When Inner Ear Stem Cell Therapy Becomes a Reality

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The clinical treatment of hearing loss is at once sophisticated and crude. Surgeons can use microsurgical techniques and lasers to manipulate ossicular prostheses fractions of a millimeter with often astounding improvement in hearing, for example, in the case of stapes fixation due to otosclerosis. For profound sensorineural impairment, the cochlea may be surgically implanted with an electrode that stimulates the spiral ganglion neurons of the cochlea, thereby enabling effective hearing for many people. Yet despite modern surgical techniques and scientific advances, outcomes for restoration of conductive hearing when there is no ossicular chain at all remain unpredictable at best. Cochlear implants are threaded into the cochlea with very little precision as to which neurons are stimulated by which electrodes. In addition, not a single surgical intervention will help the typical patient with tinnitus, for whom even sectioning of the auditory nerve would not provide relief. Scalpels and drills can only do so much.

Roughly, the same situation exists for current hearing aid technology. The historical evolution of assistive hearing devices, from the lowly ear trumpet to the modern digital hearing aid, provides irrefutable evidence of progress. For many patients, a simple hearing aid properly fitted can be life changing. However, as the severity of hearing loss worsens, hearing aid limitations become increasingly clear—for the patient with poor discrimination, for example, even the most powerful amplification available provides a fundamentally impoverished version of the auditory world. In other words, conventional amplification can be both remarkably helpful and glaringly insufficient. The more demanding a patient's auditory needs are, the clearer the limitations in our methods of intervention often appear.

It is quite plausible that molecular biology, rather than surgery or amplification, holds the key for the next transformative leap forward in our ability to treat hearing loss. As the review article ("Stem Cell Therapy for the Inner Ear: Recent Advances and Future Directions") in this issue by Okano and Kelley suggests, a great deal of research has been done in the field of stem cells for the inner ear. This field has progressed in a relatively short span of time from an intriguing area of hypothetical inquiry to a viable possibility in the not-too-distant horizon. Scientists are truly starting to unravel the mysteries of hair cells and what it would take to regenerate them in humans. Through the development of stem cell therapy for the inner ear, it is becoming increasingly plausible that our future treatments for sensorineural hearing loss will be based on neither surgery nor hearing aids, but instead on

molecular stem cell therapy. As the name suggests, stem cells offer the potential to bring the inner ear back to life, as it were, by restoring pluripotency to the cells of the inner ear—a critical step toward the reestablishment of hair cells. The easily accessible location of the inner ear just medial to the eardrum also raises the exciting possibility that transtympanic delivery of such stem cells into the inner ear may someday be accomplished as a routine office procedure.

Obviously, the issues surrounding stem cells are complex. As Okano and Kelley point out, producing a viable hair cell is only the first of many critical steps in devising an effective treatment for clinical hearing loss. More importantly, such a hair cell would need to be functional, not just alive—able to respond to acoustic energy within the cochlea. In addition and even more important still, this functional hair cell would need to transmit its message to a capable recipient—a spiral ganglion neuron presumably—that could take the incoming signal and relay it to the auditory brainstem for central auditory processing. These challenges have remained formidable obstacles to clinical treatment with stem cells for years. In fact, trying to list all of the prerequisites for clinical application of stem cell therapy only serves to emphasize how extraordinary the normal human cochlea really is. Unfortunately, unlike some other species, the human ear is stubbornly unwilling to regenerate its own hair cells. Given the fact that most sensorineural hearing loss is attributable precisely to hair cell loss or dysfunction, the ability to replace damaged hair cells is crucial. It is imperative, then, that scientists are able to continue their efforts to use stem cells in a functionally relevant manner within the inner ear.

On reading Okano and Kelley's article, I am left with a deep appreciation for how many difficulties remain in making stem cell use in the inner ear a reality. It is a daunting challenge, and it remains unclear just how far away we are from the reality of improving hearing in patients with the use of stem cells. However, these cautionary comments do not trump what I really feel, which is a sense of amazement and profound respect for just how far this field has evolved. On the basis of such impressive progress over a remarkably brief span of time as described by Okano and Kelley, it seems self-evident that one day both conventional amplification and surgical implantation will be supplanted by stem cell therapy, as the primary treatment approaches for significant sensorineural hearing loss. Even for a surgeon, that possibility is nothing if not thrilling.

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