Aarskog-Scott Syndrome: *FGD1* Gene Deletion/Duplication

**Test Code:** TH  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 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.

### Genes

*FGD1*

### Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of Aarskog-Scott syndrome in an individual in whom sequencing analysis was negative.
- Carrier testing in adult females with a family history of Aarskog-Scott syndrome in whom sequencing analysis was negative.

### Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

### Detection

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations.

Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

### Specimen Requirements

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection 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**

- **Aarskog-Scott Syndrome: FGD1 Gene Sequencing (TG)** is required before deletion/duplication analysis.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90+ genes.
- 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.