Test Definition: SUMFZ

SUMF1 Gene, Full Gene Analysis

Overview

Useful For

Confirmation of multiple sulfatase deficiency for patients with clinical features

Identification of *SUMF1* mutation to allow for genetic testing in family members

Genetics Test Information

Testing includes full gene sequencing of the *SUMF1* gene.

Reflex Tests

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

Testing Algorithm

If skin biopsy is received, fibroblast culture for genetic test will be added and charged separately.

See Lysosomal Storage Disorders Diagnostic Algorithm, Part 2 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 2
- Blood Spot Collection Instructions

Method Name

Polymerase Chain Reaction (PCR) Amplification/DNA Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Specimen preferred to arrive within 96 hours of draw.

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

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. Tubes can be supplied upon request (Eagle's minimum essential medium with 1% penicillin and streptomycin [T115]).

Specimen Volume: 4-mm punch

Specimen Stability Information: Refrigerated (preferred)/Ambient

Acceptable:

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 (T493)

Specimen Volume:2 to 5 blood spots on collection card

Collection Instructions:

1. An alternative blood collection option for a patient >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

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: 5 punches, 3-mm diameter

Reject Due To

STK11 Gene, Full Gene Analysis, Varies

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical and Interpretive

Clinical Information

Multiple sulfatase deficiency (MSD) is a rare autosomal recessive lysosomal storage disorder (LSD) caused by mutations in the sulfatase-modifying factor 1 (*SUMF1*) gene. *SUMF1* encodes for a formylglycine-generating enzyme (FGE) that performs a critical posttranslational modification of the catalytic residue necessary for activation of all human sulfatases.

MSD is often confused for a single sulfatase deficiency because it is characterized by deficiency of all known sulfatases, which results in tissue accumulation of sulfatides, sulfated glycoaminoglycans, sphingolipids, and steroid sulfates. Indeed, the clinical phenotype encompasses symptoms of every single sulfatase deficiency, including metachromatic leukodystrophy (MLD), the mucopolysaccharidoses, X-linked ichthyosis, and chondrodysplasia punctata type I. Age of onset and clinical severity are variable and correspond with the level of residual FGE enzyme activity. A severe neonatal form of MSD closely overlaps the clinical presentation of the mucopolysaccharidoses but it is often fatal within 1 year. Late-infantile MSD (onset 0-2 years) accounts for most cases and is characterized by a clinical presentation similar to MLD. Patients show progressive cognitive and motor impairment as well as skeletal changes. More rarely, MSD presents in late childhood (juvenile-onset) with more mild symptoms and slower progression. Patients with late-infantile or juvenile-onset MSD may have less severe sulfatase deficiency.

Patients with a clinical suspicion of MLD, a mucopolysaccharidosis, X-linked ichthyosis, or chondrodysplasia should be investigated for possible FGE deficiency. Urine sulfatide analysis is the recommended first tier biochemical test (CTSA / Ceramide Trihexoside/Sulfatide Accumulation in Urine Sediment, Urine). If positive, iduronate sulfatase and arylsulfatase A and B enzyme levels should be assayed and are typically decreased in patients with MSD.

While enzyme replacement therapy has been used to treat a subset of single LSD, its effectiveness is not well established for patients with MSD. Therefore, confirmation or exclusion of a diagnosis of MSD has important implications for patient management as well as prognosis.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations will be evaluated according to the American College of Medical Genetics and Genomics (AMCG) 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 multiple sulfatase deficiency (MSD) may have a mutation that is not identified by this method (eg, large genomic deletions, promoter mutations). The absence of a mutation, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of MSD. For carrier testing, it is important to first document the presence of a *SUMF1* gene mutation in an affected family member.

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 May;17(5):405-424

2. Dierks T, Schlotawa L, Frese MA, et al: Molecular basis of multiple sulfatase deficiency, mucolipidosis II/III and Niemann-Pick C1 disease-Lysosomal storage disorders caused by defects of non-lysosomal proteins. Biochim Biophys Acta 2009 Apr;1793(4):710-725

3. Schlotawa L, Ennemann EC, Radhakrishnan K, et al: *SUMF1* mutations affecting stability and activity of formylglycine generating enzyme predict clinical outcome in multiple sulfatase deficiency. Eur J Hum Genet 2011 Mar;19(3):253-261

Performance

Method Description

Bidirectional sequence analysis is performed to test for the presence of a mutation in all coding regions and intron-exon boundaries of the *SUMF1* 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 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 US Food and Drug Administration.

CPT Code Information

81479-Unlisted molecular pathology procedure code

Additional tests:

Fibroblast Culture for Genetic Testing

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

88240-Cryopreservation (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
SUMFZ	SUMF1 Gene, Full Gene Analysis	89997-1

Result ID	Test Result Name	Result LOINC Value
54027	Result Summary	50397-9
54028	Result	89997-1
54029	Interpretation	69047-9
54030	Additional Information	48767-8
54031	Specimen	31208-2
54032	Source	31208-2
54033	Released By	18771-6