HST.161 Molecular Biology and Genetics in Modern Medicine
Fall 2007

Lecture 12 Genetic Hearing Impairment

Of all the disorders we've talked about, this is probably the most prevalent.
Prevalence of hearing impairment:

- 30 million Americans affected; 2 million are profoundly deaf

Deafness: about half is acquired and half is genetic/hereditary [diagram is not hers]
75% of genetic loss is non-syndromic (70% of this is autosomal recessive)
25% autosomal dominant; more than 50 loci for mutations
Small proportions are mitochondrial, chromosomal, X-linked. May be congenital or have post-natal onset (prelingual or post-lingual).

Anatomy of the ear:

- Outer ear: ear canal up to the ear drum (tympanic membrane)
- Middle ear: malleus, stapes, incus
- "conductive" hearing loss involves outer and/or middle ear
- Inner ear: vestibular system (balance) and cochlea

Conductive hearing loss involves the outer and middle ear
Sensorineural hearing loss involves the inner ear

Cochlea:
Stereocilia: "hair" cells; the hair-like protrusion is an extension of the plasma membrane filled with rigid actin filaments. Individual protrusions on the ends are linked with "tip links." Sound waves causes a mechanical force to pivot the stereocilia, causing a shearing motion because there are taller and shorter tips layered on each other, in order. Shearing causes the tip links to stretch; this stretching pulls open ion channels, which depolarize the cell.

Endolymph has high K+ concentrations; K+ recycling is important to cellular hearing functions, so mutations in this process can cause hearing problems.

Hearing Loss:
Normal aging tends to involve high-frequency hearing loss

Obstacles to studying genetic deafness:

- inaccessible to direct observation, as cochlea is embedded inside head; need to do an autopsy to really get at it

Deaf-deaf mating: tends to happen fairly frequently, due to the common language effect (i.e. sign language)

Guest Lecture by Dr. Marley Kenna

Incidence of Hearing Loss in Newborns: very high; much higher than incidence of metabolic disorders, for example.

Tests:

- Automated auditory brainstem response
- Otoacoustic emissions looks at sounds produced by outer hair cells

20/1,000 don't pass screening for hearing impairment; 16 of these turn out to be fine

Early Hearing Detection Intervention (EHDI) Programs

Genetic heterogeneity with mutations causing deafness

- same or similar mutations can cause different symptoms
- 50 different mutations causing hearing impairment
- single phenotype can be caused by several mutations.

Usher syndrome: deaf/blind syndrome, accounts for 3-6% of childhood deafness