

## Hearing Loss: *GJB2* & *GJB6* Gene Sequencing Panel

Test Code: SX

Turnaround time: 3 weeks

CPT Codes: 81479 x1

### Condition Description

**Notice: This test has been discontinued.**

**NTD Genetics no longer accepts samples for this test. Please call: 470-378-2200 for assistance in identifying alternative testing options.**

In the United States, approximately 1 in 1000 children are diagnosed with prelingual hearing loss (HL) or deafness. Approximately half of prelingual hearing loss or deafness is attributed to environmental exposures and the remaining half to genetic causes. Approximately 30% of hereditary hearing loss is estimated to be syndromic (associated with other birth defects) while the remaining 70% is non-syndromic (isolated and not associated with other findings). Non-syndromic deafness is mainly due to recessive genes (75-80%) and over 20 such genes have been identified, but non-syndromic deafness may also be inherited in autosomal dominant, X-linked, or mitochondrial patterns.

Molecular testing can aid in rapid diagnosis of hearing loss. Early diagnosis of hearing defects can provide diagnostic information, facilitate timely intervention, and assist with genetic counseling.

Connexins are transmembrane proteins that form channels that allow rapid transport of small molecules between cells; the proteins connexin 26 and connexin 30 interact to form a channel that functions in the inner ear. The *GJB2* gene encodes the connexin 26 protein and is involved in 50% of autosomal recessive hearing loss. The *GJB6* gene is located near *GJB2*, and encodes the protein connexin 30. Patients with non-syndromic hearing loss have been found to have two mutations in connexin 26, two mutations in connexin 30, or compound heterozygosity for one mutation in connexin 26 and another in connexin 30 [1,2].

This test panel includes complete sequencing of the genes for connexin 26 and connexin 30, and testing for the common 342kb deletion in connexin 30.

Please [click here](#) for the GeneReviews summary on this condition.

#### References:

- Pandya A, *et al.* (2003) Frequency and distribution of *GJB2* (connexin 26) and *GJB6* (connexin 30) mutations in a large North American repository of deaf probands. *Genet Med* 5:295-303.
- Del Castillo I, *et al.* (2003). Prevalence and evolutionary origins of the del(*GJB6*-D13S1830) mutation in the *DFNB1* locus in hearing-impaired subjects: a multicenter study. *Am J Hum Genet* 73:1452-8.

### Genes

[GJB2](#), [GJB6](#)

### Indications

This test is indicated for:

- Individuals with clinical findings consistent with non-syndromic hearing loss when mitochondrial etiologies have been ruled out.
- For carrier testing of individuals with a family history of non-syndromic hearing loss.

### Methodology

PCR amplification of the exons and flanking regions contained in the *GJB2* and *GJB6* genes are performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions. The *GJB6* gene 342kb deletion is detected by allele-specific amplification.

### Detection

*GJB2* Sequencing:

Detects over 98% of sequence variants in the coding region and splice junctions.

*GJB6* Sequencing:

It is possible that some patients with a typical presentation may not carry a mutation detected by this analysis. This analysis may detect novel variants of unclear effect, which may require further studies. Mutations in the promoter region, some mutations in the introns, and other regulatory elements cannot be detected by sequence analysis. Large deletions such as the most common 342 kb deletion, and insertions will not be detected by sequence analysis.

**GJB6 Deletion:**

Will detect nearly all 342kb common deletion alleles in Connexin 30. Other deletion mutations reported in *GJB6*, including the 232kb (reported in Spain), 309kb (reported in UK), 140kb, and 150kb deletions will be detected by the separate *GJB6* deletion/duplication array.

**Specimen Requirements**

**Submit only 1 of the following specimen types**

**Type: DNA, Isolated****Specimen Requirements:**

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Type: Whole Blood (EDTA)****Specimen Requirements:**

EDTA (Purple Top)

Infants and Young Children ( 2 years of age to 10 years old: 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

**Type: Saliva****Specimen Requirements:**

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**Related Tests**

- The Hearing Loss: Comprehensive Panel (HL) is indicated for patients who have not have previous molecular testing and includes sequencing of the *GJB2* and *GJB6* genes, targeted mutation analysis of the *GJB6* common 342kb deletion, and testing for mitochondrial mutations associated with aminoglycoside sensitivity.
- For patients with mutations not identified by full gene sequencing, Hearing Loss: Connexin 26 and 30 Deletion/Duplication (PI) is available.
- Known Mutation Testing (KM) is available to family members if mutations are identified by sequencing.
- Mitochondrial-Related Hearing Loss: Mutation Panel (QJ) for patients with a history of aminoglycoside sensitivity.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.