Could you introduce your research at Hannover Medical School, outlining your primary aims and objectives?

TL: The Department of Otolaryngology at Hannover Medical School is recognised internationally as having one of the world’s largest cochlear implant programmes. Our vision is to provide all patients suffering from any form of hearing loss with an optimised and individualised hearing implant. Since we own one of the largest research programmes in the field of hearing, we are in the outstanding position of being able to perform basic research that can be immediately translated and transferred to the clinical side of our department – ‘from bench to bedside’ is our daily work. The research we conduct primarily involves the further development of auditory implants, neuroimplants and nanobiomaterials, as well as pharmacotherapy and laser medicine. The entire range of our work is not limited to R&D; it also encompasses design, production and testing. These services are carried out in close cooperation with industry partners.

How does the Department of Otolaryngology at Hannover Medical School work to maintain its high standards, and in what ways are you continually innovating in this field?

VS: Our position as one of the leading clinics in the cochlear implant field is based, among other things, on the fact that the German Hearing Centre Hannover (DHZ) is a part of our department. With our clinic and DHZ working hand-in-hand, we can provide an all-round service: from full audiological differential diagnosis and guidance on an adequate hearing system, to surgery and lifelong medical, technical and educational follow up, and care for patients. As our work follows a strict quality management process based on International Standards Organisation norms, we are able to maintain high standards throughout our daily work. The continuing education of all employees ensures everyone is up to date with our routine processes. Moreover, we persistently endeavour to develop novel strategies to increase our standards further.

How does the electrical stimulation (ES) of spiral ganglion neurons (SGN) via a cochlear implant work?

VS: The cochlear implant is a well-established, surgically implanted electronic device that provides hearing to patients who are deaf due to damage to sensory hair cells in their inner ear. Picking up sound by a microphone worn behind the outer ear, the cochlear implant’s processor manipulates the electrical signal and sends it to a transducer that changes the signal from an electrical to a magnetic one. This can be received through the skin by an implanted receiver. The receiver then stimulates the electrode array placed in the cochlea, leading to electrical stimulation of the auditory neuronal cells, the SGN. From those cells,afferent pathways guide the signal to the relevant structures of the brain, leading to sound sensation in the originally deaf patient. Therefore, the functional state and the number of surviving SGN are among the factors that determine the success of the cochlear implant treatment.

What methodologies do you follow when performing your research?

VS: We started our research by evaluating our hypotheses via experiments on cell lines and primary cell cultures. Here, we performed pharmacology studies of drug effects on cell survival or outgrowth, as related to applied concentrations and time points such as intervention start or treatment duration. In addition, we performed experiments on electrical stimulation of cultivated cells. When in vitro results were promising we transferred the hypothesis into in vivo experiments, choosing the relevant animal model and analysis spectrum.

How and when do you plan to translate these results into clinical applications?

TL: We are constantly developing new implant designs that are translated into clinical application in close cooperation with cochlear implant manufacturers. For example, we helped develop a short electrode array of 20 mm length that received a CE certificate this spring. This novel implant is built for optimising hearing preservation in cochlear implant patients. Transferring drug therapy strategies into the clinic is more difficult than testing medical devices, since approval for those studies is much harder to obtain from the legal authorities. However, clinical trials are running to prove the safety and efficacy of drug-based therapies in cochlear implant patients.
Hearing enhanced

Researchers at Hannover Medical School are developing pharmaceutical interventions for improved cochlear implant functionality

IT IS ESTIMATED that 10 per cent of the world’s population is hearing impaired. In the past few decades, the treatment of deaf patients has been revolutionised through the development of cochlear implants (CIs), which counteract the lost function of damaged hair cells through direct electrical stimulation of the spiral ganglion neurons (SGN).

Experts have adopted this technological advancement as a routine therapeutic option for patients with both complete and incomplete sensorineural hearing loss, especially as the proportion of CI patients with some degree of residual hearing is greater than that of individuals fitted with traditional hearing aids. However, despite its proven efficacy, levels of success among CI patients differ substantially, prompting researchers to strive to further unravel the mechanisms of hearing loss to design improved technologies and treatments.

SPIRAL GANGLION NEURONS

As the effectiveness of CIs is largely dependent on the survival and responsiveness of SGN for electrical stimulation, many studies worldwide focus on the protection and regeneration of these neurons. Dr Verena Scheper, leader of the Drug Delivery Research Group at Hannover Medical School and Professor Thomas Lenarz, Professor and Chairman of the Department of Otolaryngology, Germany, are working to optimise cochlear implants through more effective drug delivery to facilitate the protection and regeneration of auditory nerve cells. Largely, they are carrying out this research in partnership with NeuEar, an EU consortium led by NsGene A/S, Denmark, and ProHearing, The Netherlands.

MULTIMODAL TREATMENT

One area the researchers are working on is techniques for CI improvement that include local drug delivery. “The release of appropriate protective factors, so-called nerve growth factors, from the electrode matrix or a CI-linked implant, as developed in the project NeuEar, can play a role in helping to accomplish this goal,” Scheper explains. The treatment concept Scheper and her group are developing is based upon the understanding that electrical stimulation from the implant itself leads to neuronal protection. The team’s aim is thus to develop multimodal modern therapies with synergistic electrical stimulation (ES) and drug delivery.

