2014 AHRF Research Grant Awards

The AHRF Board of Directors and the Research Committee are pleased to announce this year's AHRF research grant recipients. AHRF received numerous high-quality proposals this year; therefore, we decided to fund seven research projects, two more than last year and one more than the average year. A report on the project and an accounting of funds is required at the end of the funding period, and projects are generally funded for one year unless an exception is made at the discretion of the Foundation. In addition to the seven grants awarded by AHRF in 2014, we also fund one $25,000 grant in conjunction with CORE. The AHRF grant program focuses on supporting new or beginning investigators so that they can test ideas and collect data as their research evolves. We are very pleased to introduce the recipients of the 2014 AHRF research grants and we look forward to the exciting results of these highly innovative projects!

Zonal Variations in Calyx properties of the Crista

Katherine Rennie, PhD - University of Colorado, Denver

The goal of Dr. Rennie's research project is to elucidate mechanisms of synaptic transmission and plasticity at the vestibular type I hair cell/calyx synapse. Type I hair cells have unique characteristics including a low-voltage activated K+ conductance, an unusual afferent calyx terminal that surrounds most of the hair cell's basolateral membrane, and a greater sensitivity to certain ototoxic drugs compared to other types of hair cells. The number of ribbon synapses within vestibular hair cells is known to vary across the rodent crista and afferent fibers in different zones have different responses to rotational stimuli. However, the underlying mechanisms driving synaptic transmission remain unknown. Dr. Rennie will use patch clamp and imaging techniques to study transmitter release from labeled synaptic ribbons at the rodent type I hair cell/calyx synapse. Variations in ribbon synapse numbers may have a measurable impact on glutamate release and postsynaptic responses. The role of ionic conductances in firing in calyx terminals will also be determined. Regional variations in K+ channels will be studied to better understand how they function to process vestibular signals. Defects in K+ fluxes are implicated in certain vestibular disorders including Meniere's disease, a debilitating condition characterized by episodes of vertigo. Studying ion channels in selective groups of hair cells and afferents will provide new information on processing and will help to identify future therapeutic targets for the treatment of inner ear disorders such as Meniere's.

Effects of Dexamethasone on Radiation Induced Auditory Hair Cell and Hearing Losses

Christine Dinh, MD - University of Miami Miller School of Medicine

The objective of Dr. Dinh's study is to investigate the effectiveness of dexamethasone (DXM) in preventing radiation induced auditory hair cell loss in vitro and radiation induced sensorineural hearing loss in vivo. This research project is part of a larger and more comprehensive translational research study involving the testing of various intratympanic therapies for the treatment of cisplatin, radiation, and combined cisplatin and radiation induced hearing loss. The results of this study will produce preliminary data necessary for further research through a prospective randomized, double-blind clinical trial testing the effects of several otoprotective agents against cisplatin and radiation induced hearing loss.

Cellular and Molecular Characterization of a Novel Human Deafness Dominant Mutation in Myosin IIIa

M'hamed Grati, PhD - University of Miami Miller School of Medicine

The goals of this research project include the study of the pathogenicity of this novel predicted dominant point mutation by examining its effect on myosin IIIa motility and espin-1 transport in COS7 cells, as well as its effect on myosin IIIb motility; express mutant myosin IIIa in organotypic hair cells and examine its subcellular localization, motility, and effects on hair cell stereocilia morphology; to generate transgenic mice expressing mutant myosin IIIa and evaluate, by auditory brainstem recordings and distortion product otoacoustic emissions, its effect on hearing in these mice, closely examining by whole-mount immunofluorescence and by scanning electron microscopy the morphology of their hair cell stereocilia bundle development looking for anomalies, as well as investigating by whole-mount immunofluorescence the potential deficiency in transport and the distribution of select stereocilia tip proteins.

Statistical Learning from Acoustical Simulations of Cochlear Implants

Tina Grieco-Calub, PhD and Casey Lew-Williams, PhD - Northwestern University

Drs. Grieco-Calub and Lew-Williams will test the hypothesis that fine frequency resolution is required for successful auditory statistical learning. In a series of experiments with normal hearing infants and adults, the investigators will determine whether it is possible to segment words from spectrally degraded speech. The outcomes of the experiments will converge to inform future research exploring statistical learning abilities in infants and adults with cochlear implants, with the ultimate goal of improving aural habilitation programs.

