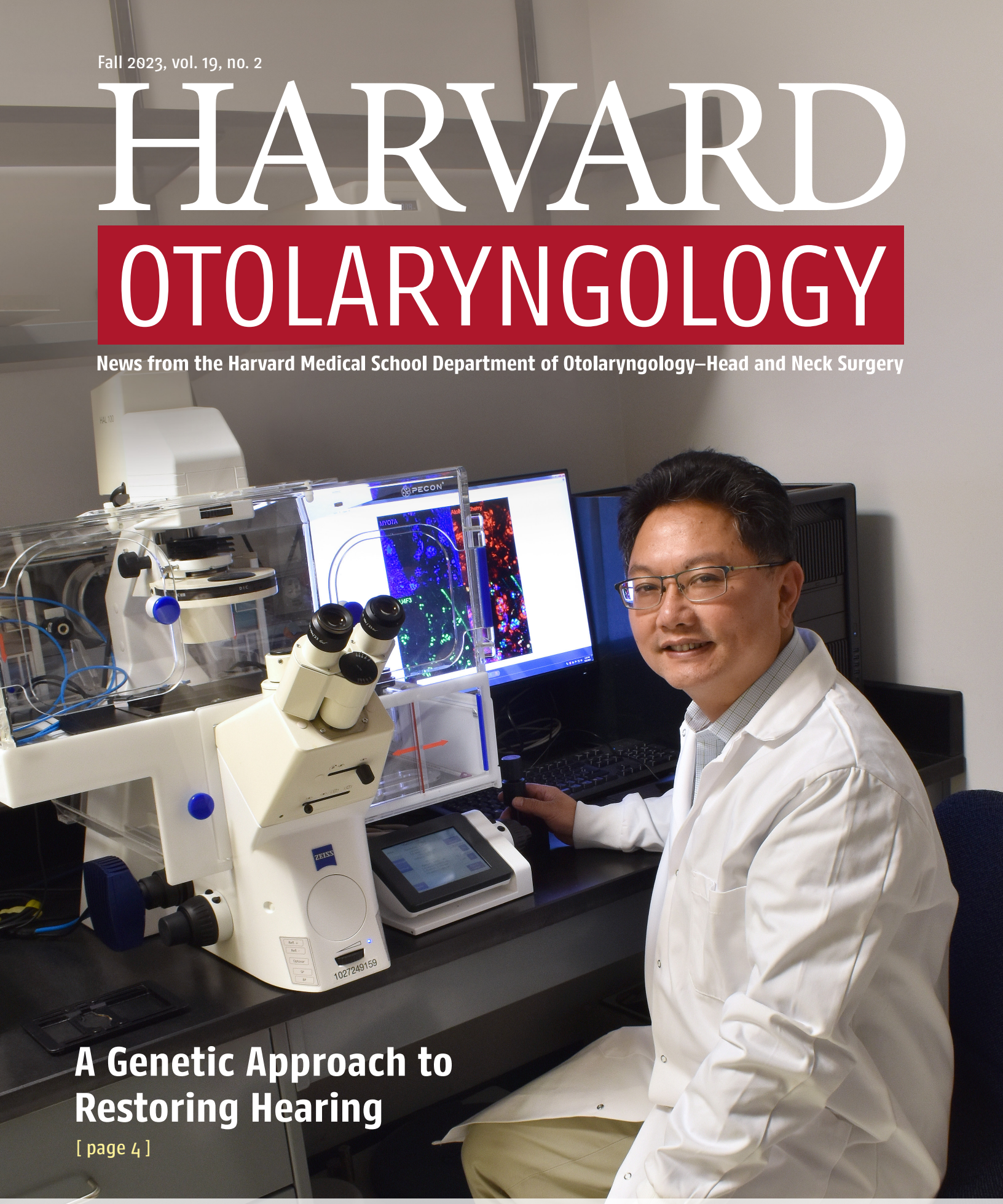
Fall 2023, vol. 19, no. 2

HARVARD OTOLARYNGOLOGY

News from the Harvard Medical School Department of Otolaryngology–Head and Neck Surgery



A Genetic Approach to Restoring Hearing

[page 4]

HARVARD MEDICAL SCHOOL | Department of Otolaryngology Head and Neck Surgery

HARVARD OTOLARYNGOLOGY

News from the Harvard Medical School Department of Otolaryngology–Head and Neck Surgery

Fall 2023 | Vol. 19, No. 2
Published twice per year.

