Test Definition: CDG

Carbohydrate Deficient Transferrin for Congenital Disorders of Glycosylation, Serum

Overview

Useful For

Screening for congenital disorders of glycosylation

This test is **not useful for** screening patients for chronic alcohol abuse.

Genetics Test Information

This testing is used to screen patients for suspected congenital disorders of glycosylation (N- and O-glycosylation defects as well as glycan structure analysis).

Congenital disorders of glycosylation (CDG) encompass over 150 genetic conditions spanning a broad clinical spectrum.

The main CDG profiles that can be identified by this analysis are type I, some type II, and mixed type CDG.

Testing Algorithm

Suggested Testing Strategy:

Disorder	Target	Mayo Test ID
N-glycan, core 1 mucin type O-glycosylation, and conserved oligomeric Golgi (COG) complex defects	Transferrin, apolipoprotein CIII	CDG / Carbohydrate Deficient Transferrin for Congenital Disorders of Glycosylation, Serum
N-glycan, core 1 mucin type O-glycosylation, and COG complex defects	Serum total N-linked glycans, transferrin, and apolipoprotein CIII	CDGN / Congenital Disorders of N-Glycosylation, Serum (includes test ID CDG) Stepwise analysis of transferrin, apolipoprotein CIII, and serum total N-glycans
alpha-dystroglycanopathies, GPI anchor disorders	Genes: *DAG1, FKRP, FKTN, ISPD, LARGE1, POMGNT1, POMGNT2, POMT1, POMT2* *PIGA, PIGL, PIGM, PIGN, PIGO, PIGT, PIGV, PIGW, PGAP2, PGAP3*	CDGGP / Congenital Disorders of Glycosylation Gene Panel, Varies

For more information see:
Congenital Disorders of Glycosylation: Screening Algorithm
Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm.

Special Instructions

- Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm
- Transferrin and Apolipoprotein-CIII Isoform Analysis
- Congenital Disorders of Glycosylation: Screening Algorithm
- Congenital Disorders of Glycosylation Patient Information

Method Name
Affinity Chromatography Mass Spectrometry (MS)

NY State Available
Yes

Specimen

Specimen Type
Serum

Ordering Guidance
This test is for congenital disorders of glycosylation. If the ordering healthcare professional is looking for evaluation of alcohol abuse, order CDTA / Carbohydrate Deficient Transferrin, Adult, Serum.

If either PMM2-CDG (CDG-Ia) or MPI-CDG (CDG-Ib) is suspected, order PMMIL / Phosphomannomutase and Phosphomannose Isomerase, Leukocytes.

Necessary Information
1. Patient's age is required.
2. Reason for testing is preferred.

Specimen Required
Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 0.1 mL Serum
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms
1. Congenital Disorders of Glycosylation Patient Information
2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume
Serum: 0.05 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	45 days	
	Ambient	7 days	
	Refrigerated	28 days	

Clinical & Interpretive

Clinical Information

Glycosylation is the post-translational modification of proteins and lipids by the addition of glycans (sugars and sugar chains) in a complex stepwise fashion in the endoplasmic reticulum, Golgi apparatus, cytosol and sarcolemmal membrane. Congenital disorders of glycosylation (CDG) are a group of over 150 inherited metabolic disorders characterized by abnormal protein and lipid glycosylation. There are 2 main groups of CDG: type I, characterized by defects in the assembly or transfer of the dolichol-linked glycan in either the cytosol or endoplasmic reticulum (ER) and type II, involving processing defects of the glycan in the ER and Golgi apparatus. In addition, there are 2 main categories of glycosylation: N-glycosylation where N-linked glycans are attached to a protein backbone via an asparagine residue on the protein, and O-glycosylation where O-glycans are attached to the hydroxyl group of threonine or serine. Apolipoprotein CIII (Apo-CIII) isoforms, with a single core 1 mucin type O-glycosylate protein, is a complementary evaluation for the CDG type II profile. This analysis will evaluate mucin type O-glycosylation, a defect involving the Golgi apparatus, which is detected biochemically by the change in ratios of the 3 isoforms.

