

Christianson Type X-Linked Mental Retardation via *SLC9A6* Gene Sequencing (Test #562)

Brief Description of Clinical Features: Mutations in the *SLC9A6* gene (OMIM 300231) cause syndromic X-linked mental retardation of the Christianson Type (OMIM 300243), a syndrome with remarkable clinical overlap with Angelman Syndrome (AS; OMIM 105830). Christianson Type XLMR is characterized by affected males with profound mental retardation, seizures, absent speech, and microcephaly (Christianson et al. *Med Genet* 36:759-766, 1999). Other features include frequent smiling and episodes of unprovoked laughter (Gilfillan et al. *Am J Hum Genet* 82:1003-1010, 2008). Cerebellar atrophy has been demonstrated in affected males (Christianson et al. 1999; Gilfillan et al. 2008), and a reduced life expectancy has also been observed. Carrier females have been reported with mild mental retardation or learning problems (Christianson et al., 1999) and severe dyslexia (Gilfillan et al., 2008). As a consequence of the significant overlap of features between Christianson Type XLMR and Angelman Syndrome, it has been suggested that males with symptoms consistent with Angelman Syndrome, but who test normal for *UBE3A* defects, are candidates for *SLC9A6* testing (Gilfillan et al. 2008).

Genetics: Christianson type X-linked mental retardation is inherited in an X-linked recessive manner. The *SLC9A6* gene encodes isoform A6 of the solute carrier family 9 proteins which is localized to the mitochondria and functions as a sodium/hydrogen exchanger (Numata et al. *J Biol Chem* 273:6951-6959, 1998). Thus far four causative *SLC9A6* mutations have been described among four families (Gilfillan et al. 2008). The types of alteration reported are: in frame deletion, nonsense, splice site, and frameshift.

Description of This Particular Test: The solute carrier family 9, subunit A6 protein is encoded by exons 1-16 of the *SLC9A6* gene located on chromosome Xq26.3. Testing is accomplished by amplifying each coding exon and ~50 bp of adjacent noncoding sequence, then determining the nucleotide sequence using standard dideoxy sequencing methods and a capillary electrophoresis instrument.

Reference Sequences: **Genomic:** NC_000023.9 **mRNA and Protein:** CCDS_14654.1

Indication for Testing: Males with microcephaly, mental retardation, absent speech, seizures, unprovoked laughter. Males with an Angelman Syndrome phenotype who have normal *UBE3A* methylation and sequencing studies.

Sensitivity of test: The etiology of this disorder has only recently been described (Gilfillan et al. 2008). Thus it is not possible to reliably predict clinical sensitivity of *SLC9A6* testing. This gene is likely one of multiple causes of the 10%-15% of Angelman Syndrome cases that are unrelated to *UBE3A*.

Turn Around Time: Maximum of 40 days.

Specimen Requirements: See page 4 of the Requisition Form.

Price: **Sequencing of *SLC9A6*** **Exons 1-16** **\$ 790**

CPT Codes:

Sample Ascertainment	83890	\$ 30	DNA Isolation	83891	\$ 40
Amplification x 15	83898	\$ 230	Sequencing x15	83904	\$ 350
Separation	83894	\$ 60	Interpretation/Report	83912	\$ 80

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

Contact for info: Thomas L. Winder, PhD, FACMG, tom.winder@preventiongenetics.com, www.preventiongenetics.com