



Soundings Newsletter

Donna Whitlon, PhD, to Chair the AHRF Research Committee

AHRF is pleased to announce that in May 2019, Donna Whitlon, PhD, assumed leadership of AHRF's Research Committee. The Committee counsels the AHRF board in the selection of research projects to fund each year. Whitlon was welcomed as a Director of the AHRF Board at this time as well.

Whitlon brings a depth of experience to the role of Committee Chair. Initially trained in biochemistry, she has over 35 years as an auditory scientist. In addition to reviewing National Institutes of Health (NIH) grants, she served as a reviewer for the AHRF Research Committee for about 11 years in the past. She notes, "I have always appreciated the idea of this Foundation, its enthusiasm and its focus on stimulating new ideas and helping to get them off the ground. So I am looking forward to joining you all again."

Whitlon also has been on the recipient side, receiving grant awards from AHRF in 2007 and 2009. "The AHRF grants made a huge difference in the work I was able to pursue. So I know what that boost can mean to others."

Since 1997, Whitlon has been faculty at Northwestern University, and is presently Research Professor of Otolaryngology – Head and Neck Surgery at Northwestern's Feinberg School of Medicine.

When asked about her research interests, Whitlon explains, "The anatomy of the cochlea, particularly the wiring of the local spiral ganglion neurons, captured my imagination

over 35 years ago. I spent the early part of my career studying the anatomy, protein expression, and development of the spiral ganglion nerve fibers. Now, in a clinical department, I am interested in a critical clinical question: How can we help to protect against or repair hearing loss?" She and her team developed an in vitro screening approach that allowed them to narrow down a library of chemical compounds to a few of the most promising. They are exploring these compounds in-depth, to determine their impact in animal models of noise induced hearing loss.



Whitlon's work has been funded by the National Institutes of Health, American Hearing Research Foundation, Knowles Leadership Fund, the Office of Naval Research and the Department of Otolaryngology, Northwestern University.

20 YEARS AT THE HELM



Alan G. Micco, MD, surgeon-educator and leading expert in otolaryngology and neurotology at Northwestern University, has guided AHRF grant evaluation for 20 years. Although stepping down from the role of Research Committee Chair, Micco will continue to share his expertise as President of the Board, and as a reviewing member of the Committee.

Colleague David Klodd, PhD, notes, "His superb organizational and communication skills have enabled the Research Committee to effectively deliberate in its annual meetings with noteworthy outcomes. On behalf of the Board, Committee, and grant recipients, we thank you for your service and dedication."

AHRF Offers Grants for 2020



In the coming year, the Foundation will offer these grants to further our understanding of hearing and balance problems related to the inner ear:

- **AHRF Regular Grants** - \$20,000 to \$50,000 - topics related to hearing and balance disorders of the inner ear
- **Causes of Sudden Hearing Loss Grant** - A one-year, one-time grant of up to \$40,000
- **Meniere's Disease Grant** - \$20,000 to \$25,000 - studies of Meniere's disease causes, diagnosis, or treatment
- **Bernard and Lottie Drazin Memorial Grants** for otolaryngology residents at specific universities - \$1,000 - topics related to hearing and balance disorders of the inner ear

Proposals will be reviewed in the coming months, and awardees will be contacted in late November.

The **Causes of Sudden Hearing Loss Grant** is supported by a donor who was affected by sudden sensorineural hearing loss (SSNHL), in two instances 38 years apart. AHRF is matching his contribution. Guidelines for evaluating and treating SSNHL recently were updated by the American Academy of Otolaryngology–Head and Neck Surgery Foundation. SSNHL can result in permanent hearing loss, tinnitus, and lower quality of life if not recognized and swiftly treated. An estimated five to 27 people per 100,000 have SSNHL. The annual incidence is 66,000 cases, according to the guideline.

AHRF Board Welcomes Michael Hoffer, MD

In May 2019, the American Hearing Research Foundation welcomed two new members to its Board of Directors: Donna Whitlon, PhD (see p.1), and Michael E. Hoffer, MD, FACS (right).

