

## Overview

### Useful For

Molecular confirmation of clinically suspected spinocerebellar ataxia type 1, 2, 3, 6, or 7

### Genetics Test Information

This test is for the assessment of specified spinocerebellar ataxia (SCA) types 1, 2, 3, 6, or 7. It assesses for CAG 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 cytosine-adenine-thymine (CAT) trinucleotides that interrupt the CAG repeat tract.

### Testing Algorithm

**For prenatal specimens only:** If amniotic fluid (nonconfluent cultured cells) is received, amniotic fluid culture will be added and charged separately. If chorionic villus specimen (nonconfluent cultured cells) is received, fibroblast culture for genetic test will be added and charged separately. 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 \(Spanish\)](#)

### 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

### 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.

**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. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

**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) 96 hours/Refrigerated

**Due to the complexity of prenatal testing, consultation with the laboratory is required for all prenatal testing.** Prenatal specimens can be sent Monday through Thursday and **must be received by 5 p.m. CST on Friday** in order to be processed appropriately. 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:** Amniotic fluid

**Container/Tube:** Amniotic fluid container

**Specimen Volume:** 20 mL

**Specimen Stability Information:** Refrigerated (preferred)/Ambient

**Specimen Type:** Chorionic villi

**Container/Tube:** 15-mL tube containing 15 mL of transport media

**Specimen Volume:** 20 mg

**Specimen Stability Information:** Refrigerated

**Acceptable:**

**Specimen Type:** Confluent cultured cells

**Container/Tube:** T-25 flask

**Specimen Volume:** 2 Flasks

**Collection Instructions:** Submit confluent cultured cells from another laboratory.

**Specimen Stability Information:** Ambient (preferred)/Refrigerated

## 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.

## Reject Due To

Specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

## Specimen Minimum Volume

Amniotic fluid: 10 mL

Blood: 0.5 mL

Chorionic villi: 5 mg

## Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies (preferred)		

## 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 3rd to 4th decade of life. Most individuals present with difficulties in gait or slurred speech. SCA1 is caused by an expansion of the cytosine-adenine-guanine (CAG) 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 cytosine-adenine-thymine (CAT) 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 repeats is considered normal and not pathogenic. In contrast, 38 repeats without CAT repeats is of uncertain significance. There is a report of

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an individual with very late onset SCA1 with 38 repeats. Reduced penetrance has been associated with 44 repeats. As with other trinucleotide repeat disorders, large CAG expansions are associated with earlier onset and a more severe clinical course.

**SCA2:**

Spinocerebellar ataxia type 2 (SCA2) is characterized by slowly progressive ataxia and dysarthria, and slow saccadic eye movements. The mean age of onset is in the 4th 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 have 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.

**SCA3:**

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 2nd to 5th 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.

**SCA6:**

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.

**SCA7:**

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 5th or 6th 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 is 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: &lt;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: &gt;38 CAG repeats

Expanded alleles with CAT interruptions: &gt;43 CAG repeats

**SPINOCEREBELLAR ATAXIA TYPE 2**

Normal alleles: &lt;32 repeats

Uncertain significance: 31 homozygous and 32 repeats

Reduced penetrance: 33-34 repeats

Expanded alleles: &gt;34 repeats

**SPINOCEREBELLAR ATAXIA TYPE 3**

Normal alleles: &lt;45 repeats

Intermediate alleles: 45-59 repeats

Expanded alleles: &gt;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 cytosine-adenine-guanine (CAG)-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

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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 (SCA) repeat regions may interfere with genotype results but are not expected to affect repeat-primed peaks.

Rare undocumented alterations (ie, polymorphisms) in 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, et al: 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 repeats. Additionally, testing assesses for CAT trinucleotides that interrupt the CAG repeat tract within the *ATXN1* gene.(Unpublished Mayo method)

### 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

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	In Process

Result ID	Reporting Name	LOINC®
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