The scientists’ hypothesis is that immediate treatment with ES or neurotrophic factor can prevent degeneration of SGN. The first phase of testing involves in vitro trials using cell lines or primary cell cultures to analyse how both pharmaceuticals and ES affect SGN survival and regeneration. Subsequently, to evaluate the therapeutic effects of these treatments on SGN in vivo, the researchers use animal models such as guinea pigs based on local or systemic deafening methods. Instead of traditional and time-consuming embedding techniques, such as the paraffin method, the group uses confocal laser scanning microscopy (CLSM) to quantify SGN. Advantages of this method are that the cochlea remain intact as organs and maintain their geometric shape. “CLSM is suitable for qualitative and quantitative determination of SGN as well as for detection of implant positions and tissue examination inside the cochlear structures,” Scheper reveals. Consistent experiments of this nature allow researchers to predict how effective interventions may be in human patients and represent a vital step prior to translation of the treatment for use in clinical settings.

PREVENTING REJECTION AND LOSS OF RESIDUAL HEARING

Alongside neuronal preservation, inner ear drug delivery can be used for other targets. Anti-inflammatory substances like dexamethasone can be delivered directly into the cochlea during the implantation surgery to quell any adverse reactions to the CI as a foreign object, which in turn helps reduce postoperative impedances and fibrosis. Moreover, the group is investigating antioxidants as potential agents for the reduction of residual hearing loss in CI patients. “In the EU-funded project ProHearing, we are evaluating the effect of a combination of the antioxidative vitamins A, C and E and magnesium on hearing preservation in CI patients,” Scheper explains. Though the project is still in its infancy (having only started in December 2013), previous studies using this formula are encouraging, and Scheper is confident that patients participating in the trial will benefit from it greatly.

PERSONALISED HEARING DEVICES

To build on the past success of enabling the preservation of residual hearing in CI patients, Scheper and Lenarz would like to focus on improving diagnostics through the analysis of the distinct differences in hearing and hearing impairment on an individual basis using functional and genetic-based evaluations. “Personalisation of hearing devices and computer- and robot-assisted surgeries will be the future in cochlear implant supply,” Lenarz concludes.
Working in harmony

NEUEAR

Coordinator of the FP7 project NeuEar, Jens Tornøe, expands upon the project’s aim to enhance existing cochlear implant technology.

Could you introduce yourself and outline your role at NeuEar?

I am Director of Research and Development for the Danish biotech company NsGene A/S, the NeuEar partner responsible for coordinating the entire three-year, €8 million EU-supported project. In addition to coordinating the NeuEar efforts, maintaining the project communication and reporting to the EC, I am heading the NsGene part of the project, which encompasses cell line and medical device engineering for cochlear implantation. The project brings together the cochlear implant technology with NsGene’s proprietary Brain Repair technology to develop a next-generation cochlear implant.

How is your collaboration with Hannover Medical School facilitating the development of new cochlear implants capable of supporting the regeneration of the auditory neurons?

The vast accumulated knowledge of hearing disorders and models of these at the Department of Otolaryngology is pivotal to the NeuEar project. The NeuEar consortium has already generated promising preliminary results with the combination treatment, and further testing is underway to demonstrate positive long-term effects. Good results in these studies will allow us to further develop our prototype into a clinical product, which we predict will be of considerable benefit to people with hearing disorders.

PROHEARING

Barry Seifer, CEO of Hearing Health Science, discusses its collaboration with Hannover Medical School and explains their joint mission to prevent hearing loss.

Could you introduce Hearing Health Science and your role as Chief Executive Officer?

Hearing Health Science is a translational research biomedical company based in Amsterdam, The Netherlands. We focus on inner ear research and therapies, and we partner with scientists at academic institutions to move basic and preclinical studies through the clinical and epidemiological phases, taking the lead role in commercialisation. My responsibility as CEO is to manage the totality of these efforts. Our first product, Soundbites, is scheduled to begin beta phase commercial testing later this year. It is the first hearing preservation treatment to target the entire range of inner ear hearing impairments.

How has a collaborative approach with Hannover Medical School proved successful in combating sensory impairments?

Hannover Medical School and Hearing Health Science are close collaborators on the cochlear implant clinical study. We supplied the clinical material and the associated pharmaceutical development documentation for approval by the German drug agency. Collaborations among public health grant-giving agencies like the EC, academic research institutions like Hannover Medical School and commercial companies like Hearing Health Science contrast with the dominant biotech/big pharma model. We believe this collaborative model helps maintain the ethical and moral integrity intrinsic to academic research. Further, we believe this approach responsibly integrates public and global health with a profitable business and accelerates progress toward a more equitable healthcare paradigm.

In the future, what promising preliminary results will allow us to further develop our prototype into a clinical product, which we predict will be of considerable benefit to people with hearing disorders.

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VERENA SCHEPER has worked in the field of otolaryngology since 2004. In 2007 she became Veterinary Research Coordinator of the Department of Otolaryngology, Hannover Medical School, Germany. Since 2009, she has lead the Drug Delivery Research Group at the Hannover Medical School, Germany, and in 2012 received EC research funds to investigate pharmaco-strategies for auditory implant optimisation.