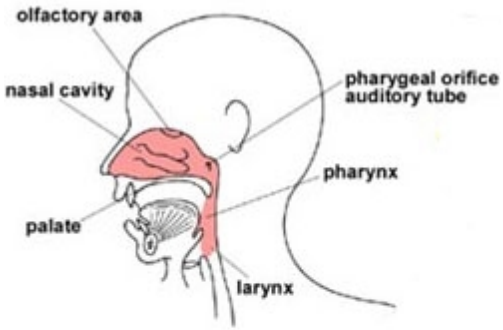
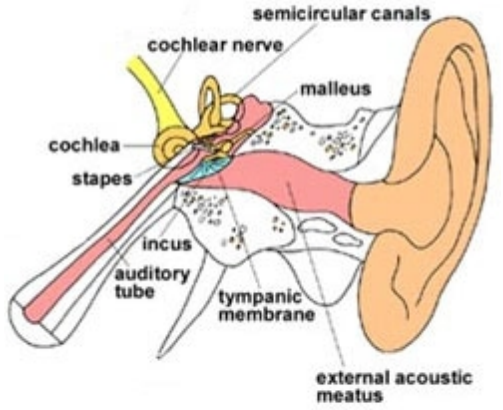
Ear, Nose, and Throat





The human ear, nose and throat are related in their functions, and thus often in the disorders that affect them. The ear is connected with the nose and throat by the auditory (or Eustachian) tube, which leads to the pharynx.

[Reproduced from University of Maryland Medical School, Otolaryngology Health guide, with permission]

Within the structures of the ear, nose and throat are complex and interrelated mechanisms that allow a person to make sound, hear, maintain balance, smell, breathe, and swallow. Traditionally, treatment of the ear — otology — was associated with that of the eye in medical practice. With the development of laryngology — the study of the throat — in the late 19th century, the connection between the ear and throat became known. Thus the birth of a discipline called otolaryngology.

Many people associate otolaryngologists with the treatment of ear infections, hearing loss and sinus problems. Otolaryngology actually encompasses the treatment of many diverse conditions, including: dizziness, facial plastic and reconstructive surgery, head and neck cancer, hearing loss, problems of the larynx and sinus, difficulties swallowing, tumors of the auditory nerve, and voice production.

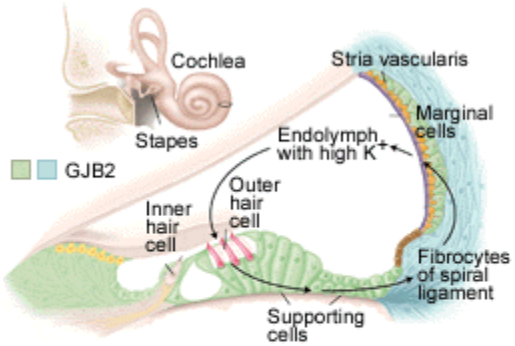
When diagnosing ear, nose, and throat disorders, it is important to differentiate genetic disorders from those due to environmental influences. This is often difficult as similar clinical features may be produced by different environmental factors or by different genes or groups of genes.

Deafness

Hearing loss is extremely common and can present at any time from infancy to old age. About 1 in 1000 infants has profound hearing impairment, with half thought to be of genetic origin. Many deafness genes exist, but the most common cause of hearing loss in American and European populations is a mutation in the *connexin 26* (*Cx26*) gene. *Cx26* has a carrier rate of 3%, similar to that for cystic fibrosis, and it causes about 20% of childhood deafness.

Mutations in *Cx26* cause congenital syndromic and nonsyndromic deafness—that is, the deafness is not accompanied by other symptoms, such as blindness. *Cx26* is located on chromosome 13q11-12 and codes for a gap junction protein called connexin 26. Gap junctions are plasma membrane channels that allow the movement of small molecules and ions between adjacent cells. Gap junctions of the inner ear may play a role in maintaining potassium homeostasis, which is important for inner-ear function and, thus, hearing. It has been proposed that mutations in *Cx26* may disrupt potassium circulation and result in deafness.

The discovery that *Cx26* mutations are a cause of congenital hearing loss can help in the early diagnosis of hearing impairment. Early identification and management of deafness is important for the development of language and social skills.



Connexin 26 (GJB2) is one of the main proteins involved in potassium (K+) homeostasis in the cochlea of the inner ear. It is found in the supporting cells, fibrocytes of the spiral ligament and in cells of the spiral limbus.[Adapted from Steel, K.P. (1999) *Science* 285, 1363-1364, with permission.]

