Gene therapies with ties to Boston hold promise for congenital deafness

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Scientists in the United States and abroad are reporting encouraging results in restoring hearing in children born with a rare form of deafness, raising the prospect that gene therapies — some developed in Massachusetts — may someday help millions of people with inherited hearing loss.

Five studies, including at least three with ties to Boston, are using rival gene therapies to treat a hearing disorder caused by mutations in a single gene, called otoferlin. Experts say the results of the studies — which have reported gains in hearing among small numbers of children — prove that gene therapy can treat this form of inherited deafness, which affects an estimated 200,000 people worldwide.

The early results, investigators say, could open the door for future use of gene therapies to treat childhood deafness caused by mutations in more than 150 other genes. Up to 60 percent of cases of hearing loss in babies have genetic causes, according to the Centers for Disease Control and Prevention.

“This was a proof-of-concept trial,” said Dr. Zheng-Yi Chen, an associate scientist at Mass Eye and Ear who helped lead the world’s first study providing gene therapy for otoferlin deafness. Each effort, he added, “is using something slightly different, but overall, the gene therapy approach is working.”

Some 1.5 billion people, 1 in 5 of the world’s population, suffer from hearing loss, according to the World Health Organization, but no medications have ever been

approved to improve hearing. Otoferlin deafness is believed to account for 2 to 8 percent of cases of congenital hearing loss, which affects about 26 million people worldwide.

The first patients began to receive a gene therapy in China in December 2022. Chen and a research team co-led by his former postdoctoral fellow, Dr. Yilai Shu, collaborated on a small clinical trial at the Eye and ENT Hospital of Fudan University in Shanghai. Their gene therapy restored at least some hearing in five of six children, ages 1 to 6.

Each received a droplet of the medicine, which contained billions of copies of what becomes a functional otoferlin gene, through an injection in one ear during a surgical procedure. So far, Chen said, the treatment has restored 60 to 70 percent of normal hearing in the five children.

The study was funded by the National Natural Science Foundation of China and the biotech Shanghai Refreshgene Therapeutics. The results of the trial were published on Jan. 24 in the medical journal The Lancet.

“These are patients who were without hearing,” said Chen, an associate professor of otolaryngology at Harvard Medical School. “Now they can hear. They can conduct a conversation.”

The children include the 19-month-old son of Lijiao Zhao, who lives in the city of Yuncheng. The toddler was profoundly deaf before he got the gene therapy in June at the Shanghai hospital. But within a few weeks, he turned his head when he heard a noise, and soon began saying “mama” and “papa,” according to his mother.

“We feel we’ve been given a new birth,” Zhao said tearfully during a Zoom conversation, with Chen interpreting, as she held her son on her lap. “It’s like a dream come true.” Zhao asked the Globe not to name her son to protect his privacy.

Investigators don’t know why the treatment didn’t work for the sixth child. They have since expanded the study to include more children, some of whom are receiving

injections in both ears, Chen said.

Other groups working on gene therapies for otoferlin deafness are Eli Lilly and its small Boston-based subsidiary Akouos; Regeneron Pharmaceuticals, which bought Boston-based Decibel Therapeutics last year for its hearing loss program; Shanghai-based Otovia Therapeutics and several entities in China; and a collaboration between the French biotech Sensorion and Institut Pasteur, a Paris-based biomedical research organization.

The condition they are targeting results in severe to complete hearing loss. Mutations in the otoferlin gene disrupt production of an inner ear protein that enables sensory hair cells to transmit sound to the brain. The only approved treatment is a cochlear implant, a small electronic device that can help to provide a limited sense of sound to a person who is profoundly deaf or severely hard of hearing.

Aissam Dam, 11, the first person to receive gene therapy in the US for congenital deafness, at the Children's Hospital of Philadelphia on Jan. 16. HANNAH BEIER/NYT

The New York Times recently reported on a gene therapy developed by Akouos and its parent company, Lilly. It restored the hearing of Aissam Dam, an 11-year-old Moroccan-born boy who received the treatment in October at Children's Hospital of Philadelphia. He was the first person to receive gene therapy for congenital deafness in the United States.

