

# NON-SYNDROMIC HEARING LOSS

## CONNEXIN 26 & 30

Non-syndromic sensorineural hearing loss (NSHL) is a common disability affecting approximately 1 in 1000 newborns. In approximately 50% of children with congenital deafness the hearing loss is due to inherited causes. The most common form of inherited hearing loss is autosomal recessive non-syndromic hearing loss (AR-NSHL), which affects approximately 1 in every 2500 children. Connexin 26 and connexin 30 are gap junction proteins important in the development of the inner ear. Mutations in the genes that encode these proteins (*GJB2* and *GJB6* respectively) can cause AR-NSHL.

### GENETICS

Many different genes have been shown to play a role in NSHL. Mutations in the *GJB2* gene are responsible for 50-80% of all AR-NSHL cases, making this the most common cause of AR-NSHL. Recurrent deletions of the *GJB6* gene are also known to cause AR-NSHL in ~20% of patients who also have one *GJB2* gene mutation, a result of digenic inheritance.

### WHO SHOULD BE TESTED?

- Individuals clinically suspected of being affected with NSHL
- Individuals with a family history of NSHL, to determine carrier status

### TEST METHODS

- Complete sequencing of the coding region and flanking exon/intron boundaries of the *GJB2* gene to identify point mutations.
- Quantitative testing of the *GJB2* or *GJB6* genes to detect larger deletions or duplications, using MLPA (Multiplex Ligation-dependent Probe Amplification).

### TEST SENSITIVITY

Most mutations in the *GJB2* gene will be detected, however 20-50% of AR-NSHL cases and other forms of sensorineural hearing loss are not caused by mutations in the *GJB2* or *GJB6* genes. These cases cannot be detected by these methodologies.

### POTENTIAL OUTCOMES & INTERPRETATION OF TEST RESULTS

Reason for referral	<i>GJB</i> Gene Mutations Allele 1 / allele 2	Explanation
Diagnosis	None detected / none detected	This result does not support a diagnosis of non-syndromic hearing loss.
Diagnosis	Mutation detected / none detected	This result is unable to confirm a diagnosis of non-syndromic hearing loss.
Diagnosis	Mutation detected / mutation detected	This result supports a diagnosis of non-syndromic hearing loss.
Carrier testing	None detected / none detected	This individual is unlikely to be a carrier of a mutation in either the <i>GJB2</i> or <i>GJB6</i> genes.
Carrier testing	Mutation detected / none detected	This individual is a carrier of non-syndromic hearing loss, and may transmit a mutation to offspring.

### For More Information

Online Mendelian Inheritance in Man: <http://www.ncbi.nlm.nih.gov/omim>. Item# 121011

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

The Canadian Association of the Deaf Homepage: <http://www.cad.ca>

Connexins and Deafness Homepage: <http://www.crg.es/deafness>.

To locate a genetics center near you, please visit the Canadian Association of Genetic Counsellors website at [www.cagc-accg.ca](http://www.cagc-accg.ca) or the National Society of Genetic Counsellors website at [www.nsgc.org](http://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 NSHL.

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.