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

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.

**GJB2 sequencing analysis**
- Sample specifications: 3-10 cc of blood in a lavender top/EDTA tube
- Cost: $500
- 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 or email.

For more information about our testing options, please visit our website at dnatesting.uchicago.edu or contact us at 773-834-0555.

References: