Overview

Useful For

Identifying mutations within genes known to be associated with congenital disorders of glycosylation (CDG)

Second-tier test for individuals with negative targeted gene mutation analyses for specific CDG-related genes

Establishing, in some cases, a diagnosis of or carrier status for a CDG

Genetics Test Information

This test includes next-generation sequencing and Sanger sequencing to evaluate for the genes listed on the panel. See Targeted Genes and Methodology Details for Congenital Disorders of Glycosylation (CDG) Genetic Panels by Next-Generation Sequencing (NGS) in Special Instructions.

This ordered service includes the option for 1 of several glycosylation disease-related panel tests to be performed. Testing options include the following:

- Comprehensive CDG Panel (116 Genes)
- Normal Transferrin CDG Panel (60 Genes)
- Abnormal Transferrin CDG Panel (51 Genes)
- Custom Gene Ordering tutorial: https://vimeo.com/299737728/23d56922f1

See Frequently Asked Questions: Custom Gene Ordering Tool in Special Instructions.

Highlights

1) CDG / Carbohydrate Deficient Transferrin for Congenital Disorders of Glycosylation, Serum is recommended as a first tier test

2) If transferrin testing (CDG / Carbohydrate Deficient Transferrin for Congenital Disorders of Glycosylation, Serum) has been performed, then _G110 / Normal Transferrin CDG Panel or _G111 / Abnormal Transferrin CDG Panel may be the more appropriate subpanel.

3) Testing can be used to confirm a diagnosis of a congenital disorder of glycosylation

Reflex Tests

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<td>Fibroblast Culture for Genetic Test</td>
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**Testing Algorithm**

The recommended first-tier test to screen for congenital disorders of glycosylation (CDDG) is a biochemical test that analyses transferrin and apolipoprotein CIII (CDG / Carbohydrate Deficient Transferrin for Congenital Disorders of Glycosylation, Serum). The results of the transferrin and apolipoprotein CIII isoform analysis should be correlated with the clinical presentation to determine the most appropriate testing strategy. If transferrin testing (CDG / Carbohydrate Deficient Transferrin for Congenital Disorders of Glycosylation, Serum) has been performed, then consider either _G110 / Normal Transferrin CDG Panel (Bill Only) or _G111/ Abnormal Transferrin CDG Panel (Bill Only) may be the more as the appropriate subpanel option. See clinical information for recommended first-tier biochemical testing.

Å

If skin biopsy is received, fibroblast culture will be added and charged separately.

See Lysosomal Storage Disorders Diagnostic Algorithm, Part 2 in Special Instructions.

**Special Instructions**

- Molecular Genetics: Biochemical Disorders Patient Information
- Informed Consent for Genetic Testing
- Targeted Genes and Methodology Details for Congenital Disorders of Glycosylation (CDG) Genetic Panels by Next Generation Sequencing (NGS)
- Frequently Asked Questions: Custom Gene Ordering Tool
- Informed Consent for Genetic Testing (Spanish)
- Lysosomal Storage Disorders Diagnostic Algorithm, Part 2

**Method Name**

Custom Sequence Capture and Targeted Next-Generation Sequencing (NGS) followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing

**NY State Available**

Yes

**Specimen**

**Specimen Type**

Varies

**Advisory Information**

1. CDG / Carbohydrate Deficient Transferrin for Congenital Disorders of Glycosylation, Serum is recommended as a first tier test

2. Targeted testing for familial variants (also called site-specific or known mutation testing) is available for all genes on this panel under FMTT / Familial Mutation, Targeted Testing, Varies. Call 800-533-1710 to obtain more information about this testing option.

**Shipping Instructions**

Specimen preferred to arrive within 96 hours of collection.
**Necessary Information**
The specific congenital disorder of glycosylation subpanel requested must be provided in order to perform this test.

