Monash University researchers have identified a new protease target for the development of treatments for acquired hearing loss. We seek a partner to develop novel inhibitors of the target and drug delivery mechanisms.

- New mechanism and target identified for the treatment of hearing loss
- Potential for ‘First in Class’ drug for the prevention of noise-induced hearing loss

THE CHALLENGE

Disabling hearing impairment due to permanent loss of sensory hair cells is a worldwide problem affecting over 360 million people of all ages and walks of life. Primary causes include overexposure to noise, treatment with ototoxic drugs or infection, resulting in death of irreplaceable hair cells.

In the USA, 13% of the population aged 12 years or older has hearing loss in both ears, based on standard hearing examinations. Approximately 15% of 26 million people between the ages of 20 and 69 have high frequency hearing loss due to exposure to noise at work or during leisure activities. Nearly 25% of those aged 65 -74 and 50% of those who are 75 and older have disabling age-related hearing loss (presbycusis).

In Australia, the prevalence of hearing loss, in the better ear, is estimated to be 3.6 million people in 2017, which is expected to more than double to 7.8 million by 2060. The financial costs of hearing loss in 2017 were estimated as $15.9 billion, and the value of the lost wellbeing as $17.4 billion, for total costs of $33.3 billion. Estimates of the potential market for auditory drugs in the USA range from $10 billion in 2005 to $22 billion in 2018.

No medicines are available to treat hearing loss, and hearing aids are used by only a small fraction of the population who could benefit from them. Hence there is clear, unmet need for a biological-based therapy that prevents hearing loss by protecting hair cells.

THE TECHNOLOGY

Individuals that lack the protease inhibitor SERPINB6 suffer severe and progressive hearing loss (DFNB91). Using their SERPINB6 knockout mouse model, Monash researchers have shown that absence of SERPINB6 results in degeneration of the Organ of Corti in the inner ear (cochlea) as discrete cell types die. Sensory hair cells die first, followed by neurons and fibrocytes.

The researchers have now identified a target protease that is responsible for this damage. The protease is normally present in the cochlea, but has not previously been implicated in inner ear function or pathology. Animals that lack the protease have better than normal baseline hearing (Fig.1).

The researchers have also established that intense noise increases the levels of the protease in the inner ear. Notably, animals lacking the protease show significantly less noise-induced hearing loss and cochlear damage (Fig.2).

It therefore appears that irreversible damage to the inner ear by this protease is responsible for noise-induced hearing loss, and possibly age-related hearing degeneration.

Developing inhibitors of the protease could lead to a first in class drug treatment for the preservation of hearing following trauma or during ageing.

THE OPPORTUNITY

Monash seeks a partner to develop novel inhibitors of the protease (including monoclonal antibodies and/or small molecules) and to explore delivery mechanisms for targeting the cochlear and inner ear.

The Monash team has extensive experience in mouse auditory anatomy and physiology, and protease biochemistry, including a biochemical assay for testing inhibitors that can be adapted for HTS.