MAYO CLINIC LABORATORIES

Test Definition: SBULB

Spinobulbar Muscular Atrophy (Kennedy Disease), Molecular Analysis, Varies

Overview

Useful For

Molecular confirmation of clinically suspected cases of sporadic or familial spinobulbar muscular atrophy (SBMA)

Presymptomatic testing for individuals with a family history of SBMA and a documented expansion in the androgen receptor (*AR*) gene

Testing Algorithm

For information see Inherited Motor Neuron Disease and Dementia Testing Algorithm

Special Instructions

- Informed Consent for Genetic Testing
- Hereditary Peripheral Neuropathy Diagnostic Algorithm
- Molecular Genetics: Neurology Patient Information
- Inherited Motor Neuron Disease Testing and Dementia Algorithm
- 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 bone marrow transplant from an allogenic donor will interfere with testing. For information about testing patients who have received a bone marrow transplant, call 800-533-1710.

Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)
Acceptable: None
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 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 is met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.

Specimen Type: Extracted DNA
Container/Tube:
Preferred: Screw Cap Micro Tube, 2mL with skirted conical base
Acceptable: Matrix tube, 1mL
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 by Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

X-linked spinal and bulbar muscular atrophy (spinobulbar muscular atrophy [SBMA] or Kennedy disease) is characterized by onset of progressive muscle weakness, atrophy, and fasciculations typically in the fourth or fifth decade of life. Affected patients also have signs of androgen insensitivity such as gynecomastia, reduced fertility, and testicular atrophy. The clinical severity and age at onset can be quite variable, even within families. Because this is an X-linked disease, males manifest this disorder and females are generally asymptomatic carriers. However, there have been reports of female carriers who exhibit symptoms such as muscle weakness and cramping.

Spinobulbar muscular atrophy is caused by an expansion of the CAG trinucleotide repeat in exon 1 of the human androgen receptor (*AR*) gene. This trinucleotide repeat is polymorphic in the general population, with the number of repeats ranging from 11 to 34. The number of repeats found in affected individuals can range from 38 to 62. There is no consensus as to the clinical significance of alleles of 35 CAG repeats and literature suggests that alleles of 36 to 37 CAG repeats may be associated with reduced penetrance. As with other trinucleotide repeat disorders, anticipation is frequently observed, and larger CAG expansions are associated with earlier onset and a more rapid clinical progression.

Reference Values

Normal alleles: 11-34 CAG repeats

Abnormal alleles: 36-62 CAG repeats

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

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-repeat amplification in the androgen receptor (*AR*) gene in an affected family member to confirm that molecular expansion is the underlying mechanism of disease in the family.

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

Predictive testing of an asymptomatic child is not recommended.

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.

Current evidence suggests that the majority of individuals with spinobulbar muscular atrophy have a CAG-repeat expansion. However, we cannot eliminate the possibility that another type of mutation not detected by our assay is present within the *AR* gene.

Clinical Reference

1. Pinsky L, Beitel LK, Trifiro MA: Spinobulbar Muscular Atrophy. In Scriver CR, Beaudet AL, Sly WS, et al. The Metabolic and Molecular Basis of Inherited Disease. Vol 4. 8th ed. McGraw-Hill Book Company, 2001;4147-4157

2. Breza M, Koutsis G. Kennedy's disease (spinal and bulbar muscular atrophy): a clinically oriented review of a rare disease. J Neurol. 2019;266(3):565-573. doi:10.1007/s00415-018-8968-7

Performance

Method Description
Direct mutation analysis. A PCR-based assay is used to detect amplification-type mutations (CAG-repeat expansion) within the *AR* gene. (Doyu M, Sobue G, Mukai E, et al. Severity of X-linked recessive bulbospinal neuronopathy correlated with size of the tandem CAG repeat in androgen receptor gene. Ann Neurol 1992;31[5]:707-710)

PDF Report
No

Day(s) Performed
Varies

Report Available
14 to 21 days

Specimen Retention Time
Whole blood: 30 days (if available); Extracted DNA: 3 months

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
81204-*AR (*androgen receptor)(eg, spinal and bulba muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; characterization of alleles (eg, expanded size or methylation status)

LOINC® Information

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Test ID	Test Order Name	Order LOINC® Value
SBULB	Spinobulbar Musc Atrophy, Kennedy's	35359-9

Result ID	Test Result Name	Result LOINC® Value
53341	Result Summary	50397-9
53342	Result	82939-0
53343	Interpretation	69047-9
53344	Reason for Referral	42349-1
53345	Specimen	31208-2
53346	Source	31208-2
53348	Released By	18771-6