Please send comments, requests for additional copies and other inquiries regarding this issue to:

Department of Otolaryngology–Head and Neck Surgery
Mass Eye and Ear
243 Charles Street, Boston, MA 02114

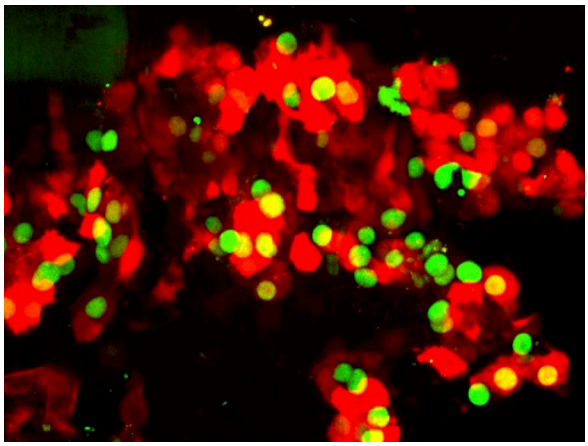
Nicole Feldman, Communications Manager
nfeldman1@meei.harvard.edu

HARVARD MEDICAL SCHOOL | Department of Otolaryngology Head and Neck Surgery

Beth Israel Deaconess Medical Center
Boston Children's Hospital
Brigham and Women's Hospital
Mass Eye and Ear
Massachusetts General Hospital

CONTENTS

FEATURE



The Regenerated HC-like cells (Green) were detected in the cultured mouse cochleae after chemical/Ad.*Atoh1* (Red) reprogramming.

Dear colleagues and friends,

Since joining the Department of Otolaryngology—Head and Neck Surgery at Harvard Medical School in 1988, I have marveled at its evolution over the decades. Most recently, I have been blown away by the way this community celebrates and supports one another. However, the unconditional support you have all shown me these past eight months as I have worked through my health concerns has been truly remarkable. My new perspective as a patient has given me an even greater appreciation for what our clinicians, researchers, nurses, physician assistants, nurse practitioners and other members of the team do so passionately for patients each day. I deeply understand the immense gratitude patients feel toward their healthcare providers when they navigate them through a serious illness. I also now have a firsthand appreciation for the incredible contributions of cutting-edge biomedical research that brings novel lifesaving treatments from the lab to the bedside. I continually stand in awe of the incredible work and accomplishments of the Harvard Otolaryngology Faculty and the immeasurable impact you have on the lives of your patients.

In the latest edition of *Harvard Otolaryngology*, our feature story highlights a research team led by Zheng-Yi Chen, DPhil, who developed a drug-like cocktail of different molecules capable of successfully regenerating hair cells in a mouse model. With this groundbreaking discovery, we are one step closer to creating a novel approach for hearing restoration, an achievement that just a few years ago was deemed unimaginable. Furthermore, we announce Daniel Polley, PhD, being named Director of Eaton-Peabody Laboratories, and we share the establishment of two new Chairs in the Mass Eye and Ear Department of Otolaryngology—Head and Neck Surgery endowed by Eugene Myers, MD, FACS, and Herbert Silverstein, MD, FACS. Finally, we celebrate our graduating residents and fellows who have participated in programs at Beth Israel Deaconess Medical Center, Brigham and Women's Hospital, Boston Children's Hospital, Massachusetts General Hospital and Mass Eye and Ear, while simultaneously welcoming our next classes of trainees.

As we move into the New Year, I look forward to re-engaging with so many of you and the important work you do on a daily basis. We have so much to look forward to in 2024.

As always, thank you for your ongoing support of our department's research initiatives, clinical activities, educational pursuits and service to the community.

