MAYO CLINIC LABORATORIES

Test Definition: SCARA

Spinocerebellar Ataxia Type 1, 2, 3, 6, or 7, Repeat Expansion Analysis, Varies

Overview

Useful For

Diagnostic or predictive testing when clinical symptoms or a family history are specific to only one type of spinocerebellar ataxia

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
MATCC	Maternal Cell Contamination, B	Yes	No
G204	ATXN1 (SCA 1) Gene Analysis	No, (Bill Only)	No
G205	ATXN2 (SCA 2) Gene Analysis	No, (Bill Only)	No
G206	ATXN3 (SCA 3) Gene Analysis	No, (Bill Only)	No
G207	ATXN7 (SCA 7) Gene Analysis	No, (Bill Only)	No
G208	CACNA1A (SCA 6) Gene Analysis	No, (Bill Only)	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

Genetics Test Information

This test is for the assessment of one type of the specified spinocerebellar ataxias (SCA), including types 1, 2, 3, 6, or 7. It assesses for CAG (cytosine-adenine-guanine) repeat expansions within the *ATXN1*, *ATXN2*, *ATXN3*, *CACNA1A*, or *ATXN7* genes, associated with SCA1, SCA2, SCA3, SCA6, and SCA7. Additionally, testing for *ATXN1* assesses for CAT (cytosine-adenine-thymine) trinucleotides that interrupt the CAG repeat tract.

Testing Algorithm

For prenatal specimens only:

-If amniotic fluid (nonconfluent cultured cells) is received, amniotic fluid culture/genetic test will be added at an additional charge.

-If chorionic villus specimen (nonconfluent cultured cells) is received, fibroblast culture for genetic test will be added at

an additional charge.
For any prenatal specimen that is received, maternal cell contamination studies will be added.

Special Instructions

- Informed Consent for Genetic Testing
- Molecular Genetics: Neurology Patient Information
- Informed Consent for Genetic Testing (Spanish)

Method Name

Polymerase Chain Reaction (PCR)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is **not a gene panel** for all types of spinocerebellar ataxia (SCA). If individual findings are not specific for one type of SCA, panel analysis is available and includes testing for SCA1, 2, 3, 6, and 7; order SCAP / Spinocerebellar Ataxia Repeat Expansion Panel, Varies.

This test and SCAP should not be ordered concurrently.

Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

Necessary Information

The type of spinocerebellar ataxia (SCA) to be assessed (SCA1, 2, 3, 6, or 7) is required. This information must be provided for testing to be performed.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. For instructions for testing patients who have received a bone marrow transplant, call 800-533-1710.

Submit only 1 of the following specimens:

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) 4 days/Refrigerated

Prenatal Specimens
Due to its complexity, consultation with the laboratory is required for all prenatal testing; call 800-533-1710 to speak to a genetic counselor.

Specimen Type: Amniotic fluid
Container/Tube: Amniotic fluid container
Specimen Volume: 20 mL
Specimen Stability Information: Refrigerated (preferred)/Ambient
Additional information:
1. A separate culture charge will be assessed under CULAF / Culture for Genetic Testing, Amniotic Fluid.
2. All prenatal specimens must be accompanied by a maternal blood specimen; order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Specimen Type: Chorionic villi
Container/Tube: 15-mL tube containing 15 mL of transport media
Specimen Volume: 20 mg
Specimen Stability Information: Refrigerated
Additional Information:
1. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing.
2. All prenatal specimens must be accompanied by a maternal blood specimen; order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Acceptable:
Specimen Type: Confluent cultured cells
Container/Tube: T-25 flask
Specimen Volume: 2 Full flasks
Collection Instructions: Submit confluent cultured cells from another laboratory.
Specimen Stability Information: Ambient (preferred)/Refrigerated
Additional Information: All prenatal specimens must be accompanied by a maternal blood specimen; order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

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: Neurology Patient Information