Important Links

Gene sequence

Genome view see gene locations

LocusLink [www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=2706] collection of gene-related information

BLink [www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=6980948&org=1] related sequences in different organisms

The literature

Research articles online full text

Books online books section

OMIM catalog of human genes and disorders

Websites

NIDCD [www.nih.gov/nidcd/] National Institute on Deafness and Other Communication Disorders

Info to Go [clerccenter.gallaudet.edu/InfoToGo/index.html] from Gallaudet University

GeneClinics [www.geneclinics.org/profiles/dfnb1/] a medical genetics resource

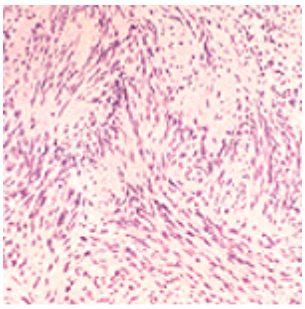
MEDLINE*plus* [www.nlm.nih.gov/medlineplus/hearingdisordersdeafness.html] links compiled by the National Library of Medicine

Neurofibromatosis

Neurofibromatosis, type 2, (NF-2) is a rare inherited disorder characterized by the development of benign tumors on both auditory nerves (acoustic neuromas). The disease is also characterized by the development of malignant central nervous system tumors as well.

The NF2 gene has been mapped to chromosome 22 and is thought to be a so-called 'tumor-suppressor gene'. Like other tumor suppressor genes (such as p53 and Rb), the normal function of NF2 is to act as a brake on cell growth and division, ensuring that cells do not divide uncontrollably, as they do in tumors. A mutation in NF2 impairs its function, and accounts for the clinical symptoms observed in neurofibromatosis sufferers. NF-2 is an autosomal dominant genetic trait, meaning it affects both genders equally and that each child of an affected parent has a 50% chance of inheriting the gene.

We are learning more about the function of the NF2 gene through studies of families with neurofibromatosis type 2 and through work in model organisms, particularly mice. The exact molecular function of NF2 in the cell is still unknown, although the protein is similar to the ERM family of cytoskeleton-membrane linker proteins. Further work on the binding partners of NF2 would help to identify potential specific targets for future drug therapies.



Microscopic section of a schwannoma, a tumor commonly found in patients with NF-2. [Image credit: K Roth and Robert Schmidt, Washington University, St. Louis, MO, USA.]

Important Links

Gene sequence

Genome view see gene locations

LocusLink [www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=neurofibromatosis&ORG=Hs&V=0] collection of gene-related information

BLink [www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4557793&org=1] related sequences in different organisms

The literature

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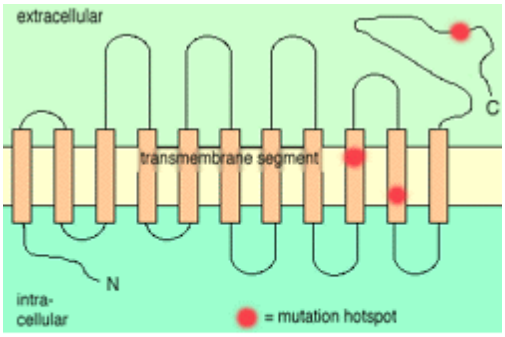
OMIM [www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=101000] catalog of human genes and disorders

Pendred syndrome

Pendred syndrome is an inherited disorder that accounts for as much as 10% of hereditary deafness. Patients usually also suffer from thyroid goiter. The recent discovery of the gene for Pendred syndrome illuminates a disorder that has confounded scientists for more than a century.

In December of 1997, scientists at NIH's National Human Genome Research Institute used the physical map of human chromosome 7 to help identify an altered gene, *PDS*, thought to cause pendred syndrome. The normal gene makes a protein, called pendrin, that is found at significant levels only in the thyroid and is closely related to a number of sulfate transporters. When the gene for this protein is mutated, the person carrying it will exhibit the symptoms of Pendred syndrome.

Because goiter is not always found in Pendred syndrome patients, it is possible that a defective pendrin gene will turn out to be responsible for some cases of deafness that had not previously been attributed to this disorder. The discovery of pendrin should also stimulate new angles of research into thyroid physiology and the role of altered sulfur transport in human disease.



Model of the human pendrin protein, based on the predicted amino acid sequence. The approximate positions of mutations in some pendred syndrome patients are shown in red.

Important Links

Gene sequence

Genome view see gene locations

LocusLink [www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=pendred%20OR%20PDS&ORG=Hs&V=0] collection of gene-related information

BLink [www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4505697&org=1] related sequences in different organisms

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Websites

Research News [www.nhgri.nih.gov/NEWS/Pendred/] from the National Human Genome Research Institute, NIH

GeneClinics [www.geneclinics.org/profiles/pendred/] a medical genetics resource