Hearing Loss: Deletion/Duplication Panel

Test Code: MD190  
Turnaround time: 2 weeks  
CPT Codes: 81228 x1, 81406 x1

Condition Description

Hearing loss can be categorized by type, onset, or severity. Sensorineural hearing loss is the result of impairment of the inner ear structures. Conductive hearing loss is the result of abnormalities of the external ear and/or the middle ear. Mixed hearing loss is a combination of sensorineural and conductive hearing loss. Central auditory dysfunction is the result of damage or dysfunction of the eighth cranial nerve, auditory brain stem, or cerebral cortex. Age of onset is characterized as prelingual (before speech develops) or postlingual (after speech develops). Severity ranges from mild to profound.

The prevalence of bilateral sensorineural hearing loss is 1 in 500 newborns and 3.5 per 1000 adolescents. While the causes of hearing loss are diverse, at least 50% (and possibly up to two-thirds) of prelingual hearing loss is genetic in origin. The remaining cases of hearing loss are thought to be due to environmental factors or unidentified genetic factors. Hearing loss can be associated with a particular genetic syndrome, such as Usher syndrome or Pendred syndrome; however, most cases of prelingual sensorineural hearing loss are the result of an autosomal recessive, nonsyndromic condition. Genetic hearing loss can be inherited in many ways. Autosomal recessive causes account for approximately 80% of hearing loss cases and are typically prelingual in onset. Autosomal dominant causes account for approximately 20% of hearing loss cases and are typically postlingual in onset. Less than 1% of hearing loss cases are inherited through the mitochondria or the X chromosome. Approximately 50% of autosomal recessive nonsyndromic hearing loss cases are caused by mutations in the \textit{GJB2} and \textit{GJB6} genes.

The Hearing Loss Panel includes deletion/duplication analysis of genes in which pathogenic variants are known to cause hearing loss or have hearing loss as part of the clinical spectrum of disease. The vast majority of genes on this panel cause sensorineural hearing loss.

References:
- GeneReviews
- OMIM

Genes

\texttt{ABHD12, ABHD5, ACTG1, ADGRV1, ARSB, ATP6V1B1, BSND, BTD, CCDC50, CDH23, CFAM16, CHD7, CIB2, CISD2, CLDN14, CLRN1, COCH, COL11A2, COL4A5, CRYM, DIABLO, DIAPH1, DNMT1, DSP, ESRRB, EYA1, EYA4, EGF3, FGFR3, FOXC1, FOXI1, GIPC3, GJB2, GJB3, GJB6, GPSM2, GRHL2, GRXCR1, GSDME, HARS2, HGFL, HSD17B4, ILDR1, KCNE1, KCNJ10, KCNQ4, LHFP5, LOXHD1, LRTOMT, MARVELD2, MAS1P, MSR3, MYH14, MYH9, MYO15A, MYO1A, MYO3A, MYO6, MYO7A, OTOA, OTOF, PCDH15, PITX2, PVJK, POU3F4, PRPS1, RDX, RPS6KA3, SALL1, SALL4, SERPINB6, SIX1, SLC17A8, SLC26A4, SLC26A5, SLC29A3, SMPX, TECTA, TIMM8A, TP2, TMC1, TMIE, TMPRSS3, TPRN, TRIOBP, USH1C, USH1G, USH2A, WFS1, WHRN}

Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of hearing loss.
- Carrier testing in adults with a family history of hearing loss.

Methodology

Deletion/Duplication Analysis: DNA isolated from peripheral blood is hybridized to a gene-targeted CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes that 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

Deletion/Duplication: Detection is limited to duplications and deletions. The CGH array will not detect point or intronic pathogenic variants. 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

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: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:

In microtainer: 10 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

**Related Tests**

- Hearing Loss: Sequencing Panel
- Hearing Loss Panel: GJB2 and GJB6 Sequencing, GJB6 Common Deletion, and Targeted Mitochondrial Analysis
- Hearing Loss: GJB2 & GJB6 Gene Sequencing Panel
- Hearing Loss: GJB2 Gene Sequencing
- Hearing Loss: GJB6 Gene Sequencing