MAYO CLINIC LABORATORIES

Test Definition: MPS1Z

Hurler Syndrome, Full Gene Analysis, Varies

Overview

Useful For

Identifying variants within the *IDUA* gene

Confirmation of a diagnosis of mucopolysaccharidosis type I (MPS-I)

Carrier testing when there is a family history of MPS- I, but disease-causing variants have not been previously identified

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No

Genetics Test Information

Testing includes full gene sequencing of the *IDUA* gene.

Testing Algorithm

For skin biopsy or cultured fibroblast specimens, fibroblast culture testing will be performed at an additional charge. If viable cells are not obtained, the client will be notified.

The following algorithms are available:
-Lysosomal Disorders Diagnostic Algorithm, Part 1
-Newborn Screen Follow-up for Mucopolysaccharidosis Type I

If the patient has abnormal newborn screening result for mucopolysaccharidosis type I, immediate action should be taken. Refer to the appropriate American College of Medical Genetics and Genomics Newborn Screening ACT Sheet.(1)

Special Instructions

- Molecular Genetics: Biochemical Disorders Patient Information
- Informed Consent for Genetic Testing
- Blood Spot Collection Card-Spanish Instructions
- Newborn Screen Follow-up for Mucopolysaccharidosis Type I
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Lysosomal Disorders Diagnostic Algorithm, Part 1
- Blood Spot Collection Instructions

Method Name

Polymerase Chain Reaction (PCR) followed by DNA Sequencing

NY State Available

Yes

Specimen

Specimen Type
Varies

Ordering Guidance
First-tier testing for mucopolysaccharidosis type I is available. Order either IDUAW / Alpha-L-Iduronidase, Leukocytes or PLSD / Lysosomal and Peroxisomal Storage Disorders Screen, Blood Spot. Be aware that these tests are not reliable for carrier testing.

For diagnostic testing or monitoring ongoing therapy, order MPSBS / Mucopolysaccharidosis, Blood Spot.

Shipping Instructions
Specimen preferred to arrive within 96 hours of collection.

Specimen Required
Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Submit only 1 of the following specimens:

Preferred:
Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)
Acceptable: Any anticoagulant
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**
Specimen Stability Information: Ambient (preferred)/Refrigerated

Specimen Type: Cultured fibroblasts
Container/Tube: T-75 or T-25 flask
Specimen Volume: 1 Full T-75 flask or 2 full T-25 flasks
Specimen Stability Information: Ambient (preferred)/Refrigerated <24 hours
Additional Information: A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks is required to culture fibroblasts before genetic testing can occur.

Specimen Type: Skin biopsy
Supplies: Fibroblast Biopsy Transport Media (T115)
Container/Tube: Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The

solution should be supplemented with 1% penicillin and streptomycin.
Specimen Volume: 4-mm punch
Specimen Stability Information: Refrigerated (preferred)/Ambient
Additional Information: A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks is required to culture fibroblasts before genetic testing can occur.

Acceptable:
Specimen Type: Blood spot
Supplies: Card - Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Collection card (Whatman Protein Saver 903 Paper)
Acceptable: PerkinElmer 226 (formerly Ahlstrom 226) filter paper, or blood spot collection card
Specimen Volume: 2 to 5 Blood spots
Collection Instructions:
1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect Dried Blood Spot Samples.
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.
Specimen Stability Information: Ambient (preferred)/Refrigerated
Additional Information:
1. Due to lower concentration of DNA yielded from blood spot, it is possible that additional specimen may be required to complete testing.
2. For collection instructions, see Blood Spot Collection Instructions
3. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
4. 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. Molecular Genetics: Biochemical Disorders Patient Information (T527)
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

Blood: 1 mL
Blood spots: 5, 3-mm diameter

Reject Due To

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

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

Mucopolysaccharidosis type I (MPS-I) can be categorized into 3 syndromes, Hurler syndrome, Scheie syndrome, and Hurler-Scheie syndrome. MPS-I, inherited in an autosomal recessive manner, is caused by variants in the *IDUA* gene. Furthermore, MPS-I is characterized by reduced or absent activity of the alpha-L-iduronidase enzyme.

