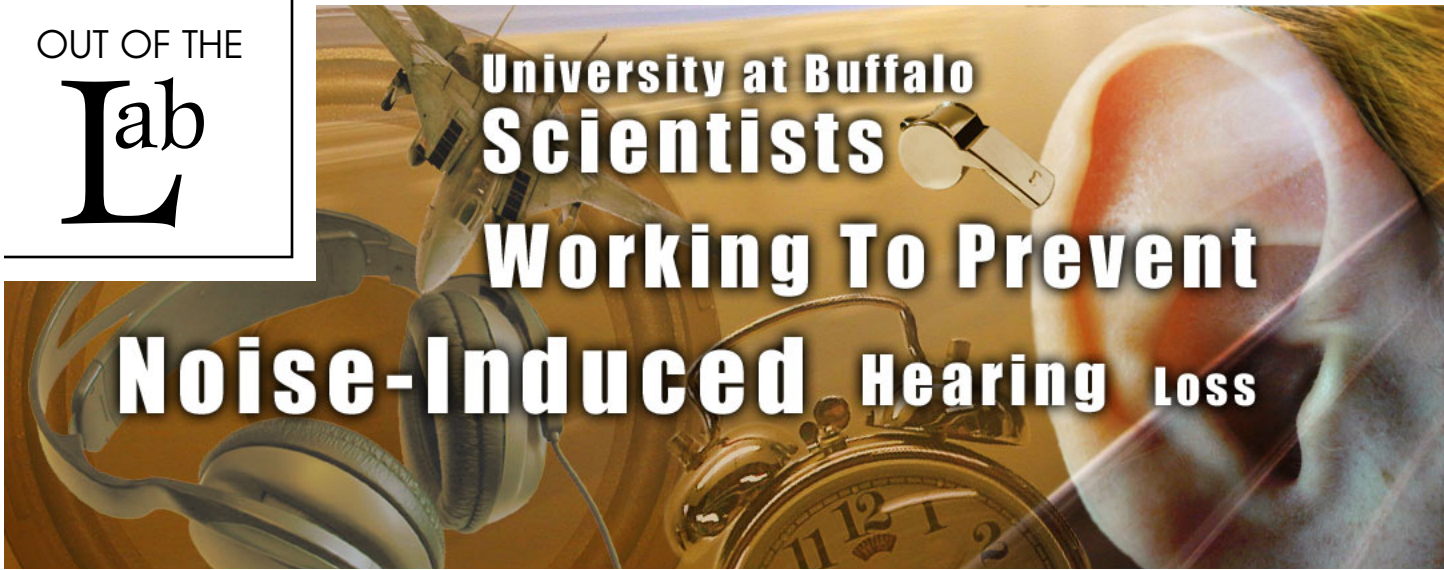


OUT OF THE
Lab



University at Buffalo Scientists Working To Prevent Noise-Induced Hearing Loss

Introduction

According to the National Institute on Deafness and Other Communication Disorders (NIDCD), more than 30 million Americans are exposed to hazardous sound levels on a regular basis. Of the estimated 28 million Americans who have some degree of hearing loss, about one-third can attribute their hearing loss, at least in part, to noise exposure. Harmful levels of sound can occur in the workplace, in recreational settings, and in the home. These exposures have the potential to temporarily or permanently damage the thousands of frequency-specific cells in the cochlea (inner ear) leading to auditory sensory deficit.

Noise-induced hearing loss might occur gradually over time or, in the case of acoustic trauma, instantaneously. Currently, the use of ear plugs or muffs and reduction of environmental sound hazards at the source are the only means of protection for those individuals exposed to

potentially damaging levels of sound. But oftentimes, hearing protection is not readily available and environmental controls are not always achievable. For example members of the military, police officers, and fire-fighters have the potential to be exposed unexpectedly to gunfire, engine noise or sirens.

When the inner ear is exposed to harmful levels of sound, excessive production of reactive oxygen species (ROS), depletion of glutathione, and damage to mitochondria eventually lead to oxidative stress in the cochlea. Glutathione is a primary inner ear antioxidant and once it is overwhelmed, sensory cells in the cochlea are injured or death occurs. The result is permanent hearing loss and often tinnitus (ringing in the ears).

An easily administered supplement or pharmaceutical product that provides protection to the delicate inner ear structures from this destructive process is considered the holy grail for those dedicating themselves to preventing noise-induced hear-

ing loss and the millions of people chronically exposed to noise.

Old Product, New Application

N-acetylcysteine (NAC) is an anti-oxidant that has been on the market for approximately fifteen years. It has been utilized clinically as a mucolytic agent for patients with chronic bronchopulmonary disease (MucoMyst) and also has indications for acetaminophen toxicity.

