AMERICAN HEARING RESEARCH FOUNDATION
SOUNDINGS NEWSLETTER

New PBS Video Sheds Light on Meniere's Disease, Educating the Public on Little-understood, Often-debilitating Hearing and Balance Disorder

The American Hearing Research Foundation has partnered with the Public Broadcasting System (PBS) to sponsor a 5-minute video, "Spotlight on Hearing and Balance," to educate the public on Meniere's disease. This difficult-to-diagnose, debilitating condition causes episodes of hearing loss, vertigo and often leads to anxiety and/or depression when symptoms become acute. PBS is airing the video across its nationwide network, with a major airing push concentrated during the summer of 2018.

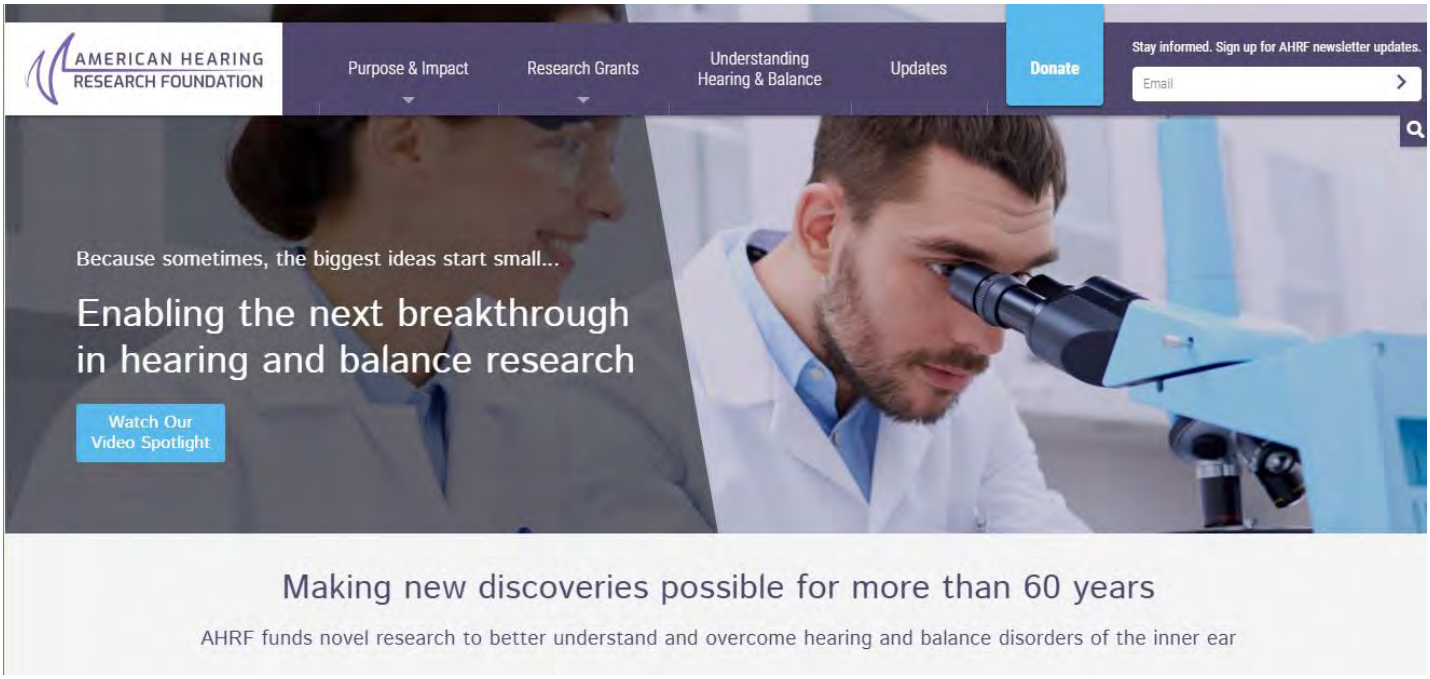
An estimated 615,000 people in the United States suffer from Meniere's disease, which becomes more common with age. Most people with Meniere's disease are over 40. Currently, there is no known cure, but evidence-based therapies and treatments can help people better manage their symptoms, which can include ringing and pressure in the ears, along with fluctuating hearing loss, extreme dizziness, and associated nausea, falls, anxiety and/or depression. (continued on p. 2)

