MAYO CLINIC LABORATORIES

Test Definition: BGA

Beta-Galactosidase, Leukocytes

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

For information see Lysosomal Disorders Diagnostic Algorithm, Part 1.

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)
- Lysosomal 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 6 days of collection to be stabilized. Pre-analytical processing is performed Monday through Friday and Sunday. This test may be canceled if specimens are outside of stability when processing occurs. Collect and package specimens for arrival on days when processing is performed.

Necessary Information

Provide a reason for testing 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 specimen in original tube. **Do not aliquot**.

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:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Biochemical Genetics Patient Information (T602)
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

5 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood ACD	Refrigerated (preferred)	6 days	YELLOW TOP/ACD
	Ambient	6 days	YELLOW TOP/ACD

Clinical & Interpretive

Clinical Information

Beta-galactosidase is a lysosomal enzyme responsible for catalyzing the hydrolysis of gangliosides. Isolated deficiency of this enzyme can be expressed clinically as 2 different diseases, GM1 gangliosidosis (GM1) and Morquio syndrome B (MPS IVB: mucopolysaccharidosis IVB), or in some patients as a disease that combines the skeletal features of MPS IVB and neurologic features of GM1. 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 autosomal recessive and absent or reduced beta-galactosidase enzyme activity leads to the accumulation of GM1 gangliosides, oligosaccharides, and keratan sulfate. The disorder can be classified into 3 subtypes that vary with respect 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 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.

In MPS IVB, reduced or absent beta-galactosidase activity leads to the accumulation of glycosaminoglycans (GAG), specifically keratan sulfate, in cells, tissues, and organs interfering with their normal function. 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, and cardiac disease but no neurological involvement.

Galactosialidosis (GS) is an autosomal recessive lysosomal storage disease caused by variants in *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 mucolipidosis 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, 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 LSDS / 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, which may include LSDGP / Lysosomal Storage Disease Gene Panel, Varies.

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 gangliosiosis, Morquio B, and galactosialidosis.

Clinical Reference

1. Suzuki Y, Nanba E, Matsuda J, Higaki K, Oshima A. Beta-galactosidase deficiency (beta-galactosidosis): GM1 gangliosidosis and Morquio B disease. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed June 9, 2025. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225547263
2. d'Azzo A, Andria G, Bonten E, Annunziata I. Galactosialidosis. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, et al, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed June 9, 2025. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225547663
3. 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;1812(7):782-790. doi:10.1016/j.bbadis.2011.03.018
4. Kingma SDK, Ceulemans B, Kenis S, Jonckheere AI. Are GMI gangliosidosis and Morquio type B two different disorders or part of one phenotypic spectrum?. JIMD Rep. 2021;59(1):90-103. doi:10.1002/jmd2.12204

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.(Ho MW, O'Brien JS. Differential effect of chloride ions on galactosidase isoenzymes: a method for separate assay. Clin Chim Acta. 1971;32[3]:443-450; Gehler J, Cantz M, Tolksdorf M, Spranger J, Gilbert E, Drube H. Mucopolysaccharidosis. VII. Beta-glucuronidase deficiency. Humangenetik. 1974;23[2]:149-158. doi:10.1007/BF00282212; Cowan T, Pasquali M. Laboratory Investigations of Inborn Errors of Metabolism. In: Sarafoglou K, Hoffman GF, Roth KS, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. 2nd ed. McGraw-Hill; 2017:1139-1158)

PDF Report

No

Day(s) Performed

Preanalytical processing: Monday through Friday, Sunday
Assay performed: Tuesday

Report Available

2 to 8 days

Specimen Retention Time

WBC homogenate: 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

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
34907	Reviewed By	18771-6
34979	Interpretation (BGA)	59462-2