

Spinal and Bulbar Muscular Atrophy DNA Screen

Background

Spinal and bulbar muscular atrophy (SBMA; also known as Kennedy's Disease) is a gradually progressive neuromuscular disorder characterized by muscle weakness, muscle atrophy, and fasciculations. SBMA is a chromosome X-linked disorder that affects only males. The cause is an abnormally high number of CAG trinucleotide repeats that encode a stretch of polyglutamine amino acids in the protein product of the androgen receptor (AR) gene. As a result of mild androgen insensitivity, affected males often show gynecomastia, testicular atrophy, and reduced fertility. Female carriers can display subclinical manifestations of disease. This is a direct DNA test that measures the number of CAG repeats in the AR gene; the mutation detection rate is 100%.

Indications for Testing

- Confirm a clinical diagnosis of a symptomatic male
- Diagnostic testing for males with adolescent-onset signs of androgen insensitivity including gynecomastia and/or small testes with oligospermia or azoospermia.
- Diagnostic testing for males with adult-onset signs of spinal lower motor neuron disease with proximal muscle weakness of the limbs or muscle cramps.
- Diagnostic testing for males with adult-onset signs of bulbar lower motor neuron disease with fasciculations of the tongue, lips, or perioral region; dysarthria and difficulty swallowing.
- Differential diagnosis of males presenting with slowly progressive bulbar ALS syndrome
- Carrier testing of females in families with X-linked SBMA
- Prenatal diagnosis of SBMA at-risk pregnancies, with appropriate genetic counseling

Genetic Counseling

Genetic counseling can be useful to patients and families considering genetic testing. The laboratory can provide referrals to genetics clinics in the patient's locale or a listing can be found at www.genetests.org

Ordering

1. Obtain blood sample.
-For prenatal testing, call the Genetics Lab; blood sample of parent(s) may also be required.
2. Fill out a Clinical Lab Request – Genetics form
(Available at <http://depts.washington.edu/labweb/Divisions/MolDiag/MolDiagGen/index.htm>).
Request: "Other: SBMA" or "Kennedy's Disease".
3. Provide information needed for test interpretation:
-Reason for ordering test
-Clinical history of patient
-Family history / pedigree
4. Call Laboratory Medicine Community Services (206) 598-6066 to arrange the best method of shipment.

Sample Requirements and Specimen Handling

Whole blood - EDTA (purple top) - 5 mL. Note: Heparin (green top) tubes are not acceptable. Samples should be received within 72 hours of collection. Samples may be refrigerated until shipped. For prenatal diagnosis specimens, consult Genetics Laboratory.

Test Frequency and Reporting

Test results usually within two weeks of specimen receipt. Prenatal samples are expedited.
A written interpretative report is provided.

References

1. La Spada, AR. Spinal and bulbar muscular atrophy. GeneClinics, 2004, Available at www.geneclinics.org
2. Greenland KJ, Zajac, JD. Kennedy's disease: pathogenesis and clinical approaches. Int Med J 34:279-286, 2004.
3. Ishihara H, et al., Clinical features and skewed X-chromosome inactivation in female carriers of X-linked recessive spinal and bulbar muscular atrophy. J Neurol 248:856-860, 2001.