

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

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

For More Information

Online Mendelian Inheritance in Man: <http://www.ncbi.nlm.nih.gov/omim>. Item# 304400

GeneReviews online clinical information resource - <http://www.genetests.org/profiles/deafness-overview>

The Canadian Association of the Deaf Homepage: <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 their 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.

