

Short Communication

Regenerative Therapy for Sensorineural Hearing Loss: Recent Progress and Future Directions

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Sensorineural Hearing Loss (SNHL) continues to be a significant public health problem with over 270 million affected people worldwide and an incidence that increases with age [1,2]. Some cases of SNHL have a genetic cause, but the majority of SNHL is the result of ototoxic insult [3]. The underlying pathophysiology is related to the loss of sensory hair cells within the organ of Corti. As this structure is post-mitotic at birth, no spontaneous replacement of damaged hair cells is thought to occur. Current therapies (hearing aids and cochlear implants) are designed to augment the function of the damaged organ of Corti [4]. Recently pre-clinical and clinical publications have suggested that hair cell regeneration may be possible in an injured, post-mitotic organ of Corti [5-11].

In addition to damage to the organ of Corti, ototoxic insults can damage structures along the auditory pathways. Modest ototoxic injury can result in Transient Threshold Shifts (TTS) where audiologic testing identifies SNHL which resolves in days to weeks following injury. More severe ototoxic insults cause a Permanent Threshold Shift (PTS) and SNHL that does not improve. Preclinical studies demonstrate that PTS inducing single noise exposure causes apoptosis mediated changes in the dorsal and ventral cochlear nuclei, the central nucleus of the inferior colliculus, the dorsal, ventral and medial subdivisions of the medial geniculate body and layers I-IV of the primary auditory cortex. Even TTS inducing insults create a decreased cell density in the ventral cochlear nucleus [12-14]. Therefore the clinical focus of regenerative therapies for SNHL should not be limited to the organ of Corti but should also include the intracranial auditory processing structures.

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In their phase 1 trial McLean et al., evaluated epigenetic modification as a treatment for SNHL. They used Histone Deacetylases (HDAC) treatment to allow cochlear stromal support cells to re-enter the mitotic cell cycle and generate new hair cells. HDACs were delivered into the middle ear in a gel preparation. The HDACs diffused into the inner ear reaching the base of the cochlea where higher frequency responsive hair cells were presumably repaired. Treated subjects showed a 10 dB improvement and ABR thresholds at higher frequencies along with improved speech discrimination test scores [10,11]. The study did not measure changes in the CNS auditory pathways.

Baumgartner et al.'s phase 1 trial, which examined intravenous autologous cord blood mononuclear fraction treatment of SNHL, showed a 15 dB improvement in Auditory Brain Stem (ABR) thresholds following treatment. The study also suggested that cord blood treatment might improve the latency of signal transmission along the eighth cranial nerve. In this study 3-Tesla MRI diffusion tensor imaging sequences were used to evaluate Fractional Anisotropy (FA). FA is a measure of white matter tract integrity. FA was shown to improve along the auditory pathways in subjects whose ABR thresholds improved following cord blood treatment. FA improvement was most evident in Heschl's gyrus [9]. Cord blood treatment was thought to act via an immunomodulatory mechanism which has been reviewed elsewhere [15].

These clinical studies are intriguing, and their results support additional phase 2/3 trials to better analyze the effects of epigenetic and immunomodulatory SNHL treatments. In addition, as both studies appear to work through alternate mechanisms, a study combining both approaches might be illuminating.

The above listed preclinical studies evaluate treatments delivered in the acute to near subacute phase following SNHL inducing ototoxic injury. The clinical trials, on the other hand, evaluated treatment administered in a more delayed time frame following SNHL onset. This area of study might benefit from preclinical experiments focusing on a more chronic SNHL model as well as clinical trials where treatment is delivered closer to the time of ototoxic insult.

We support central nervous system imaging and FA analysis in future clinical trials to evaluate the effect of new treatments on auditory pathway white matter tract integrity. As immunomodulation appears to provide some benefit in patients with SNHL, additional immunomodulatory approaches (drugs, polymers, etc.) should be evaluated in the treatment of this disabling condition.

