SickKids | Genome Diagnostics

Neuronal Ceroid Lipofuscinoses

Neuronal Ceroid Lipofuscinoses (NCLs, Batten disease) are the most common neurodegenerative disorders of childhood, with an incidence of about 1 in 25,000 births. Several subtypes of the disease are classified on the basis of age of onset, clinical features, biochemical analysis and detailed pathological examination of patient tissue with electron microscopy. NCLs are characterized by progressive motor and cognitive deterioration, seizures, early death, and often visual loss.

Genetics

Eight genes have been identified in which the occurrence of mutations can result in NCL. Several recurrent mutations accounting for ~80% of the disease in patients have been identified. In addition, more than 100 rare *CLN* gene mutations causing NCL have been detected. There is significant ethnic variation in the frequency of the recurrent mutations.

The disease is present when a child receives two copies of a defective *CLN* gene, one from each parent. Any person with one copy of the defective *CLN* gene is a Batten carrier. Carriers do not have, and will never develop, Batten disease. However, if two carriers wish to have children, there is a one in four chance (25%) that their baby will be born with Batten disease. There is a three in four chance (75%) that their baby will not have Batten disease.

Test Methods

- Direct mutation detection assay to test for the following recurrent mutations:

Gene	Mutation
CLN1	c.451C>T (p.Arg151X)
	c.223A>C (p.Thr75Pro)
CLN2	c.622C.T (p.Arg208X)
	c.851G>T (p.Gly284Val)
CLN3	1.02Kb deletion

- Complete sequencing of the coding region and flanking exon/intron boundaries to detect rare point mutations in the *CLN 1, 2, 3, 5, 6, 7, 8,* and *10* genes. Clinical, biochemical and pathological information on the patient is used to prioritize the *CLN* gene sequencing.

Who Should be Tested?

- Individuals clinically and/or biochemically suspected of being affected with Batten disease
- Individuals with a family history of Batten disease, to determine carrier status
- Pregnancies at risk due to family history of Batten disease

Potential Outcomes & Interpretation of Test Results

Reason for referral	*CLN* Gene Mutations Allele 1 / allele 2	Explanation
Diagnosis	None detected / none detected	This result does not support a diagnosis of Batten disease
Diagnosis	Mutation detected / none detected	This result is unable to confirm a diagnosis of Batten disease
Diagnosis	Mutation detected / mutation detected	This result confirms a diagnosis of Batten disease
Carrier testing	None detected / none detected	This individual is unlikely to be a carrier of Batten disease
Carrier testing	Mutation detected / none detected	This individual is a carrier of Batten disease and may transmit a mutation to offspring

For More Information

Online Mendelian Inheritance in Man http://www.ncbi.nlm.nih.gov/omim/

- *CLN1* #256730 • *CLN6* #606725
- *CLN2* #204500 • *CLN7* #610951
- *CLN3* #204200 • *CLN8* #600143
- *CLN5* #256731 • *CLN10*#256730

GeneReviews online clinical information resource http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=ncl

To locate a genetics center near you, please visit the Canadian Association of Genetic Counsellors website at www.cagc-accg.ca or the National Society of Genetic Counsellors website at www.nsgc.org

SickKids

1. Current molecular testing may not detect all possible mutations for this disease. A negative test does not rule out the possibility that the individual carries a rare CLN mutation not detected by this assay.

2. Test results should be interpreted in the context of clinical findings, family history and other laboratory data.

3. This test was developed and its performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes.