The University of Chicago Genetic Services Laboratories

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L1CAM analysis for L1 syndrome

Clinical Features:

L1 syndrome is the most common cause of congenital hydrocephalus and accounts for about 5-10% of males with congenital hydrocephalus (1). The phenotypic spectrum of L1 syndrome, which can range from severe to mild, includes X-linked hydrocephalus [OMIM#307000], MASA syndrome [mental retardation, aphasia, shuffling gait and adducted thumbs, OMIM#303350] and X-linked corpus callosum agenesis [OMIM#304100] (2). In less severely affected males, hydrocephalus may be subclinically present and only documented because of developmental delay. Intellectual disability ranges from mild to moderate. Intra- and interfamily phenotypic variations have been reported.

Molecular Genetics:

Mutations in the *L1CAM* [OMIM#308840] gene are a cause L1 syndrome. The majority of mutations in *L1CAM* are private (unique to each family) and all types of disease-causing mutations have been identified: nonsense, frameshift, splice-site and missense mutations. *L1CAM* codes for the neural L1 cell adhesion molecule and is involved in cell-to-cell adhesion at the cell surface.

Inheritance:

In general, congenital hydrocephalus is a common condition affecting 0.6 per 100 live births. The prevalence of X-linked hydrocephalus with stenosis of the aqueduct of Sylvius, the most common genetic form of congenital hydrocephalus, is approximately 1 in 30,000. L1 syndrome is inherited in an X-linked manner. Recurrence risk for a carrier female is 50%. Carrier females may manifest clinical findings related to the syndrome.

Test methods:

We offer full gene sequencing of all 28 coding exons and intron/exon boundaries by direct sequencing of amplification products in both the forward and reverse directions. Deletion/duplication analysis is performed by oligonucleotide array-CGH. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by array-CGH. Array-CGH will not detect low-level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of this assay may be reduced when DNA is extracted by an outside laboratory.

We also offer testing for Autosomal Recessive non-syndromic hydrocephalus. This testing includes full gene sequencing for the *CCDC88C* and *MPDZ* genes. Please see our information sheet on Autosomal Recessive non-syndromic hydrocephalus for more information.

L1CAM sequencing

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1980
CPT codes:	81407
Turn-around time:	4 - 6 weeks

L1CAM deletion/duplication analysis

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81406
Turn-around time:	4 weeks

Testing for a known mutation in additional family members by sequence analysis

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$390
CPT codes:	81403
Turn-around time:	3-4 weeks

Prenatal testing for a known mutation by sequence analysis

Sample specifications:	2 T25 flasks of cultured cells from amniocentesis or CVS or 10 mL of amniotic fluid
Cost:	$540
CPT codes:	81403
Turn-around time:	1-2 weeks

Results:

Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

References:

1. Verhagen JM, Schrander-Stumpel CT, Krapels IP et al. Congenital hydrocephalus in clinical practice: a genetic diagnostic approach. Eur J Med Genet 2011: 54: e542-547.
2. Vos YJ, de Walle HE, Bos KK et al. Genotype-phenotype correlations in L1 syndrome: a guide for genetic counselling and mutation analysis. J Med Genet 2010: 47: 169-175.