



The University of Chicago Genetic Services Laboratories

5841 S. Maryland Ave., Rm. L035, MC 0077, Chicago, Illinois 60637
Toll Free: (888) UC GENES (888) 824 3637
Local: (773) 834 0555 FAX: (773) 834 0556
ucgslabs@genetics.uchicago.edu www.genes.uchicago.edu
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Molecular Testing for Lissencephaly

Our testing for for lissencephaly and subcortical band heterotopia are offered in conjunction with the Molecular Genetic Studies of Brain Malformations, a research project directed by Dr. William B. Dobyns. For patients electing clinical services, participation in the research project is not required; however, it is encouraged. Frequently, after reviewing a patient's MRI films and clinical information, Dr. Dobyns can recommend a cost-effective testing strategy and provide additional information about a patient's diagnosis.

For more information about the Molecular Genetic Studies of Brain Malformations, please contact the laboratories and ask for an information packet, or visit our website at www.genes.uchicago.edu. You can also contact the research coordinator at brain@genetics.uchicago.edu.

Clinical Testing for Classical Lissencephaly

Among children with lissencephaly, FISH using a probe specific to the *LIS1* gene (such as the PAC95H6 probe) will demonstrate deletions in ~40% of patients with lissencephaly [1].

Mutation analysis by direct sequencing of the *LIS1* and or *DCX* genes will detect mutations of *LIS1* or *DCX* in ~36% of patients with lissencephaly [2]. Males and females with a posterior worse than anterior gradient of lissencephaly usually have mutations of *LIS1*, so *LIS1* sequencing is recommend first whenever a P>A gradient is seen [2]. In contrast, males with an anterior worse than posterior gradient usually have mutations of *DCX*.

Clinical Testing for Classical Subcortical Band Heterotopia

Among females with diffuse or partial frontal subcortical band heterotopia, mutation analysis of the *DCX* gene detects mutations in about 80% of patients, especially those with either diffuse bands or bilateral frontal only bands [3]. The yield in females with other atypical bands and in males with bands is lower.

Deletions/duplications

Intragenic deletions and duplications of the *LIS1* and *DCX* genes can be detected by multiplex ligation probe amplification (MLPA) and real-time quantitative PCR (RT-QPCR) analysis. We have found intragenic deletions or duplications of the *LIS1* gene in ~65%(11 of 17) of patients with lissencephaly who were normal by *LIS1* sequencing and FISH analysis. We have found intragenic deletions of the *DCX* gene in ~20%(2 of 9) of female patients with subcortical band heterotopia who were normal by *DCX* sequencing. MLPA and RT-QPCR can also detect the large *LIS1* microdeletion detectable by FISH analysis.

Deletion/duplication analysis, along with sequencing of *LIS1* and *DCX*, results in a detection rate of ~90% in patients with lissencephaly and subcortical band heterotopia.

Test methods:

We offer full gene sequencing for all coding exons and the intron/exon boundaries of *DCX* and *LIS1*. We also offer MLPA and real time-quantitative PCR to detect full gene and intragenic deletions or duplications. FISH analysis detects the 17p13 microdeletion including the *LIS1* gene, which is associated with Miller-Dieker syndrome.

Lissencephaly panel—TIER 1 (LIS1 and DCX sequencing and deletion/duplication analysis)

Sample specifications: 3 to10 cc of blood in a purple top (EDTA) tube
Cost: \$2825
CPT codes: 83891, 83898 x6, 83904 x11, 83900, 83901, 83912
Turn-around time: 6 – 8 weeks

Lissencephaly panel—TIER 2 (ARX sequencing)

Sample specifications: 3 to10 cc of blood in a purple top (EDTA) tube
Cost: \$1000
CPT codes: 83891, 83898 x2, 83904 x4, 83912
Turn-around time: 4 – 6 weeks

LIS1 mutation analysis (sequencing and deletion/duplication analysis)

Sample specifications: 3 to10 cc of blood in a purple top (EDTA) tube
Cost: \$2000
CPT codes: 83891, 83898 x3, 83904 x7, 83900, 83901 x2, 83912
Turn-around time: 4 – 6 weeks

LIS1 Sequencing analysis

Sample specifications: 3 to10 cc of blood in a purple top (EDTA) tube
Cost: \$1675
CPT codes: 83891, 83898 x4, 83904 x7, 83912
Turn-around time: 4 – 6 weeks

DCX mutation analysis (sequencing and deletion/duplication analysis)

Sample specifications: 3 to10 cc of blood in a purple top (EDTA) tube
Cost: \$1575
CPT codes: 83891, 83898 x2, 83904 x5, 83900, 83901 x2, 83912
Turn-around time: 4 – 6 weeks

DCX Sequencing analysis

Sample specifications: 3 to10 cc of blood in a purple top (EDTA) tube
Cost: \$1250
CPT codes: 83891, 83898 x3, 83904 x5, 83912
Turn-around time: 4 – 6 weeks

LIS1/DCX deletion/duplicaton analysis

Sample specifications: 3 to10 cc of blood in a purple top (EDTA) tube
Cost: \$350
CPT codes: 83891, 83900, 83912
Turn-around time: 4 weeks

Deletion analysis (FISH)

Sample specifications: 3 to10 cc of blood in a green top (sodium heparin) tube
Cost: \$325
CPT codes: 88230, 88271, 88291, 88273
Turn-around time: 10-12 days

Testing for a known mutation in additional family members

Sample specifications: 3 to10 cc of blood in a purple top (EDTA) tube
Cost: \$390-\$450
CPT codes: please contact us for specific CPT codes
Turn-around time: 2 – 3 weeks

Prenatal testing for a known mutation

Sample specifications: 2 T25 flasks of cultured cells from amniocentesis or CVS
Cost: \$590-\$650
CPT codes: please contact us for specific CPT codes
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:

Soma Das, Ph.D.
Director, Molecular Genetics Laboratory
ABMG Certified Molecular Geneticist

Stuart Schwartz, Ph.D.
Director, Cytogenetics Laboratory
ABMG Certified Cytogeneticist

Melissa Dempsey, M.S.
ABGC Certified Genetic Counselor

Darrel J. Waggoner, M.D., and William B. Dobyns, M.D.
Clinical Advisors/ABMG Certified Clinical Geneticists

References

1. Pilz DT, et al. (1998) Fluorescence in situ hybridization analysis with LIS1 specific probes reveals a high deletion mutation rate in isolated lissencephaly sequence. *Genet Medicine* 1:29-33.
2. Pilz DT, et al. (1998) LIS1 and XLIS (DCX) mutations cause most human classical lissencephaly, but different patterns of malformation. *Human Molec Genet* 7(13): 2029-37.
3. Matsumoto N, et al. (1999) Mutation Analysis of the DCX gene and genotype/phenotype correlation in subcortical band heterotopia. *European Journal of Human Genetics* 9(1): 5-12.

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