**Specimen Required**
Submit only 1 of the following specimens:

**Specimen Type:** Whole blood

**Patient Preparation:** A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

**Container/Tube:**
- **Preferred:** Lavender top (EDTA) or yellow top (ACD)
- **Acceptable:** Any anticoagulant

**Specimen Volume:** 3 mL

**Collection Instructions:**
1. Invert several times to mix blood.
2. Send specimen in original tube.

**Specimen Stability Information:** Ambient (preferred)/Refrigerated

**Additional Information:** To ensure minimum volume and concentration of DNA is met, the preferred volume of blood must be submitted. Testing may be canceled if DNA requirements are inadequate.

**Specimen Type:** Cultured fibroblasts

**Container/Tube:** T-75 or T-25 flask

**Specimen Volume:** 1 Full T-75 or 2 full T-25 flasks

**Specimen Stability Information:** Ambient (preferred)/Refrigerated <24 hours

**Acceptable**

**Specimen Type:** Confluent cultured cells

**Container/Tube:** T-25 flask

**Specimen Volume:** 2 flasks

**Collection Instructions:** Submit confluent cultured cells from another laboratory.

**Specimen Stability Information:** Ambient (preferred)/Refrigerated
**Specimen Type:** Skin biopsy

**Supplies:** Fibroblast Biopsy Transport Media (T115)

**Container/Tube:** Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin. Tubes can be supplied upon request; Eagle's minimum essential medium with 1% penicillin and streptomycin.

**Specimen Volume:** 4-mm punch

**Specimen Stability Information:** Refrigerated (preferred)/Ambient

**Forms**
1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

   - Informed Consent for Genetic Testing (T576)
   - Informed Consent for Genetic Testing-Spanish (T826)

2. **Molecular Genetics: Biochemical Disorders Patient Information** (T527) in Special Instructions

3. If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.

**Reject Due To**
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

**Specimen Stability Information**

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**Clinical and Interpretive**

**Clinical Information**

Congenital disorders of glycosylation (CDG), formerly known as carbohydrate-deficient glycoprotein syndrome, are a group of disorders affecting several steps of the pathway involved in the glycosylation of proteins. CDG are classified into 5 groups. CDG types I and II will have abnormal biochemical findings detected by serum transferrin and serum total N-glycan analyses (see CDG / Carbohydrate Deficient Transferrin for Congenital Disorders of Glycosylation, Serum). In the other 3 groups these analyses will be normal.

CDG type I disorders are characterized by defects in the assembly or transfer of the dolichol-linked glycan, while CDG type II includes defects of the glycan moiety processing.

The third group includes disorders of glycosylphosphatidylinositol (GPI) anchor protein glycosylation. If clinically
suspected, a flow cytometry analysis could facilitate the diagnostic workup.

The fourth group involves disorders of O-mannosylation, a process which takes place predominantly in the muscle and brain tissues.

The fifth group involves deglycosylation defects (eg, NAGLY1-CDG). The urine oligosaccharide profile by matrix-assisted laser desorption/ionization time-of-flight/time-of-flight mass spectrometer (MALDI-TOF/TOFMS) may be abnormal and facilitate the diagnostic workup.

CDG typically present as multisystemic disorders with a broad range of clinical features including developmental delay, hypotonia, abnormal magnetic resonance imaging findings, skin manifestations, and coagulopathy. There is considerable variation in the severity of this group of diseases, ranging from hydrops fetalis to a mild presentation in adults. Almost all types of CDG are autosomal recessive in inheritance, but some are X-linked.

The broad clinical spectrum and genetic heterogeneity of CDG make a comprehensive panel a helpful tool in establishing a diagnosis for patients with suggestive clinical features.


Custom Gene Panel:

Custom gene ordering allows the creation of a custom gene list to tailor testing to a patient's exact need. After selection of a specific disease state, the custom gene panel can be modified to add or remove genes. Through this option, single gene testing can be performed.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics and Genomics (ACMG) recommendations. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

Clinical Correlations:

An online research opportunity called GenomeConnect (genomeconnect.org), a project of ClinGen, is available for the recipient of this genetic test. This patient registry collects deidentified genetic and health information to advance the knowledge of genetic variants. Mayo Clinic is a collaborator of ClinGen. This may not be applicable for all tests.

