

Aarskog-Scott Syndrome: *FGD1* Gene Sequencing

Test Code: TG

Turnaround time: 4 weeks

CPT Codes: 81479 x1

Condition Description

Aarskog-Scott syndrome (faciogenital dysplasia) is an X-linked disorder characterized by facial, skeletal, and genital anomalies, although expressivity is highly variable. The main features are:

- Short stature
- Ocular hypertelorism
- Anteverted nostrils
- Broad upper lip
- Brachydactyly
- "Shawl scrotum" in males.

Other symptoms can include ligamentous laxity manifested by hyperextensibility of the fingers, genu recurvatum, and flat feet. Congenital heart defects have been demonstrated in some patients. A spectrum of behavioral disorders and intellectual disability may also be part of the Aarskog-Scott syndrome phenotype. Female carriers may show some minor manifestations of the disorder, especially in the face and hands.

Mutations in the *FGD1* gene (Xp11.21) have been associated with both Aarskog-Scott syndrome and non-syndromic X-linked intellectual disability. One study identified *FGD1* mutations in 8 of 46 male patients with a clinical diagnosis of Aarskog-Scott syndrome, including 4 deletions, 1 insertion, and 3 missense mutations. The mutations were scattered over the entire coding sequence, and there were no apparent genotype/phenotype correlations. No global differences in clinical findings were found between probands with or without mutations, but those with mutations presented with a fuller clinical spectrum of the phenotype. Mutations have also been found in a male with attention deficit-hyperactivity disorder (ADHD) and low intelligence quotient with dysmorphic features reminiscent of Aarskog-Scott syndrome, and in three brothers with non-syndromal X-linked mental retardation who lacked distinct craniofacial, skeletal, or genital findings, suggestive of Aarskog-Scott syndrome.

For patients with suspected Aarskog-Scott syndrome, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

Please [click here](#) for the OMIM summary on this condition.

Genes

[FGD1](#)

Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of Aarskog-Scott syndrome.
- Carrier testing in adult females with a family history of Aarskog-Scott syndrome.

Methodology

Next Generation Sequencing: In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Detection

Clinical Sensitivity:

One study identified *FGD1* mutations in 8 of 46 male patients with a clinical diagnosis of Aarskog-Scott syndrome. Mutations in the promoter region, some mutations in the introns, other regulatory element mutations and large deletions will not be detected by this analysis.

Analytical Sensitivity: ~99%.

Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Whole Blood (EDTA)

Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old): 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: Saliva**Specimen Requirements:**

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Type: DNA, Isolated**Specimen Requirements:**

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Special Instructions

Please submit copies of diagnostic biochemical test results along with the sample, if appropriate. Contact the laboratory if further information is needed. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

Related Tests

- *FGD1* Gene Deletion/Duplication (TH) is available for those individuals in whom sequence analysis is negative.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90+ genes.
- [Known Mutation Analysis \(KM\)](#) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- [Prenatal Custom Diagnostics](#) is available to adult females who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.