Overview

Useful For

Identifying variants within the *SGSH, NAGLU, HGSNAT,* and *GNS* genes

Confirmation of a diagnosis of mucopolysaccharidosis type III, also known as Sanfilippo syndrome

Highlights

Testing can be used to confirm a diagnosis of mucopolysaccharidosis type III, also known as Sanfilippo syndrome

Testing includes sequencing of the *SGSH, NAGLU, HGSNAT,* and *GNS* genes.

Reflex Tests

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

Testing Algorithm

If a skin biopsy is received, fibroblast culture 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

Method Name

Polymerase Chain Reaction (PCR) followed by DNA Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Advisory Information

For aid in diagnostic testing or monitoring ongoing therapy, order either MPSBS / Mucopolysaccharidosis, Blood Spot or MPSQU / Mucopolysaccharides Quantitative, Random, Urine.

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 specimenin 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 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

Acceptable:

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

Specimen Type: Blood spot

Container/Tube:

Preferred: Blood Spot Collection Card

Acceptable: Whatman Protein Saver 903 Paper

Specimen Volume: 5 blood spots

Collection Instructions:

1. Let blood dry on the filter paper at ambient temperature in a horizontal position for 3 hours.

2. Do not expose specimen to heat or direct sunlight.

3. Do not stack wet specimens.

4. Keep specimen dry.

Specimen Stability Information: Ambient (preferred)/Refrigerated

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

3. If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.

Specimen Minimum Volume

Blood: 1 mL
Blood Spots: 3

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 and Interpretive

Clinical Information

Mucopolysaccharidosis type III (MPS-III), also known as Sanfilippo syndrome, is an autosomal recessive condition that consists of 4 different types (A, B, C, and D). Each type of MPS-III results from the absence of 1 of 4 lysosomal enzymes, which leads to the accumulation of heparan sulfate in various tissues.

Sanfilippo syndrome A is caused by variants in *SGSH* and is characterized by reduced or absent activity of the sulfamidase enzyme. Sanfilippo syndrome B is caused by variants in *NAGLU* and is characterized by reduced or absent activity of the N-acetyl-alpha-D-glucosaminidase. Sanfilippo syndrome C is caused by variants in *HGSNAT* and is characterized by reduced or absent activity of the acetyl-CoA:alpha-glucosaminide N-acetyltransferase enzyme. Sanfilippo syndrome D is caused by variants in *GNS* and is characterized by reduced or absent activity of the N-acetylglucosamine-6-sulfatase enzyme.

Sanfilippo syndrome presents with a spectrum of central nervous system degeneration and physical disease. Onset of clinical features, most commonly behavioral problems and delayed development, usually occurs between 2 and 6 years in a child who previously appeared normal. Severe neurologic degeneration occurs in most patients by 6 to 10 years, accompanied by a rapid deterioration of social and adaptive skills.

Measurement of mucopolysaccharides in blood or urine can aid in diagnosis and ongoing therapeutic monitoring (MPSBS / Mucopolysaccharidosis, Blood Spot or MPSQU / Mucopolysaccharides Quantitative, Random, Urine).

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations will be evaluated according to American College of Medical Genetics and Genomics (ACMG) recommendations.(1) Variants will be 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 III (MPS-III) 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-III.

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

Rare polymorphisms 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 our 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;17(5):405-424

2. Ruijter GJ, Valstar MJ, van de Kamp JM, et al: Clinical and genetic spectrum of Sanfilippo type C (MPS IIIC) disease in The Netherlands. Mol Genet Metab. 2008;93(2):104-111

3. Valstar MJ, Ruijter GJ, van Diggelen OP, et al: Sanfilippo syndrome: a mini-review. J Inherit Metab Dis. 2008;31(2):240-252

4. Yogalingam G, Hopwood JJ: Molecular genetics of mucopolysaccharidosis type IIIA and IIIB: Diagnostic, clinical, and biological implications.Hum Mutat. 2001;18(4):264-281

Performance

Method Description

Bidirectional sequencing is performed to test for the presence of a variant in all coding regions and intron/exon boundaries of the *SGSH, NAGLU, HGSNAT,* and *GNS* genes.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Performed Weekly, Varies

Analytic Time

14 days

Maximum Laboratory Time

20 days

Specimen Retention Time

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

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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 U.S. Food and Drug Administration.

CPT Code Information

81479-Unlisted molecular pathology procedure

88233-Tissue culture, skin or solid tissue biopsy (if appropriate)

88240-Cryopreservation (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
SFPAN	MPS III, Multi-Gene Panel	In Process

Result ID	Test Result Name	Result LOINC Value
54458	Result Summary	50397-9
54459	Result	82939-0
54460	Interpretation	69047-9
54461	Additional Information	48767-8
54462	Specimen	31208-2
54463	Source	31208-2
54464	Released By	18771-6