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Genes that control cell death fingered in age-related hearing loss

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Several genes that play a role in how our body's cells normally auto-destruct may play a role in age-related hearing loss, according to research published online in the journal *Apoptosis* – a journal devoted to the topic of cell suicide, or programmed cell death.

Doctors know that genetics play some role in such hearing loss, which affects nearly everyone older than 60, as well as many people somewhat younger. But while more than 100 genes are known to play a role in congenital deafness, scientists have yet to pinpoint any gene in humans that plays a role in presbycusis, or age-related hearing loss.

The research in mice, done by using sophisticated technology comparing gene activity in older mice to their younger counterparts, offers a sort of roadmap to researchers who are confident they are closing in on some of the genetic factors that are part of the process in people.

"It's very likely that multiple genes contribute to age-related hearing loss," said Robert D. Frisina, Ph.D., the lead investigator and professor of Otolaryngology at the University of Rochester Medical Center. "We know the same is true for other diseases, for instance some types of cancer and heart disease."

Frisina is co-director of the International Center for Hearing and Speech Research, which is based both at the University of Rochester Medical Center and at the National Technical Institute for the Deaf in Rochester, N.Y. The group comprises one of the largest research groups in the

world devoted to studying, and preventing, the problem of hearing loss as we get older.

The team has spent nearly 20 years looking at the problem. More than 800 people have been put through a rigorous battery of tests that analyze the condition of their ears, their brain performance, and their genes. Despite the effort and that of other groups around the world, there is currently no way to reverse the hearing loss, largely because of the complexity of the process. In addition to genetics, other factors that play a role in presbycusis include sound exposure, medications that can damage hearing, the condition of the brain as it deteriorates with age, and changes in the delicate cells in the inner ear that translate a sound into a signal that the brain "hears."

"Age-related hearing loss is a very serious problem for patients, and it's also challenging for scientists who study it," said Frisina. "There are many potential reasons. It could be a problem in the brain, or the problem could rest with any number of cells in the inner ear. The causes are more complicated than in a condition like Parkinson's disease, where we know exactly which type of cell dies in which part of the brain."

To begin to understand the genetics of human hearing, the group has been charting the activity of more than 22,000 genes in mice, comparing young mice to their older counterparts. In the study in Apoptosis, the team used two different methods to study gene expression, thanks to funding from the National Institute on Aging and the National Institute on Deafness and Other Communication Disorders, both part of the National Institutes of Health.

First, scientists put more than 300 genes through a broad gene-array study, looking at genes whose activity in the inner ear differed greatly between normal mice and those with hearing loss. Then the team narrowed its focus to 35 such genes, employing a newer technique

known as a PCR array to measure activity. Through that test the scientists identified eight genes, all part of the apoptotic process, whose activity differed between the two groups.

Apoptosis itself is certainly nothing new. Such programmed cell death happens constantly – it's the body's way of getting rid of cells that are damaged or no longer needed. When apoptosis happens, a cell's structure breaks up, and the cell disintegrates, with the cell "blebbing," or bulging outward, ultimately blowing apart. It's a familiar process to scientists who know that it also happens as part of the course of many diseases. For instance, after a stroke, many brain cells perceive a threat – low oxygen – and "jump ship," killing themselves and dramatically worsening the effects of the stroke.

The new research is the first demonstration that such activity also occurs in the aging inner ear. The work offers a potential new target as scientists work to find ways to stop age-related hearing loss, such as a drug that would stop cells from committing cell suicide as they age.

"The goal, of course, is to prevent and even reverse age-related hearing loss, which is the third most common chronic medical condition among the elderly," said Frisina, who also has appointments in the departments of Biomedical Engineering and Neurobiology and Anatomy. "Right now, there is nothing we can do to treat it or reverse it, so prevention is the focus."

Frisina advises avoiding exposure to loud noise wherever possible, and wearing ear protection when working with power tools or hunting, for example. Since many medications can damage hearing, patients should speak at length with their doctors about side effects before going on medications, particularly antibiotics, hormone therapy, and drugs that fight cancer. Since conditions like diabetes can also damage hearing, heed the timeless advice to eat right and exercise.

Source: University of Rochester