Sincerely,

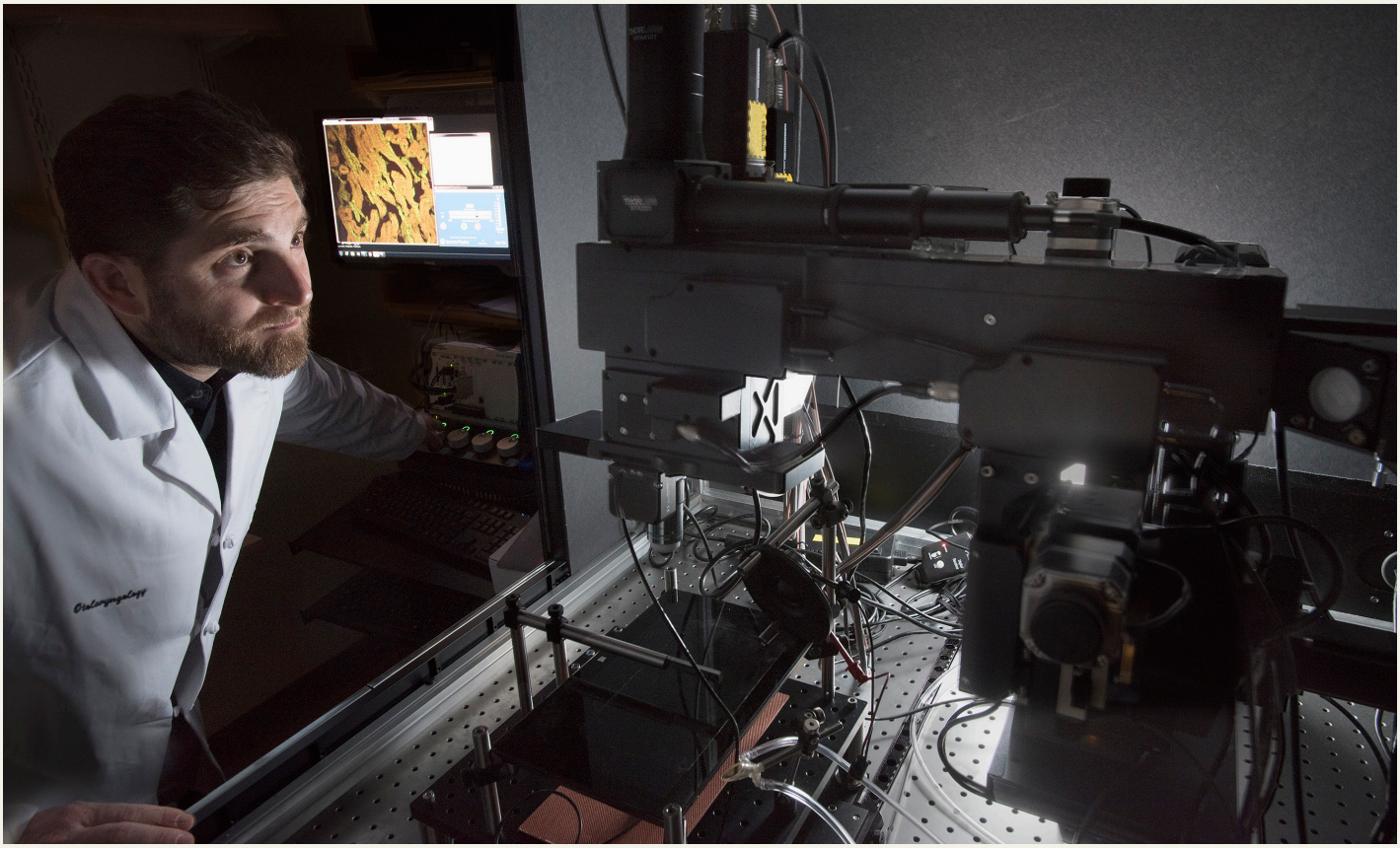
Mark A. Varvares, MD, FACS

The John W. Merriam and William W. Montgomery Professor and Chair Department of Otolaryngology–Head and Neck Surgery, Harvard Medical School

Chief, Departments of Otolaryngology–Head and Neck Surgery, Massachusetts Eye and Ear
Massachusetts General Hospital

Dr. Daniel Polley Named Director of Eaton-Peabody Laboratories, Otolaryngology Vice Chair of Basic Science Research at Mass Eye and Ear

Daniel B. Polley, PhD, the Amelia Peabody Chair in Otolaryngology–Head and Neck Surgery (OHNS) at Mass Eye and Ear, has been named Director of the Eaton-Peabody Laboratories (EPL), the world's largest and most productive private research enterprise focused on hearing and deafness, as well as Vice Chair for Basic Research for the hospital's Department of OHNS.



