specimen Requirements:**

Microtainer

3µg

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 &amp; 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.

**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 EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the *GNE* 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.
- [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 to adult couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.