Predicting prognosis
Assisting researchers in understanding the molecular basis of disease in the pursuit for improved treatments and cures
Assessing the possibility of therapy for some forms of CDG
Providing the opportunity for carrier testing in at-risk family members of those with a known mutation

Interpreting Test Results

- **Positive result:** A biochemical finding and mutations have been identified that are of particular diagnostic and clinical significance
- **Negative result:** No abnormal biochemical pattern or mutation has been identified. A negative result does not exclude the presence of a glycosylation defect or a mutation that cannot be identified by the current panel and technology.
- If **variants of unknown significance** with or without abnormal biochemical findings are detected, follow-up testing of parents and other available family members is generally recommended to aid in determining the segregation pattern of the identified variant(s).

Sample requirements

**Transferrin Analysis:**
3-5 ml blood in a red top (serum) or green top (plasma) tube. Centrifuge to separate serum or plasma. Ship frozen.

**DNA Analysis:**
3-5 ml whole blood in a purple top (EDTA) tube. Ship at room temperature within 5 days of collection.

- **GeneReviews:**
- **National Organization for Rare Diseases (NORD):**
  - [www.rarediseases.org](http://www.rarediseases.org)
- **Euroglycanet:**
  - [www.euroglycanet.org/uz/CDG](http://www.euroglycanet.org/uz/CDG)
- **The CDG Family Network:**
  - [www.cdgf.com](http://www.cdgf.com)

**Contact Information**

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Emory Genetics Laboratory (EGL) is a comprehensive clinical genetics testing laboratory specializing in molecular cytogenetics, rare disease testing, and newborn screening confirmatory testing.
Congenital Disorders of Glycosylation

Congenital disorders of glycosylation (CDGs), formerly called carbohydrate deficient glycoprotein syndromes, are a group of genetic disorders caused by alterations in protein and lipid glycosylation. Glycosylation is a process whereby sugars (glycans) are linked together in a specific pattern and are attached to proteins and lipids. The sugar complexes are used as signals for the proper cellular localization of the proteins and lipids. These sugar-protein and sugar-lipid complexes are called glycoproteins and glycolipids, and they are needed for normal function and growth of all tissues and organs in the human body.

The process of glycosylation is very complex, involving at least 100 separate enzymes used to create and modify the sugar chains and add them to thousands of different proteins and lipids. Incorrect glycosylation, and therefore mislocalization of proteins and lipids, is the underlying basis of the different clinical features seen in individuals with CDG.

Classification

CDGs can be classified into four major groups depending on the nature of the abnormal sugar chain: disorders of N-glycosylation, disorders of O-glycosylation, multiple glycosylation disorders, and glycolipid disorders. Disorders of N-glycosylation are the most common, and can be divided into type I and type II (CDG I, CDG II) based on the location in the glycosylation pathway in which the defect occurs. Different subtypes in each group are defined by the specific gene involved and are designated by a small letter code (Ia, Ib, Ic, etc.).

Type I CDGs are caused by defects in genes coding for enzymes that create the sugar chain precursors or that attach them to proteins and lipids. Type II CDGs are caused by defects in genes coding for enzymes that modify the sugar chains after they are added to the protein or lipid. Currently, more than 30 variants of CDG have been described. CDG type Ia is the most common form of CDG, having been reported in more than 700 individuals.

Symptoms

The symptoms and severity of CDGs vary significantly between people. Clinical manifestations can range from severe developmental delay, failure to thrive, seizures, and hypotonia with multiple organ system involvement, to hypoglycemia and protein-losing enteropathy with normal development. The specific symptoms a person displays will depend upon the tissues affected by the mislocalization of glycoproteins and glycolipids.

Most commonly, CDG disorders begin in infancy and are associated with minor dysmorphic features (e.g., inverted nipples, sub-cutaneous fat pads, strabismus, cerebellar atrophy and hypoplasia). Some of the symptoms may become more or less prominent at later ages. Failure to thrive is often a good indicator for a CDG diagnosis.

Testing for CDG

Most CDG patients can be diagnosed by biochemical analysis of transferrin isoforms and glycan structural analysis to determine the glycosylation status of proteins in serum. Once CDG is diagnosed biochemically, genetic testing is required to determine the type and subtype of CDG.

Because of the wide variety and overlap of symptoms seen in affected individuals, it is very difficult to identify which CDG gene may be responsible for the symptoms in any given patient. While single gene testing is available, our panel allows for simultaneous testing of multiple CDG genes which provides a significant diagnostic advantage over single gene sequencing. Because DNA analysis is available for some but not all forms of CDG, biochemical analysis is an integral component of CDG testing. If you have questions about what testing would be best for your patient, please contact the lab.

Additional benefits of testing include:

- Providing information for recurrence risk, prenatal diagnosis, and family planning
- Helping physicians to determine appropriate follow-up testing and develop a health maintenance plan