Test Definition: MPS4W

Mucopolysaccharidosis IV Enzyme Panel, Leukocytes

Overview

Useful For

Supporting the biochemical diagnosis of mucopolysaccharidosis type IVA and IVB in whole blood specimens

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

Genetics Test Information

This test provides diagnostic testing for individuals with clinical signs and symptoms suspicious for mucopolysaccharidosis type IVA or IVB. If an enzyme deficiency is detected by this test, additional biochemical or molecular testing is required to confirm a diagnosis.

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

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

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

1. Patient's age is required.

2. Reason for testing is required.

Specimen Required

Container/Tube:
Preferred: Yellow top (ACD solution B)
Acceptable: Yellow top (ACD solution A) or lavender top (EDTA)
Specimen Volume: 6 mL
Collection Instructions: Send whole blood 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	
	Ambient	6 days	

Clinical & Interpretive

Clinical Information

Mucopolysaccharidosis IVA, (MPS IVA; Morquio A syndrome) is caused by reduced or absent *N*-acetylgalactosamine-6-sulfate sulfatase (GALNS) enzyme activity. The glycosaminoglycans (GAGs), keratan and chondroitin sulfate, accumulate in multiple tissues but mainly bone, cartilage, heart valves, and cornea. Clinical features and severity of symptoms of MPS IVA are widely variable affecting multiple body systems, in particular the skeletal system. Other clinical features may include short stature, dental anomalies, corneal clouding, respiratory insufficiency, and cardiac disease. Cognitive abilities are generally unaffected.

Mucopolysaccharidosis type IVB (MPS IVB or Morquio syndrome B) is caused by reduced or absent beta-galactosidase activity leading to the accumulation of GAGs, particularly keratan sulfate. 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.

GM1 gangliosidosis is also caused by reduced or absent beta-galactosidase activity, however the clinical features include neurological involvement in addition to the skeletal and other systemic findings associated with MPS IVB. The disorder can be classified into 3 subtypes that vary with respect to age of onset and clinical presentation.

Galactosialidosis is 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 includes 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.

A diagnostic workup for MPS also includes glycosaminoglycan determination in urine (MPSQU / Mucopolysaccharides Quantitative, Random, Urine) or blood (MPSBS / Mucopolysaccharidosis, Blood Spot or MPSER / Mucopolysaccharidosis Quantitative, Serum) and molecular genetic analysis of the relevant gene. For MPS IVA, molecular analysis of the *GALNS* gene (CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies; specify Gene List ID: IEMCP-JUFPRX) and for MPS IVB and GM1 gangliosidosis, molecular analysis of the *GLB1* gene (CGPH; specify Gene List ID: IEMCP-D5F3YS) allows for detection of disease-causing variants in affected patients and subsequent carrier detection in relatives.

A diagnostic workup for galactosialidosis traditionally includes determination of beta-galactosidase enzyme activity in leukocytes or fibroblasts and molecular analysis of *CTSA* (CGPH; specify Gene List ID: IEMCP-D1J7U5). Analysis of urine mucopolysaccharides, oligosaccharides, ceramide trihexoside, and sulfatides (LSDS / Lysosomal Disorders Screen, Random, Urine) can help differentiate between galactosialidosis, MPS IVA, and MPS IVB/GM1 to guide physicians in choosing the best confirmatory molecular testing option. See Lysosomal Disorders Diagnostic Algorithm, Part 1.

Reference Values

N-acetylgalactosamine-6-sulfatase: >1.60 nmol/h/mg protein
Beta-galactosidase: >0.28 nmol/h/mg protein

An interpretive report will be provided.

Interpretation

Abnormal results are not sufficient to establish a diagnosis of a particular disease. To verify a preliminary diagnosis based on this assay, additional biochemical or molecular genetic analyses are required.

When abnormal results are detected, a detailed interpretation is given, including an overview of the results and of their significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional biochemical testing, and in vitro, confirmatory studies (enzyme assay, molecular analysis), and a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

Cautions

Beta-galactosidase is also reduced in patients with galactosialidosis. Those patients will also demonstrate deficient activity of neuraminidase which is not evaluated on this panel. If there is clinical suspicion of galactosialidosis, please

order follow up testing to include test OLIGU / Oligosaccharide Screen, Random, Urine

Individuals with pseudodeficiency alleles can show reduced enzyme activity.

Carrier status (heterozygosity) for these conditions cannot be reliably detected.

Enzyme levels may be normal in individuals receiving enzyme replacement therapy or who have undergone hematopoietic stem cell transplant.

Clinical Reference

1. Neufeld EF, Muenzer J. The mucopolysaccharidoses. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; Accessed September 11, 2025. https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225544161
2. Hopwood JJ, Ballabio A. Multiple sulfatase deficiency and the nature of the sulfatase family. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; Accessed September 11, 2025. https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225546905
3. Regier DS, Oetgen M, Tanpaiboon P. Mucopolysaccharidosis Type IVA. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 1993-2025. Updated June 11, 2021.Accessed September 11, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK148668/

Performance

Method Description

Leukocytes are incubated with four cocktail mixes in 96-well plates: 1) substrate and internal standard (IS) for iduronate 2-sulfatase, heparan N-sulfatase, alpha-N-acetylglucosaminidase, N-acetylgalactosamine-sulfate, beta-galactosidase, arylsulfatase B, beta-glucuronidase, and tripeptidyl peptidase 1; 2) substrate and IS for acetyl-CoA:alpha-glucosaminide N-acetyltransferase; 3) substrate and IS for N-acetylglucosamine-6-sulfatase; and 4) substrate and IS for palmitoyl-protein thioesterase 1. Following overnight incubation, the plates are combined and purified by liquid-liquid extraction. The extracts are evaporated, reconstituted with mobile phase, and analyzed by tandem mass spectrometry.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

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

Report Available

3 to 9 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
MPS4W	MPS IV Panel, WBC	104072-4

Result ID	Test Result Name	Result LOINC® Value
BG769	Reason for Referral	42349-1
618462	N-acetylgalactosamine-6-sulfatase	24096-0
618463	Beta-galactosidase	24061-4
618464	Interpretation	59462-2
618461	Reviewed By	18771-6