Israeli find could mean cure to deafness

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JUDY SIEGEL-ITZKOVICH

An Israeli discovery on the function of tiny molecules called microRNAs (miRNAs) in the inner ears of mice could lead to the cure of human deafness in adults caused by aging, disease, drugs and noise, or genetic disease in children.

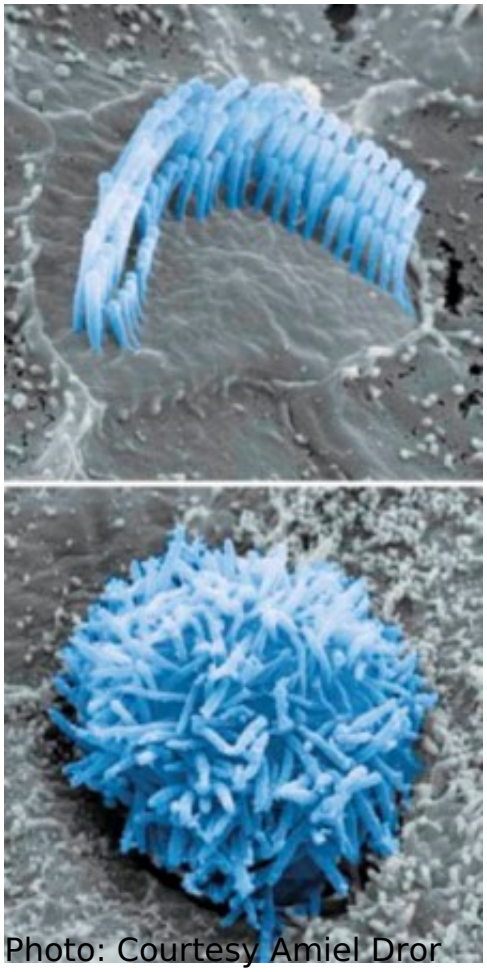

Photo: Courtesy Amiel Dror

Inner ears with normal mouse hair cells and without

The research, carried out over three years by world-renowned geneticist Prof. Karen Avraham of Tel Aviv University's Sackler School of Medicine and Dr. Lilach Friedman and other post-doctoral researchers in her lab, has just been released for publication in the prestigious journal PNAS (Proceedings of the National Academy of Sciences of the United States of America).

About one out of every two elderly people suffers from some degree of hearing disability, while one in 1,000 infants is born deaf due to mutant genes. Healthy babies are born with 15,000 sensory hair cells in each ear that allow them to hear. These hair cells are responsible for translating sounds to electrical pulses that the

brain can interpret.

When these cells die off in a process called apoptosis, it results in hearing disability, and when the hair cells are all gone, profound deafness follows. Finding the mechanism in which apoptosis occurs might make it possible to prevent it.

MicroRNAs, first described by US labs in 1993 and named in 2001, are single-stranded RNA molecules that regulate gene expression and decide whether proteins will be produced.

They are known to be responsible for the normal functioning of cells in plants and animals. More recently, it was discovered that microRNAs are involved in diseases, including some types of cancer and liver and cardiovascular disorders.

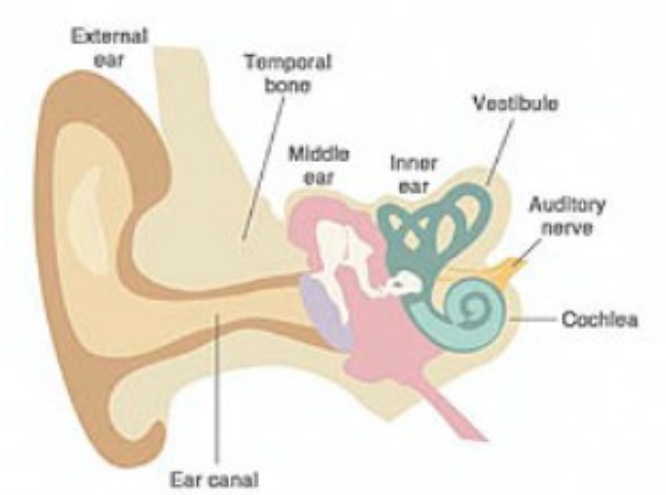

Photo: Courtesy

A Diagram of the human ear.

MicroRNAs are involved in every part of a cell and can already be used to predict what kind of cancer a person has. Great effort is being made to develop strategies for inserting these tiny molecules into cells and using them as new drugs and potential cures.

The TAU team - working with cooperation from the Weizmann Institute of Science molecular genetics department and biologists at Indiana's Purdue University - has discovered for the first time that these molecules are vital to the development and survival of hair cells in the inner ear and for normal hearing. This important discovery opens an entirely new window for possible treatments and a cure for all types of deafness, whether age-related or genetic.

"The internal ears of mice and humans are very similar," Avraham told The Jerusalem Post on Monday.

Prof. Donna Fekete of Purdue helped Avraham and her post-doctoral students by

working on the common black-and-white-striped aquarium-dwellers whose inner ears are very similar in structure and function to those of mammals and are translucent so their development can be easily viewed.

"Donna 'knocked down' [blocked the functioning of] a specific miRNA in them," explained Avraham, who recently received the Prof. Michael Bruno Award from Yad Hanadiv/The Rothschild Foundation.

Her team blocked the functioning of the microRNA molecules in the inner ears of mice, preventing a protein from being made, causing them to degenerate and thus preventing hearing. As mice are born deaf and remain so for two weeks, when they were supposed to show the development of this sense, "the mice were found at one month to be completely deaf, with evidence that they had never heard. This suggested that a lack of normal microRNAs could also lead to progressive hearing loss in people born with normal hearing, said Avraham. "This understanding of miRNAs is a new phenomenon in genetic knowledge and gene regulation."

The study investigated both mice and zebrafish, but the model holds true for all vertebrates - including humans, she said. It's a whole new level of looking at our genome," said the TAU geneticist, who is originally from New Jersey.

"We hope that both diagnostic and therapeutic applications for hearing loss will follow in the near future," Avraham added.

The Israelis made a "catalogue of all microRNAs they thought were important to the inner ear of the mouse. There probably are about 600 different ones, and each one is responsible for turning off and on as many as 200 genes. We 'knocked out' an enzyme called Dicer, causing the tiny hair cells in the inner ear to disappear, unlike in a normal inner ear where they are very numerous. Until now science knew only that mutations in protein-coding genes caused deafness. We went a layer deeper and discovered that the loss of microRNAs leads to deafness as well," she said.

She believes that further work could lead to treating and even curing deafness.

"We are continuing to work on this," said Avraham, who previously discovered four deafness genes and novel mutations in 10 deafness genes, among 46 known ones.

Avraham, who collaborates with Palestinian researchers to help them understand and fight the high rate of genetic deafness in the offspring of Arabs who marry first cousins, concludes that if scientists can figure out how microRNAs regulate hair cells, they could be used to rescue the cells that are dying.

"During the past five years, genomics has shown that disease is a combination of events, not one mutation causing one disease but an enormous domino effect, a cascade that makes things fall apart," Avraham explained. "It is very complex."

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