Research Advances for the Treatment of Hearing Loss

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The Amazing System of Human Hearing

The cochlea of the inner ear, where sound is first detected, is a unique and beautiful structure like no other in the human body. Encapsulated in a boney case, the auditory organ (called the organ of Corti) is a spiral containing very specialized cells that are bathed in fluid. This spiral, akin to a snail or nautilus shell, creates a tonotopic or frequency map. High frequency sounds, like the chirping of a bird, are detected in the basal turn of the cochlea and low frequency sounds, like the rumbling of a car engine, are detected in the apex.

Sound is transmitted from the vibration of middle ear bones to the fluid inside the cochlea that bathes the organ of Corti. Here, specialized cells (called hair cells) are sensitive to mechanical stimuli. The “hairs” that crown the surface of hair cells are very different from the hair on your head and are technically called stereocilia bundles. When stereocilia bundles are deflected by sound waves, hair cells become activated (or depolarized). This produces a chemical signal that allows the activated hair cells to stimulate the nerves that are connected to the brain for the perception of speech, music, and other sounds.

Another group of important cells in the cochlea are aptly named supporting cells because they surround hair cells and offer structural support. They also release substances that keep the hair cells and auditory nerves healthy. When hair cells are killed by exposure to loud noise or drugs, supporting cells engulf the dying hair cells to isolate the insult and prevent the spread of damage to neighboring cells.

Children with Hearing Loss

In the United States, 2 to 3 in every 1,000 infants is born with a detectable amount of hearing loss. If a child is born hearing, the most common cause of acquired hearing loss is damage to hair cells caused by exposure to loud noise or specific types of drugs. It is estimated that ~15% of children between the ages of 6 and 19 have hearing loss in one or both ears and this number is increasing due to the popularity of iPods and headphones. According to a recent report by the World Health Organization, more than 1 billion teenagers are at risk for noise-induced hearing loss. In addition to noise, over 100 drugs have been found to kill hair cells and cause hearing loss.

Treatment of Hearing Loss

Unfortunately there are no treatments approved by the US Food & Drug Administration (FDA) to prevent or reverse hearing loss. Hearing aids and cochlear implants are commonly used, but they do not produce normal hearing. However, there have been great advances in hearing research over the past 10 to 15 years. Several drugs are now being tested in clinical trials for the prevention of hearing loss (see
the link below for more information) and recent findings from my lab and others demonstrate that regeneration of hair cells may be possible.

**Fascinating Research on Regenerating Hair Cells**

In 1988, hair cell regeneration was discovered to occur in birds, which allowed the recovery of hearing function. After hair cells were killed by loud noise, neighboring supporting cells either proliferated and became new hair cells or directly changed into a hair cell without cell division. In the years that followed, hair cell regeneration was also observed in other animals including fish, amphibians, and reptiles. However there was no evidence that hair cell regeneration could occur in humans or other mammals until very recently.

During my training, I became fascinated with the cochlea and hair cell regeneration. In studying the mouse cochlea and how it matures in the weeks after birth, I felt that the best chance we had of stimulating hair cell regeneration in mammals was in the newborn mouse. However this was much easier said than done because killing hair cells in newborn mice is very difficult (and likely why the idea had not been tested before). Mice do not hear until they are 2 weeks of age and ototoxic drugs also cause kidney damage, so both of these commonly used methods to damage hair cells were ineffective in the neonate. Instead we used state-of-the-art genetic tools to precisely control the expression of a toxin specifically in hair cells in the newborn mouse. **To our surprise, after the toxin killed the hair cells, spontaneous regeneration of hair cells occurred.** The new hair cells came from neighboring supporting cells, in a process that was similar to what occurs in birds and other non-mammals. However when we killed hair cells in mice that were 1 week old, regeneration no longer occurred. Despite this limited window, the discovery of hair cell regeneration has been very exciting and our results have been confirmed by research groups at Stanford and Harvard Universities.

**Hope for Future Generations**

Our findings offer the opportunity to study the hair cell regeneration process in mammals, which is much closer process to humans than birds and fish. I am now an assistant professor at Southern Illinois University School of Medicine where my research lab focuses on learning more about the hair cell regeneration process that occurs in newborn mice. We have recently been awarded a 3 year research grant from the U.S. Office of the Assistant Secretary of Defense for Health Affairs, a division of the Department of Defense, to advance our research. Understanding the genes and proteins involved in the hair cell regeneration process in young mice is a first step to stimulating successful hair cell regeneration in adult mice and potentially translating these findings to humans. We hope that our work in the coming years will make hair cell regeneration a feasible treatment for persons with hearing loss who are interested in exploring this option.

For more information about hair cell regeneration in newborn mice:
[http://dev.biologists.org/content/141/4/816](http://dev.biologists.org/content/141/4/816)

For more information about Dr. Cox’s new grant from the Department of Defense:

For more information about clinical trials for the prevention of hearing loss:

Please share this information with families who may be interested in future developments.