A budding application of NAC relates to the prevention of hearing loss as a result of noise. Considering a key mechanism of cochlear damage is the depletion of glutathione, and studies have shown NAC to be effective in replenishing cochlear supplies of glutathione depleted by loud noise exposure, this was an area that warranted further investigation.

Donald Henderson, Ph.D. is a Professor in the Department of Communicative Disorders and Sciences at the University at Buffalo. As a highly respected auditory neuroscientist, Dr. Henderson has been chipping

away at the noise-induced hearing loss issue for over 36 years.

Initial studies in Dr. Henderson's UB lab attempted to provide support to the concept that NAC would exhibit its protective properties in the cochlea. NAC was placed on the round window of the cochleas of chinchillas that acted as subjects for a noise exposure experiment. Following NAC administration and defined noise treatments, electrophysiological measures and histological studies of the animals' cochleas were completed. The results were as Dr. Henderson's group hypothesized. The NAC-treated cochleas sustained less of a sensory cell insult from the noise exposures than the cochleas of the animals that did not receive

the compound.

According to Dr. Henderson, "the first controlled study, supervised by Army Colonel Richard Kopke, MD, is about to get underway to determine if the effects of NAC are generalizable to humans with regard to hearing conservation". A group of newly recruited Marines moving through basic training and war games will be separated into treatment and control groups. The treatment group will be provided with NAC throughout the study and the control group with a placebo. Both groups will have their audiological status monitored closely. The hope is that Dr. Henderson's findings in the chinchilla model will replicate in the basic trainees receiving NAC supplementation.

Currently, Drs. Henderson and Bohua Hu from UB, and Drs. Richard D. Kopke and Michael Hoffer from the DOD Spatial Orientation Center, Naval Medical Center in San Diego, jointly hold the patent on NAC as it applies to hearing conservation. In 2002 the technology was licensed to start-up biotechnology company American BioHealth Group in San Diego, CA. According to David Karlman, CEO, "the company is taking a neutraceutical and over-the-counter approach to address hearing and related disorders". American BioHealth Group was founded 2.5 years ago with an initial influx of capital from founders and the California State University system. The company is currently in discus-



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sions with potential investors and hopes to raise an additional \$6.5 million. The funds will be dedicated to the development of new technology through phase I, and the marketing of current products including NAC that has been named “The Hearing Pill”.

New Technology, New Application

Another potential fighter in the battle against noise-induced hearing loss evolved out of a different UB laboratory. Former Merck scientist and current UB Associate Professor of Medicinal Chemistry, David Hangauer, Ph.D. has dedicated himself to the study of kinases for the past ten years. Originally focusing on cancer, Dr. Hangauer has developed a chemical compound that has been shown to bind to kinase Src and inhibit tumor growth.

“Noise exposure has been shown to not only affect the sensory cells of the cochlea, but also the junction between the cells, specifically at the Deiter’s

cupps in which they rest”, according to Dr. Henderson. He continues, “Dr. Hangauer’s compound is a small molecule that prevents a certain kind of apoptosis and therefore we believe we can reduce or prevent damage we see occurring at the cell junctions”.

Dr. Henderson and his Center for Hearing and Deafness colleagues put a small amount of Dr. Hangauer’s compound (CH-65) on the round window of chinchillas and then exposed the animals to noise. The results suggested that blockage of apoptotic signaling at the cell matrix can indeed prevent hair cell loss. As a result, this could play a significant role in reducing noise-induced hearing loss. Administration through IP route is next on the agenda.

Dr. Hangauer’s technology has been licensed to Buffalo based start-up Kinex Pharmaceuticals, LLC. The company was founded in late 2002 and is led by Allen Barnett, former Vice President of Technology Acquisition for

Schering-Plough. Dr. Hangauer is the company’s Senior Vice President of Research and Development and Lyn Dyster, Ph.D., a prominent figure in Buffalo’s biotechnology community, is acting as the company’s Vice President for Drug Discovery.

According to Dr. Hangauer, one primary differentiating component of Kinex’s technology is that “Kinex is developing a small molecule that competes with the peptide substrate, other technologies in the area of kinase inhibition focus on ATP”. Kinex is vigorously pursuing applications for their Src technology in the area of cancer. They also have an SBIR grant pending (in collaboration with Dr. Henderson’s Center for Hearing and Deafness) in the area of noise-induced hearing loss. To date, the company has been funded by the founders and angel investors. They are currently seeking \$6 million to support research activities and overall structural growth of the company. 