Behavioral Testing for Hidden Hearing Loss in Chinchillas: Towards Human Diagnostics

Ann E. Hickox, PhD and Michael G. Heinz, PhD - Purdue University

Drs. Hickox and Heinz will measure physiological and behavioral signs of hidden hearing loss on a chinchilla model and, within the same individual animals, assess the relationship between physiological damage and perceptual consequences. The timelines and methods of the project are designed for immediate application to a large-scale study of hidden hearing loss and the development of diagnostic assays, led by Dr. Chris Plack at the University of Manchester in the United Kingdom. By combining invasive histological analysis, available in the animal model, with electrophysiology and behavioral tasks that are applicable to both animal and human listeners, the study in chinchillas can directly address the hypothesis that a history of noise exposure leads to perceptual deficits based in hidden auditory nerve damage. Collaborative efforts with the team in the U.K. ensures that results from the chinchilla model will directly and immediately inform the design of the human-subject studies, and ultimately contribute to the development of new and more sensitive clinical diagnostics.

Role of Resident Immune Cells in the Development of Cochlear Innervation

Tejbeer Kaur, PhD and Mark Rutherford, PhD - Washington University School of Medicine

Recent work in the developing central nervous system has demonstrated that selective synaptic pruning involves the activity of microglia, the macrophages of the brain. Using a genetically engineered mouse model in which all macrophages are labeled with green fluorescent protein, the researchers have observed a large population of resident macrophages in the developing organ of Corti. However, the possible role of these cells in synaptic pruning and refinement has not been explored. Through this project, Drs. Kaur and Rutherford will determine whether macrophages in the developing cochlea are involved in the developmental refinement of cochlear innervation. The study will test for this unprecedented role of macrophages by depleting them, using both pharmacological and genetic approaches, during the postnatal period of cochlear development. This work will quantify synapse numbers and innervation patterns, and also assess auditory function after macrophage depletion. The outcomes of the experiments will indicate whether macrophages play an essential role in the refinement of cochlear innervation and may provide new insights into the nature of cellular dialogue between the innate immune system and the inner ear.

Central Neurophysiological Markers Underlying Degraded Speech Recognition

Gavin M. Bidelman, PhD - School of Communication Sciences & Disorders, University of Memphis

Extracting speech from background noise is fundamental for real-world communication as everyday listening environments, such as noisy classrooms and restaurants, contain competing sounds. Recognizing speech within the auditory scene is challenged by two types of acoustic interference: noise and reverberation. These interferences are particularly problematic for elderly and hearing impaired people who perform poorer in noise than their hearing loss would predict. While modern hearing aids provide audibility, they fail to restore speech intelligibility in noisy/reverberant settings. Advancements in assistive hearing technologies could be dramatically improved with knowledge of how central brain mechanisms affect speech coding in adverse listening situations. The long-term goal of Dr. Bidelman's research project is to elucidate the neural substrates that contribute and interact to yield robust perceptual abilities. The project results will offer new and fresh insights for improved auditory prostheses and signal processing strategies by evaluating how noise and reverberation each affect the neural correlates of speech at multiple computational levels of the auditory pathway.

2013 AHRF Research Grant Reports

We asked our 2013 AHRF researchers to provide some information about the scientific productivity and knowledge that emerged from their research grants by providing an assessment of the impact the grants may have had on their scientific career advancement, or if the grants helped to develop skills in young researchers. We would like to share their stories as to how scientific research also advances the important human elements of discovery and working together towards common goals.

Mechanism of Cochlear Fibrosis Following Cochlear Electrode Implantation Trauma

Esperanza Bas Infante, PharmD, PhD - University of Miami Ear Institute, Miami, FL

The main aim of this AHRF research grant was to gain insight into the molecular mechanism of fibrotic tissue and bone formation that can occur following electrode insertion trauma (EIT) in a mouse model of cochlear implantation trauma. The translational aspect of the project is to target the mediators involved in fibrogenesis after an EIT event to reduce the formation of scar tissue deposition around the CI electrode, which can ultimately improve the hearing perception of implanted patients and their quality of life.

