Translational Hearing Research Summit:
Biological and Pharmacological Approaches

ACTION ON HEARING LOSS
A national charity since 1911

22 March 2018, London

IN PARTNERSHIP WITH

NHS National Institute for Health Research | UCL THE EAR INSTITUTE

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The summit and its purpose

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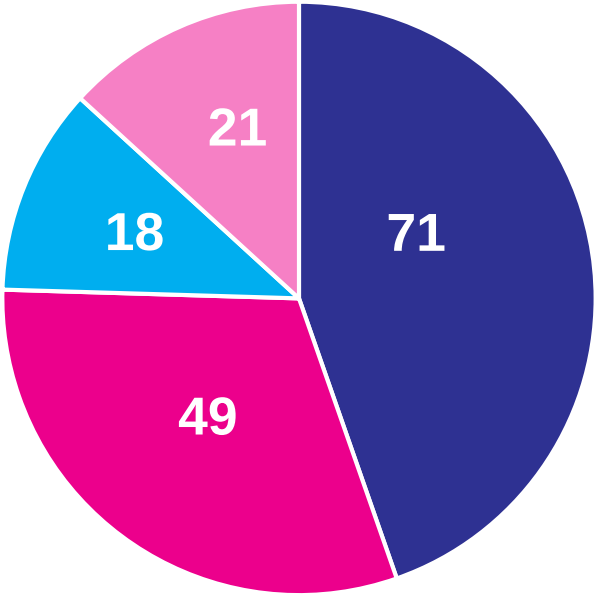
The "*Translational Hearing Research Summit: Biological and Pharmacological Approaches"* was an international summit that gathered 159 delegates, from 14 countries to discuss the current challenges and opportunities in the development of treatments for hearing loss and tinnitus.

Number of delegates divided by sector



- Academia
- Industry
- Clinical
- Patients, Investors & Funders

The unmet need

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- 466 million people in the world have disabling hearing loss (WHO, 2018)
- 1.1 billion young people (12-35 years old) are at risk of developing hearing loss due to recreational noise (WHO, 2018)
- Hearing Loss was identified as one of the top risk factors for dementia (Livingston, G et al (2017) The Lancet)
- 1 in 10 adults in the UK has tinnitus (Action on Hearing Loss)

BUT…

There are NO treatments for hearing loss or tinnitus currently available in the market.

Summit Programme

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9am **Arrival refreshments**

9.15am **Welcome**

Paul Breckell, Chief Executive, Action on Hearing Loss, UK

Prof Jonathan Gale, Interim Director, UCL Ear Institute, UK

Dr Ralph Holme, Executive Director of Research, Action on Hearing Loss, UK

Session 1 – Clinical trials: the learning curve

Chair: Prof Anne Schilder, evidENT, UCL Ear Institute, NIHR UCLH BRC Deafness and Hearing Problems Theme, UK

9.30am **What do patients and clinicians need?**
Prof Douglas Hartley, University of Nottingham, UK

9.45am **Early phase trials in hearing disorders; challenges and opportunities**
Prof Anne Schilder, evidENT, UCL Ear Institute, NIHR UCLH BRC Deafness and Hearing Problems Theme, UK

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10am **Questions and answers: the patient view**
Hugh Strickland, Corporate Finance Partner at Aaron & Partners Solicitors, UK. Hugh suffers from hereditary hearing loss.

10.20am **Refreshments and networking**

10.40am **Atoh1 gene therapy for hearing loss – preclinical and early clinical development**
Dr Richard A Colvin, Novartis, USA

11am **Developing drugs for central hearing loss and tinnitus**
Dr Charles Large, Autifony Therapeutics, UK

11.20am **Targeted drug delivery to treat hearing loss disorders**
Dr Alan C Foster, Otonomy, USA

11.40am **Sodium thiosulfate (STS) as otoprotectant to reduce the incidence of cisplatin-induced hearing loss: final results of the siopel 6 trial for standard risk hepatoblastoma (SR-HB)**
Dr Penelope R Brock, Retired Consultant Paediatric Oncologist Great Ormond Street Hospital for Children NHS Foundation Trust, UK