Congenital disorders of glycosylation typically present as multi-systemic disorders with a broad clinical spectrum including, but not limited to, developmental delay, hypotonia, with or without neurological abnormalities, abnormal magnetic resonance imaging findings, skin manifestations, and coagulopathy. There is considerable variation in the severity of this group of diseases ranging from a mild presentation in adults and children to severe multi-organ dysfunctions causing infant lethality. In some subtypes, phosphomannose isomerase-CDG (MPI-CDG or CDG-Ib) in particular, intelligence is not compromised. CDG should be suspected in all patients with neurological abnormalities including developmental delay and seizures, brain abnormalities such as cerebellar atrophy or hypoplasia as well as unexplained liver dysfunction. Abnormal subcutaneous fat distribution and chronic diarrhea may be present. The differential diagnosis of abnormal transferrin patterns also includes liver disease not related to CDG including galactosemia, hereditary fructose intolerance in acute crisis, and liver disease of unexplained etiology.

Transferrin and apolipoprotein CIII isoform analysis are the initial screening tests for CDG. The results of the transferrin and apolipoprotein CIII isoform analysis should be correlated with the clinical presentation to determine the most

appropriate follow-up testing strategy including enzyme, molecular, and research-based testing. Enzymatic analysis for phosphomannomutase and phosphomannose isomerase in leukocytes (PMMIL / Phosphomannomutase and Phosphomannose Isomerase, Leukocytes) should be performed if either PMM2-CDG (CDG-Ia) or MPI-CDG (CDG-Ib) is suspected.

Other glycosylation pathways, in addition to N- and O-glycosylation, have been elucidated, in particular glycophosphatidylinositol (GPI)-anchored protein glycosylation disorders in which there is absent or decreased expression of all the GPI-linked antigens, and alpha-dystroglycanopathies caused by impaired synthesis of O-mannose glycans. Neither class of disorders are picked up by CDG analysis in serum but are typically diagnosed using molecular methods (CDGGP / Congenital Disorders of Glycosylation Gene Panel, Varies).

Reference Values

Ratio	Normal	Indeterminate	Abnormal
Transferrin mono-oligo/di-oligo ratio	< or =0.06	0.07-0.09	> or =0.10
Transferrin A-oligo/di-oligo ratio	< or =0.011	0.012-0.021	> or =0.022
Transferrin tri-sialo/di-oligo ratio	< or =0.05	0.06-0.12	> or =0.13
Apo CIII-1/Apo CIII-2 ratio	< or =2.91	2.92-3.68	> or =3.69
Apo CIII-0/Apo CIII-2 ratio	< or =0.48	0.49-0.68	> or =0.69

Interpretation

Positive test results could be due to a genetic or nongenetic condition; additional confirmatory testing is required.

In serum, the bi-antennary transferrin (di-oligo) fraction is the most abundant transferrin isoform. Congenital disorders of glycosylation (CDG)-I generally show increases in mono-oligo- and/or a-oligo transferrin isoforms whereas CDG-II shows elevated increased transferrin with truncated glycans of varying degree depending on the type of defect.(1)

Results are reported as the mono-oligosaccharide/di-oligosaccharide transferrin ratio, the a-oligosaccharide/di-oligosaccharide transferrin ratio, the tri-sialo/di-oligosaccharide transferrin ratio, and the apolipoprotein CIII-1/apolipoprotein CIII-2 ratio, and the apolipoprotein CIII-0/apolipoprotein CIII-2 ratio. The report will include the quantitative results and interpretation.

The congenital disorders of glycosylation (CDG) profiles are categorized into 5 types:
1. CDG type I profile. Mono-oligosaccharide/di-oligosaccharide transferrin ratio or the a-oligosaccharide/di-oligosaccharide transferrin ratio is abnormal. This group should have the apolipoprotein C-III profile within the normal ranges, because the Golgi system is not affected in CDG type I.
2. CDG type II profile. The tri-sialo/di-oligosaccharide transferrin ratio is abnormal. In this category, the apolipoprotein C-III profile will have 2 scenarios:
A. The apolipoprotein CIII-1/apolipoprotein CIII-2 ratio or the apolipoprotein CIII-0/apolipoprotein CIII-2 ratio will be abnormal. In this case, the defect is most likely glycan processing in the Golgi apparatus; therefore, a CDG (conserved oligomeric Golgi [COG]) defect or defect that alters the Golgi apparatus is likely.
B. The apolipoprotein CIII-1/apolipoprotein CIII-2 ratio or the apolipoprotein CIII-0/apolipoprotein CIII-2 ratio are

