1. WHAT IS GENE THERAPY?

Genes carried on chromosomes, are the basic physical and functional units of heredity. Genes are specific sequences of bases that encode instructions on how to make proteins. Although genes get a lot of attention, it's the proteins that perform most life functions and even make up the majority of cellular structures. When genes are altered so that the encoded proteins are unable to carry out their normal functions, genetic disorders can result. Gene therapy is a technique for correcting defective genes responsible for disease development. Researchers may use one of several approaches for correcting faulty genes:

- A normal gene may be inserted into a nonspecific location within the genome to replace a nonfunctional gene. This approach is most common.
- An abnormal gene could be swapped for a normal gene through homologous recombination.
- The abnormal gene could be repaired through selective reverse mutation, which returns the gene to its normal function.
- The regulation (the degree to which a gene is turned on or off) of a particular gene could be altered.

2. CURE HEARING LOSS WITH GENE THERAPY?

An experiment was performed using guinea pigs and gene therapy. The study shows that, the supporting cells of the ear migrate and partially restored the hearing, indicating that gene therapy could improve hearing in deaf animals. This means that possibly not one, but a combination of therapies, could be used in the future to restore hearing. The researchers carried out experiments for getting DNA into the cells of the developing ear. They attached DNA containing a gene that produced a fluorescent protein (a sort of “marker”) to other bits of DNA that would cause the gene to be activated once inside a cell. They then injected the DNA into the developing ear of embryonic mice in the womb (on about the 11th day after conception), and applied a weak electrical current to help the DNA get into the cells. They then checked to see whether the gene was working (whether it was switched on), which cells it was working in, how long it took to work, and whether the process had disrupted normal development of the ear by about 18 days after conception. The researchers also tested the hearing of some of the mice one month after their birth to see if it had been affected. The researchers then repeated their experiments using a similar piece of DNA that contained the Atoh1 gene. They looked the development of the ear in these mice. Their technique did not appear to disrupt normal structural development of the ear, and the mice treated seemed to have normal hearing one month after they were born.

Liposomes are the traditional nonviral vector used in inner ear research. They are easy to repare, can be complexed with DNA of any size, and have a very low risk of insertional mutagenesis, Liposome complexed with LacZ and GFP reporter genes has successfully transfected nearly all tissue types of mice and guinea pig cochleae in vivo. A broader investigation of vectors and promoters, and the incorporation of nuclear localization sequences and targeting ligands could result in an efficient vector. Better insight into cell membrane composition and nuclear transport may also result in improvements. Other methods such as electroporation and the gene gun have yielded significant in vitro results but have not been developed for effective use in vivo.

The majority of inner ear gene therapy research has been carried out with replication-deficient Adenoviral (Ad) vectors, which can be generated at high concentrations and can accommodate large (8 kb) fragments of DNA. The replication defective Ad vector transfects hair cells in vivo. It is important to note a large degree of variation in the specific expression. This variation may result from variation in Ad concentrations, Ad vector generations, and methods of vector inoculation and transgenic protein detection. The mechanisms involved in Ad transfection need to be elucidated, ideally through a study of the expression of Ad receptors in the inner ear. Recent

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studies have used the Ad vector to prevent deafness in animals.

**3. CONCLUSION**

This study illustrates the feasibility of gene transfer in the developing ears of mice, and the effects of using this technique to introduce the Atoh1 gene. This technique will undoubtedly be useful in the study of the biology of deafness and potential gene therapies. However, this research is at a very early stage, and it is too early to say whether it will result in successful treatments for human deafness.