12pm **Lunch and networking**

Session 2 – Building on success: opportunities and challenges

Chair: Dr Carina Santos, Action on Hearing Loss, UK

1.10pm **An overview of the mechanisms of hearing loss (and tinnitus) and their potential as therapeutic targets**
Prof Jonathan Gale, UCL Ear Institute, UK

1.30pm **Showcase presentations**
(10 minutes each)

- **Developing stem cell therapies for the treatment of hearing loss**
  Prof Marcelo Rivolta, Sheffield University, UK
- **Targeted somatic cell neurotrophin gene electrotransfer promotes spiral ganglion neurite outgrowth to enhance cochlear implant performance**
  Prof Gary Housley, UNSW Sydney, NSW, Australia
- **Development of a unique therapeutic approach for the treatment of noise-induced hearing loss: the allosteric modulation of the mGlu7 receptor**
  Dr Guillaume Duvey, Pragma Therapeutics, France
- **Magnetic delivery of therapy to the cochlea**
  Dr Benjamin Shapiro, Otomagnetics, USA

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- **Development of ORC-13661: A medicine to prevent aminoglycoside-induced ototoxicity**
  Prof Edwin W Rubel, University of Washington and Oricula Therapeutics Inc, USA
- **A gerbil model to evaluate the effects of drugs on neural correlates of tinnitus and functional hearing**
  Dr Roland Schaette, UCL Ear Institute, UK
- **Getting the measure of tinnitus**
  Prof Deborah Hall, University of Nottingham and NIHR Nottingham Biomedical Research Centre
- **Exploring the views and expectations of patients and professional stakeholders on novel hearing therapies; a qualitative study**
  Dr Matthew Topping, evidENT, UCL Ear Institute, UK

3pm **Medicines discovery for auditory disease: right drug, right dose, right time, right patient**
Dr Rick Cousins, GSK, UK

3.20pm **Afternoon refreshments**

3.40pm **Panel discussion:**

"How to accelerate the development of biological and pharmacological treatments for hearing loss and tinnitus?"

Chair: Dr Sohaila Rastan, Independent Advisor, UK

Participants:

1 Dr Erik Larsen
Senior Director of Hearing Science and Technology, Decibel Therapeutics, USA

2 Rolf-Jan Rutten
CEO, Audion Therapeutics, Netherlands

3 Dr August Wilke
Principal Research Scientist at Chorus, a division of Eli Lilly and Company, USA

4 Prof Karen Steel
Professor of Sensory Function at the Wolfson Centre for Age-Related Diseases, King's College London, UK

5 Prof Gary Housley
Professor of Physiology and Director of the Translational Neuroscience Facility, School of Medical Sciences, UNSW Sydney, Australia

6 Prof Deborah Hall
Professor of Hearing Sciences, Faculty of Medicine & Health Sciences, University of Nottingham; Deputy Director of the NIHR Nottingham Biomedical Research Centre and Hearing Theme Lead, UK

7 Dr Ralph Holme
Executive Director of Research, Action on Hearing Loss, UK

5.30pm **Drinks reception and networking**

About this report

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This is a non-exhaustive summary of the current challenges and opportunities in the development of treatments for hearing loss and tinnitus discussed at the “Translational Hearing Research Summit: Biological and Pharmacological Approaches” :

1- What do patients and clinicians need?

2- Current challenges in the development of treatments for hearing loss and tinnitus.

3- What can be done to tackle those challenges and accelerate the development of treatments?

What do patients and clinicians need?

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- **Better diagnostics**

Better diagnostics are necessary to be able to distinguish among problems in the hair cells, synapses, stria vascularis or central auditory pathway and to predict the progression of hearing loss.

- **Better hearing tests**

Hearing tests should assess hearing problems in the real world.

- **Ways to prevent progression of hearing loss – otoprotection**

“Prevention is better than cure”.