2019: Grants up to $50K to be offered

"The applications we see have more innovation and potential than ever before. So we're renewing our commitment to support the ideas of these scientists." - AHRF Chairman Richard Muench

Starting in 2019, AHRF will increase the upper limit on its Regular Grants by $10,000. Now researchers can request $20,000 to $50,000 for novel studies related to the hearing or balance functions of the ear. Since 2010, AHRF has provided over $1.4 million in grant monies, and in 2018 grants were provided for 10 studies. In the past two years, four researchers have gotten articles published, one person's study has led to funding from the National Institutes for Health.

Coming soon: a new look!



The American Hearing Research Foundation is just weeks away from launching a new website (which you still will find at www.american-hearing.org). The launch includes a refreshed brand and logo, plus entirely new website content.

AHRF's Executive Director, Joan Wincentsen, notes, "AHRF funds leading edge science and innovation. Our website – our public face – needs to reflect this amazing work." She added, "We're excited to recommit to our mission. Our goal is to draw attention to the importance of advancing scientific knowledge of hearing and balance disorders of the inner ear.

New PBS Video (continued from p. 1)

"Until someone suffers themselves from Meniere's disease, or is close to a friend or loved one with the condition, it's difficult to imagine the impact that it can have on everyday life," says President of AHRF, Alan Micco, MD. "Most of us take our hearing and especially our balance for granted. But when a condition like Meniere's disease strikes, entire lives change. At AHRF, we're committed to investing in research to better understand Meniere's disease and other hearing and balance disorders of the inner ear so we can identify treatments that will make a difference."

"Spotlight on Hearing and Balance" illuminates the connection between hearing and balance and features people who live with Meniere's disease. Nashville country singer, JesseLee Jones, and Wisconsin-based physical therapist, Kim Mayer, share their stories, bringing the reality of living with Meniere's disease into focus for PBS viewers.

To view this eye-opening video online, visit the AHRF YouTube channel at https://www.youtube.com/watch?v=S0JDvIJH0Oc.

You and AHRF Support... *Collaboration!*

Anna Lysakowski, PhD
University of Illinois Chicago
Antonio Lopez-Escamez, MD, PhD,
University of Granada, Spain
AHRF grant recipients (Meniere's disease research), 2018

It started at a castle in Denmark.

Anna Lysakowski met Anthony Lopez-Escámez at Hindsgavl Castle during the 2012 Grete Lundbeck European Brain Research Foundation Brain Prize meeting.

Dr. Lysakowski: "I gave a talk on the striated organelle in vestibular hair cells at the Brain Prize meeting and mentioned that I was trying to figure out its protein composition. Antonio's colleagues Teresa and Carmen (Teresa Requena and Carmen Martin-Sierra, two PhD candidates with Antonio's lab in Granada, Spain) approached me afterwards, saying 'We think we have an idea of what you're looking for.' Later, over dinner, Antonio and I discussed a potential collaboration to locate the candidate genes of familial Meniere disease.

"Turns out the protein suggested by Teresa and Carmen wasn't a Meniere's disease protein, but instead it led us to investigate other avenues, using mice models.

"Since then I've continued to collaborate with Antonio's team in Granada trying to find the cell types involved in the vestibular organs. As a practicing clinician and geneticist, he has collected DNA samples from over 1,700 Meniere's disease patients, and has found evidence of several types of patients with Meniere's disease."

Dr. Lopez-Escámez: "Anna has made significant contributions in the field of anatomy and cell biology of the vestibular system by using immunohistochemistry and electron microscopy. Since our first conversation, we've been working to identify gene sequences associated with Meniere's disease. Our partnership gave Teresa an opportunity to work in Anna's lab in 2014."

Dr. Lysakowski: [At that time] "we conducted mouse experiments to localize two candidate gene proteins for familial Meniere's Disease, DTNA and FAM136A, and found the protein in inner ear hair ll mitochondria. Teresa (now Dr. Requena) published a paper in Human Molecular Genetics partially based on her work in our lab in Chicago. This year she's back in our lab, doing much of the molecular and genetic studies for the project supported by AHRF and the Spanish government. "

Dr. Lysakowski's and Dr. Lopez-Escámez's teams currently are researching cellular and animal models of familial Meniere's disease for different genes, so that specific treatments can be tested.