normal. In this case, the defects most likely do not involve the Golgi system, thus the molecular defect is different.
3. CDG mixed type profile (type I and II together). In this type of profile one can have abnormal tri-sialo/di-oligosaccharide transferrin ratio with the mono-oligosaccharide/di-oligosaccharide transferrin ratio or the a-oligosaccharide/di-oligosaccharide transferrin ratio abnormal and may have the apolipoprotein CIII-1/apolipoprotein CIII-2 ratio and the apolipoprotein CIII-0/apolipoprotein CIII-2 ratio normal or abnormal, depending on if the defects involve Golgi apparatus.
4. CDG with normal transferrin and apolipoprotein profile. Some CDG (eg, PGM3, some ALG13, MOGS, NGLY1, SLC35C1, Fut8) pose a problem for their detection. Thus, careful medical history, physical exam, and analysis of other protein status may be informative for general protein glycosylation defects. If suspicious for either NGLY1- or MOGS-CDG, specific oligosaccharides in urine can be detected (OLIGU / Oligosaccharide Screen, Random, Urine).
5. When the profile cannot be categorized following the above classification, the abnormalities will be reported descriptively according to the molecular mass of the glycan isoform structures.

Reports of abnormal results will include recommendations for additional biochemical and molecular genetic studies to identify the correct form of CDG more precisely. If applicable, treatment options, the name and telephone number of contacts who may provide studies, and a telephone number for one of the laboratory directors (if the referring healthcare professional has additional questions) will be provided.

For more information, see Transferrin and Lipoprotein-CIII Isoform Analysis.

Cautions

Other conditions such as acute crisis of hereditary fructose intolerance, galactosemia, substance abuse, and acute liver disease may have a congenital disorder of glycosylation (CDG) profile that is indistinguishable from any other true CDG type I cases. Relevant clinical information and the indication for the analysis should be provided with the specimen.

Transferrin glycosylation patterns may normalize so repeat testing is warranted in patients with significant clinical suspicion.

Clinical Reference

1. Lefeber DJ, Morava E, Jaeken J. How to find and diagnose a CDG due to defective N-glycosylation. J Inherit Metab Dis. 2011;34(4):849-852
2. Peanne R, de Lonlay P, Foulquier F, et al. Congenital disorders of glycosylation (CDG): Quo vadis? Eur J Med Genet. 2018;61(11):643-663
3. Freeze HH, Eklund EA, Ng BG, Patterson MC. Neurology of inherited glycosylation disorders. Lancet Neurol. 2012;11(5):453-466
4. Hennet T, Cabalzar J. Congenital disorders of glycosylation: a concise chart of glycocalyx dysfunction. Trends Biochem Sci. 2015;40(7):377-384
5. Freeze HH, Chong JX, Bamshad MJ, Ng BG. Solving glycosylation disorders: fundamental approaches reveal complicated pathways. Am J Hum Genet. 2014;94(2):161-175
6. Sparks SE, Krasnewich DM. Congenital disorders of N-linked glycosylation and multiple pathway overview. In: Adam MP, Bick S, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2005. Updated January 12, 2017. Accessed February 23, 2026. Available at www.ncbi.nlm.nih.gov/books/NBK1332/
7. Ng BG, Freeze HH. Human genetic disorders involving glycosylphosphatidylinositol (GPI) anchors and glycosphingolipids (GSL). J Inherit Metab Dis. 2015;38(1):171-178. doi:10.1007/s10545-014-9752-1

8. Bouchet-Seraphin C, Vuillaumier-Barrot S, Seta N. Dystroglycanopathies: About numerous genes involved in glycosylation of one single glycoprotein. J Neuromuscul Dis. 2015;2(1):27-38

Performance

Method Description
Serum is diluted with water and then subjected to online immunoaffinity chromatography coupled to a quadrupole time-of-flight mass spectrometer. Relative quantitation of carbohydrate deficient transferrin and apolipoprotein CIII is achieved by comparing glycoform ratios in each protein.(Unpublished Mayo method).

PDF Report
No

Day(s) Performed
Monday, Thursday

Report Available
3 to 6 days

Specimen Retention Time
1 month

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
82373

LOINC® Information

Test Definition: CDG

Carbohydrate Deficient Transferrin for
Congenital Disorders of Glycosylation, Serum

Test ID	Test Order Name	Order LOINC® Value
CDG	CDG, S	90417-7

Result ID	Test Result Name	Result LOINC® Value
BG160	Reason for Referral	42349-1
31721	Mono-oligo/Di-oligo Ratio	35469-6
31720	A-oligo/Di-oligo Ratio	35475-3
50820	Interpretation	53808-2
50822	Reviewed By	18771-6
34474	Tri-sialo/Di-oligo Ratio	90420-1
34476	Apo CIII-1/Apo CIII-2 Ratio	90421-9
34475	Apo CIII-0/Apo CIII-2 Ratio	90419-3