

Test Descriptions:

Congenital disorders of glycosylation (CDGs) are a group of inherited diseases characterized by abnormal protein and lipid glycosylation. To date, over 120 separate genetic deficiencies have been linked to a CDG and the breadth of causative genes leads to highly variable clinical presentation with multi-systemic involvement. The severity and long term outcome is dependent on the specific causative CDG, and shows significant inter- and intra-familial variability. While a common phenotype cannot be reported, The majority of CDGs may be associated with a significant neurologic component including hypotonia, seizures, cerebellar hypoplasia and developmental delay/intellectual disability. Additional common features may include abnormal fat distribution, coagulation defects, feeding difficulties, gastrointestinal abnormalities, ocular abnormalities and cardiac abnormalities including cardiomyopathy

CDGs can be classified into two groups based on the pathway defect. Type I CDG (CDG-I) refers to defects in glycan assembly and transfer from the dolichol phosphate lipid to the asparagine residue on nascent proteins. Type II CDG (CDG-II) refers to defects in processing of the N-glycan to its mature form. CDG-II can also affect serine/threonine-linked glycosylation (O-glycosylation). Complete biochemical analyses for screening of CDGs include carbohydrate deficient transferrin (CDT), N-glycan profiling, and O-glycan profiling in serum or plasma.

Carbohydrate deficient transferrin (CDT) analysis: Transferrin (Tf) is immunopurified from patient plasma and analyzed by Quadrupole Time-of-Flight Mass Spectrometry (Q-TOF MS). The ratios of carbohydrate deficient Tf (a-oligo, mono-oligo and tri-sialo) to the mature fully-glycosylated di-oligo Tf are reported to evaluate the glycosylation status of Tf. This assay is clinically useful in screening type I CDG. In addition, certain type II CDG and combined defects can also be identified by the presence of Tf with abnormal glycan structures.

N-glycan profiling: Plasma N-glycan profiling involves removal of N-glycans from proteins, purification, permethylation and MALDI-TOF/TOF analysis. A total of 42 glycans are monitored and their relative abundance provides a comprehensive view of N-glycan metabolism, particularly in regard to the processing after glycan transfer in the ER or Golgi-localized steps that are associated with type II CDGs. This assay can also reveal abnormalities associated with certain type I CDGs.

O-glycan profiling: Plasma O-glycan profiling involves removal of O-glycans from proteins, purification, permethylation and mass spectrometry analyses. Thomsen-Friedenreich antigen (T-antigen) is an unsubstituted core 1 O-GalNAc glycan that is used for assessing the O-glycosylation function. The quantification of T-antigen and its sialylated species (ST) is performed by LC-MS/MS. An elevated level of T-antigen and elevated T/ST ratio are indicative of an O-glycosylation defect or a combined defect. The O-glycan profile is qualitatively analyzed by MALDI-TOF/TOF. This assay is also useful in the diagnosis of GNE-CDG (sialuria).

In patients suspected of having a CDG, all three tests can be ordered to provide the most comprehensive view of the glycosylation status. These tests can also be utilized for monitoring patients on dietary treatment. Results should be correlated with the patient's clinical findings. Positive biochemical findings should be confirmed with molecular analysis. Secondary glycosylation abnormalities have been reported in patients with alcoholism and other metabolic diseases such as fructose intolerance and galactosemia.

Related tests:

PMM2, ALG6, MPI molecular testing can be ordered for diagnostic purposes via the expanded carrier screening panel

Specimen Requirements:

- 1-2 mL in EDTA tube (lavender top) or sodium heparin tube (green top) or serum tube (red top). Minimum of 0.5 mL is required.
- 1 mL plasma or serum, minimum of 100 µL.

Shipping:

- Separate plasma immediately and ship frozen plasma on dry ice
- Plasma should be stored frozen until analysis

Turnaround Times: 10 days

CPT Codes:

Shipping Address:

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