- **Treatments that are safe**

Treatments should not present risks to residual hearing or induce any kind of systemic or balance problems. Therapies need to be future proofed so that they do not compromise the efficacy of other and better treatments that may appear in the future.

What do patients and clinicians need?

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- **Treatments that are effective in real world situations**

Treatments should improve patients ability to localize sounds, listen in noisy environments, use a phone and appreciate music.

- **Treatments that are suitable for the patient's lifestyle**

Delivery methods of the therapy to the inner ear and frequency of administration of the treatments should be compatible with the patient's work and social life.

- **Treatments that are equitable for all**

Although ~14 million people worldwide can potentially benefit from cochlear implants (CI), current market penetration is ~20% in developed countries & <1% in developing countries due to the high costs of CIs (Zeng IEEE 2017).

- **Quality hearing**

Patients need quality hearing which can only be achieved with a step change in treatments.

Current challenges in the development of treatments

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- **There are no therapies approved in the market**

Therefore there are no established and proven routes through clinical trials to market that companies can follow. This creates challenges when choosing a CRO and designing clinical trials, uncertainty around patient selection, appropriate clinical endpoints and regulatory approval. There is also uncertainty around how new treatments would be viewed by national healthcare providers/insurers.

- **Preclinical models may not always translate to the clinic and need to be standardized**

We need better preclinical models that can predict the outcomes in patients.

- **Lack of accurate diagnostics**

Better diagnostics are necessary to distinguish the site of lesion i.e. problems in the hair cells, synapses, stria vascularis or central auditory pathway and to predict the progression of hearing loss. This is needed to improve patient stratification, ensuring the right patient gets the right treatment at the right time.

Current challenges in the development of treatments

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- **Lack of hearing tests that assess hearing in real world situations**

We need hearing tests that assess hearing problems in the real world to properly test the benefit of the treatments that are being developed.

- **Lack of efficient delivery methods**

The inner ear is a particularly difficult area to access and new delivery methods need to be developed to ensure that new therapies can efficiently reach their targets.

- **Lack of suitable targets and genetic insight**

We need to identify more suitable targets and have a better understanding of the molecular pathways of hearing.

Current challenges in the development of treatments

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- **Lack of understanding of the patient population necessary for adequate patient segmentation**

We need to better characterize the patient population and improve understanding of the sub-types of hearing loss; of the state of the inner ear and of how the patient will respond to different therapies. We need better methods and criteria to classify and choose the patient populations that could most benefit from the treatments that are being developed.

- **Lack of robust biomarkers**

Biomarkers are necessary for better diagnostics, patient selection and assessment of treatment efficacy. Biomarkers need to predict real world functional gains.

- **Lack of good and standardized outcome measures**

Patient relevant outcome measures need to be developed and standardized to evaluate the benefit of the treatments to the patients. We should move from subjective to objective measures.

Current challenges in the development of treatments

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- **Difficulty in accessing patient populations**

We need national and international patient registries to easily access the patient population relevant to specific trials.

- **Not enough ENT surgeons and audiologists to deliver clinical trials**

The next generation of ENT surgeons and audiologists need to be trained to deliver clinical trials.

- **Lack of funding**

More funding is necessary to support: a) basic research to understand the molecular basis of hearing; b) translational research to develop new therapies to treat hearing loss and tinnitus and c) multidisciplinary projects to tackle the current challenges around patient stratification and design of relevant and predictive outcome measures.

What can be done to tackle those challenges and accelerate the development of treatments?

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- **Establish multidisciplinary teams**

Teams need to include researchers from different preclinical and clinical areas (psychophysics, electrophysiology, computational modeling, biologists, ENT, audiology, mental health, etc) to help develop better diagnostics and hearing tests, better patient selection methods and suitable outcome measures.

- **Establish effective collaborations**

More effective collaborations between different sectors (discovery scientists, clinicians and industry) should be established to share and complement expertise and skills and therefore accelerate the development of treatments.

