NON-SYNDROMIC RECESSIVE DEAFNESS

London Health Sciences Centre | St. Joseph's Health Care London

Pathology and Laboratory Medicine

Orderable – E-order/Requisition

Turnaround Time: 6 weeks

Laboratory:
Molecular Diagnostics Lab

Requisition:
MOLECULAR DIAGNOSTICS REQUISITION

Method of Analysis:
All coding exons and 20 bp of flanking intronic sequence are enriched using an LHSC custom targeted hybridization protocol (Roche Nimblegen), followed by high throughput sequencing (Illumina). Sequence variants and copy number changes are assessed and interpreted using clinically validated algorithms and commercial software (SoftGenetics: Nextgene, Geneticist Assistant, Mutation Surveyor; and Alamut Visual). All exons have >300x mean read depth coverage, with a minimum 100x coverage at a single nucleotide resolution. This assay meets the sensitivity and specificity of combined Sanger sequencing and

Alternate Name(s):

RD

Specimen:

Whole blood-2 x 4 mL Lavender EDTA top Vacutainer tube

Collection Information:

Blood samples must be maintained at room temperature.

Reference Ranges:

See report

Interpretive Comments:

Severe deafness or hearing impairment is the most prevalent inherited sensory disorder, affecting about 1 in 1,000 children. Although a number of mutant genes have been identified that are responsible for syndromic (multiple phenotypic disease) deafness such as Waardenburg syndrome and Usher 1B syndrome, little is known about the genetic basis of non-syndromic (single phenotypic disease) deafness (PMID:9139825). Mutations in the GJB2 (Cx26) gene, which codes for a gap junction protein, may be responsible for either autosomal recessive (DFNB1) or dominant (DFNA3) forms of hereditary hearing impairment (PMID:11438992). In addition a recurrent ~340kb deletion (D GJB6-D13S1830), which includes a significant portion of the coding sequence of the GJB6 (Connexin 30) gene, has been reported to be associated with an inherited hearing impairment (PMID:11807148). Studies (PMID:9529365) indicate that DFNB1 (13q11-12) causes 20% of all childhood deafness and may have a carrier rate as high as 2.8%.

NON-SYNDROMIC RECESSIVE DEAFNESS

London Health Sciences Centre
St JOSEPH'S HEALTH CARE LONDON
Pathology and Laboratory Medicine

Comments:

Genes Tested (hg19; HGVS nomenclature): GJB2(NM_004004.5), GJB6(NM__001110219.2)

Critical Information Required:

Pedigree required

Storage and Shipment:

Must be received within 5 days of collection, shipped at room temperature by courier/overnight delivery.

MLPA copy number analysis. All variants interpreted as either ACMG category 1, 2, or 3 (pathogenic, likely pathogenic, VUS; PMID: 25741868) are confirmed using Sanger sequencing, MLPA, or other assays. ACMG category 4 and 5 variants (likely benign, benign) are not reported, but are available upon request. This assay has been validated at a level of sensitivity equivalent to the Sanger sequencing and standard copy number analysis (>99%; PMID: 27376475).

Test Schedule:
As required,
Monday to Friday 0800-1600 hours