Dr. Hoffer will be a tremendous resource to both AHRF and its Research Committee. He has had 20-plus years in the Navy studying mild Traumatic Brain Injury (mTBI), tinnitus, hearing loss, and vestibular disorders on active duty service members. Today, Hoffer is a Professor of Otolaryngology and Neurological Surgery at the University of Miami. As a clinician-scientist, he performs both basic and clinical research along with his Otolaryngology/Neurotology practice. Hoffer focuses much of his research on traumatic damage to the inner ear and brain, including pioneering work on the treatment of noise-induced hearing loss and tinnitus, pharmaceutical countermeasures for mTBI, and optimized diagnosis and management of neurosensory disorders seen after mTBI. He has published extensively and received research grants from the Department of Defense, National Institutes of Health, and industry.



Report on Diplomat Symptoms in Cuba

Hoffer was lead author of the first report of acute symptoms and clinical findings in 25 diplomatic personnel living in the U.S. Embassy in Havana, Cuba. These individuals experienced severe neurosensory symptoms after exposure to a unique sound and pressure phenomenon. The study, "Acute Findings in an Acquired Neurosensory Dysfunction," was published in the August 2019 journal *Laryngoscope Investigative Otolaryngology*.



“This protein must be doing something very important, so much so that it can’t change over millions of years of evolution. I needed to find out what it was.”

RESEARCHER PROFILE

David C. Martinelli, PhD

Assistant Professor
University of Connecticut Health Center

DAVID MARTINELLI, PhD, uses colorful metaphors to explain his AHRF-funded study *“Determination of the auditory function of the outer hair cell afferent synapses in the mammalian cochlea.”* But what drew him to this area of research is two words: “luck and fate.”

A Family of Proteins

“I was a post-doc at Stanford University, studying C1Q-like (C1QL) proteins that make up a family of genes. I noticed how well these proteins are conserved when comparing mice and humans. By that I mean the percentage that these proteins are the same in both species, and have not changed despite the way each has evolved. Other proteins in this comparison might be 70% or even 90% conserved, but this protein is 99% conserved. It had to be doing something very important.”

At the time “I was far removed from studying the auditory system. My post-doctoral research [with the gene C1QL3] had everything to do with brain function.” But in 2013, a paper was published by the lab of David He; it reported a gene in the same family – C1Q1 – was expressed specifically in the cochlea.

“We know there are two types of hair cells in the cochlea – inner and outer. Each cell has small protrusions that look like hairs. When a soundwave bends these protrusions, the hair cell neurons (or “afferents”) send a signal to the brain via the auditory nerve. Up to 95% of our hearing comes through *inner* hair cell afferents. But the *outer* hair cells have afferents, too. I was surprised to learn that the function of the outer hair cell afferents is unknown.”

“This is where my AHRF-funded project comes in. One of the genes I’d been studying is significantly expressed in outer – but not inner – hair cells.” Martinelli believed he could create a “knockout mouse” – one that does not have the gene C1QL1. “If we can determine what’s wrong with the mouse, we may be able to discover the function of C1QLs.”

UConn Opportunity

At the University of Connecticut, researchers “had done groundbreaking work” exploring the auditory system. “I had knowledge of these proteins, and there was an opportunity for us to collaborate.”

To date, Martinelli has achieved what he proposed to do with his AHRF funding. He was able to breed the C1QL1 knockout mouse, and determine these mice hear normally. Next he wants to explore what the outer hair cells do. He proposes “that in the cochlea, the inner hair cells are responsible for hearing, and the outer hair cells are responsible for detecting auditory pain. The afferent neurons under the microscope look like pain sensors. This could have applications for treating hyperacusis – when a person finds normal sound levels painful.”

“AHRF funding is what got this project started. Anything I learn on the AHRF project will inform what I do next.”



RESEARCHER UPDATE
Jessy Alexander, PhD
Research Professor
The University of New York at Buffalo

“Just as the globe is getting smaller – reducing distances and bringing people from different places together, research is enabling scientists to join hands from different fields to get a better understanding of life and what it entails.”



