MAYO CLINIC LABORATORIES

Test Definition: MPS2Z

Hunter Syndrome, Full Gene Analysis

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

Genetics Test Information

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

Testing Algorithm

If a skin biopsy is received, fibroblast culture and cryopreservation for biochemical studies will be performed at an additional charge.

See Lysosomal Storage Disorders Diagnostic Algorithm, Part 1 in Special Instructions.

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 Storage Disorders Diagnostic Algorithm, Part 1
- Blood Spot Collection Instructions

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
FIBR	Fibroblast Culture	Yes	No
CRYOB	Cryopreserve for Biochem Studies	No	No

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 specimen in original tube.

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

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

Specimen Type: Blood spot

Supplies: Card - Blood Spot Collection (Filter Paper) (T493)

Container/Tube:

Preferred: Collection card (Whatman Protein Saver 903 Paper)

Acceptable: Ahlstrom 226 filter paper, or Blood Spot Collection Card

Specimen Volume: 2 to 5 Blood Spots on collection card

Collection Instructions:

1. An alternative blood collection option for a patient older than 1 year of age is finger stick.

2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 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 in Special Instructions.

2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) in Special Instructions.

3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) in Special Instructions.

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

Reject Due To

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

Specimen Minimum Volume

Blood: 1 mL

Blood Spots: 5 punches, 3-mm diameter

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies (preferred)		

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

Specimen Retention Time

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

Performing Laboratory Location

Rochester

Fees & Codes

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

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	Reporting Name	LOINC®
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