MAYO CLINIC LABORATORIES

Test Definition: MPS2Z

Hunter Syndrome, Full Gene Analysis, Varies

Overview

Useful For

Confirmation of a diagnosis of mucopolysaccharidosis type II (Hunter syndrome)

Carrier testing when there is a family history of mucopolysaccharidosis type II (Hunter syndrome), 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 *IDS* 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.

For more information see the following:
-Lysosomal Disorders Diagnostic Algorithm, Part 1
-Newborn Screening Follow up for Mucopolysaccharidosis type II

Special Instructions

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

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 II is available. Order either I2SW / Iduronate-2-Sulfatase, Whole Blood or I2SBS / Iduronate-2-Sulfatase, 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.

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.
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 in Special Instructions:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Molecular Genetics: Biochemical Disorders Patient Information (T527) in Special Instructions
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 punches, 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 II (MPS-II), also known as Hunter syndrome, is a rare X-linked condition caused by variants in the *IDS* gene. MPS-II is characterized by reduced or absent activity of the iduronate 2-sulfatase enzyme.

The clinical features and severity of symptoms of MPS-II are widely variable, ranging from severe disease to an attenuated form, which generally presents at a later onset with a milder clinical presentation. In general, symptoms may include coarse facies, short stature, enlarged liver and spleen, joint contractures, cardiac disease, and profound neurologic involvement leading to developmental delays and regression. Female carriers are usually asymptomatic.

The *IDS* gene is located on the X chromosome and has 9 exons and is the only known gene to be associated with MPS-II. The recommended first-tier test for mucopolysaccharidosis type II is biochemical testing that measures iduronate 2-sulfatase enzyme activity in blood: I2SW / Iduronate-2-Sulfatase, Whole Blood or blood spots: I2SBS / Iduronate-2-Sulfatase, Blood Spot.

Individuals with decreased or absent enzyme activity are more likely to have a variant in the *IDS* gene identifiable 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.(1) 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 II (MPS-II) 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-II. The preferred approach to carrier testing is to first document the presence of an *IDS* 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. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015 May;17(5):405-424
2. Martin R, Beck M, Eng C, et al: Recognition and diagnosis of mucopolysaccharidosis II (Hunter syndrome). Pediatrics. 2008;121(2):e377-386

3. Wraith JE, Scarpa M, Beck M, et al: Mucopolysaccharidosis type II (Hunter syndrome): a clinical review and recommendations for treatment in the era of enzyme replacement therapy. Eur J Pediatr. 2008;167(3):267-277

Performance

Method Description

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

In addition, a PCR-based assay is utilized to examine DNA for the presence of rearrangements between the *IDS* gene and pseudogene, *IDSP1*.(Lagerstedt K, Karsten SL, Carlberg BM, et al: Double-strand breaks may initiate the inversion mutation causing the Hunter syndrome. Hum Mol Genet. 1997;6[4]:627-633)

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

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

81405-*IDS* (iduronate 2-sulfatase) (eg, mucopolysacchridosis, type II), 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
MPS2Z	Hunter Syndrome, Full Gene Analysis	76030-6

Result ID	Test Result Name	Result LOINC® Value
53526	Result Summary	50397-9
53527	Result	82939-0
53528	Interpretation	69047-9
53529	Additional Information	48767-8
53530	Specimen	31208-2
53531	Source	31208-2
53532	Released By	18771-6