MAYO CLINIC LABORATORIES

Test Definition: SMN1Z

SMN1 Gene, Full Gene Analysis, Varies

Overview

Useful For

Confirming a diagnosis of spinal muscular atrophy due to nucleotide variants in *SMN1* gene

Second-tier carrier screening when there is a family history of spinal muscular atrophy, but an affected individual is not available for testing, or when disease-causing variants are unknown

Second-tier carrier screening for the reproductive partner of a known spinal muscular atrophy carrier

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No
CULFB	Fibroblast Culture for Genetic Test	Yes	No
MATCC	Maternal Cell Contamination, B	Yes	No

Genetics Test Information

Testing includes full gene sequencing of the *SMN1* gene.

Testing Algorithm

Skin biopsy or cultured fibroblast specimens:

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.

Cord blood:

For cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will be performed at an additional charge.

For more information see Inherited Motor Neuron Disease and Dementia Testing Algorithm

Special Instructions

- Molecular Genetics: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Inherited Motor Neuron Disease Testing and Dementia Algorithm

- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions

Method Name
Polymerase Chain Reaction (PCR) followed by DNA Sequencing

NY State Available
Yes

Specimen

Specimen Type
Varies

Ordering Guidance
This is **not** the preferred genetic test for first-tier carrier screening or diagnosis in individuals with suspicion of spinal muscular atrophy (SMA). For these situations, order SMNCS / Spinal Muscular Atrophy Carrier Screening, Deletion/Duplication Analysis, Varies or SMNDX / Spinal Muscular Atrophy Diagnostic Assay, Deletion/Duplication Analysis, Varies.

This test is appropriate for second-tier carrier screening following SMNCS / Spinal Muscular Atrophy Carrier Screening, Deletion/Duplication Analysis, Varies when:
-There is a family history of SMA, but an affected individual is not available for testing
-The disease-causing variants are unknown
-Testing the reproductive partner of a known SMA carrier

Additionally, this test is appropriate when there is a strong clinical suspicion for SMA, and SMNDX / Spinal Muscular Atrophy Diagnostic Assay, Deletion/Duplication Analysis, Varies was not diagnostic.

Specimen Required
Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor will interfere with testing. For information about testing patients who have received a hematopoietic stem cell transplant, call 800-533-1710.
Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube: Lavender top (EDTA) or yellow top (ACD)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information
Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days
Additional Information:

1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
3. For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood and maternal blood specimens under separate order numbers.

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 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 a Dried Blood Spot Sample.
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. Blood spot specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from blood spots, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.
2. Due to lower concentration of DNA yielded from blood spot, it is possible that additional specimen may be required to complete testing.
3. For collection instructions, see Blood Spot Collection Instructions
4. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
5. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800

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: Ambient (preferred) <24 hours/Refrigerated <24 hours
Additional Information:
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An

additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Cultured fibroblasts
Source: Skin or tissue
Container/Tube: T-25 Flask
Specimen Volume: 2 Flasks
Collection Instructions: Submit confluent cultured fibroblast cells from a biopsy. Cultured cells from a prenatal specimen will not be accepted.
Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours
Additional Information:
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Extracted DNA
Container/Tube:
Preferred: Screw Cap Micro Tube, 2mL with skirted conical base
Acceptable: Matrix tube, 1 mL
Collection Instructions:
1. The preferred volume is at least 100 mcL at a concentration of 75 ng/mcL.
2. Include concentration and volume on tube.
Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated
Additional Information: DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

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: Congenital Inherited Diseases Patient Information (T521)

Specimen Minimum Volume

See Specimen Required

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

Spinal muscular atrophy (SMA) is an autosomal recessive neuromuscular disorder characterized by motor neuron degeneration leading to muscular atrophy with progressive paralysis. It is a genetically complex condition that is traditionally divided into 5 subtypes, depending on the age at which symptoms present and the motor milestones that are achieved. Presentation can range from in utero joint contractures and lack of fetal movement (type 0), to loss of ambulation in adolescence or adulthood (type IV). All patients with SMA develop symmetrical loss of muscle control, most commonly affecting proximal muscles. The American College of Medical Genetics and Genomics (ACMG) recommends offering SMA carrier screening to all couples, regardless of race or ethnicity, before conception or early in pregnancy.(1,2)

