MAYO CLINIC LABORATORIES

Test Definition: SCAP

Spinocerebellar Ataxia Repeat Expansion Panel, Varies

Overview

Useful For

Molecular confirmation of clinically suspected spinocerebellar ataxia when a specific subtype isn't suspected

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
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No
MATCC	Maternal Cell Contamination, B	Yes	No

Genetics Test Information

This test assesses for CAG (cytosine-adenine-guanine) repeat expansions within the *ATXN1*, *ATXN2*, *ATXN3*, *CACNA1A*, and *ATXN7* genes, associated with spinocerebellar ataxia (SCA) type 1, SCA2, SCA3, SCA6, and SCA7. Additionally, testing for *ATXN1* assesses for CAT trinucleotides that interrupt the CAG repeat tract.

Testing Algorithm

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

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

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:
Preferred: 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: 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: 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
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
Spinocerebellar Ataxia Type 1:
Spinocerebellar ataxia type 1 (SCA1) is characterized by progressive ataxia, dysarthria, eventual deterioration of bulbar functions, and ophthalmoplegia.(1) 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.(2)

Spinocerebellar Ataxia Type 2:
Spinocerebellar ataxia type 2 (SCA2) is characterized by slowly progressive ataxia, dysarthria, and slow saccadic eye movements.(1) 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.(2)

Spinocerebellar Ataxia Type 3:
Spinocerebellar ataxia type 3 (SCA3), also known as Machado-Joseph disease, is characterized by progressive cerebellar ataxia and pyramidal signs.(1) 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.(2)

Spinocerebellar Ataxia Type 6:
Spinocerebellar ataxia type 6 (SCA6) is characterized by adult-onset, slowly progressive cerebellar ataxia, dysarthria, and nystagmus.(1) 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.(2)

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.(1) 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.(2)

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 Type7
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

The interpretive report includes an overview of the findings as well as the associated clinical significance.

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;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* genes 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

Varies

Report Available

21 to 28 days

Specimen Retention Time

Whole blood: 28 days (if available); Extracted DNA: 3

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

81178
81179
81180
81181
81184
81479 (if appropriate for government payers)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SCAP	Spinocerebellar Ataxia Panel	21769-5

Result ID	Test Result Name	Result LOINC® Value
609506	Result Summary	21769-5
609507	Result	36911-6
609508	Interpretation	69047-9
609509	Additional Information	48767-8
609510	Specimen	31208-2
609512	Method	85069-3
609513	Disclaimer	62364-5
609514	Released By	18771-6
609511	Source	31208-2