**Complement, hearing loss and lupus:
A project update from Dr. Alexander**

Systemic lupus erythematosus (SLE) is an autoimmune disorder, affecting 1.5 million patients in the USA. Patients are usually young women: men at a ratio of 9:1. The most common otologic symptom found in SLE patients is sensorineural hearing loss (SNHL) and tinnitus. The decline in hearing in these young patients lowers their quality of life.

The current treatments for SLE are mainly immunosuppressants which have toxic side effects. Therefore, identification of new biomarkers and therapeutic targets is an urgent need. The AHRF funds helped me begin studies to understand the role of complement proteins in hearing loss in SLE patients using established lupus mouse models. Our focus was the complement protein factor H (FH), a critical protein that regulates the alternative complement pathway.

Our results show deposition of immune complexes in the spiral ganglion and damage of outer hair cells resulting in decreased sensitivity.

Our future studies will be directed toward understanding the role of infiltrating immune cells into the ear using the same mouse model that will be genetically engineered to be deficient in different complement proteins. The immune cells are driven towards the immune complex deposits by anaphylatoxins that are proteins generated during complement activation. It will be exciting to study whether manipulating the signaling between the anaphylatoxins and their receptors will help alleviate the hearing pathology in these patients.

How did you get into the biochemical research field?

I believe it is how one's brain is wired. I enjoyed music, admired paintings, read books and spent time cooking new dishes or sewing. I could appreciate architectural and engineering wonders.

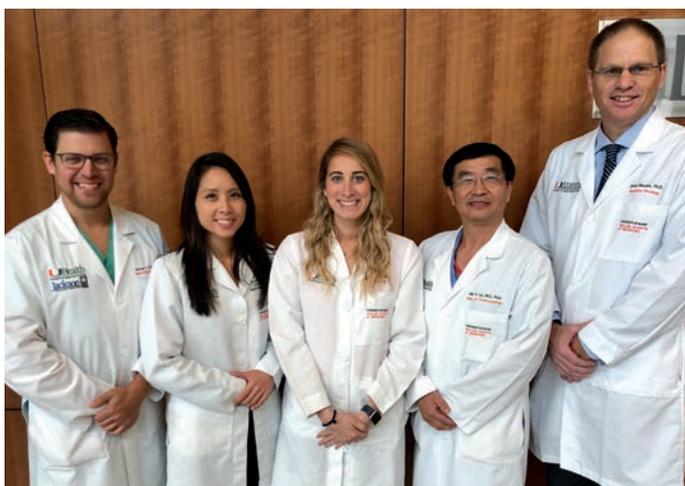
But nothing excited me more than watching an earthworm after the rain move by pulling each body segment forward while the body segment in front waited for the one behind to catch up. When I fell and hurt my knee... what was telling the body segments of the earthworm to move or the skin on my knee to grow back? How did an organism grow from a single cell to a complex, thinking and functioning adult? I always had the curiosity to understand how biological systems work which made my career choice very simple.

What aspects of this work are the most interesting?

I have not felt bored yet. The ups, the downs, the good days and the bad, the times with funding and the hard days without funding are all a part of the wholesome experience of biomedical research. It is an amazing time in science and I consider myself fortunate to be a part of it.

The AHRF Mission:

To fund significant research to better understand and overcome hearing and balance disorders of the inner ear, and to educate the public about these life-altering conditions. AHRF is a 501(c)(3) nonprofit organization.



Cohen (center), pictured with colleagues M. Ivan, C. Dihn, X. Liu, and B. Marples

THE BERNARD AND LOTTIE DRAZIN Memorial Research Grant is offered to third-year otolaryngology residents to support their work and encourage fledging research careers. Erin Cohen, MD, received this grant in 2019.

