
# Hearing Biochemistry

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| Overview |
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| **Resources** (Where to go for more) |
| **Hearing organization** (What it looks like) |
| **Hearing genes and proteins** (Who's involved and what can go wrong) |

| Resources |
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| Neuromuscular Home Page (Washington University) |
| **Brown, R. H., Jr., and J. R. Mendell.** 2001. Disorders of smell, taste, and hearing, pp. 178-187. *In* E. Braunwald, A. S. Fauci, D. L. Kasper, S. L. Hauser, D. L. Longo, and J. L. Jameson (ed.), Harrison's principles of internal medicine, 15th ed. McGraw-Hill, Inc., New York. |
| **Petit, C., J. Levilliers, and J.-P. Hardelin.** 2001. Molecular genetics of hearing loss. Annu. Rev. Genet. **35:**589-646. |
| **Petit, C., J. Levilliers, S. Marlin, and J-P. Hardelin.** 2001. Hereditary hearing loss, pp. 6281-6328. *In* C. R. Scriver, A. L. Beaudet, W. S. Sly, D. Valle, B. Childs, K. W. Kinzler, & B. Vogelstein (ed.), The metabolic and molecular bases of inherited disease, 8th ed. McGraw-Hill, Inc., New York. |

| Hearing Organization |
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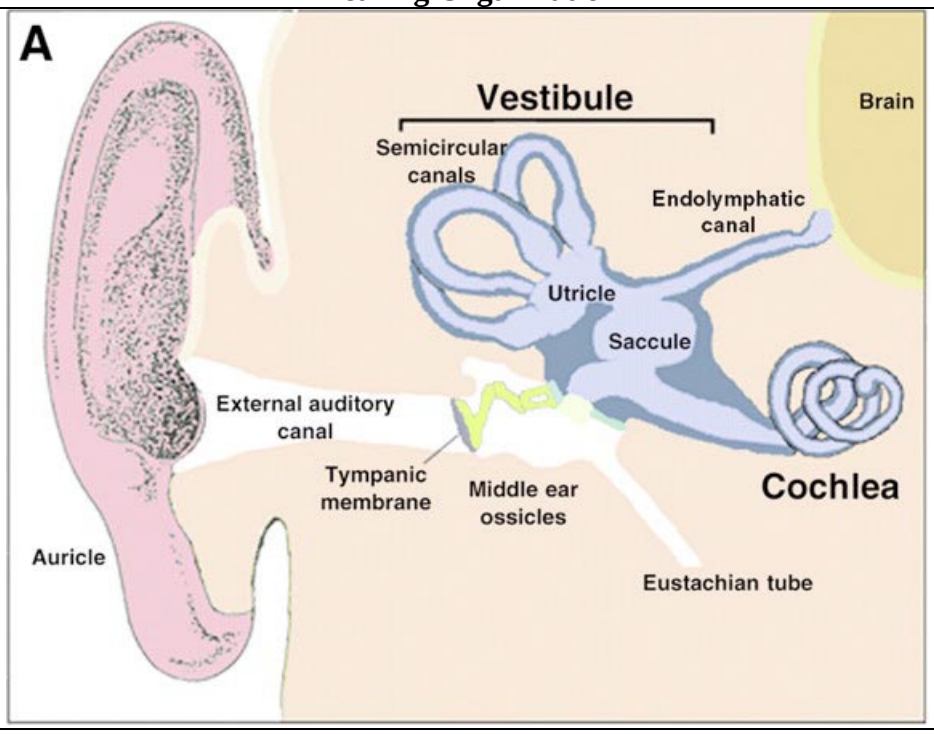
| **Human ear** |
| **Cochlear duct** |
| **Inner hair cell** |