The results obtained from this project confirm cooperation between Transforming Growth Factor- beta and Wnt/beta-catenin pathways that influence the induction of fibrosis and neo-osteogenesis within implanted cochleae. The activation of these pathways lead to the modulation of certain genes involved in cell- cell interactions, cell growth, cell to cell adhesion, migration and differentiation of cells to form fibrotic tissue and new bone. At early stages we observed infiltration of monocytes into the wounded area. Macroscopic and microscopic images of the implanted ears at 1 month post-surgery show new tissue growth in the area were the electrode was inserted. We are excited with these results because it provides important baseline information that can be applied to the screening of new and novel drug therapies that can be applied to the cochlea during the implantation and help to control the growth of fibrotic tissue and new bone around the electrode array.

Some of the results obtained from this project have been presented in international meetings such as:
Esperanza Bas, Yamil Selman, Bradley Goldstein, Chhavi Gupta, Adrien Eshraghi and Thomas R. Van De Water. Cochlear electrode implantation trauma causes over-expression of TGF-β1 and activation of the Wnt/β-catenin pathway in an in vitro model. Association for Research in Otolaryngology. Baltimore, MD, USA, 2013.

Esperanza Bas, Yamil Selman, Bradley Goldstein, Chhavi Gupta, Adrien Eshraghi and Thomas R. Van De Water. Electrode implantation trauma (EIT) initiates fibrosis by over-expression of TGF-β 1 and activation of the Wnt/β-catenin pathway in an in vitro model of cochlear implantation in an in vitro model. Experimental Biology. Boston, MA, USA, 2013, American Society of Biochemistry and Molecular Biology. Travel Award Recipient.

Esperanza Bas, Chhavi Gupta, Adrien Eshraghi and Thomas R. Van De Water. Dexamethasone prevents electrode insertion trauma-initiated inflammatory response and fibrosis. Inner Ear Biology, Alcala de Henares, Madrid, Spain, 2013.

And will be presented at:
Esperanza Bas, Bradley Goldstein, Michelle Adams and Thomas R. Van De Water. Dexamethasone modulates the inflammatory and fibrogenic responses in cochlear tissue explants initiated by electrode insertion trauma. Association for Research in Otolaryngology. San Diego, CA, USA, 2014.

This grant also gave Michelle Adams, a student who will be graduating with a Baccalaureate Degree in Exercise Science with a pre-med track and invited to the Honor's College at FIU, an opportunity of getting introduced into this field of research. Michelle rapidly learned different research techniques and actively participated in the execution of this project. Ms. Adams is excited to come back to the lab during her summer break and she stated that due to her experience with this research project, she would like to become an ENT doctor and also continue to pursue translational science in the lab.

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2013 AHRF Research Grant Reports - continued

Video Games as an Alternative to Traditional Auditory Training After Hearing Loss
Noah Ledbetter, PhD - Department of Biomedical Engineering, Washington University, St. Louis, MO

This has been an exciting project for both the professors and the graduate students involved due to the high level of professional interest in these games and their potential to influence hearing health. Because of the work made possible by the grant, we have had the opportunity to present these ideas at several public events. We have received enthusiastic feedback about the entertainment value of our games as well as their scientific and diagnostic applications.

We are currently cultivating relationships with business and clinical professionals about the potential expansion of the ideas funded by this grant. In conjunction with audiologists based at the Central Institute for the Deaf, we have begun collecting data from a group of hearing impaired subjects to demonstrate efficacy of game-based auditory training for future publication. Additionally, we are collecting data from normal hearing listeners in partnership with the Psychology department at Washington University in St. Louis.

We have presented this work at the Entertainment Software and Cognitive Neurotherapeutics Society 2013 annual meeting (Training the Brain with Auditory Games), and will be presenting at the Association for Research in Otolaryngology 2014 annual meeting (Auditory Games as a Novel Tool for Aural Rehabilitation).

