

# PENDRED SYNDROME

Pendred syndrome is characterized by congenital sensorineural hearing loss, temporal bone anomalies, and the development of euthyroid goiter in late childhood to early adulthood. Pendred syndrome is caused by mutations in the *SLC26A4* gene which result in a deficiency of the protein pendrin. A form of non-syndromic deafness (DNFB4) is also caused by mutations in this gene. Individuals with DNFB4 have sensorineural hearing loss and may have temporal bone malformations, but do not have thyroid abnormalities.

## GENETICS

Pendred syndrome is an autosomal recessive disorder that is present when a child receives two copies of a defective *SLC26A4* gene, one from each parent. A person with one copy of the defective *SLC26A4* gene is a Pendred syndrome carrier and is not affected, however has a 50% chance of transmitting the defective gene to a child.

The gene responsible for Pendred syndrome, *SLC26A4*, has been localized to chromosome 7q31. Three recurrent mutations account for ~50% of the Pendred mutant alleles in Caucasians of northern European descent who have a confirmed diagnosis of Pendred syndrome: p.Leu236Pro (26%), p.Thr416Pro (15%), and c.1001+G>A (14%).

## TEST METHODS

- Complete sequencing of the 22 exon coding region and flanking exon/intron boundaries of the *SLC26A4* gene to identify point mutations
- Quantitative testing of the *SLC26A4* gene to detect larger deletions, using MLPA (Multiplex Ligation-dependent Probe Amplification)

## TEST SENSITIVITY

Mutations in the *SLC26A4* gene are responsible for ~50% of individuals affected with Pendred syndrome from multiplex families, and 20% of individuals from simplex families.

## WHO SHOULD BE TESTED?

- Individuals clinically suspected of being affected with Pendred syndrome or DNFB4
- Individuals with a family history of Pendred syndrome or DNFB4, to determine carrier status

## POTENTIAL OUTCOMES & INTERPRETATION OF TEST RESULTS

Reason for referral	<i>SLC26A4</i> Gene Mutations allele 1 / allele 2	Explanation
Diagnosis	None detected / none detected	This result does not support a diagnosis of Pendred syndrome / DNFB4.
Diagnosis	Mutation detected / none detected	This result is unable to confirm a diagnosis of Pendred syndrome / DNFB4.
Diagnosis	Mutation detected / mutation detected	This result supports a diagnosis of Pendred syndrome / DNFB4.
Carrier testing	None detected / none detected	This individual is unlikely to be a carrier of Pendred syndrome / DNFB4.
Carrier testing	Mutation detected / none detected	This individual is a carrier of Pendred syndrome / DNFB4, and may transmit a mutation to offspring.

## For More Information

Online Mendelian Inheritance in Man: <http://www.ncbi.nlm.nih.gov/omim>. Item # 274600

GeneTests online clinical information resource - <http://www.genetests.org/profiles/pendred>

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 that the individual has a rare mutation not included in the assay and is affected with Pendred syndrome.

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. This test was developed and its performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. It has 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. This test is used for clinical purposes.