

Overview

Useful For

Diagnosis of GM1 gangliosidosis, Å Morquio syndrome B, and galactosialidosis in whole blood specimens

This test is **not useful** for carrier detection.

Genetics Test Information

Beta-galactosidase enzyme is deficient in the following conditions: GM1 gangliosidosis, Morquio syndrome B, and galactosialidosis.

Testing Algorithm

See [Lysosomal Storage Disorders Diagnostic Algorithm, Part 1](#) in Special Instructions.

Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Biochemical Genetics Patient Information](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)
- [Lysosomal Storage Disorders Diagnostic Algorithm, Part 1](#)

Method Name

Fluorometric Enzyme Assay

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Additional Testing Requirements

Careful review of clinical findings will help distinguish between GM1 gangliosidosis and Morquio syndrome type B. A diagnosis of galactosialidosis must be additionally demonstrated by a deficiency of neuraminidase (NEURF / Neuraminidase, Fibroblasts).

Necessary Information

Provide a reason for referral with each specimen.

Specimen Required

Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Yellow top (ACD)

Specimen Volume: 2 mL

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. [Biochemical Genetics Patient Information](#) (T602) 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

0.5 mL

Reject Due To

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

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	7 days	
	Refrigerated	7 days	

Clinical and Interpretive

Clinical Information

Beta-galactosidase is a lysosomal enzyme responsible for catalyzing the hydrolysis of gangliosides. Isolated deficiency of this enzyme is expressed clinically as 2 different autosomal recessive diseases, GM1 gangliosidosis and Morquio syndrome B (MPS IVB, Morquio B). Galactosialidosis (GS) is also associated with a deficiency of beta-galactosidase, but in conjunction with neuraminidase deficiency secondary to a defect in protective protein cathepsin A (PPCA). Enzymatic testing is not reliable for carrier detection of these conditions.

In GM1 gangliosidosis, reduced or absent beta-galactosidase activity leads to the accumulation of GM1 gangliosides, oligosaccharides, and keratan sulfate. The disorder can be classified into 3 subtypes that vary with regard to age of onset and clinical presentation. Type 1, or infantile onset, typically presents between birth and 6 months with a very rapid progression of hypotonia, dysostosis multiplex, hepatosplenomegaly, central nervous system degeneration, and death usually by 1 to 2 years. Type 2 is generally classified as late infantile or juvenile with onset between 7 months and 3 years presenting with developmental delays and a slower progression. Type 3 is an adult or chronic variant with onset between 3 and 30 years and is typically characterized by slowly progressive dementia with Parkinsonian features and dystonia. The incidence has been estimated to be 1 in 100,000 to 200,000 live births.

In MPS IVB, reduced or absent beta-galactosidase activity leads to the accumulation of glycosaminoglycans (GAG) in lysosomes and interferes with normal functioning of cells, tissues, and organs. MPS IVB typically manifests as a systemic skeletal disorder with variable severity ranging from early severe disease to a later onset attenuated form. Virtually all patients have dysostosis multiplex and short stature along with other symptoms that may include coarse facies, hepatosplenomegaly, hoarse voice, stiff joints, cardiac disease, but no neurological involvement.

Galactosialidosis is an autosomal recessive lysosomal storage disease caused by variants in the cathepsin A gene (CTSA) resulting in a combined deficiency of the enzymes beta-galactosidase and neuraminidase. The disorder can be classified into 3 subtypes that vary with regard to age of onset and clinical presentation. Typical clinical presentation includes coarse facial features, cherry-red spots, and skeletal dysplasia. The early infantile form is associated with fetal hydrops, visceromegaly, skeletal dysplasia, and early death. The late infantile form typically presents with short stature dysostosis multiplex, coarse facial features, corneal clouding, hepatosplenomegaly, and/or heart valve problems. The majority of individuals with the juvenile/adult form of GS are of Japanese ancestry and develop symptoms after 4 years of age, which include neurologic degeneration, ataxia, and angiokeratomas.

A diagnostic workup in an individual with GM1 gangliosidosis, MPS IVB, or GS typically demonstrates decreased beta-galactosidase enzyme activity in leukocytes or fibroblasts; however, additional testing and consideration of the patient's clinical findings are necessary to differentiate between these conditions. Follow-up testing may include LYSDU / Lysosomal Storage Disorders Screen, Urine, which analyzes urine mucopolysaccharides, oligosaccharides, ceramide trihexosides, and sulfatides. The Lysosomal storage disorders screen can help differentiate between the 3 conditions to guide physicians in choosing the best confirmatory molecular testing option.

