

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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NSDHL analysis for CHILD syndrome

Clinical Features:

Patients with CHILD syndrome (Congenital Hemidysplasia with Ichthyosiform erythroderma and Limb Defects [OMIM #308050], have a specific lateralization pattern and midline demarcation of an inflammatory epidermal nevus. These skin lesions are usually present at birth and persist throughout life. Alopecia and nail abnormalities are also common. Limb defects (typically hypoplasia or aplasia) occur ipsilateral to the skin defects. Epiphyseal stippling may be noted on radiographs in infancy. Underdevelopment of other organs, including the brain, lungs, heart or kidneys, on the same side as the skin defects may also occur [1-3].

Molecular and Biochemical Genetics:

Mutations of the *NSDHL* [OMIM #300275] gene that codes for a NADH steroid dehydrogenase-like protein (3 β -hydroxysteroid dehydrogenase) have been identified in patients with CHILD syndrome [2]. This protein functions in the cholesterol biosynthetic pathway and mutations are thought to result in a loss of function. The *NSDHL* gene has 7 coding exons, and over 20 mutations have been identified. Intragenic deletions of one or more exons of the *NSDHL* gene have been reported in a small percentage of patients [1,4]. No clear genotype-phenotype correlations have been reported, most likely due to random X-inactivation. The *NSDHL* gene is the human homolog of *bare patches* (Bpa) and *striated* (Str) in mice that show an X-linked dominant male-lethal phenotype [5]. Bornholdt, et al [2005] found mutations in the *NSDHL* gene in 14/14 patients with a clinical and histopathological diagnosis of CHILD syndrome [1].

Patients with CHILD syndrome have increased levels of 4-methyl- and carboxysterols in cultured lymphoblasts. Sterol analysis of plasma and scales from skin lesions is currently used for diagnosis and is available at the Clinical Mass Spectrometry Laboratory at Kennedy Krieger Institute. This test may also distinguish CHILD syndrome from CDPX2 (X-linked dominant chondrodysplasia punctata), a phenotypically similar condition caused by mutations in the *EBP* (emopamil binding protein) gene [1].

Inheritance:

CHILD syndrome is an X-linked condition that is thought to be lethal in males. A heterozygous male has been reported with somatic mosaicism [3]. Penetrance appears to be 100%, and incidence does not vary between populations. Recurrence risk for affected individuals and carrier mothers is 50%.

Test methods:

We offer full gene sequencing of all 7 coding exons and intron/exon boundaries. Our lab is currently working on setting up testing to identify intragenic deletions/duplications.

Mutation analysis (sequencing)

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	\$1325
CPT codes:	83891, 83898 x 4, 83904 x 5, 83912
Turn-around time:	4 – 6 weeks

Testing for a known mutation in additional family members

Sample specifications:	3 to 10 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:

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

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

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

Melissa Dempsey, M.S.
Certified Genetic Counselor

References:

1. Bornholdt D, et al. Mutational spectrum of *NSDHL* in CHILD syndrome (2005) *J Med Genet* 42(2): e17.
2. Konig A, et al. Mutations in the *NSDHL* gene, encoding a 3 β -hydroxysteroid dehydrogenase, cause CHILD syndrome (2000) *Am J Med Genet* 90: 339-46.
3. Herman GE. Disorders of cholesterol biosynthesis: prototypic metabolic malformation syndromes (2003) *Human Molecular Genetics* 12: R75-R88.
4. Kim CA, et al. CHILD syndrome caused by a deletion of exons 6-8 of the *NSDHL* gene (2006) *Dermatology* 211; 155-158.
5. Liu et al. The gene mutated in bare patches and striated mice encodes a novel 3 β -hydroxysteroid dehydrogenase (1999) *Nat. Genet.* 22:182-187

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