Clinical Features:  
Mutations in *GJB2* (Connexin 26) [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:  
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

Hereditary Hearing Loss Homepage  
http://webh01.ua.ac.be/hhh/

Test methods:  
We offer mutation analysis of both coding exons and intron/exon boundaries of *GJB2* by direct sequencing of amplification products in both the forward and reverse directions. We also offer deletion/duplication analysis of the *GJB2* gene by MLPA or oligonucleotide array-CGH to identify deletions/duplications of one or more exons. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by array-CGH. Array-CGH will not detect low-level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of this assay may be reduced when DNA is extracted by an outside laboratory. For best results, please provide a fresh blood sample for this testing.

**GJB2 sequencing analysis**  
Sample specifications: 3-10 cc of blood in a lavender top/EDTA tube  
Cost: $450  
CPT codes: 81252  
Turn-around-time: 4 weeks
**GJB2 deletion/duplication analysis**

Sample specifications: 3-10 cc of blood in a lavender top/EDTA tube  
Cost: $1000  
CPT codes: 81402  
Turn-around-time: 4 weeks

**GJB2 targeted analysis in additional family member by sequence analysis**

Sample specifications: 3-10 cc of blood in a lavender top/EDTA tube  
Cost: $500  
CPT codes: 81253  
Turn-around time: 3 weeks

**Results:**

Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

**References:**


*Committed to CUSTOMIZED DIAGNOSTICS, TRANSLATIONAL RESEARCH & YOUR PATIENTS’ NEEDS*