Hearing Loss: GJB2 & GJB6 Gene Deletion/Duplication Panel

**Condition Description**

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 involves deletion/duplication analysis of the entire coding sequence of the GJB2 and GJB6 genes that encode the connexin 26 and connexin 30 proteins.

Please [click here](#) for the GeneReviews summary on deafness and hereditary hearing loss.

**References**


**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 and testing of connexin 30 has resulted in either no mutations/one mutation found.

**Methodology**

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient’s phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations.

Results of molecular analysis must be interpreted in the context of the patient’s clinical and/or biochemical phenotype.

**Specimen Requirements**

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:
In EDTA (purple top) tube:
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

Type: Saliva

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

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.
- 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.