

## Aarskog-Scott Syndrome via *FGD1* Gene Sequencing (Test #837)

**Brief Description of Clinical Features:** Aarskog-Scott syndrome (ASS; OMIM#305400), also known as Faciogenital dysplasia, is characterized by short stature, hypertelorism, shawl scrotum, and brachydactyly. There is wide phenotypic variability and other features, such as joint hyperextensibility, short nose, widow's peak, and inguinal hernia. Most patients do not have mental retardation, but some may have neurobehavioral features. Carrier females may present with subtle features, such as widow's peak or short stature (Orrico et al. *Am J Med Genet* 152A:313-318, 2010).

**Genetics:** Aarskog-Scott syndrome is an X-linked disorder caused by mutations in the *FGD1* gene. FGD1 protein (also known as FYVE, RhoGEF and PH domain containing protein 1) has strong homology to RAS-like RHO/RAC guanine nucleotide exchange factors (GEFs), and contains a cysteine-rich zinc finger-like region and 2 potential Src homology-3 (SH3)-binding sites (Hou et al. *Hum Molec Genet* 12:1981-1993, 2003). This protein is proposed to play an important role in regulating cell shape (Hou et al., 2003). The majority of mutations in *FGD1* are missense, nonsense and frameshift mutations. There is no apparent genotype/phenotype correlation in studied patient cohort (Orrico et al. 2010).

**Description of This Particular Test:** This test involves bidirectional sequencing using genomic DNA of all coding exons of the *FGD1* gene plus ~50 bp of flanking non-coding DNA on each side. As indicated, we will also sequence any single exon (Test #100, \$190) in family members of patients with a known mutation, or to confirm research results.

**Reference Sequences:** **Genomic:** NC\_000023.10                      **mRNA:** NM\_004463.2  
**Protein:** NP\_004454.2    **mRNA and Protein:** CCDS14359.1

**Indications for Test:** Candidates for this test are patients with clinical features consistent with Aarskog-Scott syndrome, and family members of patients who have a known *FGD1* mutation.

**Sensitivity of Test:** This test is predicted to detect disease mutations in up to 30% of individuals with ASS (Schwartz et al. *Eur J Hum Genet* 8: 869-874, 2000; Orrico et al. *Eur J Hum Genet* 12:16-23, 2004; Orrico et al., 2010)

**Turnaround Time:** Maximum of 40 calendar days, although many tests are completed in 2-3 weeks.

**Specimen Requirements:** See page four of the Requisition Form.

**Prices:**                      **Sequencing of all coding exons of the *FGD1* gene:**      **\$ 940**

**CPT Codes:**

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x17	83898 \$ 300	Sequencing x17	83904 \$ 440
Separation x1	83894 \$ 50	Interpretation/Report x1	83912 \$ 80

**Accreditation:** CLIA ID:52D1027685 (expires 1/18/13) CAP ID:7185561, AU ID:1407125 (expires 12/20/12)

**Contact:** Ying Wang, MD, PhD, [ying.wang@preventiongenetics.com](mailto:ying.wang@preventiongenetics.com), [www.preventiongenetics.com](http://www.preventiongenetics.com)