National Institutes of Health

Fact Sheet *Hair Cell Regeneration and Hearing Loss*

Our ability to hear relies on hair cells, small sensory cells in the inner ear. Hair cells are named for microscopic hair-like extensions, called stereocilia, projecting from their tops in bundles. These "hair bundles" convert sound vibrations into electrical signals, which travel to the brain by way of the auditory, or hearing, nerve. When hair cells are damaged—by disease, injury, or aging—a person experiences hearing loss, sometimes profound. Although fish, amphibians, and birds are able to grow new hair cells to replace damaged ones, mammals cannot regenerate hair cells on their own. Through gene therapy and stem cell research, however, scientists have been able to grow new hair cells in laboratory animals, in some cases restoring some hearing to deafened mammals. Such promising results have led researchers to wonder if we might be able to regenerate hair cells in people one day.

Yesterday

- More than 90 percent of hearing loss occurs when either hair cells or auditory nerve cells are destroyed. Scientists believed that hair cells in mammals could never be replaced if they were injured or destroyed.
- Early studies suggested that when a hair cell develops, it inhibits its neighbor from becoming a hair cell which, instead, becomes a supporting cell. Scientists wondered if supporting cells had the ability to become hair cells if neighboring hair cells were injured or destroyed.
- To test this theory, NIH-supported scientists destroyed hair cells in a mouse inner ear. Time lapse photography showed neighboring supporting cells migrating to the hair cell region and growing hair bundles on their surfaces. Although the process did not result in restored hearing in the mice, researchers began to investigate whether experimental augmentation of the process might improve hearing loss.

Today

- Scientists have made a number of critical discoveries about hair cell growth and development that are contributing to new ideas about the possibility of regenerating hair cells in people one day.
- Knowing that supporting cells have the ability to become hair cells under certain conditions, scientists focused on identifying specific molecules that might be involved in a hair cell developing from a supporting cell.
- In studies in experimental animals, scientists identified specific genes necessary for hair cells to detect sound. They found that these genes were similar even though they were from different animals. For example, a gene in mice, called *Atoh1* is similar to a sound-detecting gene in fruit flies.
- In a landmark study, NIH-supported scientists treated deafened guinea pig ears with a harmless virus carrying the gene *Atoh1*. The *Atoh1* gene caused supporting cells to become hair cells in the deafened guinea pigs and, importantly, the treated animals were able to regain some of their hearing. This was the first demonstration of gene therapy that improved hearing in formerly deaf animals.
- NIH-supported scientists identified a gene in mice, called *Rb1*, that shuts down the growth of new hair cells early in development. Mice bred to be missing the gene were able to grow more hair cells than mice possessing the gene. In addition, mature hair cells growing in culture dishes were able to regenerate when the *Rb1* gene was deleted.
- NIH-supported researchers demonstrated that mouse embryonic stem cells can develop into hair cells in the laboratory. The researchers are now studying whether embryonic stem cells injected into the developing inner ear of deaf mouse embryos can give rise to healthy hair cells that restore hearing.

- The ability to regrow hair cells will not restore hearing without properly reconnected nerve endings. NIH-supported scientists found that newly formed hair cells and nerve cells successfully reestablish connections in an organized way, although the reconnected nerve endings are simpler than those generated during normal development. This and other research will help reveal how nerve cells form connections with newly generated hair cells.

Tomorrow

The NIH is poised to make major discoveries in the study of hair cells and hearing loss. Areas of emphasis will include the *prediction* of hearing loss through genetic testing, the *personalization* of treatments for hearing loss through the development of a wider range of possible treatment options, and the *preemption* of hearing loss through the study of possible ways to protect hair cells from damage.

- *Predicting hearing loss.* As scientists learn more about the genes that cause deafness, hearing health professionals will be better able to predict which individuals are at risk of losing some or all of their hearing from damage to hair cells or auditory nerve cells.
- *Personalized treatments.* Progress continues to be made in the treatment of hearing loss, including the enhancement of technologies such as cochlear implants and hearing aids. Continued research in hair cell regeneration could one day offer another powerful treatment option, if not a cure, for individuals with hearing loss.
- *Preemptive approaches.* NIH-supported scientists are investigating the cellular and molecular mechanisms the body uses to protect auditory hair cells against damage. With improved understanding, they can work to develop methods to enhance survival of hair cells following trauma or disease.

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