MAYO CLINIC LABORATORIES

Test Definition: BGABS

Beta-Galactosidase, Blood Spot

Overview

Useful For

Diagnosis of beta-galactosidase deficiency (GM1 gangliosidosis, Morquio syndrome B, and galactosialidosis) using blood spot 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

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Lysosomal Storage Disorders Diagnostic Algorithm, Part 1
- Blood Spot Collection Instructions

Method Name

Fluorometric Enzyme Assay

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Necessary Information

Provide a reason for testing with each specimen.

Specimen Required

Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Blood spot collection card (T493)

Acceptable: PerkinElmer 226 (formerly Ahlstrom 226) filter paper and Whatman Protein Saver 903 paper
Specimen Volume: 2 blood spots
Collection Instructions:
1. An alternative blood collection option for a patient 1 year of age or older is a fingerstick. For infants younger than 1 year, a heel stick should be used. See Dried Blood Spot Collection Tutorial for how to collect blood spots via fingerstick.
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.
Additional Information:
1. For collection instructions, see Blood Spot Collection Instructions
2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800)

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

1 Blood spot

Reject Due To

Shows serum rings Multiple layers	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	28 days	FILTER PAPER
	Frozen	90 days	FILTER PAPER
	Refrigerated	90 days	FILTER PAPER

Clinical & Interpretive

Clinical Information

Beta-galactosidase is a lysosomal enzyme responsible for catalyzing the breakdown of gangliosides. The deficiency of this enzyme can be seen in the following conditions: GM1 gangliosidosis, Morquio syndrome B, and galactosialidosis.

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 respect to age of onset and clinical presentation. Type 1, or infantile onset, typically presents between birth and 6 months of age with a very rapid progression of hypotonia, dysostosis multiplex, hepatosplenomegaly, central nervous system degeneration, and death usually by 1 to 2 years of age. Type 2 is generally classified as late infantile or juvenile with onset between 7 months and 3 years of age, presenting with developmental delays, and a having a slower progression. Type 3 is an adult or chronic variant with onset between 3 and 30 years of age 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.

Mucopolysaccharidosis type IVB (MPS IVB or Morquio syndrome B) is an autosomal recessive lysosomal storage disorder caused by reduced or absent beta-galactosidase activity leading to the accumulation of glycosaminoglycans, particularly keratan sulfate, 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 (GS) is an autosomal recessive lysosomal storage disease associated with a combined deficiency of beta-galactosidase and neuraminidase secondary to a defect in the cathepsin A protein. The disorder can be classified into 3 subtypes that vary with respect to age of onset and clinical presentation. Typical clinical presentation is coarse facial features, cherry-red spots, and skeletal dysplasia. The early infantile form is associated with fetal hydrops, skeletal dysplasia, and early death, while the late infantile form is characterized by short stature, dysostosis multiplex, coarse facial features, corneal clouding, hepatosplenomegaly, and heart valve problems. Individuals of Japanese ancestry makeup the majority of patients with the juvenile/adult form of GS and typically develop symptoms after 4 years of age. These include neurologic degeneration, ataxia, and angiokeratomas.

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 LSDS / Lysosomal Storage Disorders Screen, Random, Urine, which analyzes urine mucopolysaccharides, oligosaccharides, ceramide trihexosides, and sulfatides. The LSDS test can help differentiate between the 3 conditions to guide physicians in choosing the best confirmatory molecular testing option. See Lysosomal Storage Disorders Diagnostic Algorithm, Part 1

Reference Values

> or =5.0 nmol/hour/mL
An interpretive report will be provided.

Interpretation

Properly submitted specimens with results less than 5.0 nmol/h/mL are consistent with beta-galactosidase deficiency (GM1 gangliosidosis, Morquio syndrome B, or galactosialidosis). Further differentiation between GM1, Morquio syndrome B, and galactosialidosis is dependent on the patient's clinical findings and results of additional biochemical testing.

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

Cautions

This test cannot reliably determine carrier status.

This test does not differentiate between GM1 gangliosidosis, Morquio syndrome 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: Valle D, Antonarakis S, Ballabio A, Beaudet A, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed January 5, 2022. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225547263
2. Regier DS, Tifft CJ: GLB1-related disorders. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews. Updated 29 Aug 2019. Accessed January 5, 2022. Available at www.ncbi.nlm.nih.gov/books/NBK164500/
3. d'Azzo A, Andria G, Bonten E, Annunziata I: Galactosialidosis. In: Valle D, Antonarakis S, Ballabio A, Beaudet A, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed January 5, 2022. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225547663
4. Arash-Kaps L, Komlosi K, Seegraber M, et.at: The clinical and molecular spectrum of GM1 gangliosidosis. Pediatr. 2019 Dec;215:152-157.e3. doi: 10.1016/j.jpeds.2019.08.016

Performance

Method Description

A one-eighth inch (3-mm) disk is punched out of the dried blood spot into a 96-well, round-bottom plate with citrate-phosphate buffer as elution liquid and 4-methylumbelliferyl-beta-D-galactopyranoside in water as the substrate. A blank is prepared using only elution liquid, substrate, and filter paper punches containing no blood. All patients, controls, and blank are set up in duplicate. After the incubation period, the liquid from the plate is 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. Stop buffer is added to all wells (patients, quality controls, 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 Oct;372(1-2):98-102; 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

Wednesday

Report Available
8 to 15 days

Specimen Retention Time
1 year

Performing Laboratory Location
Rochester

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. This test 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
BGABS	Beta-Galactosidase, BS	55916-1

Result ID	Test Result Name	Result LOINC® Value
60986	Beta-Galactosidase, BS	55916-1
34429	Reason for Referral	42349-1
34431	Reviewed By	18771-6
34430	Interpretation	69047-9