- **Share data and experience**

Teams and sectors need to share data and analyse the clinical data that already exists in order to inform future trials, eg. there is already a significant amount of data from cochlear implant studies. Companies should share experiences and learn from each other's experience to accelerate the learning process and the development of treatments in this field.

What can be done to tackle those challenges and accelerate the development of treatments?

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- **Change public's attitudes towards hearing loss**

The general public is still very dismissive towards hearing loss. All stakeholders, and especially patient advocacy groups, need to make the public more aware of the condition and of its consequences.

- **Funding bodies should support projects that aim to tackle the challenges identified and promote multidisciplinary work**

Funding bodies should support projects that aim to solve the challenges currently faced in the development of treatments for hearing loss and tinnitus and favor multidisciplinary teams to tackle those challenges. Innovate UK and European funds are increasingly supporting networking and multidisciplinary projects.

- **Start looking into health economics of hearing loss disorders**

We need to look forward and start considering the health economics and implementation of future therapies.

What can be done to tackle those challenges and accelerate the development of treatments?

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- **Create multidisciplinary clinical trials consortiums (national and international)**

The consortium/network would work as the go-to place for companies wanting to test their drugs for hearing loss and tinnitus (eg. similar to cardiac and oncology networks). This would avoid companies looking at different places to do their clinical trials and identify different patients populations. This consortium would facilitate the design of clinical trials and maximize resources.

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In the last 5 years hearing loss companies have attracted an increasing amount of private (2007-12: $86.4million vs 2013-17: $299.3 million) and public (2007-12: $57million vs 2013-17: $469.7 million) funding (Li, V (2017) Biocentury). Although big pharma and investors are still cautions they are aware of the huge unmet need and potential of the hearing loss market.

The first successful therapy will bring traction to the field and will open up the regulatory and clinical pathway to hearing loss and tinnitus therapies, encouraging pharma and investors to engage more deeply.

Effective collaborations and communication among all stakeholders (academia, industry, clinicians and patients) is essential to leverage experience and skills, thus maximizing resources to ramp-up the development of treatments for hearing loss and tinnitus.

This summit was organized by:

ACTION ON HEARING LOSS
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Action on Hearing Loss

We are the largest not-for-profit organisation representing people with hearing loss and tinnitus in the UK. A national charity since 1911, our vision is a world where deafness, tinnitus and hearing loss do not limit or label people, and where people value their hearing. We are the largest charity dedicated to funding research into hearing loss and tinnitus.

Our Translational Research Initiative for Hearing (TRIH) funds worldwide translational hearing research and works globally with companies, academics, clinicians and investors to accelerate the development of pharmaceutical and biological therapies for hearing loss and tinnitus.

Find out more about TRIH.

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UCL Ear Institute

The UCL Ear Institute brings exceptional discovery scientists and excellent clinicians together on one site with a unified goal of understanding hearing and fighting deafness. It is a multi-disciplinary state-of-the-art research institute within UCL's Faculty of Brain Sciences. Research at the Ear Institute is truly interdisciplinary and collaborative, enabling individual researchers to pool their expertise. In addition, partnerships other UCL departments, centres and institutes, and across the world, ensure that research at the Ear Institute is world-leading and at the cutting edge.

Find out more about the UCL Ear Institute.

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NIHR UCLH BRC Deafness and Hearing Problems theme

The NIHR UCLH BRC Deafness and Hearing Problems theme builds on the unique partnership of the UCL Ear Institute and the Royal National Throat, Nose and Ear Hospital (RNTNEH). The RNTNEH is the only dedicated ENT hospital in the UK, with dedicated clinical research space and adjacent to the NIHR UCLH Clinical Research Facility. This university and hospital partnership provides the infrastructure and excellence to deliver world-leading translational research in the field of hearing loss.
Researchers within the NIHR UCLH BRC Deafness and Hearing Problems theme aim to develop and deliver targeted and transformative therapies to prevent or alleviate deafness and hearing problems and to regenerate the hearing system.

The new BRC theme commenced work in April 2017. You can find regular updates on the key target area on their dedicated web page.