Test results should be interpreted in context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

If testing was performed because of a family history of congenital disorders of glycosylation, it is often useful to first test an affected family member. Identification of a specific gene mutation in this family would lead to more informative testing of at risk individuals.

Technical Limitations:

Due to the limitations of next-generation sequencing, small deletions and insertions may not be detected by this test. If a diagnosis of one of the syndromes on this panel is still suspected, consider full gene sequencing using traditional
Sanger methods.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Bone marrow transplants from allogenic donors will interfere with testing. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

Evaluation Tools:

Multiple in-silico evaluation tools were used to assist in the interpretation of these results. These tools are updated regularly; therefore, changes to these algorithms may result in different predictions for a given alteration. Additionally, the predictability of these tools for the determination of pathogenicity is currently unvalidated.

Unless reported or predicted to cause disease, alterations found deep in the intron or alterations that do not result in an amino acid substitution are not reported.

Reclassification of Variants-Policy:

All detected alterations are evaluated according to ACMG recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. At this time, it is not standard practice for the laboratory to systematically rereview likely pathogenic alterations or variants of uncertain significance that have been previously detected and reported. The laboratory encourages health care providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time.

Clinical Reference


Performance

Method Description

Next-generation sequencing (NGS) and/or Sanger sequencing is performed to test for the presence of a mutation in the following genes: ALDOB, ALG1, ALG11, ALG12, ALG13, ALG14, ALG2, ALG3, ALG5, ALG6, ALG8, ALG9, ATP6VOA2, B3GALNT2, B3GALNT3, B3GLCT, B3GAT3, B4GAT1, B4GALNT1, B4GALNT2, B4GALNT7, C1GALT1C1, CHST14, CHST3, CHST6, CHST8, CHSY1, COG1, COG2, COG4, COG5, COG6, COG7, COG8, DDOST, DOLK, DPAGT1, DPM1, DPM2, DPM3, DSE, EOGT, EXT1, EXT2, FKRPI, FKTP, G6PC3, GALE, GALK1, GALNT3, GALT, GMF1, GFT1, GMPPA, GMPPB, GNE, GNPTAB, GOLM4, GORAB, ISPDL, LARGE1, LNF1, MAGT1, MAN1B1, MGAT1, MGAT2, MOGS, MPDU1, MPI, MV17, NGLY1, PAPSS2, PGAP2, PGAP3, PGM1, PGM2, PGM3, PIGA, PIGL, PIGM, PIGN, PIGO, PIGT, PIGW, PMM1, PMM2, PNPLA4, POFUT1, POGUT1, POMGNT1, POMK, POMT1, POMT2, PRKCSH, RFT1, RPN2, SEC23A, SEC23B, SEC63, SLC26A2, SLC35A1, SLC35A2, SLC35A3, SLC35C1, SLC35D1, SLC37A4, SRD5A3, SSR3, SSR4, ST3GAL3, ST3GAL5, STT3A, STT3B, STXBP1, SYP, TF, TMEM165, TMEM5, TRIP11, TSTA3, TUSC3, and XYL1.
There are regions of the gene ALG13 that cannot be effectively amplified and sequenced as a result of technical limitations of the assay. Regions of homology, high GC-rich content, and repetitive sequences may not provide accurate sequence. Therefore, all reported alterations detected by NGS are confirmed by an independent reference method when appropriate. However, this does not rule out the possibility of a false negative result in these regions.

Additionally, NGS is used to test for the presence of large deletions and/or duplications in all genes on the panel listed above, except B3GALT6, CHSY1 exon 1, and LFNG exon 1.

PCR and/or Sanger sequencing is used to confirm alterations detected by NGS when appropriate. (Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Performed weekly, Varies

Analytic Time

4 weeks

Maximum Laboratory Time

5 weeks

Specimen Retention Time

Whole Blood: 2 weeks (if available) Extracted DNA: 3 months

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

81404

81405 x4

81406 x7

81479

Fibroblast Culture for Genetic Test
Test Definition: CDGP
CDG Molecular Panel

88233 (if applicable)
88240 (if applicable)

LOINC® Information

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