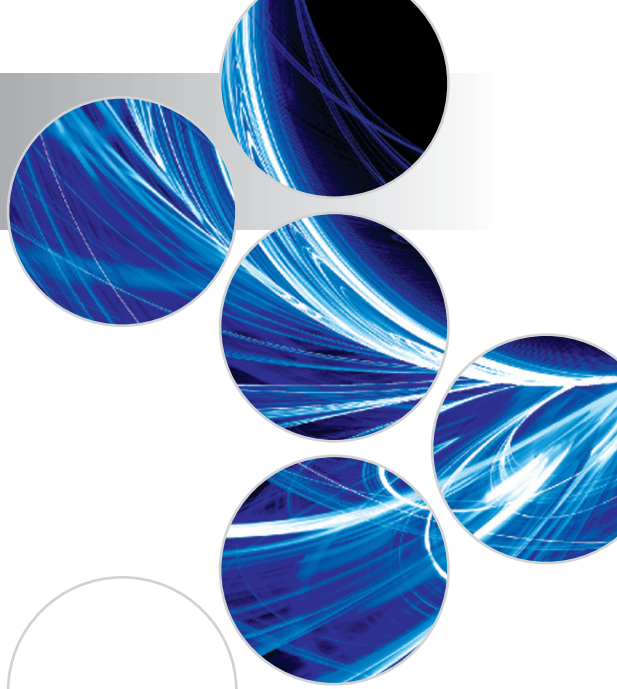
Nonsyndromic Hearing Loss secondary to *GJB2* (connexin 26) mutations



Disorder: Hearing loss affects about 1 in 500 newborns and a genetic etiology is suspected in two thirds of these patients. Hearing loss can be caused by mutations in many different genes which can be inherited in an autosomal dominant, autosomal recessive, X-linked or mitochondrial (maternal inheritance) manner.

Mutations in the *GJB2* gene, which encodes for the connexin 26 protein, are the most frequent cause of autosomal recessive nonsyndromic hereditary hearing loss, known as DFNB1. Mutations in the *GJB2* gene are found in various populations, with carrier rates of approximately 1-in-30 in the United States Caucasian population and 1-in-20 in the Ashkenazi Jewish population.

Indications:

- Sensorineural hearing loss of unknown etiology
- Carrier testing in a relative of a patient with a proven *GJB2* mutation

Specimen: At least 2 mLs whole blood in a lavender top (EDTA) tube. Alternately, two cytobrushes (cheek swabs) may be collected. (Please call 1-513-636-4474 for a free cytobrush collection kit). Label each tube or brush with patient's name, birth date, and date of collection.

Testing Methodology: PCR-based sequencing of the exon/intron boundaries and the entire coding sequence which is contained within exon 2 of the *GJB2* gene.

Analysis of *GJB2* is also offered as part of our **Hearing Loss Panel Tier 1 and OtoSeq® Hearing Loss Panel** which includes analyses for additional genes which cause hereditary hearing loss. Please refer to our web site for additional information.

Test Sensitivity: PCR-based sequencing detects 99% of the reported mutations in *GJB2*. Mutations in *GJB2* account for 18% of congenital sensorineural hearing loss in the U.S. population.

The sensitivity of DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed. Mutations in regulatory regions or other untranslated regions are not detected by this test. Large deletions involving entire single exons or multiple exons, large insertions and other complex genetic events are not identified using this test methodology. Rare primer site variants may lead to erroneous results.

Cincinnati Children's®

Human Genetics

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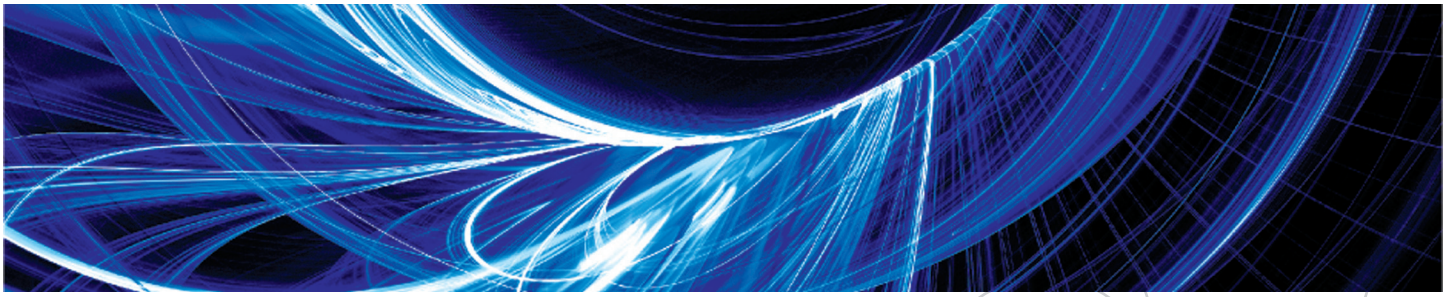

Turn-Around Time: 28 days

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

CPT Codes:

***GJB2* full gene sequence analysis**
81252

Family specific mutation analysis
81403

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.

References:

del Castillo, F. J., M. Rodriguez-Ballesteros, et al. (2005). "A novel deletion involving the connexin-30 gene, del(GJB6-d13s1854), found in trans with mutations in the GJB2 gene (connexin-26) in subjects with DFNB1 non-syndromic hearing impairment." J Med Genet 42(7): 588-594.

Lim, L. H., J. K. Bradshaw, et al. (2003). "Genotypic and phenotypic correlations of DFNB1-related hearing impairment in the Midwestern United States." Arch Otolaryngol Head Neck Surg 129(8): 836-840.

Lin, J. W., N. Chowdhury, et al. (2011). "Comprehensive diagnostic battery for evaluating sensorineural hearing loss in children." Otol Neurotol 32(2): 259-264.

Marlin, S., D. Feldmann, et al. (2005). "GJB2 and GJB6 mutations: genotypic and phenotypic correlations in a large cohort of hearing-impaired patients." Arch Otolaryngol Head Neck Surg 131(6): 481-487.

Preciado, D. A., L. H. Lim, et al. (2004). "A diagnostic paradigm for childhood idiopathic sensorineural hearing loss." Otolaryngol Head Neck Surg 131(6): 804-809.

Scott, D. A., M. L. Kraft, et al. (1998). "Identification of mutations in the connexin 26 gene that cause autosomal recessive nonsyndromic hearing loss." Hum Mutat 11(5): 387-394.

Additional information and test requisitions are available at: **www.cchmc.org/hearing-loss**

Shipping Instructions

Please enclose a completed **test requisition, audiogram and MRI/CT report, if available** with the sample. **All information must be completed before the 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
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Cincinnati, OH 45229
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