

Study shows isolation of stem cells may lead to a treatment for hearing loss

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Have you ever walked by someone listening to their i-Pod loud enough for you recognize the song? Studies have shown noise-induced hearing loss is going to become the next big epidemic affecting our younger generation though the effects won't show until it is too late to treat. In addition to loud noise, certain cancer drugs or genetic factors can cause hearing loss in humans due to loss or faulty development of the sensory 'microphones' (hair cells) inside the ear – the cochlea.

Lost hair cells are not replaced and people exposed to these conditions face permanent hearing loss. Identification of the stem cells from the adult cochlea would be a major step forward to develop new therapeutic approaches to hearing loss.

Members of the National Center for Regenerative Medicine research team, Dr. Robert Miller and Dr. Kumar Alagramam, both of Case Western Reserve University School of Medicine, recently published research findings in *Developmental Neuroscience* which suggest new ways of treating hearing loss. These researchers have isolated "cochlear stem cells" located in the inner ear and already primed for development into ear-related tissue due to their proximity to the ear and expression of certain genes necessary for the development of hearing.

"Previous work in our lab with young-adult mouse cochlear tissue showed expression of genes normally found in stem cells and neural progenitors. This led us to hypothesize that cochlea harbors stem cells and neural precursor cells. Our work in collaboration with Miller's lab supports our hypothesis" Dr. Alagramam said. They say that in early life, these precursor cells may be able to regenerate hair cells, but their capacity to do so becomes limited as the ear develops and ages. The team's research is a major step in devising a therapy to reverse permanent hearing loss because it may lead to the activation of cochlear stem cells in the inner ear to

regenerate new hair cells. "Clearly we have miles to go before we reach our end goal, but the exciting part is now we can test compounds that could promote regeneration of hair cells from these precursor cells in vitro, we can study the genes expressed during the transition from stem cells to hair cells, and we can think of developing strategies for cell replacement, i.e. transplanting these cochlear stem cells into the adult cochlea to affect hair cell replacement in the mouse, by extension, in humans" remarked Dr. Alagramam.

In this paper, Drs. Miller and Alagramam offer further evidence for the existence of cochlear stem cells in the mouse cochlea by confirming the ability to form 'stem cell' spheres in culture and by characterizing these cells in terms of neural and hair cell development using a panel of stem cell development and hair cell markers. The formation of spheres from early postnatal cochlear tissues and their expression of a wide range of developmental markers unique to hair cells confirm the possibility that self-supporting hair cell precursors exist in or can be derived from the postnatal mammalian cochlea.

Currently there are no clinical treatments to repair these hair cells vital to normal hearing. In the United States, 30% of people over the age of 65 have a handicapping hearing loss and of those, one in 500 people become deaf before reaching adulthood. In most cases, the target is the highly specialized hair cells. Docked inside the spiral duct of the human cochlea are ~15,000 hair cells, which are highly specialized neuroepithelial cells that enable us to hear a violin or a whisper. These hair cells differ in length by minuscule amounts and are set in motion by specific frequencies of sound. We hear this sound because this motion induces the hair cell to release an electrical impulse which passes along the auditory nerve to the brain. If the sound is too loud, the hair cells are damaged and no longer send signals to the brain. Severely damaged hair cells do not repair themselves nor do

they regenerate naturally.

While further research is necessary, the researchers believe these precursor cells have the potential to regenerate the damaged hair cells and restore normal hearing. The team has already begun animal studies to explore the use of cochlear stem cells in well-established hair cell ablation models and in deaf mouse mutants with predictable patterns of early hair cell loss. This line of research will evaluate the in vivo survival and differentiation of self-renewing cochlear cell populations and potentially lead to new therapies for the numerous individuals that are going to suffer from noise-induced hearing loss in the near future.

Source: Case Western Reserve University

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