Hearing Loss Prevention Drug is Closer to Reality

By Edwin W. Rubel, PhD

Many hearing disorders result from the death of inner ear hair cells. As such, it’s not surprising for physicians to sometimes think: Wouldn’t it be wonderful if we could cure hearing and balance disorders by putting a drug in the ear?

That dream became a potential reality in the late 1980s when my laboratory, along with Doug Cotanche, PhD, discovered that birds regenerate the inner ear hair cells that are lost due to excessive noise exposure or ototoxic therapeutic drug treatments. Although a drug that could stimulate humans to regenerate inner ear hair cells is still years away, drugs that can prevent hearing loss are much closer to reality. This is not a novel idea, but a new company developed a different approach and is preparing to test a new drug in patients.

Aminoglycoside (AG) antibiotics are some of the earliest and most effective antibiotics. They continue to be used worldwide to treat a variety of life-threatening bacterial infections, including pulmonary infections in patients with cystic fibrosis, endocarditis, neonatal septicemia, pseudomonas respiratory infections, and multiple drug-resistant tuberculosis. However, AG use is associated with ototoxicity that results in permanent hearing loss in as many as 20 percent of the 2 million to 4 million individuals treated with parenteral AGs annually. Not only can this unwanted side effect cause untold pain and expense to the patients, but this serious liability can also cause an extremely effective class of medications to be withheld from patients who might otherwise benefit from their use.

We believe that relief is in sight. My colleague, David Raible, PhD, and I took advantage of the externally located lateral line hair cells in larval zebrafish to develop a high-throughput screening platform to evaluate drugs and drug-like small molecules that might alter the response of hair cells to ototoxic medications. Using this model, we discovered a new chemical entity (NCE) that completely protects hearing in laboratory animals exposed to very high doses of amikacin, one of the most commonly used AG antibiotics. This NCE has now been patented by the University of Washington, and is exclusively licensed to a start-up biotechnology company, Oricula Therapeutics, LLC. Oricula has previously received grants from the National Institutes of Health to examine the preliminary safety of the compound, which has been named ORC-13661. It demonstrated a therapeutic index in excess of 20-fold. In January 2016, Oricula was awarded a $2 million grant from the National Institute of Allergy and Infectious Disease to manufacture ORC-13661 and to advance it through preclinical safety and toxicology tests needed to get FDA approval for human testing.

We expect the first-in-human testing of the compound by early 2018. These tests will only involve human volunteers exposed to ORC-13661, but not to AG antibiotics. The purpose is to demonstrate the safety of the drug in humans and to estimate the appropriate dose to test in actual clinical trials. We also aim to identify the appropriate clinical indication for the initial testing of ORC-13661 as a hearing protectant. Indeed, we are excited about the prospect of saving people from unnecessary hearing loss.

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