

The University of Chicago Genetic Services Laboratories



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Connexin 26/GJB2 Sequencing

Clinical Features:

Mutations in *GJB2* [OMIM#121011] are typically characterized by congenital, non-syndromic, and non-progressive sensorineural deafness. This type of hearing loss is referred to as DFNB1 [OMIM#220290]. Individuals with homozygous *GJB2* mutations can present with varying degrees of hearing loss from mild to profound [1]. Individuals with a heterozygous *GJB2* mutation have been found to have subtle differences in their otoacoustic emissions [2]. A few studies have also linked *GJB2* to syndromic forms of deafness, including Palmoplantar keratoderma, Keratitis-Ichthyosis-Deafness (KID), Vohwinkel's syndrome, and Bart-Pumphrey syndrome [1].

Inheritance:

Congenital deafness affects 1 in 1,000 births [3]. One in 31 non-Hispanic White Americans is a carrier of one of the number of reported mutations in the gene *GJB2* [4]. *GJB2* mutations occur in 50% of families in the United States with an identified autosomal recessive non-syndromic deafness, but may also be cause autosomal dominant forms of deafness and interact with mutations in *GJB6*, which encodes connexin 30, to form a double heterozygote [1].

Molecular Genetics:

GJB2 encodes for the gap junction protein connexin 26 [4]. Mutations in the *GJB2* are the most common genetic cause of non-syndromic deafness and account for 40% of all cases of pre-lingual hearing loss. The single base deletion 35delG is responsible for 20% of all childhood hereditary hearing loss [5] and 70% of all *GJB2* mutations [6]. Of individuals with DFNB1, 98% have two identifiable *GJB2* mutations and 2% are double heterozygotes, having one mutation in *GJB2* and one of two large deletions in *GJB6* [OMIM#604418].

Additional Resources:

Hereditary Hearing Loss Homepage

<http://webh01.ua.ac.be/hhh/>

Hearing Loss Association of America

7910 Woodmont Avenue
Suite 1200
Bethesda, MD USA 20814
Phone (v-tty): 301-657-2248
Fax: 301-913-9413
<http://www.hearingloss.org>

Test methods:

Our laboratory offers full gene analysis of both exons of *GJB2*. In addition, samples from individuals heterozygous for a mutation in the gene will be analyzed for the 342 kb deletion in *GJB6*.

GJB2 mutation analysis (sequencing)

Sample specifications:	3-10 cc of blood in a lavender top/EDTA tube
Turn-around-time:	4 - 6 weeks
Cost:	\$430
CPT codes:	83891, 83898, 83904, 83894, 83912

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: 2 - 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.

Molecular Diagnostics Laboratory Faculty and Staff:

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References:

1. Smith, R. and G. Van Camp. *Nonsyndromic Hearing Loss and Deafness, DFNB1*. (2008) GeneReviews from www.genetests.com.
2. Morell, R.J., et al., *Mutations in the connexin 26 gene (GJB2) among Ashkenazi Jews with nonsyndromic recessive deafness*. N Engl J Med, 1998. **339**(21): p. 1500-5.
3. Cohn, E.S., et al., *Clinical studies of families with hearing loss attributable to mutations in the connexin 26 gene (GJB2/DFNB1)*. Pediatrics, 1999. **103**(3): p. 546-50.
4. CDC. *Annual EHDI data*. 2005 [cited; Available from: <http://www.cdc.gov/ncbddd/ehdi/data.htm>].
5. Green, G.E., et al., *Carrier rates in the midwestern United States for GJB2 mutations causing inherited deafness*. Jama, 1999. **281**(23): p. 2211-6.
6. Kelley, P.M., E. Cohn, and W.J. Kimberling, *Connexin 26: required for normal auditory function*. Brain Res Brain Res Rev, 2000. **32**(1): p. 184-8.

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