### 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 lipid linked oligosaccharide (LLO) precursor 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 mannos-6-phosphate to mannos-1-phosphate. CDG-Ib (phosphomannose isomerase, MPI deficiency) is the only known treatable form, by giving mannos orally. CDG type II (CDGII) includes defects in the 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, thus understanding of the phenotypes is limited.

The current diagnostic test for CDG is the 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.

Paesold-Burda et al. (2009) identified a homozygous mutation in the COG5 gene (7q22.3) in an individual with CDGIIi. Her features include developmental delay, moderate intellectual disability, a slow and inarticulate speech, mild hypotonia, truncal ataxia, and pronounced diffuse atrophy of the cerebellum and brain stem.

### References:

- OMIM #606821: COG5 gene
- OMIM #613612: CDGIIi

### Genes

**COG5**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Congenital Disorder of Glycosylation Type IIi.
- Carrier testing in adults with a family history of Congenital Disorder of Glycosylation Type IIi.

### Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

### 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

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:
In EDTA (purple 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, if appropriate. Contact the laboratory if further information is needed.

**Related Tests**

- Analysis of other CDG genes is also available, including single gene analysis and a next generation sequencing panel.
- 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 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.