3. If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

Specimen Minimum Volume

Amniotic fluid: 10 mL
Blood: 0.5 mL
Chorionic villi: 5 mg

Reject Due To

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

Spinocerebellar Ataxia Type 1:
Spinocerebellar ataxia type 1 (SCA1) is characterized by progressive ataxia, dysarthria, eventual deterioration of bulbar functions, and ophthalmoplegia.
Onset typically occurs in the third to fourth decade of life. Most individuals present with difficulties in gait or slurred speech. SCA1 is caused by an expansion of the CAG (cytosine-adenine-guanine) trinucleotide repeat in the *ATXN1* gene. This trinucleotide repeat is polymorphic in the general population, with the number of benign repeats ranging from 6 to 37. The pathogenicity of the repeat is dependent on the presence or absence of CAT (cytosine-adenine-thymine) trinucleotide repeats that interrupt the CAG repeats. Therefore, individuals with 36 to 37 uninterrupted CAG repeats are predisposed to having a child with an expanded allele. In affected individuals, the CAG expansions are greater than 38 uninterrupted CAG repeats or greater than 44 repeats, regardless of the presence or absence of CAT repeat interruptions. The presence of CAT repeats in an individual with 36 to 43 CAG repeats is considered normal and not disease-causing. In contrast, 38 CAG repeats without CAT repeats are of uncertain significance. There is a report of an individual with very last onset SCA1 with 38 CAG repeats. Reduced penetrance has been associated with 44 CAG repeats. As with other trinucleotide repeat disorders, large CAG expansions are associated with earlier onset and a more severe clinical course.

Spinocerebellar Ataxia Type 2:
Spinocerebellar ataxia type 2 (SCA2) is characterized by slowly progressive ataxia, dysarthria, and slow saccadic eye movements. The mean age of onset is in the fourth decade, but symptoms may appear from childhood to later adulthood. SCA2 is caused by an expansion of the CAG trinucleotide repeat in the *ATXN2* gene. This trinucleotide repeat is polymorphic in the general population, with the number of benign repeats less than 32. However, 29 to 31 heterozygous repeats have been associated with an increased exponential risk for amyotrophic lateral sclerosis (ALS). Additionally, there has been a report of an individual homozygous for 31 repeats with late-onset cerebellar ataxia. In contrast, 27 repeats have been associated with a protective effect for ALS. In affected individuals, the CAG expansion is

greater than 34 repeats, with the most common disease-causing alleles having 37 to 39 repeats. Larger CAG expansions are associated with an earlier age of onset but repeat length cannot predict age of onset or disease severity. A CAG expansion of 32 repeats is of unclear clinical significance. Repeats in the 33 to 34 range are associated with reduced penetrance.

Spinocerebellar Ataxia Type 3:
Spinocerebellar ataxia type 3 (SCA3), also known as Machado-Joseph disease, is characterized by progressive cerebellar ataxia and pyramidal signs. The age of onset is highly variable but most commonly occurs in the second to fifth decade of life. Individuals may present with gait problems, speech difficulties, clumsiness, or visual blurring. SCA3 is caused by an expansion of the CAG trinucleotide repeat in the *ATXN3* gene. This trinucleotide repeat is polymorphic in the general population, with the number of benign repeats ranging from 12 to 44. In affected individuals, the CAG expansion ranges from 60 to 87 repeats. A loose correlation exists between repeat length and clinical phenotype. Individuals with 45 to 59 CAG repeats are predisposed to having a child with an expanded allele and may or may not have symptoms themselves. There have been reports of reduced penetrant and nonpenetrant alleles with repeats in this range.

Spinocerebellar Ataxia Type 6:
Spinocerebellar ataxia type 6 (SCA6) is characterized by adult-onset, slowly progressive cerebellar ataxia, dysarthria, and nystagmus. The mean age of onset is 43 to 52 years. Initial symptoms include unsteadiness, stumbling, and imbalance. SCA6 is caused by an expansion of the CAG trinucleotide repeat in the *CACNA1A* gene. This trinucleotide repeat is polymorphic in the general population, with the number of benign repeats less than 19. In affected individuals, the CAG expansion ranges from 20 to 33 repeats. Larger CAG expansions are associated with an earlier age of onset. A CAG expansion of 19 repeats is of unclear clinical significance. Individuals with 19 CAG repeats are predisposed to having a child with an expanded allele. Additionally, homozygous abnormal expansions have been reported in individuals with younger age of onset and a more severe phenotype.

Spinocerebellar Ataxia Type 7:
Spinocerebellar ataxia type 7 (SCA7) is characterized by progressive cerebellar ataxia, including dysarthria and dysphagia, and con-rod and retinal dystrophy. Onset ranges from infancy to the fifth or sixth decade of life. SCA7 is caused by an expansion of the CAG trinucleotide repeat in the *ATXN7* gene. This trinucleotide repeat is polymorphic in the general population, with the number of benign repeats less than 19. In affected individuals, the CAG expansion is greater than 36 repeats. A CAG expansion of 19 to 27 repeats is of unclear clinical significance. Individuals with 28 to 33 repeats are predisposed to having a child with an expanded allele but are unlikely to have symptoms themselves. Thirty-four to 36 repeats are associated with reduced penetrance, and when symptoms do occur, they are more likely to be associated with later onset and a milder phenotype.

