DFN3 X-Linked (POU3F4, DFNX2) Hearing Loss

DFN3-related hearing loss accounts for ~50% of all cases of X-linked hearing loss. DFN3-related X-linked hearing loss is caused by mutations in the X chromosome gene POU3F4. Hearing loss in affected males is prelingual, progressive, and mixed conductive-sensorineural. Affected individuals may have temporal bone abnormalities, stapedial fixation, and perilymphatic gusher if the stapes is disturbed during surgery. Female carriers with one POU3F4 mutation may show no or slight hearing loss, and mild perilymphatic gusher during surgery.

**Genetics**

Many different genes play a role in hearing loss. Mutations in the POU3F4 gene are responsible for ~50% of all X-linked cases, making this the most common cause of X-linked hearing loss. Mutations in the POU3F4 gene are typically deletions that remove a part of all of the POU3F4 gene, or less often point mutations within the POU3F4 gene.

**Who Should be Tested?**
- Individuals clinically suspected of being affected with X-linked hearing loss
- Individuals with a family history of X-linked hearing loss to determine carrier status

**Test Methods**
- Quantitative testing of the POU3F4 gene to detect large deletions using MLPA (Multiplex Ligation-dependent Probe Amplification).
- Complete sequencing of the coding region and flanking exon/intron boundaries of the POU3F4 gene to identify point mutations.

**Test Sensitivity**

Most mutations in the POU3F4 gene will be detected. As other forms of hearing loss may be caused by mutations in genes other than the POU3F4 gene, these cases cannot be detected by this test.

**Potential Outcomes & Interpretation of Test Results**

<table>
<thead>
<tr>
<th>Sex of Patient</th>
<th>POU3F4 Gene Mutation</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>None detected</td>
<td>This result does not support a diagnosis of POU3F4-related hearing loss</td>
</tr>
<tr>
<td>Male</td>
<td>Mutation detected</td>
<td>This result confirms a diagnosis of POU3F4-related hearing loss</td>
</tr>
<tr>
<td>Female</td>
<td>None detected / none detected</td>
<td>It is unlikely that this person is affected with, or is a carrier of POU3F4-related hearing loss</td>
</tr>
<tr>
<td>Female</td>
<td>Mutation detected / none detected</td>
<td>This individual is affected with, or is a carrier of POU3F4-related hearing loss</td>
</tr>
</tbody>
</table>

For More Information


GeneReviews online clinical information resource - [http://www.genetests.org/profiles/deafness-overview](http://www.genetests.org/profiles/deafness-overview)

The Canadian Association of the Deaf Homepage: [http://www.cad.ca](http://www.cad.ca)

To locate a genetics center near you, please visit the Canadian Association of Genetic Counsellors website at www.cagc-accg.ca or the National Society of Genetic Counsellors website at www.nsgc.org

1. Current molecular testing may not detect all possible mutations for this disease. A negative test does not rule out the possibility of X-linked hearing loss.
2. The clinical course or severity of symptoms cannot be predicted by molecular analysis.
3. Test results should be interpreted in the context of clinical findings, family history and other laboratory data.
4. These tests were developed and the performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. They have not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. These tests are used for clinical purposes.