Overview

Useful For

Confirmation of a diagnosis of Gaucher disease

Carrier screening in cases where there is a family history of Gaucher disease, but an affected individual is not available for testing or disease-causing alterations have not been identified

Genetics Test Information

Testing includes full gene sequencing of the *GBA* gene.

Risk alleles for Parkinson disease with no known beta-glucocerebrosidase enzyme reduction or Gaucher disease association will only be reported in patients over 18 years old unless otherwise requested.

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
FIBR	Fibroblast Culture	Yes	No
CRYOB	Cryopreserve for Biochem Studies	No	No

Testing Algorithm

If a skin biopsy is received, fibroblast culture and cryopreservation for biochemical studies will be added at an additional charge.

See Newborn Screen Follow-up for Gaucher Disease in Special Instructions.

For more information, see Newborn Screening Act Sheet Gaucher Disease: Decreased Acid Beta-Glucosidase in Special Instructions.

Special Instructions

- Molecular Genetics: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing
- Blood Spot Collection Card-Spanish Instructions
- Newborn Screening Act Sheet Gaucher Disease: Decreased Acid Beta-Glucosidase
- Newborn Screen Follow-up for Gaucher Disease
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions

Method Name

Polymerase Chain Reaction (PCR) followed by DNA Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This is not the preferred genetic test for carrier screening or diagnosis in individuals of Ashkenazi Jewish ancestry. For these situations, order GAUP / Gaucher Disease, Mutation Analysis, *GBA*, Varies.

For diagnostic testing in potentially affected individuals, enzyme testing should be performed prior to molecular genetic analysis. Order GBAW / Beta-Glucosidase, Leukocytes.

For ongoing therapeutic monitoring, order GPSY / Glucopsychosine, Blood Spot.

Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

Specimen Required

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.

Submit only 1 of the following specimens:

Specimen Type: Whole blood

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

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

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.

Specimen Volume: 4-mm punch

Specimen Stability Information: Refrigerated (preferred)/Ambient

Specimen Type: Blood spot

Supplies: Card - Blood Spot Collection (Filter Paper) (T493)

Container/Tube:

Preferred: Collection card (Whatman Protein Saver 903 Paper)

Acceptable: Ahlstrom 226 filter paper, or Blood Spot Collection Card

Specimen Volume:2 to 5 Blood Spots on collection card

Collection Instructions:

1. An alternative blood collection option for a patient older than 1 year is finger stick.

2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 3 hours.

3. Do not expose specimen to heat or direct sunlight.

4. Do not stack wet specimens.

5. Keep specimen dry

Specimen Stability Information: Ambient (preferred)/Refrigerated

Additional Information:

1. For collection instructions, see Blood Spot Collection Instructions in Special Instructions.

2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) in Special Instructions.

3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) in Special Instructions.

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: Congenital Inherited Diseases Patient Information (T521) in Special Instructions

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

Specimen Minimum Volume

Blood: 1 mL
Blood Spots: 5 punches, 3-mm diameter

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical and Interpretive

Clinical Information

Gaucher disease is a relatively rare lysosomal storage disorder resulting from a deficiency of acid beta-glucocerebrosidase. Reduced or absent activity of this enzyme results in accumulation of its substrate in lysosomes, interfering with cell function. There are 3 major types of Gaucher disease: nonneuropathic (type 1), acute neuropathic (type 2), and subacute neuropathic (type 3). In addition, there are 2 rare presentations of Gaucher disease: a perinatal lethal form associated with skin abnormalities and nonimmune hydrops fetalis, and a cardiovascular form presenting with calcification of the aortic and mitral valves, mild splenomegaly, and corneal opacities. Gaucher disease demonstrates large clinical variability, even within families.

Type 1 accounts for over 95% of all cases of Gaucher disease and is the presentation commonly found among Ashkenazi Jewish patients. The carrier rate of Gaucher disease in the Ashkenazi Jewish population is 1:18. There is a broad spectrum of disease in type 1 Gaucher disease, with some patients exhibiting severe symptoms and others very mild disease. Type 1 disease does not involve nervous system dysfunction; patients may display anemia, low blood platelet levels, massively enlarged livers and spleens, lung infiltration, and extensive skeletal disease. Type 2 is characterized by early-onset neurologic disease with rapid progression to death by 2 to 4 years of age. Type 3 may have early onset of symptoms, but generally a slower disease progression than type 2.

Alterations in the *GBA* gene cause the clinical manifestations of Gaucher disease. Over 250 variants have been reported to date. The N370S and L444P alterations have the highest prevalence in most populations. N370S is associated with type 1 Gaucher disease, and individuals with at least 1 copy of this alteration do not develop the primary neurologic disease seen in types 2 and 3. Conversely, L444P is associated with neurologic disease.

Alterations in the *GBA* gene have also been reported to cause an increased risk for Parkinson disease. Alterations associated with Parkinson disease, but not Gaucher disease, are not routinely reported for patients under the age of 18, but are available upon request.

For carrier screening of the general population, the recommended test is GAUP / Gaucher Disease, Mutation Analysis, *GBA*, Varies, which tests for the 8 most common *GBA* alterations. For diagnostic testing (ie, potentially

affected individuals), enzyme testing (GBAW / Beta-Glucosidase, Leukocytes) should be performed prior to variant analysis. In individuals with abnormal enzyme activity and 1 or no variants detected by a panel of common alterations, sequence analysis of the *GBA* gene should be utilized to detect private variants. Additionally, measurement of the glucopsychosine biomarker can aid in diagnosis and ongoing therapeutic monitoring (GPSY / Glucopsychosine, Blood Spot).

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.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

A small percentage of individuals who are carriers or have a diagnosis of Gaucher disease may have a variant that is not identified by this method (eg, large genomic deletions, promoter alterations). The absence of a variant, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of Gaucher disease. For carrier testing, it is important to first document the presence of a *GBA* gene variant in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified.

Rare alterations 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.

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

Clinical Reference

1. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015 May;17(5):405-424

2. Guggenbuhl P, Grosbois B, Chales G: Gaucher disease. Joint Bone Spine. 2008 Mar;75(2):116-124

3. Hruska KS, LaMarca ME, Scott CR, Sidransky E: Gaucher disease: mutation and polymorphism spectrum in the glucocerebrosidase gene (GBA). Hum Mutat. 2008 May;29(5):567-583

4. O'Regan G, deSouza RM, Balestrino R, Schapira AH: Glucocerebrosidase mutations in Parkinson disease. J Parkinsons Dis. 2017;7(3):411-422

Performance

Method Description

Bidirectional sequence analysis is performed to test for the presence of a variant in all coding regions and intron/exon boundaries of the *GBA* gene.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Varies

Report Available

14 to 20 days

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

81479-Unlisted molecular pathology procedure code

88233-Tissue culture, skin, or solid tissue biopsy (if appropriate)

88240-Cryopreservation (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
GBAZ	Gaucher Disease, Full Gene Analysis	94230-0

Result ID	Test Result Name	Result LOINC Value
53477	Result Summary	50397-9
53478	Result	82939-0
53479	Interpretation	69047-9
53480	Additional Information	48767-8
53481	Specimen	31208-2
53482	Source	31208-2
53483	Released By	18771-6