Ongoing research holds great promise in the treatment of SNHL. The quantitative measures available in the evaluation of SNHL make hearing loss a model system to evaluate regenerative medical treatments which cannot be easily analyzed in other conditions. In addition to improving the communication skills of patients with SNHL, continued research in SNHL may result in an improved understanding of broad areas of regenerative medicine.

References

1. Lin FR, Niparko JK, Ferrucci L (2011) Hearing loss prevalence in the United States. *Arch Intern Med* 171:1851-1852.
2. Mehra S, Eavey RD, Keamy DK Jr (2009) The epidemiology of hearing impairment in the United States: newborns, children and adolescents. *Otolaryngol Head Neck Surg* 140: 461-472.
3. Shibata SB, Shearer AD, Smith RJH (2014) Genetic sensorineural hearing loss. In: Flint PW, Haughey BH, Lund VJ, Niparko JK, Robbins KT, et al., editors. *Cummings Otolaryngology-Head and Neck Surgery*. 6th ed. Philadelphia, PA: Saunders, an imprint of Elsevier; 2014. Pp. 2285-2300.
4. Canalis RH, Lambert PR (2020) *The ear: comprehensive otology*. 1st ed. Philadelphia (PA): Lippincott Williams and Wilkins, 2000.
5. Revoltella RP, Papini S, Rosellini A, Michelini M, Franceschini V, et al. (2008) Cochlear repair by transplantation of human cord blood CD133+ cells to nod-scid mice made deaf with kanamycin and noise. *Cell Transplant* 17: 665-678.
6. Bettini S, Franceschini V, Astolfi L, Simoni E, Massanti B, et al. (2018) Human mesenchymal stromal cell therapy for damaged cochlear repair in non-scid mice deafened with kanamycin. *Cytotherapy* 20:189-203.
7. Choi MY, Yeo SW, Park KH (2012) Hearing loss restoration in a deaf animal model with intravenous transplantation of mesenchymal stem cells derived from human umbilical cord blood. *Biochem Biophys Res Commun* 427: 629-636.
8. Da Costa V, O'Grady D, Jackson L, Kaylie D, Raynor E (2012) Improvements in sensorineural hearing loss after cord blood transplant in patients with mucopolysaccharidosis. *Arch Otolaryngol Head Neck Surg* 138: 1071-1076.
9. Baumgartner LS, Moore E, Shook D, Messina S, Day MC, et al. (2018) Safety of autologous umbilical cord blood therapy for acquired sensorineural hearing loss in children. *J Audiol Otol* 22: 209-222.
10. McClean WJ, Hinton AS, Herby JTJ, Salt AN, Hartsock JJ, et al. (2021) Improved speech intelligibility in subjects with stable sensorineural hearing loss following intratympanic dosing of FX-322 in a phase 1b study. *Otol Neurotol* 42: e849-e857.
11. McLean WJ, McLean DT, Eatcock RA, Edge AS (2016) Distinct capacity for differentiation to inner ear cell types by progenitor cells of the cochlea and vestibular organs. *Development* 143: 4381-4393.
12. Yang WP, Henderson D, Hu BH, Nicotera TM (2004) Quantitative analysis of apoptotic and necrotic outer hair cells after exposure to different levels of continuous noise. *Hear Res* 196: 69-76.
13. Groschel M, Gotze R, Ernst A, Basta D (2010) Differential impact of temporary and permanent noise-induced hearing loss on neural cell density in the mouse central auditory pathway. *J Neurotrauma* 27: 1499-1507.
14. Froelich F, Ernst A, Strubing I, Basta D, Gröschel M (2017) Apoptotic mechanisms after repeated noise trauma in the mouse medial geniculate body and primary auditory cortex. *Exp Brain Res* 235: 3673-3682.
15. Baumgartner JE, Baumgartner LS, Baumgartner ME, Moore EJ, Messina SA, et al. (2020) Progenitor cell therapy for acquired pediatric nervous system injury: Traumatic brain injury and acquired sensorineural hearing loss. *Stem Cells Transl Med* 10: 164-180.



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