Manny Simons, founder and chief executive of Akouos and senior vice president of gene therapy for Lilly, said the boy's results were particularly impressive because he had lived in silence for so long.

"This is the first time that somebody who has been profoundly deaf for over a decade has seen restoration of hearing," Simons said. Lilly plans to expand the study to other trial sites, including Boston Children's Hospital.

In October, Regeneron announced that its therapy restored partial hearing to a child younger than 2 years old in the United Kingdom. The child, who received the gene therapy in one inner ear, has continued to improve and had only moderate hearing loss after 12 weeks, the company said at the J.P. Morgan Healthcare Conference in San Francisco in early January. (Regeneron declined to share the child's gender or exact age.)

"We're very proud of this," said Dr. Aris Baras, who helps run the genetic medicine program at Regeneron, based in Tarrytown, N.Y. "This is a historic moment for science and for biotechnology."

Researchers involved in the five studies plan to update their status at a meeting of the Association for Research in Otolaryngology in Anaheim, Calif., scheduled to start on Saturday. Otolaryngology is a medical specialty focusing on the ears, nose, and throat.

Although some people with hearing loss, or relatives with it, are excited by the prospect of gene therapies, others in the deaf community criticize the notion that deafness is something that needs a remedy.

“The world loves to celebrate ASL [American Sign Language] and deaf culture and give Oscars to movies about it and call it beautiful — and then turn around and work to destroy it,” said Danielle Loughlin, head of clinical services for the Deaf and Hard of Hearing program at Perspectives Corporation in North Kingstown, R.I., who is herself deaf. “To me this is a case of just because you can doesn’t mean you should.”

Scientists have investigated using gene therapy to restore hearing for more than two decades. Jeffrey Holt, a professor of otolaryngology at Boston Children’s Hospital and Harvard Medical School, wrote a paper in 1999 that showed a virus could ferry genes into the inner ear. He spent years trying to figure out which version of the virus, known as an adeno-associated virus, would work best. In 2017, his laboratory settled on the virus that Akouos and Lilly ended up using.

“We’ve been working [on viruses to carry the gene] for 25 years,” Holt said. “To see this work begin to come to fruition and have benefits to patients is deeply satisfying.”

Gene therapy has become one of the hottest areas in medicine as the Food and Drug Administration greenlighted therapies for spinal muscular atrophy (a rare inherited disease that affects nerves and muscles), sickle cell disease, two forms of hemophilia, and other disorders. The drugs are breathtakingly expensive; one hemophilia treatment costs $3.5 million per patient.

No one knows when the FDA might approve a gene therapy for otoferlin deafness. But Chen, of Mass Eye and Ear, estimated that the efforts could lead to a drug approval “within the next three to five years.”

Dr. Margaret A. Kenna, a professor of otolaryngology at Boston Children’s Hospital and Harvard Medical School who is serving as an investigator in the Lilly-Akouos trial, said it’s too soon to say which of the five gene therapies holds the most promise.

“Maybe one will be better than the other,” said Kenna. “Maybe they will all be equally good. Maybe they won’t hold up. We don’t know.”

If the FDA does eventually approve a gene therapy for otoferlin deafness, she is worried about how much the treatment would cost and how easily patients would be able to get it.

Nonetheless, she was delighted to see the science advancing.

“Even though I could see the progress in the field all around me, I didn’t think we’d see a gene therapy that works in my practice lifetime,” said Kenna, who has been in practice for 40 years. “I was hoping it would happen, but I wasn’t holding my breath.”

The vast majority of cases of hearing loss are age-related and treated with hearing aids, according to Chen. Scientists, including some in his lab, are working on a variety of medical approaches, including drugs, gene therapies, and regeneration of sensory hair cells to transmit sound.

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