



Division of Human Genetics



Tier 2 Testing for Hearing Loss
Genes Tested: *OTOF*, *MYO7A*, *CDH23*

Molecular Genetics Laboratory

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Additional information and test requisitions are available at:

www.cincinnatichildrens.org/molecular-genetics



Helping you fit the pieces together

Shipping Instructions

Please enclose completed test requisition, audiogram and MRI/CT report, if available with sample. All information must be completed before sample can be processed.

Place samples in Styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday

Ship to:

Cytogenetics and Molecular Genetics Laboratories

3333 Burnet Avenue NRB 1042

Cincinnati, OH 45229

513-636-4474

Hereditary hearing loss affects about 1 in 1500 infants and accounts for more than 50% of the causes of childhood deafness. Mutations in many different genes result in hereditary hearing loss. These genes may be inherited in an autosomal dominant, autosomal recessive, X-linked, or mitochondrial manner.

RATIONALE FOR TESTING:

Identification of the specific cause of a child's hearing loss is an important part of a comprehensive hearing loss evaluation. Identification of a specific genetic mutation provides important information about long-term prognosis and medical management. It also provides very specific information on which to base genetic counseling for parents and other at-risk family members. Finally, identification of a genetic mutation, early in the evaluation process, may eliminate the need for further, more invasive and costly medical procedures and tests.

⦿ OTOSEQ testing is indicated for patients with sensorineural hearing loss of unknown etiology who have had normal *GJB2* (connexin 26) or Tier 1 test results previously.

⦿ OTOSEQ testing identifies three less common genetic causes of childhood sensorineural hearing loss and includes testing for mutations in the otoferlin (*OTOF*), cadherin (*CDH23*) and myosin 7A (*MYO7A*) genes. Mutations in *CDH23* and *MYO7A* account for approximately 70% of the mutations which cause Usher syndrome type I. Usher syndrome type I is associated with severe to profound congenital sensorineural hearing loss and retinitis pigmentosa with onset in childhood. Conversely, mutations in both of these genes may also be associated with nonsyndromic hearing loss. Mutations in *OTOF* are associated with auditory neuropathy in some patients and nonsyndromic hearing loss in other patients.

INDICATIONS:

Sensorineural hearing loss of unknown etiology and with normal *GJB2* (connexin 26) or Tier 1 results previously.

Note: Children with enlarged vestibular aqueduct(s) may benefit from molecular testing for mutations in the *SLC26A4* gene for Pendred syndrome prior to Tier 2 testing.

METHODOLOGY:

This test is performed by enrichment of the exons, flanking intronic and untranslated regions (5' and 3') of *OTOF*, *MYO7A* and *CDH23* using microdroplet PCR technology followed by next generation sequencing with > 40 fold coverage at every target base. All pathogenic and novel variants, as well as variants of unknown (indeterminate) significance, as determined bioinformatically, are confirmed by Sanger sequencing.

SENSITIVITY:

Overall, approximately 15-20% of the genetic causes of hearing loss can be identified through this test. Mutations in the *OTOF*, *MYO7A* and *CDH23* genes account for approximately 5% each of all congenital sensorineural hearing loss in our Midwestern U.S. population. The sensitivity of next generation sequencing is over 99% for the detection of nucleotide base changes and small deletions and insertions (<10 bases) in the regions analyzed. Larger deletions, insertions and genetic recombinational events are not identified using this test methodology. Rare primer site variants may lead to erroneous results.

SPECIMEN:

At least 5 mLs whole blood in lavender top (EDTA) tube. Label each tube with patient's name, birth date, and date of collection.

TURN-AROUND TIME:

3 months

COST:

Please call 1-866-450-4198 for current pricing or for insurance precertification and with any billing questions.

CPT CODES:

83891, 83900, 83901(x50), 83894, 83892, 83898(x50), 83904(x10), 83909(x10), 83912

RESULTS:

Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.