Hearing loss affects 466 million people worldwide. People experience hearing loss due to loss of, or damaged hair cells in the cochlea, the inner ear. Hair cells lose their ability to convert mechanical energy from sound waves into neural impulses. Cochlear implants (CIs) are auditory prostheses which replace the function of damaged sensory cells in the cochlea. Despite the huge success of CIs, some individuals do not do as well with their implants and for some people their implants do not work at all.

We hypothesise that the priming of innate immune cells in the cochlea and auditory pathway, in response to inflammatory insults, play a role in this.

We propose that the variability between individuals after cochlea insult linked to microglial/macrophage priming?

What is priming?

Priming describes a change in phenotype and expression profile whereby microglia and macrophages exhibit an exaggerated inflammatory response to a second stimulus having previously been exposed to an initial ‘trigger’ stimulus.

Methods

Immunohistochemistry (IHC): The presence and immunoreactivity of inflammatory markers will be measured from tissue collected from the cochlea and central auditory pathway of noise-exposed and control (sham-exposed) CBA mice. Auditory Brainstem Response (ABR): ABR were recorded using sub-dural electrodes positioned on the bullae and vertex in response to 50 µs clicks and tone pips at sound levels from 10-80 dB SPL. All stimuli were presented from a pre-calibrated, free-field speaker positioned 45° from midline. µCT: A single scan will image the cochlea samples complete internal 3D structure at high resolution with the aim to corroborate this information with IHC data, to determine damaged regions of the cochlea after cochlear implantation.

Mouse strain: Male CBA mice

Initial insult - Noise exposure: Octave-band noise (8-16 kHz), 100 dB SPL was presented free-field to anaesthetised mice for 2 hours.

Secondary insult - Cochlear implantation: Implanted with a functional electrode array provided by Oticon.

Gene expression: The expression of genes that may be involved in the priming of innate immune cells will be investigated in situ, with high specificity and sensitivity using RNAseq.

Findings and Future Work

• This level of noise exposure causes an increase in hearing threshold 3 days post-injury.
• Iba1-positive cells are expressed across the cochlea and auditory pathway indicating a population of microglia/macrophages that could become primed as a result of a cochlear or systemic insult.
• Changes in phenotype and regional distribution of microglia and macrophages after cochlear insult will be investigated using different antibodies. Whether priming leads to a heightened inflammatory response upon a secondary insult (cochlear implantation) will be determined by measuring cytokine production.

Understanding whether microglia and macrophages become primed after initial insults and the effect on the subsequent inflammatory response, will contribute to determining whether robust control of inflammation will improve hearing outcomes after cochlear implantation.