Genomics study identifies unique set of proteins that restores hearing in zebrafish
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Hearing loss affects around 37.5 million Americans, and most cases come from the loss of hearing receptors known as "hair cells" in the inner ear. Bristles that stick out of these microscopic hair cells move and bend when sound travels into our ears, resulting in electric signals sent through nerves and into our brains that allow us to process sound.

Humans and zebrafish are visually quite different, but at a genomic level, they share more than 70% of their genes. This genomic similarity offers the potential for researchers to understand the biology of cell regeneration in zebrafish before translating the findings to humans.

Erin Jimenez, Ph.D., a postdoctoral fellow in the laboratory of Shawn Burgess, Ph.D., senior investigator in the National Human Genome Research Institute's (NHGRI) Translational and Functional Genomics Branch, led the study in collaboration with researchers Ivan Ovcharenko, Ph.D., and Wei Song, Ph.D., at the National Library of Medicine's National Center for Biotechnology Information.

"Humans and other mammals are born with a set number of hair cells that are slowly lost through aging and trauma. However some animals, such as zebrafish, can regenerate hair cells and recover hearing after injury," said Burgess. "How and why regeneration happens in these animals remain a mystery that many scientists would like to unravel."

Confocal image of adult zebrafish hair cells (green) in the auditory organ of the inner ear. Credit: Erin Jimenez, Ph.D.

National Institutes of Health researchers have discovered a specific network of proteins that is necessary to restore hearing in zebrafish through cell regeneration. The study, led by investigators at the National Human Genome Research Institute (NHGRI), may inform the development of treatments for hearing loss in humans. The findings were published in Cell Genomics.

Although hair cell loss cannot be replaced in humans, many animals, including zebrafish, can restore hearing after injury through the regeneration of hair cells. The regenerative properties of zebrafish hair cells prompted researchers to use this animal to understand some fundamental properties of regeneration.
"Our study identified two families of transcription factors that work together to activate hair cell regeneration in zebrafish, called Sox and Six transcription factors," said Jimenez.

First, the Sox transcription factors initiate the regeneration response in surrounding cells, called support cells. Next, the Sox and Six transcription factors cooperate to turn those support cells into hair cells.

When hair cells die in zebrafish, nearby support cells start replicating. These support cells are like stem cells because of their ability to become other cell types. Researchers had identified some of the factors that convert support cells into hair cells, but what was not understood is how and where the genes encoding those factors turn on and are coordinated with other unknown factors.

"We have identified a unique combination of transcription factors that trigger regeneration in zebrafish. Further down the line, this group of zebrafish transcription factors might become a biological target that may lead to the development of novel therapy to treat hearing loss in humans," Jimenez said.


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