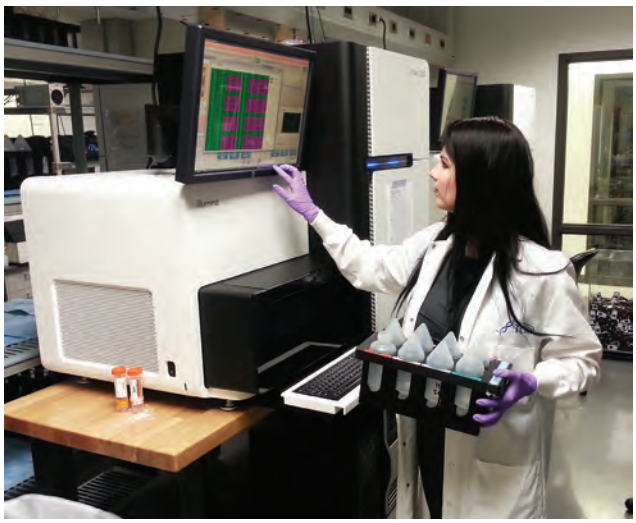
Research Update: Genetics and ear malformations

Isabelle Schrauwen, PhD
Baylor College of Medicine
(seated 3rd from left in team photo)

Dr. Schrauwen's study, *"Identification of genes for non-syndromic rare congenital inner ear malformations in children,"* was funded in part by a 2018 AHRF grant.

Dr. Schrauwen and her team are studying the molecular basis of rare ear malformations in children. She reports:

Congenital inner ear malformations affecting both the osseous and membranous labyrinth can have a devastating impact on hearing and language development. Using exome sequencing in eight children and their parents (the children have severe inner ear malformations), we have identified two previously unreported de novo loss-of-function mutations in GREB1L (a protein coding gene) [c.4368G>T;p.(Glu1410fs) and c.982C>T;p.(Arg328*)] in two children with absent cochleae and 8th cranial nerve malformations.



The cochlear aplasia in these children suggests that a developmental problem at a very early stage during inner ear development exists, such as during the otic pit formation. We went on to investigate expression of this gene in developing tissues. Overall craniofacial Greb1l RNA expression peaks in mice during this time-frame (E8.5). It also peaks in the developing inner ear during E13-E16, after which it decreases during adulthood. We also have been able to show that homozygote greb1lsa16374 knockout zebrafish exhibit a loss of or abnormal sensory epithelia innervation.

In conclusion, we provide evidence that GREB1L is a key player in early inner ear and 8th cranial nerve development. Abnormalities in cochleovestibular anatomy can provide challenges for cochlear implantation. Combining a molecular diagnosis with imaging techniques might aid the development of individually tailored therapeutic interventions in the future.

Study results published in Human Genetics: Schrauwen, I., Kari, E., Mattox, J. et al. Hum Genet (2018) 137: 459. https://doi.org/10.1007/s00439-018-1898-8.

Research Update: Audition and balance

Timothy E. Hullar, MD
Oregon Health and Science University
(2nd from left in team photo)

Dr. Hullar's study, "Audition and balance," was funded in part by a 2017 AHRF grant.

Dr. Hullar explains: We have long known that visual, vestibular (inner-ear balance), and proprioceptive sensory cues are combined by the brain to help us maintain balance when standing and walking. Our work here involved demonstrating that auditory cues are also important for this vital task.

We looked for this effect in hearing aid users while walking, and in cochlear implant users when standing and walking. For the walking experiments, we had adult subjects walk across a room toward a sound source while wearing sensors that measured their speed, stride length, and gait symmetry both with their devices on and off. We found that some individuals clearly had better walking performance with their hearing devices on.

For the standing experiment, we used similar sensors to look at how much our cochlear implant patients swayed with and without their speech processors. We found that wearing cochlear implants improved balance enough to reduce the chance of falling.

These studies showed fundamental impact of audition on balance, and that hearing assistive devices can improve balance.

This work supported by AHRF has already gained national and international attention for its novelty and importance. Our article by Weaver et al. in *Otology and Neurotology* inspired a complimentary letter to the editor from a Dutch research group. Our invited response allowed us an additional opportunity to show otolaryngologists the importance of auditory contributions to balance. This additional exposure will help disseminate our findings and improve the patient care provided by professionals in the field.

