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# Inherited form of hearing loss stems from gene mutation

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Pat Phalin learned she had hearing loss at 30, when she volunteered to give hearing tests at her local school. The pupils heard sounds she could not hear.

Her husband Larry, a genealogy enthusiast, saw a pattern in his wife's family history. Her mother, grandfather and great-grandfather had severe hearing loss as adults. One of the Phalins' children had hearing problems before he reached school age.

The hearing loss must be hereditary, Larry Phalin thought, though his wife's family didn't seem to realize it. "They blamed it on everything else under the sun: They worked in loud factories, they listened to loud music. One got hit by a tractor," he says.

Phalin, who lives near Chicago, heard 14 years ago that scientists were seeking families for studies of hereditary hearing loss. He got in touch with Marci Lesperance, M.D., now a hearing researcher at the University of Michigan Health System.

That contact sent Lesperance and her colleagues on a decade-long search. In 2001, her lab identified chromosome 12 as the one containing the responsible gene. Finally, after considering dozens of genes on this chromosome that could possibly play a role, they were able to identify one gene mutation that explains a previously unknown form of hereditary hearing loss.

In results published online today in the American Journal of Hearing Genetics, Lesperance and researchers in Iowa, France and Germany report they have identified a mutation in a gene, SLC17A8, that accounts for a form of hearing loss that diminishes one's ability to hear high-frequency sounds. The severity of the mutation's effects varies among individuals. The loss may occur early or later in life.

The researchers show that the mutation accounts for hearing loss in the Phalin family and another unrelated extended family in Iowa. Since the exact mutation occurs in two families that appear completely unrelated, the mutation may be an ancient one and not particularly rare. Future research may find that it affects others who have an unexplained family history of hearing loss, says Lesperance, an associate professor of pediatric otolaryngology at the U-M Medical School.

The form of deafness, which the researchers have named DFNA25, also is of interest for further research because it closely resembles the hearing loss common in people as they age, called presbycusis.

"Some people with the mutation have hearing loss in their 40s of the kind we normally see in people a decade or more older," says Lesperance. "Often, identifying a gene in individuals who have early onset of a disorder will help explain why the disorder occurs in the general population."

The key to identifying which gene was responsible for the families' hearing loss occurred in French scientist Jean-Luc Puel's laboratory. Puel and his research team, also authors of the study, discovered that a mouse lacking the SLC17A8 gene was deaf.

Through extensive studies, the French research team and colleagues in Germany also were able to discover precisely how the SLC17A8 gene and the protein it encodes, VGLUT3, are needed in the inner ear to

process the hearing signal. There, VGLUT3 normally promotes the presence of glutamate, a neurotransmitter important in allowing the ear's inner hair cells to convey signals to the auditory nerve, which carries them to the brain. The mutation in the families most likely interferes with that process.

Implications:

Lesperance hopes the research will encourage families and physicians to be alert to the possibility that hearing problems are inherited. That may spur more people to take prompt action such as frequent hearing tests in the young and early use of hearing aids, as well as genetic counseling to understand the chances of occurrence in future children.

"In many types of hereditary hearing loss, it's likely that environmental factors that people can control, such as smoking and exposure to noise, also can influence how severe the hearing loss is, and how early in life it begins," says Lesperance.

Lesperance has previously been involved in the discovery of three other genes related to particular types of hearing loss. It's thought that hereditary factors may play a role in as many as 50 percent of people with hearing loss.

Genetic testing is possible for more than two dozen genes involved in hearing loss, but testing is available in the United States for only a handful of the most common genes.

Larry Phalin says that he's going to urge family members to be tested for the SLC17A8 mutation – an option that now exists for them as a result of the study.

"Then you can be prepared for it," he says. "You can have children tested early, so they don't have speech or school problems."

For his own now-grown son and other family members who have gotten help early on for hearing loss, hearing tests and hearing aids made a big difference. "They get along fine," he says.

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