Hurler syndrome (severe MPS-I) has early onset and consists of skeletal deformities, coarse facial features, corneal clouding, hepatosplenomegaly, cardiac involvement, hearing loss, and respiratory tract infections. Developmental delay is noticed as early as 12 months with death occurring usually before 10 years of age.

Hurler-Scheie syndrome and Scheie syndrome (attenuated MPS-I) have onset between 3 to 10 years of age and consist of corneal clouding, cardiac involvement, moderate-to-severe hearing loss, and progressive pulmonary disease. Typically skeletal and joint involvement is the most significant source of discomfort for attenuated MPS-I. Intellect with attenuated MPS-I is typically normal or nearly normal.

The *IDUA* gene is located on chromosome 4 and has 14 exons. *IDUA* is the only known gene to be associated with MPS-I, and the 3 syndromes appear to be caused by different combinations of variants.

The recommended first-tier test for MPS-I is biochemical testing that measures alpha-L-iduronidase enzyme activity in blood: IDUAW / Alpha-L-Iduronidase, Leukocytes or PLSD / Lysosomal and Peroxisomal Storage Disorders Screen, Blood Spot. Individuals with decreased or absent enzyme activity are more likely to have 2 identifiable variants in the *IDUA* gene by molecular genetic testing. However, enzymatic testing is not reliable to detect carriers. Additionally, measurement of mucopolysaccharides in blood can aid in diagnosis and ongoing therapeutic monitoring (MPSBS / Mucopolysaccharidosis, Blood Spot).

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics and Genomics (ACMG) recommendations.(2) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

A small percentage of individuals who are carriers or have a diagnosis of mucopolysaccharidosis type I (MPS-I) may have a variant that is not identified by this method (eg, large genomic deletions, promoter alterations). The absence of a variant, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of MPS-I. The preferred approach to carrier testing is to first document the presence of an *IDUA* gene variant in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified.

Rare alterations exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in the interpretation of results may occur if information given is inaccurate or incomplete.

Clinical Reference

1. Newborn Screening ACT Sheet [alpha-L-iduronidase deficiency with or without glycosaminoglycan (GAG) accumulation] Mucopolysaccharidosis Type I (MPS I). American College of Medical Genetics and Genomics; 2023. Updated November 2023. Accessed June 10, 2024. Available at www.acmg.net/PDFLibrary/MPSI-ACT-Sheet.pdf
2. Muenzer J, Wraith JE, Clarke LA, International Consensus Panel on Management and Treatment of Mucopolysaccharidosis I: Mucopolysaccharidosis I: management and treatment guidelines. Pediatrics. 2009 Jan;123(1):19-29
3. Scott HS, Bunge S, Gal A, Clarke LA, Morris CP, Hopwood JJ: Molecular genetics of mucopolysaccharidosis type I: diagnostic, clinical, and biological implications. Hum Mutat. 1995;6(4):288-302
4. Terlato NJ, Cox GF: Can mucopolysaccharidosis type I disease severity be predicted based on a patient's genotype? A comprehensive review of the literature. Genet Med. 2003 Jul-Aug;5(4):286-294
5. Vijay S, Wraith JE: Clinical presentation and follow-up of patients with the attenuated phenotype of mucopolysaccharidosis type I. Acta Paediatr. 2005 Jul;94(7):872-877

Performance

Method Description

Bi-directional sequence analysis is performed to test for the presence of a variant in all coding regions and intron/exon boundaries of the *IDUA* gene.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Varies

Report Available

14 to 20 days

Specimen Retention Time

Whole Blood: 2 weeks (if available); Extracted DNA: 3 months

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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81406 IDUA (iduronidase, alpha-L-) (eg, mucopolysaccharidosis type I), full gene sequence
88233-Tissue culture, skin or solid tissue biopsy (if appropriate)
88240-Cryopreservation (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MPS1Z	Hurler Syndrome, Full Gene Analysis	76028-0

Result ID	Test Result Name	Result LOINC® Value
53950	Result Summary	50397-9
53951	Result	82939-0
53952	Interpretation	69047-9
53953	Additional Information	48767-8
53954	Specimen	31208-2
53955	Source	31208-2
53956	Released By	18771-6