We will continue with a series of experiments examining the basic mechanisms by which sound assists balance. We also have begun a collaboration with Oculus VR, a leading virtual reality company, to develop an auditory-based device for improving balance. Both of these research directions have grown directly from our AHRF support.

Publications:

Weaver, T.S., Shayman, C.S., and Hullar, T.E. The Effect of Hearing Aids and Cochlear Implants on Balance During Gait. *Otology and Neurotology* 2017;38(9):1327-1332.

Shayman, C.S., Mancini, M., Weaver, T.S., King, L., and Hullar, T.E. The Contribution of Cochlear Implants to Postural Stability. *Laryngoscope* https://doi.org/10.1002/lary.26994.

Research Update: Improving hearing when two cochlear implants are used

Justin Aronoff, PhD
University of Illinois at Urbana-Champaign
(pictured)

David Landsberger, PhD
New York University Langone Medical Center

The study conducted by Drs. Aronoff and Landsberger, *"The Importance of Coordination of Binaural Cochlear Implant Processors,"* was funded by a 2016 AHRF grant.

Dr. Aronoff explains: Having two ears provides a number of benefits in difficult listening environments, including helping people locate from where a sound originates and understand what someone is saying to them in a noisy environment.

These benefits primarily arise from two effects. First, the head partially blocks sound such that a sound that comes from the left will be louder at the left ear than the right ear. This phenomenon is referred to as an interaural level difference (interaural means between the ears). Second, sound travels across space at a fixed speed such that a sound coming from the left will reach the left ear before it reaches the right ear. This phenomenon is referred to as an interaural time difference.

Having a cochlear implant for each ear can provide many of the benefits of having two ears. However, cochlear implant users generally are not able to benefit from interaural time differences. There are a number of potential reasons for this. One potential reason is that the timing of the signals in the two ears is distorted because each cochlear implant processor works independently with slightly different timing. In principal, this could be addressed by physically linking the cochlear implant processors together to coordinate the timing, but this would require substantial changes to the hardware. This study investigated another option: using the sound that each cochlear implant processor receives to coordinate the timing for the two processors. The results from the study suggest that this approach can be as effective as physically linking the two cochlear implant processors together. In other words, we have successfully demonstrated a method that would make interaural timing differences more perceptible for cochlear implant users without changing the hardware design. This could result in improved performance in difficult or noisy listening environments for cochlear implant users.

The results from this study have been presented at the Conference on Implantable Auditory Prostheses, the American Auditory Society Scientific and Technology Meeting, and the Association for Research in Otolaryngology midwinter meeting. We are also currently preparing a manuscript based on this study.

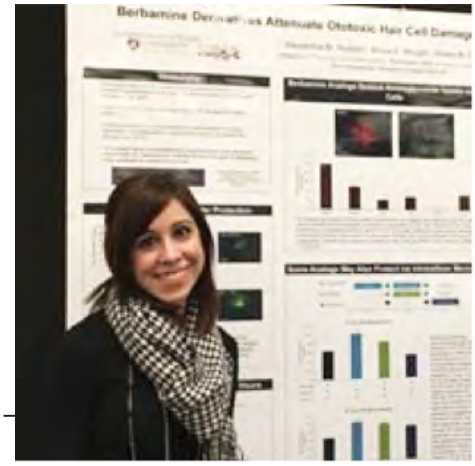
You and AHRF Support... *Inspiration!*

Erika Skoe, PhD
University of Connecticut
AHRF grant recipient, 2016 and 2018

Dr. Skoe commented, "I was in an interview a while back, and they asked me, 'Where will you be five research grants from now?' I don't want to know. There is so much being done that could inspire me to go in a new direction. I don't want to be locked in to a specific topic.

"For instance, today I heard a speaker talk about his work that connects circadian rhythms and hearing. Think about it: your ears don't have a lid, so even in sleep they're taking in information from environmental sounds. [My team's] data collection process could be used to track hearing with those circadian rhythms and environmental noise. So I'm going to think more about this." (*ARO 2018 Conference, San Diego*)

You and AHRF Support... *Aha Moments!*



Alexandria Hudson, PhD candidate
Washington State University Vancouver
Supporting the work of Allison Coffin, PhD

Ms. Hudson studied berbamine analogs as potential drugs to prevent certain forms of antibiotic-induced hearing loss.

