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Study breaks new ground in understanding drug-induced deafness

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Peter Steyger's research on hearing is very personal.

That's because Steyger — a research scientist with the Oregon Hearing Research Center at Oregon Health & Science University — is deaf.

Now Steyger has published groundbreaking research that is as personal as it gets. The study gives scientists new insight into why a specific class of antibiotics causes deafness — the same class of antibiotics that caused Steyger's deafness as a child in England 48 years ago. The study was published this month in *Scientific Reports*, part of the Nature Publishing Group.

"Compared to a lot of other papers I've published, this paper is intensely personal," Steyger says. "And that's why I'm extraordinarily proud of it."

Aminoglycoside antibiotics are widely used to prevent, among other things, tuberculosis in people in developing countries, and to prevent life-threatening bacterial infections, particularly in premature infants across the world. But Steyger and co-author Hongzhe Li, also at OHSU, examined a long-known and significant problem with the use of aminoglycoside antibiotics — how they find their way into the inner ear and kill the sensory "hair" cells that enable us to hear. The killing of these sensory hair cells is a major cause of deafness.

For 60 years, scientists have questioned how these antibiotics get into the inner ear. The Steyger and Li paper provides the strongest evidence yet

for a definitive answer — they cross a specific "blood-labyrinth" barrier in the inner ear that protects its sensory hair cells from potentially damaging components in the blood.

The blood-labyrinth barrier actively transports important minerals and nutrients into the inner ear for sensitive auditory function — ions, amino acids and glucose, for example. Steyger says the aminoglycoside antibiotics likely use particular nutrient pathways for "drug trafficking" into the inner ear.

Now that Steyger has learned the predominant trafficking route, he and other scientists can test individual nutrient transport pathways to identify the mechanism that moves aminoglycoside antibiotics across the blood-labyrinth barrier. So the Steyger paper represents a significant milestone toward the ultimate goal — blocking the trafficking of these drugs into the inner ear and preventing the killing of hair cells and subsequent hearing loss and deafness.

"We could give an inhibitor at the same time as the antibiotics that will protect the ear but still allow the drug to kill bacteria — thereby saving the patient's hearing," Steyger says.

In the United States alone, about 80 percent of premature infants are given aminoglycoside antibiotics to prevent infections that would otherwise kill them. The smaller percentage of premature infants with infections must remain on the antibiotics for several days, and are in significant danger of hearing loss, Steyger says.

With those infants and other patients, "if we could find a blocker, then we could save the hearing of up to 50,000 individuals from drug-induced deafness in the United States every year," Steyger says.

Steyger's own hearing loss occurred when he was 14 months old, after he

developed meningitis. Living with his family in Stockport, England, Steyger was treated with streptomycin, one of the first aminoglycoside antibiotics in wide use. The drug "literally saved my life," Steyger says, but it also caused his severe-to-profound hearing loss.

Steyger's mother was coached to provide him with daily speech and listening therapy from ages 2 to 7 — unusual for that time in the United Kingdom. The success of that program meant that Steyger then went to a traditional elementary school in the U.K., also unusual for deaf children at the time.

After high school, he studied zoology at the University of Manchester before enrolling into a hearing research Ph.D. program at Keele University in the U.K. After obtaining his doctorate, he was recruited to a NASA vestibular research program in San Antonio, Texas, in 1992. He's been at the Oregon Hearing Research Center at OHSU for the past 14 years, where he currently is an associate professor of otolaryngology/head and neck surgery.

Steyger's study was funded by the National Institute of Deafness and Other Communications Disorders, a branch of the National Institutes of Health. After this key finding, Steyger and his lab are already researching the precise molecular mechanisms of how aminoglycoside antibiotics (and other ototoxic drugs) cross the blood-labyrinth barrier. As they learn more, they hope to develop new and more effective strategies to prevent drug-induced hearing loss.

Because, he says "hearing loss from these drugs is entirely preventable. And my team and I will continue working hard to find ways to prevent it."

Beyond his work at OHSU, Steyger is also scientific director at the national Hearing Health Foundation and for 10 years has been a board

member at the Tucker-Maxon Oral School in Portland, Ore., where children with hearing loss can learn to listen and speak.

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