Reference Values

SPINOCEREBELLAR ATAXIA TYPE 1
Normal alleles: <36 CAG repeats
Normal alleles with CAT interruptions: 36-43 repeats
Intermediate alleles without CAT interruptions: 36-37 repeats
Uncertain significance: 38 repeats
Expanded alleles without CAT interruptions: >38 CAG repeats
Expanded alleles with CAT interruptions: >43 CAG repeats

SPINOCEREBELLAR ATAXIA TYPE 2
Normal alleles: <32 repeats
Uncertain significance: 31 homozygous and 32 repeats
Reduced penetrance: 33-34 repeats
Expanded alleles: >34 repeats

SPINOCEREBELLAR ATAXIA TYPE 3
Normal alleles: <45 repeats
Intermediate alleles: 45-59 repeats
Expanded alleles: >59 repeats

SPINOCEREBELLAR ATAXIA TYPE 6
Normal alleles: <19 repeats
Intermediate alleles: 19 heterozygous repeats
Uncertain significance: 19 homozygous repeats
Expanded alleles: >19 repeats

SPINOCEREBELLAR ATAXIA TYPE 7
Normal alleles: <19 repeats
Uncertain significance: 19-27 repeats
Intermediate alleles: 28-33 repeats
Reduced penetrance: 34-36 repeats
Expanded alleles: >36 repeats

An interpretive report will be provided.

Interpretation
An interpretive report will be provided.

Cautions
For predictive testing, it is important to first document the presence of a CAG (cytosine-adenine-guanine)-repeat expansion in an affected family member to confirm that the repeat expansion is the underlying mechanism of disease in the family.

It is strongly recommended that patients undergoing predictive testing receive genetic counseling both prior to testing and after results are available.

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.

Due to somatic mosaicism, repeat size identified in the peripheral blood specimen may not reflect the repeat size in untested tissues (eg, central nervous system). In addition, a negative result does not rule out the presence of a variant in the mosaic state that may be present but below the limit of detection of this assay (approximately 10%).

Rare sequence variants immediately downstream of the spinocerebellar ataxia repeat regions may interfere with genotype results but are not expected to affect repeat-primed peaks.

Rare undocumented alterations (ie, polymorphisms) in the polymerase chain reaction primer binding regions may lead to false-negative results.

Clinical Reference

1. Soong BW, Morrison PJ: Spinocerebellar ataxias. Handb Clin Neurol. 2018;155:143-174. doi: 10.1016/B978-0-444-64189-2.00010-X
2. Buijsen RAM, Toonen LJA, Gardiner SL, van Roon-Mom WMC: Genetics, mechanisms, and therapeutic progress in polyglutamine spinocerebellar ataxias. Neurotherapeutics. 2019 Apr;16(2):263-286. doi: 10.1007/s13311-018-00696-y

Performance

Method Description

A polymerase-chain reaction-based assay is used to amplify across the region of the *ATXN1*, *ATXN2*, *ATXN3*, *CACNA1A*, or *ATXN7* gene containing CAG (cytosine-adenine-guanine) repeats. Additionally, testing assesses for CAT (cytosine-adenine-thymine) trinucleotides that interrupt the CAG repeat tract within the *ATXN1* gene.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday, Wednesday

Report Available

21 to 28 days

Specimen Retention Time

Whole blood: 2 weeks (if available); Extracted DNA: 3 months; Amniotic fluid, chorionic villi, cultured chorionic villi: 1 month

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

88233-Fibroblast Culture (if appropriate)
88235-Amniotic Fluid Culture (if appropriate)
88240-Cryopreservation (if appropriate)
81265-Maternal Cell Contamination (if appropriate)
81178 (if appropriate)
81179 (if appropriate)
81180 (if appropriate)
81181 (if appropriate)
81184 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SCARA	SCA 1,2,3,6, or 7 Repeat Analysis	21769-5

Result ID	Test Result Name	Result LOINC® Value
609700	Result Summary	21769-5
MG323	Test Code	21768-7
609701	Result	36911-6
609702	Interpretation	69047-9
609703	Reason for Referral	42349-1
609704	Specimen	31208-2
609705	Source	31208-2
609706	Method	85069-3
609707	Disclaimer	62364-5
609708	Released By	18771-6