AHRF: Did you have a moment when you said, "Hey, look at this!"?

Ms. Hudson: I did! It was when I saw the results for one compound that not only gave protection to hearing cells before and during the use of antibodies, but *after* as well. This might have applications for a broader audience, not just those who need ongoing protection like those with cystic fibrosis. (*ARO 2018 Conference, San Diego*)

Research Update: High-throughput drug discovery for prevention of noise-induced hair cell loss

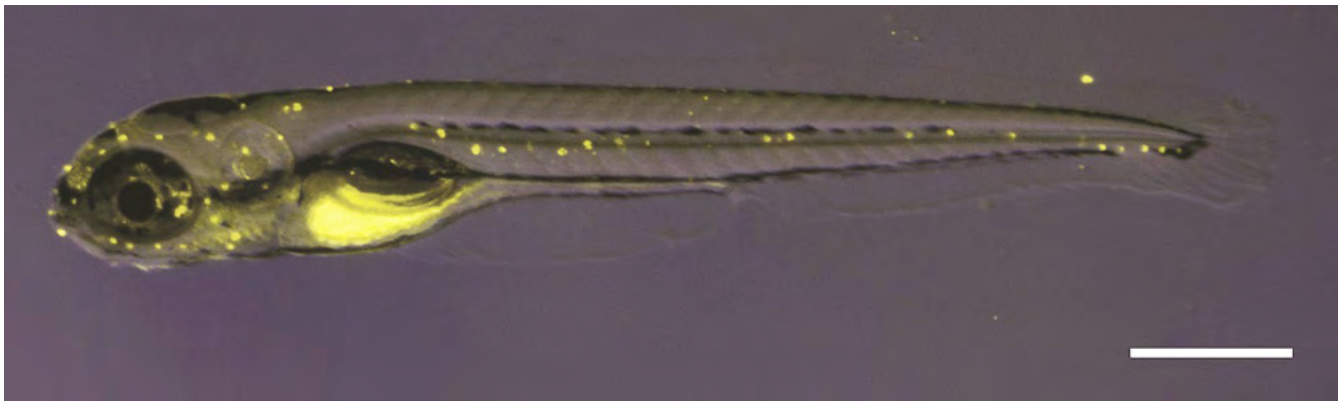
Allison Coffin, PhD
Washington State University Vancouver
(Pictured in her off hours!)

Dr. Coffin's study was funded by a 2017 AHRF grant.

She explains: We aimed to 1) determine the extent to which MM-201, a small molecule therapeutic, protects hair cells from acoustic trauma, and 2) interrogate a library of FDA-approved drugs to identify drugs that may be repurposed as hearing protectants.

We have data showing that MM-201 protects hearing cells from noise damage, suggesting that it may be an effective therapeutic. We also have shown that some antioxidants also protect hearing cells. We will follow up with these findings in the next year, and continue to work towards a therapy to prevent noise-induced hearing loss. MM-201 is of particular interest, as it will be used this year for clinical trials in Alzheimer's patients, meaning that MM-201 is further along in the process to FDA-approval and use as a drug.

Dr. Coffin notes that her team collaborated with Dr. Jie Xu, University of Illinois at Chicago, on this project.



Coffin lab results: Zebrafish responds with luminescence during test of protective compound.

Who Supports AHRF? *James Erbach*

"I lost hearing in my left ear in 8th grade, and had reduced hearing in my right hear. I was in the Signal Corps. In the service it didn't help being near cannons going off for artillery practice. I've been going to an audiologist, Larry Hable, for 45 years, and I've done well with hearing aids. My friend has hearing aids through the V.A. and struggles with them. You don't learn to use these things overnight."

Partner with Us!

General Fund. You can support the vital work of hearing and balance innovations by donating online at www.American-Hearing.org. Or mail your contribution in the enclosed postage-paid envelope. If you wish, you can designate your gift to honor someone dear to you.

