

Overview

Useful For

Aiding in the diagnosis of GM1 gangliosidosis, Morquio B disease, and galactosialidosis

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

Genetics Test Information

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

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.

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

NY State Available

Yes

Specimen

Specimen Type

Whole Blood ACD

Shipping Instructions

For optimal isolation of leukocytes, it is recommended the specimen arrive refrigerated within 72 hours of collection to be stabilized. Collect specimen Monday through Thursday only and not the day before a holiday. Specimen should be collected and packaged as close to shipping time as possible.

Necessary Information

Provide a reason for referral with each specimen.

Specimen Required

Container/Tube:

Preferred: Yellow top (ACD solution B)

Acceptable: Yellow top (ACD solution A)

Specimen Volume: 6 mL

Collection Instructions: Send in original tube. Do not transfer blood to other containers.

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

5 mL

Reject Due To

Gross hemolysis	Reject
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Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood ACD	Refrigerated (preferred)	72 hours	YELLOW TOP/ACD
	Ambient	72 hours	YELLOW TOP/ACD

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 diseases, GM1 gangliosidosis and Morquio syndrome B. Galactosialidosis is also associated with a deficiency of beta-galactosidase but in conjunction with neuraminidase secondary to a defect in protective protein cathepsin A (CTSA). Enzymatic testing is not reliable for carrier detection of these conditions.

GM1 gangliosidosis is an autosomal recessive lysosomal storage disorder caused by reduced or absent beta-galactosidase activity. Absent or reduced 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 and presenting with developmental delays or regression and a slower clinical course. 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 mucopolysaccharidosis type IVB (MPS IVB, Morquio B), 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 (LSD) 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 respect 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, 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.

Patients with mucopolipidosis II/III (I-cell disease) may also demonstrate deficiency of beta-galactosidase in leukocytes, in addition to deficiency of other hydrolases. I-cell disease is an autosomal recessive lysosomal storage disorder resulting in impaired transport and phosphorylation of newly synthesized lysosomal proteins to the lysosome due to deficiency of N-acetylglucosamine 1-phosphotransferase (GlcNAc). Characteristic clinical features include short stature, skeletal and cardiac abnormalities, and developmental delay. Measurement of beta-galactosidase activity is not the preferred diagnostic test for I-cell disease, but may be included in the testing strategy.

A diagnostic workup in an individual with GM1 gangliosidosis, Morquio B, or galactosialidosis 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, Random, Urine, which analyzes mucopolysaccharides, oligosaccharides, ceramide trihexosides, and sulfatides to help differentiate between the 3 conditions and guide physicians in choosing the best confirmatory molecular testing option.

Reference Values

> or =1.56 nmol/min/mg

Interpretation

Very-low enzyme activity levels are consistent with GM1 gangliosidosis and Morquio B disease. Clinical findings must be used to differentiate between those 2 diseases. The deficiency of beta-galactosidase combined with neuraminidase deficiency is characteristic of galactosialidosis.

Cautions

This test does not differentiate between GM1 gangliosidosis, Morquio B, 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 March 11, 2019, Available at <https://ommbid.mhmedical.com/content.aspx?sectionid=225547263&bookid=2709&Resultclick=2>
2. 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, 2014, Accessed March 11, 2019, Available at <https://ommbid.mhmedical.com/content.aspx?sectionid=225547663&bookid=2709&Resultclick=2>

3. Brunetti-Pierri N, Scaglia F: GM1 gangliosidosis: review of clinical, molecular, and therapeutic aspects. *Mol Genet Metab* 2008 Aug;94(4):391-396

4. Caciotti A, Garman SC, Rivera-Colon Y, et al: GM1 gangliosidosis and Morquio B disease: an update on genetic alterations and clinical findings. *Biochim Biophys Acta* 2011 Jul;1812(7):782-790

Performance

Method Description

The deficiency of beta-galactosidase is demonstrable using the artificial substrate 4-methylumbelliferyl-beta-D-galactopyranoside. The enzyme hydrolyzes the artificial substrate to produce 4-methylumbelliferone, which is measured fluorometrically. (Modified from Ho MW, O'Brien JS: Differential effect of chloride ions on galactosidase isoenzymes: a method for separate assay. *Clin Chim Acta* 1971 May;32[3]:443-450; Gehler J, Cantz M, Tolksdorf M, et al: Mucopolysaccharidosis. VII. Beta-glucuronidase deficiency. *Humangenetik* 1974 July 15;23[2]:149-158; 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

Specimens are processed Monday through Sunday.

Assay is performed: Varies

Analytic Time

8 days

Maximum Laboratory Time

15 days

Specimen Retention Time

WBC homogenate stored 1 month

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
BGA	Beta-Galactosidase, Leukocytes	24061-4

Result ID	Test Result Name	Result LOINC Value
8486	Beta-Galactosidase, Leukocytes	24061-4
34979	Interpretation (BGA)	59462-2
34907	Reviewed By	18771-6