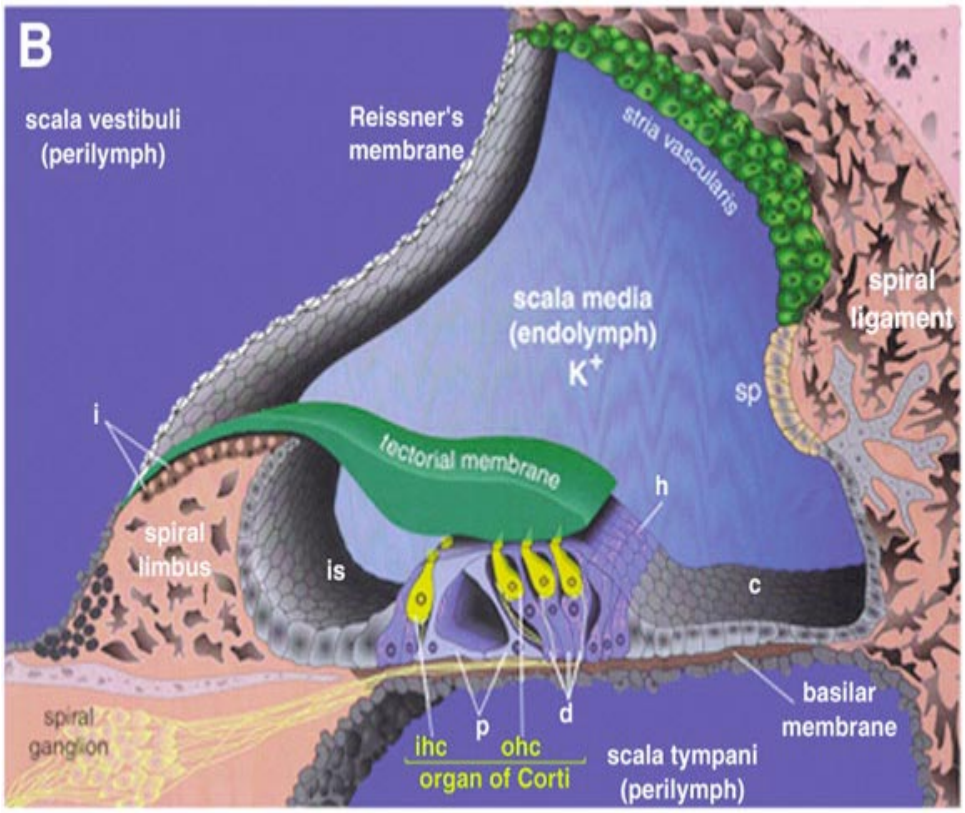
**Hearing Organization**




(http://arjournals.annualreviews.org/doi/full/10.1146/annurev.genet.35.102401.091224)

Figure 1 (A) Schematic representation of the human ear. The mammalian ear is composed of three compartments: the outer ear is made up of the auricle and external auditory canal, the middle ear contains the ossicles within the tympanic cavity, and the inner ear consists of six sensory organs, namely the cochlea and the five vestibular end organs (saccule, utricle, and three semicircular canals).

**Hearing Organization**




(http://arjournals.annualreviews.org/doi/full/10.1146/annurev.genet.35.102401.091224)

Figure 1 (B) Cross-section through the cochlear duct. The membranous labyrinth of the cochlea (cochlear duct) divides the bony labyrinth in three canals, the scala vestibuli and the scala tympani, both filled with perilymph, and the scala media, filled with endolymph. The organ of Corti, which is the auditory transduction apparatus, protrudes in the scala media. This organ is made up of an array of sensory cells (in yellow), i.e., the single row of inner hair cells (ihc) and the triple row of outer hair cells (ohc); and different types of supporting cells that include pillar cells (p), cells of Deiters (d), and cells of Hensen (h). It is covered by an acellular gel, the tectorial membrane. The organ of Corti is flanked by the epithelial cells of the inner sulcus (is) on the medial side and by the cells of Claudius (c) on the lateral side. The stria vascularis, on the lateral wall of the cochlear duct, is responsible for the secretion of K+ into the endolymph and for the generation of the endocochlear potential. Different types of fibrocytes surround the cochlear epithelium. Other abbreviations: (i) interdental cells, (sp) spiral prominence. (Adapted from a figure drawn by P. Küssel-Andermann.)