The most common form of SMA is associated with the loss of survival motor neuron (SMN) protein, which is encoded by 2 or more genes on chromosome 5. The majority of SMN protein is expressed by the survival motor neuron 1 (*SMN1*) gene, but a small portion of SMN is also contributed by the survival motor neuron 2 (*SMN2*) gene. Indeed, *SMN1* produces more than 90% of SMN protein, while *SMN2* produces less than 10% of residual SMN protein. This occurs because *SMN2* differs from *SMN1* by 5 nucleotides, 1 of which leads to alternative exon 7 splicing, and a reduction of *SMN2* expression. Most individuals have 2 copies of *SMN1*, but individuals with as many as 5 copies of *SMN1* are detected. In addition, individuals may also have 0 to 5 copies of *SMN2*.(3,4)

Spinal muscular atrophy is most commonly caused by a homozygous deletion of exon 7 in *SMN1*. However, some patients with this disorder may be compound heterozygotes, with a deletion of 1 copy of *SMN1* and a nucleotide variant in the other allele. The severity of a patient's disease course is associated with the number of copies of *SMN2* that are present, and 3 or more *SMN2* copies are associated with a milder SMA phenotype.(3)

This test aims to specifically identify nucleotide variants in *SMN1* by direct sequencing and to distinguish these nucleotide variants from changes within *SMN2*. However, *SMN1* exon 1 variants are still unable to be distinguished from changes within *SMN2* exon 1.(5,6)

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics and Genomics recommendations.(7) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

Variants detected in *SMN1* exon 1 cannot be distinguished from variants in*SMN2* exon 1. Therefore, additional molecular analyses are required to confirm results in this region.

A small percentage of individuals who are carriers or have a diagnosis of spinal muscular atrophy 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 spinal muscular atrophy. For carrier testing, it is important to first document the presence of an *SMN1* 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. Committee Opinion No. 690. Carrier screening in the age of genomic medicine. Obstet Gynecol. 2017;129(3):e35-e40. doi:10.1097/AOG.0000000000001951
2. Committee Opinion No. 691. Carrier screening for genetic conditions. Obstet Gynecol. 2017;129(3):e41-e55. doi:10.1097/AOG.0000000000001952
3. Prior TW, Leach ME, Finanger EL. Spinal Muscular Atrophy. In: Adam MP, Feldman J, Mirzaa GM, et al., eds. GeneReviews [Internet]. University of Washington, Seattle; 2000. Updated September 19, 2024. Accessed November 14, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK1352/
4. Carre A, Empey C. Review of spinal muscular atrophy (SMA) for prenatal and pediatric genetic counselors. J Genet Couns. 2016;25(1):32-43. doi:10.1007/s10897-015-9859-z
5. Clermont O, Burlet P, Benit P, et al. Molecular analysis of SMA patients without homozygous SMN1 deletions using a new strategy for identification of SMN1 subtle mutations. Hum Mutat. 2004;24:417-427
6. Kubo Y, Nishio H, Saito K: A new method for SMN1 and hybrid SMN gene analysis in spinal muscular atrophy using long-range PCR followed by sequencing. J Hum Genet. 2015;60: 233-239
7. 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
8. Butchbach MER. Genomic variability in the survival motor neuron genes (SMN1 and SMN2): Implications for spinal muscular atrophy phenotype and therapeutics development. Int J Mol Sci. 2021;22(15):7896. doi:10.3390/ijms22157896

Performance

Method Description

Long-range polymerase chain reaction (PCR) of *SMN1* exons 2-8, followed by bidirectional Sanger sequence analysis for nucleotide variants in all protein-coding regions and intron/exon boundaries of *SMN1*. *SMN1* exon 1 is PCR-amplified and bidirectionally Sanger-sequenced.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Varies

Report Available
14 to 20 days

Specimen Retention Time
Whole blood: 28 days (if available); Extracted DNA: 3 months, Blood spots: 1 year (if available)

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
81336
88233-Tissue culture, skin, or solid tissue biopsy (if appropriate)
88240-Cryopreservation (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SMN1Z	SMN1 Full Gene Analysis	94221-9

Result ID	Test Result Name	Result LOINC® Value
602754	Result Summary	50397-9
602755	Result	82939-0
602756	Interpretation	69047-9
602757	Additional Information	48767-8
602758	Specimen	31208-2
602759	Source	31208-2
602760	Released By	18771-6