Reference Values

> or =5.0 nmol/hour/mL

An interpretive report will be provided.

Interpretation

Results below 5.0 nmol/hour/mL in properly submitted specimens are consistent with beta-galactosidase deficiency (GM1 gangliosidosis, MPS IVB, or galactosialidosis). Further differentiation between GM1, MPS IVB, and galactosialidosis is dependent on the patient's clinical findings and results of additional biochemical testing.

Normal results (> or =5.0 nmol/h/mL) are not consistent with beta-galactosidase deficiency.

Cautions

This test cannot reliably determine carrier status.

This test does not differentiate between GM1 gangliosidosis, MPS IVB, and galactosialidosis.

Clinical Reference

1. Suzuki Y, Nanba E, Matsuda J, et al: Beta-Galactosidase Deficiency (Beta-Galactosidosis): GM1 Gangliosidosis and Morquio B Disease. In *The Online Metabolic and Molecular Bases of Inherited Disease*. Edited by D Valle, AL Beaudet, B Vogelstein, et al. New York, McGraw-Hill. Accessed 3/11/2019. Available at

<https://ommbid.mhmedical.com/content.aspx?sectionid=225547263&bookid=2709&Resultclick=2>

2. Chamoles NA, Blanco M, Gaggioli D, Casentini C: Hurler-like phenotype: enzymatic diagnosis in dried blood spots on filter paper. *Clin Chem* 2001 Dec;47(12):2098-2102

3. Regier DS, Tiftt CJ: GLB1-Related Disorders. In *GeneReviews*. Edited by RA Pagon, MP Adam, HH Ardinger, et al. Updated 29 Aug 2019. Accessed 1/30/2017. Available at www.ncbi.nlm.nih.gov/books/NBK164500/

4. d'Azzo A, Andria G, Bonten E, Annunziata I: Galactosialidosis. In *The Online Metabolic and Molecular Bases of Inherited Disease*. Edited by D Valle, AL Beaudet, B Vogelstein, et al. New York, McGraw-Hill. Accessed 3/11/2019. Available at <https://ommbid.mhmedical.com/content.aspx?sectionid=225547663&bookid=2709&Resultclick=2>

Performance

Method Description

Whole blood collected in ACD or EDTA anticoagulant tubes is spotted onto filter paper. A one-eighth inch (3-mm) disk is punched out of the dried blood spot (DBS) into a 96-well, round-bottom plate. Forty microliters of 50 mM cit-phos buffer as elution liquid and 20 microliters of 0.8 mM 4-methylumbelliferyl-beta-D-galactopyranoside in water as the substrate (60 microliters total volume + DBS). A blank is prepared using only elution liquid, substrate, and filter paper punches containing no blood (60 microliters total volume + blank punches). All patients, controls, and blank are set up in duplicate (2 punches total, 1 punch per well). After the incubation period (3 hours at 37 degrees C), all of the liquid from the plate is manually transferred to a 96-well, flat-bottom black plate. A calibration curve is prepared and analyzed on every plate to calculate enzyme activity results, based on fluorescence units in patient wells vs calibrators. The calibration is derived from 4-methylumbelliferone (4-MU) that is serially diluted manually in the plate with the highest calibrator being equivalent to an enzyme activity of 10.4 nmol/hour/mL. Two hundred microliters of stop buffer (150 mM EDTA, pH 11.4) is added to all wells (patients, QC, blanks, calibrators). The plate is then read on the spectrofluorometer. Fluorescence readings for duplicate wells are averaged, and the average fluorescence is used to calculate the enzyme activity result. (Civallero G, Michelin K, de Mari J, et al: Twelve different enzyme assays on dried-blood filter paper samples for detection of patients with selected inherited lysosomal storage diseases. Clin Chim Acta 2006;372:98-102; Cowan T, Pasquali M: Laboratory Investigations of Inborn Errors of Metabolism. In Pediatric Endocrinology and Inborn Errors of Metabolism. Second Edition. Edited by K Sarafoglou, GF Hoffman, KS Roth. 2017. pp 1139-1158)

PDF Report

No

Day(s) and Time(s) Test Performed

Varies

Analytic Time

8 days

Maximum Laboratory Time

15 days

Specimen Retention Time

1 year

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

82657

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
BGAW	Beta-Galactosidase, B	16454-1

Result ID	Test Result Name	Result LOINC Value
60987	Beta-Galactosidase, B	16454-1
34428	Interpretation	69047-9
34427	Reason for Referral	42349-1
34432	Reviewed By	18771-6