NeuEar Final Report - Publishable Summary

Sixteen percent of adult Europeans suffer from hearing loss, great enough to adversely affect their daily life. Over the age of 80, 50% of the population is suffering from hearing loss. A large portion of this population is affected by sensorineural hearing loss (SNHL), the consequence of a progressive degeneration of the primary auditory neurons (ANs), the afferent neurons of the cochlea. The only current therapeutic intervention for these patients is the use of a cochlear implant (CI), a neural prosthesis designed to directly electrically stimulate the ANs (see picture from Zeng et al 2008). Despite improvements in CI technology, the hearing experience with these devices remains far from normal, with many patients reporting difficulties discriminating speech in noise and poor perception of temporally encoded sounds such as music.

During the course of the grant, NeuEar partners have designed a neurotrophic cochlear implant – a novel neural prosthesis - to provide both electric auditory cues and regenerative neurotrophic factor(s) to severe-profoundly deaf patients. As the ongoing degeneration of ANs that occurs over time is a limiting factor in current cochlear implant efficacy, the ANs have been the target cells in the implant design strategy. The project aims were to develop an encapsulated cell (EC) therapy device capable of long-term intracochlear delivery of neurotrophic factors to prevent the degeneration of ANs, and to further combine this new EC device with a cochlear electrode implant for joint implantation in the cochlea.

Parts of cochlear implant
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As a first step, several clones based on a human retinal pigment epithelial cell line were developed to express high levels of either Glial cell-line Derived Neurotrophic Factor (GDNF) or Brain-Derived Neurotrophic Factor (BDNF). To test the clones in a relevant animal deafness model, a novel encapsulated cell device was engineered to allow for cochlear implantation in guinea pig and cat. In a one-month short-term guinea pig study, we showed that the encapsulated cells expressing either GDNF or BDNF successfully protected the animals from normally deafening, injected doses of neomycin. These very encouraging proof-of-concept results show that intracochlear delivery of neurotrophic factor from an encapsulated cell device can indeed provide a positive effect to diminish hearing loss.

In a following long term, 6-month cat study, encapsulated cell devices were implanted together with custom-made cochlear implants designed by the consortium. Good results on safety and the lack of adverse effects in the cats were obtained, but the cochlear implants were generally broken over the six months due to the natural movements of the cats. Furthermore, encapsulated cell devices implanted over the same time were found to be rejected by the cats, leading to their loss of function. Compared to the good results obtained in guinea pigs, this indicates that the cat deafness model could be difficult to work with for chronic cochlear implantations.

In parallel to the in vivo studies, several design concepts for a final clinical product were made, resulting in functional prototypes that can be employed in coming clinical studies. These designs are currently being patented and will, based on the very encouraging NeuEar data, be used in a clinical Phase I trial planned to start shortly after the end of the NeuEar project.

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