Schedule of Events

SAVE THE DATE - Friday, April 25, 2014 - Tinnitus Symposium

The American Hearing Research Foundation is proud to present a half-day long learning opportunity for patients and healthcare providers interested in knowing more about tinnitus. Our primary goal with this event is to give attendees the opportunity to learn more about this condition directly from the experts and to be able to ask questions in an informative and interactive setting. The afternoon symposium will feature Carol A. Bauer, MD, from the Southern Illinois University School of Medicine, and will be held in the greater Chicago area. Dr. Bauer is certified as a diplomate in otolaryngology by the American Board of Otolaryngology. Please call the Foundation office at (630) 617-5079 for more information, or check our website for updates as they become available.

Association for Researchers in Otolaryngology (ARO) 37th Annual Mid-Winter Meeting February 22-26, 2014 Manchester Grand Hyatt Hotel in San Diego, CA
AHRF Chairman Richard Muench and Executive Director Kimberly LaBounty will be hosting a dinner for the 2014 AHRF research grant recipients on Sunday February 23rd at 6:30pm. Also, look for AHRF on Monday, February 24th from 12:30 pm - 1:30 pm during the "Get Your Research Funded" presentation.

Partner with Us!

Each of us has special people and loved ones who play important roles in our lives – a parent, sibling, spouse, grandparent, or teacher - a "special hero" who shaped us into who we are today. Honor or memorialize that special person by making a tax-deductible donation to AHRF in their honor or memory. You could also:

- Make an investment in the future by giving a tax-deductible donation in honor of your children and grandchildren.
- Tell your friends about the work we do.
- Share this newsletter with someone you care about.
- Help us reduce our mailing costs by providing us with your email address.

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A non-profit foundation dedicated to scientific research, and the preventive care and cure of deafness.

Winter 2014

AMERICAN HEARING RESEARCH FOUNDATION SOUNDINGS NEWSLETTER

Dear Friends of the American Hearing Research Foundation

We are pleased to announce that AHRF has joined the Healthy People 2020 Consortium, a diverse and dedicated group of organizations committed to achieving goals set through a national agenda that communicates a vision for improving health and preventing disease. This is accomplished through a framework, set in ten year increments, for public health prevention priorities and actions as developed thirty years ago by the U.S. Department of Health and Human Services' Office of Disease Prevention and Health Promotion (ODPHP).

For the past thirty years, the Healthy People program has been grounded in the principle that setting national objectives and monitoring progress can motivate action and, in just the last decade, preliminary analyses indicate that the country has either progressed toward or met 71 percent of its Healthy People targets. In the decade between 2010 and 2020, there are eleven new topic areas of focus that now include hearing and other sensory communication disorders. The goal is to reduce the prevalence and severity of disorders of hearing and balance; smell and taste; and voice, speech, and language.

Communication and other sensory processes contribute to our overall health and well-being. Protecting these processes is critical, particularly for people whose age, race, ethnicity, gender, occupation, genetic background, or health status places them at increased risk. The Healthy People 2020 objectives are designed to ensure that all Americans, from birth through old age, will benefit from scientific advances in prevention, diagnosis, and treatment of hearing and other sensory or communication disorders.

Because our mission is rooted in scientific research and preventive care, AHRF is particularly interested in emerging issues in hearing disorders. Researchers are identifying the genetic components of many disorders, which may lead to earlier and more accurate diagnoses. Research is also adding to our understanding of co-occurring conditions and the way the presence of one disorder may lead to diagnosis and treatment of another disorder. Hearing loss may be a largely unrecognized complication of diabetes, which suggests that people with diabetes should be screened for hearing loss. Through federal and private funding, researchers explore new ideas, make discoveries that lead to cures, and otherwise create solutions that can lead to treatment and prevention of a disorder affecting 40 million Americans. We are pleased to support this worthwhile endeavor along with all the Consortium members and the U.S. Department of Health and Human Services.

Sincerely,

Richard Muench, Chairman of the Board of Directors