



Preventing noise-induced hearing loss with a novel pharmaceutical

Background

Hearing loss is one of the most prevalent chronic health conditions worldwide and one of the fastest-growing conditions facing Canadians. Age-related hearing loss is common but another leading cause of hearing loss worldwide is excessive exposure to loud noise. This could be environmental (e.g. city noise), recreational (e.g. loud music) or workplace (e.g. industry or military) related noise.

Hearing loss has huge implications on our ability to communicate effectively, and there is clear evidence that it increases the risk for developing dementia, including Alzheimer's disease, and accelerates age-related cognitive decline.

The Research

It is well known that noise exposure leads to oxidative stress in the sensory cells in the cochlea, as well as in the brain. Since oxidative stress appears to be a common factor in noise trauma, we really need a trusted pharmaceutical to take after noise exposure that could effectively reduce the oxidative stress in both the cochlea and the brain. Unfortunately, no such treatment exists. There have been attempts to flood the body with traditional antioxidants but without success. A new approach was warranted to address this unmet clinical need.

Our plan is to therapeutically increase the levels of a natural antioxidant, catalase, in the cochlear and brain to reduce the oxidative stress. We have two problems to overcome - we have to target the catalase inside the cochlear and brain cells where it can most effectively combat oxidative stress, and we have to develop a delivery mechanism to cross the blood-brain barrier.

The Findings

Through *in vitro* experiments with two models, we demonstrated that targeted catalase provides protection for cochlear cells against oxidative stress, including compared to a non-targeted antioxidant which was unable to provide any protection.

We used tiny membrane structures, known as exosomes, to package the catalase. These exosomes are part of the body's own transport mechanism for moving biomolecules between cells and have proved suitable here.

We were able to demonstrate production of this catalase in larger quantities necessary for future *in vivo* testing.

Finally, any new pharmaceutical must be demonstrated as safe overall before *in vivo* testing can take place. We chose to administer the catalase through the nose and we were able to show that it did cross the blood-brain barrier, without causing negative impacts on other organs in the body.

Key Points

A targeted catalase, packaged and delivered via exosomes intranasally, provides protection for cochlear cells against oxidative stress, the kind of stress that results from loud noise exposure. It is able to cross the blood-brain barrier and does not result in negative outcomes elsewhere in the body.

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Next Steps

Having established that targeted catalase can safely protect cochlear cells from oxidative stress, that we can package it and transport it through the blood-brain barrier and that we can produce it in large quantities, the next step is to test the level of protection *in vivo* against actual noise-induced cochlear damage, hearing loss and auditory processing deficits, as well as the cognitive impairment that persists post-noise exposure.

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