**Hearing Organization**

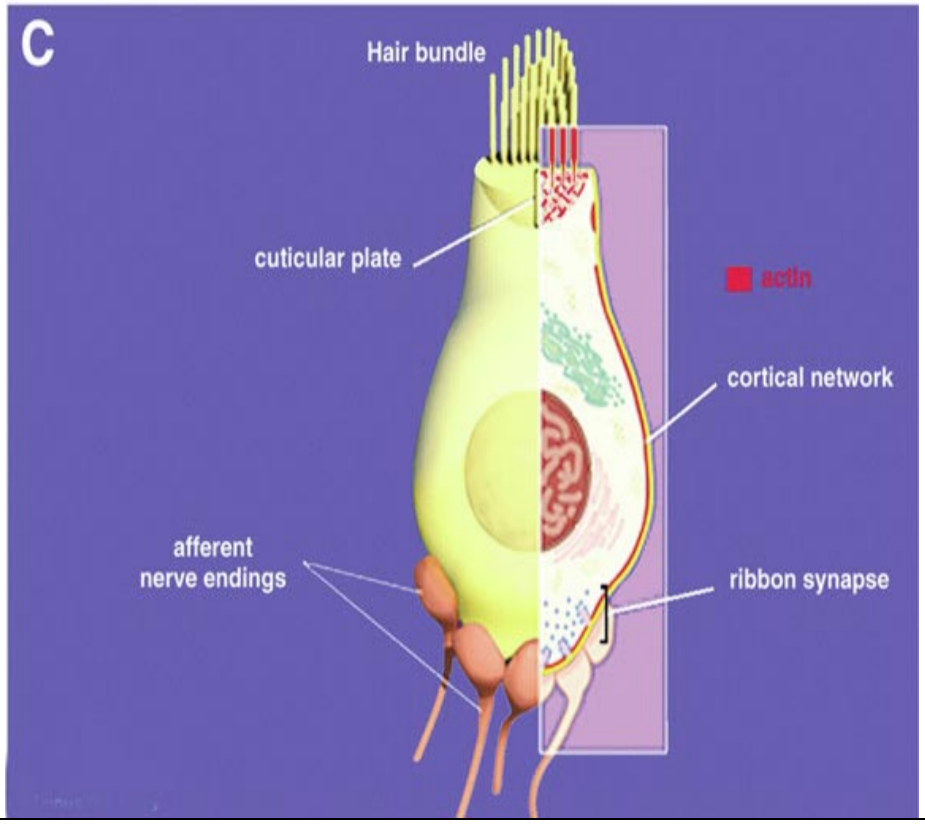



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Figure 1 (C) Schematic representation of an inner hair cell. Note the highly organized hair bundle, made of several rows of stereocilia, at the apical pole of the cell. The ribbon synapse has particular structural and functional features. Three specific structures of the actin cytoskeleton are shown (in red), namely the filaments of the stereocilia, the cuticular plate (a dense meshwork of horizontal filaments running parallel to the apical cell surface), and the cortical network (beneath the plasma membrane). Unconventional myosins form a large family that has been divided into 16 classes. These motor proteins move along the actin filaments using the energy generated by the hydrolysis of ATP. The structure of unconventional myosins consists of (a) the N-terminal motor head containing the highly conserved actin and ATP-binding sites; (b) a neck region, composed of a variable number of IQ (isoleucine-glutamine) motifs that are expected to bind to calmodulin; and (c) a tail, which differs substantially from one myosin to another. The tail sequence determines the functional specificity of each myosin because it contains various putative protein-protein interacting domains that bind to cargo molecules, regulatory factors, and components of the transduction pathways. Unconventional myosins have been implicated in the formation and the movements of cytoplasmic expansions, in the movements of vesicles and in signal transduction.

| Hearing Genes and Proteins | | | |
|---|---|---|---|
| **Primary defect** | **Gene** | **Protein** | **Type of molecule** |
| Filaments | *MYO7A* | **Myosin** VIIA | **Motor protein** |
| | *MYO15* | **Myosin** XV | **Motor protein** |
| | *MYO6* | **Myosin** VI | **Motor protein** |
| | *USH1C* | Harmonin | PDZ domain-containing protein |
| | *CDH23* | **Cadherin**-23 | **Cell adhesion protein** |
| | *Espn* | Espin | Actin-binding protein |
| | *KCNQ4* | **KCNQ4** | **$K^+$ channel subunit** |
| | *Atp2b2/Pmca2* | $Ca^{2+}$-ATPase 2 | Calcium pump |
| | *OTOF* | Otoferlin | Vesicle trafficking protein |
| | *POU4F3* | POU4F3 | Transcription factor |
| Nonsensory cells | *CX26/GJB2* | **Connexin** 26 | **Gap junction protein** |
| | *CX30/GJB6* | **Connexin** 30 | **Gap junction protein** |
| | *CX31/GJB3* | **Connexin** 31 | **Gap junction protein** |
| | *Slc12a2/Nkcc1* | NKCC1 | $Na^+K^+2Cl^-$ cotransporter |
| | *PDS* | Pendrin | Iodide/chloride transporter |
| | *CLDN14* | Claudin-14 | Tight junction component |
| | *COCH* | Cochlin | Extracellular matrix component |
| | *EYA4* | EYA4 | Transcriptional coactivator |
| | *POU3F4* | POU3F4 | Transcription factor |
| Tectorial membrane | *COL11A2* | **Collagen** XI ($\alpha$2 chain) | **Extracellular matrix** |
| | *TECTA* | $\alpha$-tectorin | Extracellular matrix |
| | *Otog* | Otogelin | Extracellular matrix |
| Unknown | *TMPRSS3* | TMPRSS3 | Transmembrane serine protease |
| | *PCDH15* | Proto**cadherin**-15 | **Cell adhesion protein** |
| | *HDIA1* | Diaphanous-1 | Regulator of actin cytoskeleton |
| | *DFNA5* | | |
| | *MYH9* | **Myosin** IIA | **Motor protein** |
| | *MTRNR1* | | Mitochondrial 12SrRNA |
| | *MTTS1* | | Mitochondrial $tRNA^{ser(UCN)}$ |

| Myosin | | |
|---|---|---|
| **Head** | **Rod** | **Tail** |
| Actin-binding, ATPase | calmodulin-binding | variable, binding to other proteins |