

Can Hearing Loss be Reversed? Research Reveals Clues that could Regrow the Cells that Help us Hear

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The most common cause of hearing loss is progressive because the cochlear hair cells—the primary cells to detect sound waves—cannot regenerate if damaged or lost. People who are repeatedly exposed to loud noises, such as soldiers, construction workers and musicians, are at the highest risk of developing this type of hearing loss. But it can happen to anyone over time. Birds and fish, however, can regenerate these hair cells, and now researchers at the Del Monte Neuroscience Institute are beginning to identify the mechanisms that can promote such regeneration in mammals, as explained in a recent study published in the journal, *Frontiers in Cellular Neuroscience*. Patricia White, professor of neuroscience and otolaryngology at the University of Rochester Medical Center, said, based on her previous work, expression of the active growth gene ERBB2 may be possible to activate the growth of new hair cells (in mammals), but they did not fully understand why. A 2018 study led by Jingyuan Zhang found that activation of the ERBB2 growth gene pathway triggered a series of sequential cellular events in which cochlear supporting cells began to multiply and activate other neighboring stem cells to become new sensory hair cells. This new study tells us how this activation occurs - a big step towards the ultimate goal of creating new cochlear cells in mammals. Using single-cell RNA sequencing in mice, the researchers compared cells with an overactive growth gene (ERBB2 signalling) with similar cells that lacked such a signal. They found that the growth gene - ERBB2 - promoted stem cell-like development by triggering the expression of several proteins, including SPP1, a protein that signals through the CD44 receptor. The CD44 receptor can be present on supporting cells of the inner ear. This increase in

cellular response promoted mitosis in supporting cells, a key event in regeneration. When Dorota Piekna-Przybylska and her White Lab team controlled this process in adult mice, they were able to show that the expression of ERBB2 controlled the expression of the SPP1 protein which is necessary for activation of CD44 and the growth of new hair cells. This discovery made it clear that regeneration is not limited to early stages of development. They believe they can use these findings to drive regeneration in adults. They plan to further investigate this phenomenon from a mechanistic perspective to see if it can improve auditory function after damage in mammals; found that activating the growth gene ERBB2 pathway triggered a cascading series of cellular events by which cochlear support cells began to multiply and activate other neighboring stem cells to become new sensory hair cells; that is the ultimate goal...