The Project

Cohen's study, *Radiation Toxicity and Biology in Merlin-Deficient and Normal Schwann Cells in Vitro*, addresses the clinical problem of hearing loss following radiosurgery of vestibular schwannoma (a benign tumor on the balance and hearing nerves of the inner ear). She is looking for a radiation dosing protocol that will maximize control of schwannoma and minimize radiation injury to adjacent normal Schwann cells.

Looking for radiation thresholds that preserve hearing

"One main treatment option for vestibular schwannoma is stereotactic radiation. Although tumor control rates with radiation are more than 85% at 10 years, hearing preservation rates are extremely low at 25%. It is known that radiation can cause cochlear hearing loss, however the effect of radiation on other components of the hearing pathway, e.g. Schwann cells, is unknown. I chose this topic to analyze the effect of radiation on normal Schwann cells and schwannoma cells and determine if there are radiation thresholds that optimize tumor control and hearing preservation."

Findings

"We did indeed identify differences in DNA damage and repair that may help explain why tumor cells are more susceptible to radiation than normal Schwann cells and identified radiation thresholds. We are preparing a manuscript for submission now."

RESIDENT GRANT RECIPIENT Erin Cohen, MD University of Miami/Jackson Memorial Hospital



Research is a part of training

"At our institution, we have dedicated research time during the third year of residency. Our program also encourages research longitudinally throughout residency. We have a lot of research opportunities both in the lab, as well as clinical, translational, and quality improvement studies. I enjoy research because it gives me the opportunity to identify targets for improvement and to become familiar with other research projects and papers through extensive literature review. I feel that research will ultimately make me a better clinician. It can be challenging to get all of the logistical portions of a project together; however, I have found that once the research has begun, challenges with a certain aspect of a project are merely learning take-home points for future research."

Cohen hopes to incorporate research into her clinical practice, which will likely be in the academic setting.



One Step Leads to the Next

"Good news, the data from the grant funded by AHRF is now going into an R01 [National Institutes for Health] grant proposal. So, again, thank you for the funding, it was much needed!"

Lina Reiss, PhD, Oregon Health & Science University
2016 AHRF grant recipient

YOU CAN HELP

“She said it was like a freight train was in her head at night.”

- Debbie Richmond, describing the severe Meniere’s disease symptoms her sister, Loretta Lynn Ammon, experienced

When you support AHRF, you’re helping to search for answers to hearing loss, tinnitus, vertigo, sensitivity to sound, and many other challenges related to problems of the inner ear. These have a ripple effect on careers, schooling, families, relationships, and simple pleasures of day-to-day life. Let’s work together to find solutions.

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Would you like to find hearing and balance answers for the next generation? When you remember AHRF through a gift in your will (a “bequest”), you can ensure cutting-edge research projects continue. You can choose to leave a specific amount, or a percentage of your estate. Or consider other forms of planned giving: securities, life insurance policy, or a retirement plan. A qualified financial planner can guide you with your decisions.

SUPPORT MENIERE’S DISEASE RESEARCH

When she learned there are few treatment options for her mother’s Meniere’s disease symptoms of tinnitus, vertigo, and hearing loss, Katie Mertz decided to raise funds for research. She began the initiative *run because*, a grassroots effort to raise the profile of Meniere’s. To date, Katie has completed 24 half-marathons, nearly half of her goal of 51 (one in every state plus DC), and raised \$37,000 for Meniere’s investigation. You can follow Katie’s progress at www.facebook.com/runbecause. Donations for Meniere’s research can be made via the AHRF website.



COMBINED FEDERAL CAMPAIGN

The American Hearing Research Foundation is a designated charity for the Combined Federal Campaign (CFC) – the largest workplace giving campaign in the world that raises more than \$265 million each year. AHRF is on the CFC National List, number 10571.



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General Funds sustain the core programs central to the Foundation's mission. Donations to the General Fund also can be restricted to use for research into certain areas such as Meniere's disease.

There are several levels from which to choose:

- Chairman's Circle \$5,000 and above
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Frances Meredith, PhD, University of Colorado Denver, presents AHRF-funded study results at ARO conference, February, 2019