Support Meniere's Disease Research. Over three years ago, the Foundation joined forces with Katie Mertz, founder of *"run because."* As her mother dealt with the debilitating effects of Meniere's disease, Katie embarked on a grassroots effort to raise awareness and research funding for this illness by aiming to run 51 half-marathons – one in each state plus DC – by age 50. She completed race #19 in Arkansas this past November, and has raised over $27,000 to date. You can follow Katie's efforts – and support her cause at www.facebook.com/runbecause.

Helping Future Generations. Will you work with us to find hearing and balance solutions for generations to come? When you remember AHRF through a gift in your will, known as a bequest, you can ensure these cutting-edge research projects continue. You can choose to leave a specified sum of money or a percentage of your estate. Other forms of planned giving include securities, life insurance policies, or retirement plans. A qualified financial planner can guide your decision and help you consider tax consequences.

PLANNED GIVING

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.

CFC® Combined Federal Campaign

AHRF Leadership

Contact Us

Joan Wincentsen
Executive Director

Phone: (630) 617-5079
Fax: (630) 563-9181
E-mail: Info@American-Hearing.org
www.American-Hearing.org

American Hearing Research Foundation

A nonprofit foundation dedicated to funding significant research in hearing and balance disorders, and helping to educate the public about these disorders.

"Ultimately, what AHRF gives us is a shot at applying novel science to interventions that help kids learn, the aging stay connected, and adults of all ages function more effectively-and more happily-in their everyday lives."

-Nina Kraus, PhD
AHRF Research Committee Member

Thank You to Our Donors

This list reflects donations received from December 15, 2017 through July 31, 2018.

Chairman's Circle

Stephen Goode

Research Supporter

Mark Callicotte
Bernard Chan
Sallyann Cowles
James Erbach
Janet Fullmer
Bev Herrmann
Robert B. Howland
Bruce and Lena Kennedy
David Klodd, PhD
Barry and Susan Kneisel
Paul Lurie
Nancy Masterson
Kim and Richard Mayer
Richard G. Muench
John W. Muldoon
John and Erin Robertson
Catherine Schagh
Carol Schneider
Marilyn Snyder
David Wuertz

Research Champion

David L. Holman
Alan G. Micco
John Carey
Kathryn E. Wise

Friends of the Foundation

Laura Bautista
Dan Fenton
Gail Grantschnig
Anthony Haugen
Agnes Hite
Dave Hostetler
Michael Kaufman
James F. Jackson
Cheryl Lee
Judy Love
Mark Mayer
Robert Moise
Eugene Ring
Frank Serdar

Thomas Snook

In Memory / Honor

In Memory of Bernice Benson
Kasie Bennett
Sonya and Ronnie Keith

In Memory of Dr. Eugene Derlacki
Roger F. Vaughn

In Memory of Wiley Harrison
C. Richard Kriebel

In Memory of Daniel J. Knight
William L. Lederer

In Memory / Honor

In Memory of Natalie McGlathery
Doug Ballew
Darlene Caldwell
Katherine Hagler
George and Lana Thompson
Brenda Villanueva

In Memory of Ann Moody
George Bolles
Roger Bolles
Linda Davidson
Karen Ishitani
Beverly Peters

In Honor of Brien Dix
Julia Dix

In Honor of Jessie and Dean Duffy's 50th Wedding Anniversary
Sherry Gibbon

In Honor of Louis and Tamara Freedman
Robert Freedman

In Honor or Dave German
Tom German

In Honor of Milton Kats
David Michael Keeter

In Honor of Trish and Rick Kapustka
Eileen Welch

In Honor of Huey Lewis, of Huey Lewis and the News
Nutty Brown Enterprises, LP

Giving to the General Fund

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
- Research Champion $1,000 to $4,999
- Research Supporter $100 to $999
- Friends of the Foundation $99 or under

The Foundation also appreciates the support of the following organizations:

amazonsmile You shop. Amazon gives.
America's Charities
CardinalHealth FOUNDATION
COMMUNITY HEALTH CHARITIES Give. Connect. Help.
CUNY The City University of New York
SECC Indiana State Employee's Community Campaign (SECC)
Network for Good
tix4cause
United Way of Central New York
United Way of the National Capital Area
WELLS FARGO

AMERICAN HEARING RESEARCH FOUNDATION

Non-Profit Org.
U.S.Postage
Paid
Chicago, Illinois
Permit No. 1693

275 N. York Street
Suite 401
Elmhurst, IL 60126

Address Service Requested