

# The University of Chicago Genetic Services Laboratories



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## SLC9A6 sequencing for X-linked Angelman-like syndrome

### Clinical Features:

Features of patients with *SLC9A6* mutations include mental retardation, microcephaly, truncal ataxia, grand mal epilepsy and lack of speech [1] [OMIM #300243]. The clinical features of these patients suggest a similarity to Angelman syndrome, with developmental delay, ataxia, flexed arms, excessive drooling, happy demeanor with spontaneous smiling and laughter, as well as progressive microcephaly by two years of age [2]. Patients have minimal to absent language skills despite normal hearing. Seizures typically occur before two years of age. Characteristic physical features can include a long face with pointed jaw, ophthalmoplegia, swallowing difficulties, kyphoscoliosis and poor growth [1,2]. Most patients are found to have a slender body habitus, which differs from Angelman syndrome, where patients tend to become obese with age [2]. Heterozygous females can show variability in phenotype, with a range from normal to mild cognitive handicaps [1,2].

Male patients exhibiting an Angelman-like syndrome phenotype who are negative for relevant genetic testing (normal methylation of the 15q11-q13 region as well as normal *UBE3A* sequencing), as well as *MECP2* negative patients, may be considered for mutations in the *SLC9A6* gene.

### Molecular and Biochemical Genetics:

Mutations of the *SLC9A6* [OMIM #300231] gene have been identified in patients with X-linked mental retardation with features similar to Angelman syndrome [2]. *SLC9A6* has 16 coding exons and is ubiquitously expressed, with the highest expression in mitochondrion-rich tissues such as brain and skeletal muscle [3]. It is thought that the *SLC9A6* protein product, the Na<sup>+</sup>/H<sup>+</sup> exchanger protein NHE6, is important for sodium/hydrogen exchange as well as normal mitochondrial function [3].

### Inheritance:

Mutations in *SLC9A6* are inherited in an X-linked pattern and result in clinical features in affected males and occasionally some mild features in carrier females. Multiple families have been identified with *SLC9A6* mutations, including several families with multiple affected boys over several generations [1,2]. A woman who has more than one affected son is an obligate carrier. Recurrence risk for carrier mothers is 50%.

### Additional Resources:

#### Angelman Syndrome Foundation

4255 Westbrook Drive, Ste. 216, Aurora, IL 60504  
Phone: 630-978-4245; 800-432-6435  
Email: [info@angelman.org](mailto:info@angelman.org)  
[www.angelman.org](http://www.angelman.org)

### Testing Methods:

The University of Chicago Genetic Services Laboratories offers sequence analysis of all 16 coding exons and intron/exon boundaries of *SLC9A6* by direct sequencing of amplification products in both the forward and reverse directions.

#### SLC9A6 sequencing:

Sample specifications:	3 to 10cc of blood in a purple top (EDTA) tube
Cost:	\$1675
CPT codes:	83891, 83898 x 4, 83904 x 7, 83912
Turn-around time:	4 - 6 weeks

### Testing for a known mutation in additional family members

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	\$390
CPT codes:	83891, 83898 x 2, 83894, 83912
Turn-around time:	3 – 4 weeks

### Prenatal testing for a known mutation

Sample specifications:	2 T25 flasks of cultured cells from amnio or CVS or 10ml of amniotic fluid
Cost:	\$590
CPT codes:	83891, 83898 x 2, 83894, 83912, 99051
Turn-around time:	1-2 weeks

### **Results:**

You will be informed of the results of your case as soon as it has been completed. Results, along with an interpretive report, will be faxed and mailed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

### **Laboratory Faculty and Staff:**

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ABMG Certified Molecular Geneticist

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### **References:**

1. Christianson A, et al. X-linked severe mental retardation, craniofacial dysmorphism, ophthalmoplegia, and cerebellar atrophy in a large Sough African kindred is localised to Xq24-q27 (1999). J. Med. Genet. 36:759-766.
2. Gilfillan G, et al. *SLC9A6* mutations cause X-linked mental retardation, microcephaly, epilepsy and ataxia, a phenotype mimicking Angelman syndrome (2008). Am. J. Hum. Genet. 82:1003-1010.
3. Numata M, et al. Identification of a mitochondrial NA<sup>+</sup>/H<sup>+</sup> exchanger (1998). J. Biol. Chem. 273:6951-6959.

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