Congenital Disorders of Glycosylation: O-glycan Analysis, Quantitative and Qualitative, Plasma

Condition Description

The congenital disorders of glycosylation (CDG) are autosomal recessive disorders characterized by alterations in protein glycosylation (Jaelen et al., 2001). Protein glycosylation in CDG involves N- and/or O-glycosylation. Primary defects in the N- and/or O-glycosylation pathways lead to defective glycogen conjugate biosynthesis. In the past decade, over 40 genetic diseases have been identified that alter glycan synthesis and structure and ultimately the function of nearly all organ systems.

Congenital disorders of glycosylation are divided into types based on the type of glycosylation. CDG group I (CDGI) disorders result from impaired synthesis of the incomplete lipid linked oligosaccharide (LLO) and/or its attachment to the growing polypeptide chain. Group II (CDGII) includes defects in processing of N-glycans and/or O-glycans which leads to accumulation of glycans with abnormal structure. Multiple glycosylation defects impair both glycan synthesis and processing, such as defects in the conserved oligomeric Golgi complex (COG). Other types of multiple glycosylation defects may also present as a combined CDG type I and type II. Currently, multiple glycosylation disorders include at least 14 different genetic defects. Lastly, there are an increasing number of patients with strong evidence of a glycosylation defect, whose molecular basis has not yet been identified (CDG-x). More recent discoveries point to genetic defects in chaperones, transporters, and Golgi-trafficking complexes.

Educational Materials:
- CDG Handout for Parents
- CDG Handout for Clinicians

References:


Indications

The plasma/serum O-glycan profile is principally used to identify multiple glycosylation disorders, such as COG deficiency.

Manifestations of CDG range from severe developmental delay and hypotonia with multiple organ system involvement to hypoglycemia and protein-losing enteropathy with normal development. Consider CDG in all patients with:

- failure to thrive
- mental retardation
- hypotonia
- hypoglycemia
- cerebellar hypoplasia
- liver dysfunction
- coagulopathy
- partial TBG deficiency
- perinatal dysmorphism
- microcephaly
- loose wrinkled skin
- skeletal anomalies
- short stature
- recurrent infections
- thrombocytopenia
- neutropenia
- seizures and stroke-like episodes
- dandy-walker malformation
- ataxia
- absence of speech
- myopathy and polynuropathy

Methodology

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Detection

Interpretation of O-glycan profiles from MALDI-TOF is based on pattern recognition: presence of abnormal O-glycans and significant elevations/reductions of normal glycans.

The final interpretation of plasma O-glycosylation will be based on the O-glycan profile and quantification of T antigen, Sialyl T antigen, and the ratio of T antigen to Sialyl T antigen.

O-glycan profiles of patients with cancer and diabetes must be interpreted with caution. It is possible that other acquired disorders, such as cancer and diabetes, may alter O-glycans at the cellular level. However, there are no documented reports of alterations in O-glycan profiles in blood. Molecular and enzymatic analysis are recommended to confirm a specific diagnosis.

Reference Range

Normal ranges:
- T antigen \( \leq 1.03 \mu\text{mol} \)
- Sialyl T antigen \( \geq 13 \mu\text{mol} \)
- T antigen/Sialyl T ratio \( \geq 0.06 \)

Specimen Requirements

Additional Specimen Collection/Handling Instructions Required for this Test
Only one specimen type is required for this test: Whole blood or frozen plasma. If whole blood cannot be received at EGL within 24 hours of collection, please send frozen plasma. (See instructions below)

Submit only 1 of the following specimen types

Type: Whole Blood

Specimen Requirements:
- Sodium heparin (green top) tube:
  - Children under 2 years: 1 ml blood
  - Older Children & Adults: 3 - 5 ml blood

  Blood drawn 2-4 hours postprandial is preferred.

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample overnight at room temperature for receipt at EGL within 24 hours of collection.

Type: Plasma

Specimen Requirements:
- Sodium heparin (green top) tube:
  - Children under 2 years: 1 ml blood
  - Older Children & Adults: 3 - 5 ml blood

  Centrifuge immediately to separate plasma and freeze.

  Blood drawn 2-4 hours postprandial is preferred.

Specimen Collection and Shipping: Ship frozen sample on dry ice with overnight delivery.

Special Instructions

Click here for the clinical presentation form.

Related Tests

- Oligosaccharide Screen in Urine (OS)
- Carbohydrate Deficient Transferrin for Congenital Disorders of Glycosylation (BCDGS)
- N-glycan Structural Analysis for CDG (BNGLY)
- N-glycan and Carbohydrate Deficient Transferrin panel for CDG’s (BCDGP)

- Sequencing analysis of individual CDG genes is available
- Sequencing analysis by panels for CDG genes is also available
- Custom diagnostic mutation analysis (KM) is available to family members if mutations have been 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 sample.