Deafness Gene Panel

Preface:

Hearing loss has an incidence of 1 in 500 newborns and a genetic etiology is suspected in two thirds of these patients. This can be caused by mutations in many different genes with a pattern of autosomal dominant, autosomal recessive, X-linked or mitochondrial (maternal) inheritance.

The Otogenetics Deafness Gene Panel (cat# Oto-DA3) allows the clinician or researcher to sequence one hundred and twenty-nine (129) genes known to cause both nonsyndromic hearing loss and syndromes that can present themselves as nonsyndromic.

Testing Rationale:

The Otogenetics DA3 panel plays a vital role when performing a comprehensive hearing loss evaluation. The DA3 panel can drastically reduce the time it take to identify the specific cause of a child’s hearing loss through the thorough sequencing of these 129 genes, including GJB2 (connexin 26), one of the most common genetic causes. This genetic information is critical when identifying and providing information for:

- Long-term prognosis
- Medical management/intervention
- Specific information for genetic counseling

Access to this information may significantly reduce medical costs and eliminate unnecessary procedures. This information may also may provide treatment options in a more timely fashion.

Methodology:

The Otogenetics DA3 Panel is performed by next generation sequencing using custom oligonucleotide-based target capture followed by Illumina HiSeq sequencing of the coding regions of the DA3 panel genes; with > 100 fold coverage at every target base.

Clinically significant variants are identified using the Burrows-Wheeler Aligner (BWA) and confirmed by Sanger sequencing.

Results:

Each Otogenetics DA3 Panel report includes a detailed explanation of all clinically-relevant variants.

Visit www.otogenetics.com for more information.

Test Name:
Otogenetics DA3 Panel, Cat# Oto-Da3

Turn-Around-Time:
Approximately 5-6 weeks

Specimen Requirement:
5 mL whole blood, or by saliva collection kit

Cumulative Percentage Coverage of Target Genes (%)

Oto-DA3 Panel, 500x Coverage

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Cumulative Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>150</td>
<td>95.3%</td>
</tr>
<tr>
<td>350</td>
<td>99.3%</td>
</tr>
<tr>
<td>550</td>
<td>99.1%</td>
</tr>
<tr>
<td>750</td>
<td>99%</td>
</tr>
<tr>
<td>950</td>
<td>95.3%</td>
</tr>
<tr>
<td>1150</td>
<td>90%</td>
</tr>
<tr>
<td>1350</td>
<td>80%</td>
</tr>
</tbody>
</table>

Mean = 490
Bases = 213545

> 20x = 99.5%
> 30x = 99.3%
> 40x = 99.1%
> 50x = 99%
> 100x = 95.3%
**Deafness Gene Panel**

**DA3 Gene List**

- ACTB, ACTG1, ATP6V1B1, ATP6V1B2
- BC51L, BSND
- CATSPER2, CCDC50, CDH23, CEACAM16, CLDN14, CLRN1, COCH, COL11A2, COL9A2, COL9A3, CRYP
- DFNA5, DFNB31, DFNB59, DIAPH1, DSPP
- ECE1, EDNRA, EDNRB, ERCC2, ERCC3, ESPN, ESRRB, EYA4
- FAS, FGFR3, FGFR3, FOXI1
- GATA3, GIPC3, GJA1, GJB1, GJB2, GJB3, GJB4, GJB6, GPR98, GPSM2, GRHL2, GRXCR1, GSTP1
- HAL, HGF
- ILDR1
- JAG1
- KCNE1, KCNJ10, KCNQ1, KCNQ4, KIAA1199

**TotSeq™ Targeted Human DA3 Genes Sample Preparation Flowchart**

**STEP**

- DNA Fragmentation, End Repair, Tailing, Ligation (Oto-DLP-001)
- DNA Library Amplification Using LM-PCR (Oto-DLP-001)
- Pooling of Amplified Multiplex DNA Libraries
- Hybridize Samples to Oto-DA3-Probe (Oto-DA3-Primer)
- Wash and Recover Captured DNA (Oto-Enrich-001)
- Amplify Captured DNA (Oto-Enrich-001)
- Assess Enrichment Using qPCR (Oto-DA3-Primer)
- Proceed to Sequencing via Illumina HiSeq/MiSeq

**TIME**

- 4 hours
- 2 hours
- 2 hours
- 3 days
- 2.5 hours
- 2 hours
- 2 hours
- 10 days
- 27 hours

**References:**

- [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3881369/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3881369/)

**For Research Use Only**

Copyright 2014 by Otogenetics Corporation. Products and specifications are subject to review and change without notice.