As the EPL director, Dr. Polley will oversee a multi-disciplinary group of more than 20 investigators dedicated to the study of hearing and deafness, with a primary focus on acoustics and biomechanics, inner ear biology and central auditory processing. He had served as interim director of the EPL since 2022, when M. Charles Liberman, PhD, the Harold F. Schuknecht Professor of OHNS at Harvard Medical School, stepped down from the position.

Dr. Polley arrived at Mass Eye and Ear and Harvard Medical School in 2011 after beginning his faculty career at Vanderbilt University. He has served as Director of the Lauer Tinnitus Research Center since 2017 and was promoted to Professor of OHNS in 2021. His research has primarily focused on the neurobiology of sound perception and the development of new biomarkers and treatment avenues for tinnitus, hyperacusis and other types of "hidden" hearing disorders. He has pursued questions to these topics using cutting-edge neuro-technology in mouse genetic models and has pioneered new approaches for hearing assessments and hearing rehabilitation in human subjects.

"I am humbled and honored to lead the EPL and serve the broader basic science endeavor in our department as Vice Chair," said Dr. Polley. "With first-in-human clinical trials for cochlear gene therapy just around the corner and an aging society that abuses its ears with higher and higher levels of environmental noise, the importance for maintaining EPL's primacy as the hearing research institution the world can turn to for guidance, insight and inspiration has never been greater."

Dr. Polley begins his tenure at a pivotal moment in the history of the lab. Last year, the EPL began major renovations to its central facilities, including additional lab space for expanded research capabilities and reconfigured space for cross-discipline research collaborations. The renovations were funded in large part by a generous gift from the Amelia Peabody Charitable Fund, champions of the EPL since it was founded in 1958 through a partnership between Miss Amelia Peabody, a philanthropist and former Mass Eye and Ear Board Member, and the late Nelson Kiang, PhD, the EPL's Founding Director.

According to Mark A. Varvares, MD, FACS, Chief of the Departments of OHNS at Mass Eye and Ear and Massachusetts General Hospital, Dr. Polley's strategic vision has been integral in the complex planning of the 10,000 square feet of renovations that will ensure the hospital continues to foster an optimal space for groundbreaking hearing advances.

"Dr. Polley's cutting-edge research on experience-dependent brain plasticity and its therapeutic applications for hearing loss, hyperacusis and tinnitus—not to mention his outstanding leadership—made him the clear choice to direct the EPL," said Dr. Varvares. "I am confident that Dr. Polley will help propel the EPL to even greater heights at such a pivotal moment in the lab's history." ■

M. Charles Liberman, PhD, left, and Daniel B. Polley, PhD, right.

"Dr. Polley is a world-class researcher, who elegantly combines optogenetic, neurophysiological and behavioral approaches in animal models and human subjects to study mechanisms and develop treatments for key aspects of sensorineural hearing loss. He has the international respect and scientific vision needed for the Director position, and I couldn't be more pleased with the outcome of the search."

– M. Charles Liberman, PhD

Top left of image on computer are regenerated hair cells labeled with one marker (Blue); top right of image, cells that are infected by Ad-Atoh1 (Red); bottom left, regenerated hair cells labeled with another marker (Green); bottom right image is the merged image on screen.

A Genetic Approach to Restoring Hearing

Researchers at Mass Eye and Ear learn how to regenerate lost hair cells–a feat once thought to be unattainable.

Hearing loss affects more than 45 million people in the United States alone, including about half of all adults over age 70. As the population ages, it is becoming a growing concern. That is especially true because hearing loss has been linked to increased feelings of isolation in older people and also can worsen dementia.

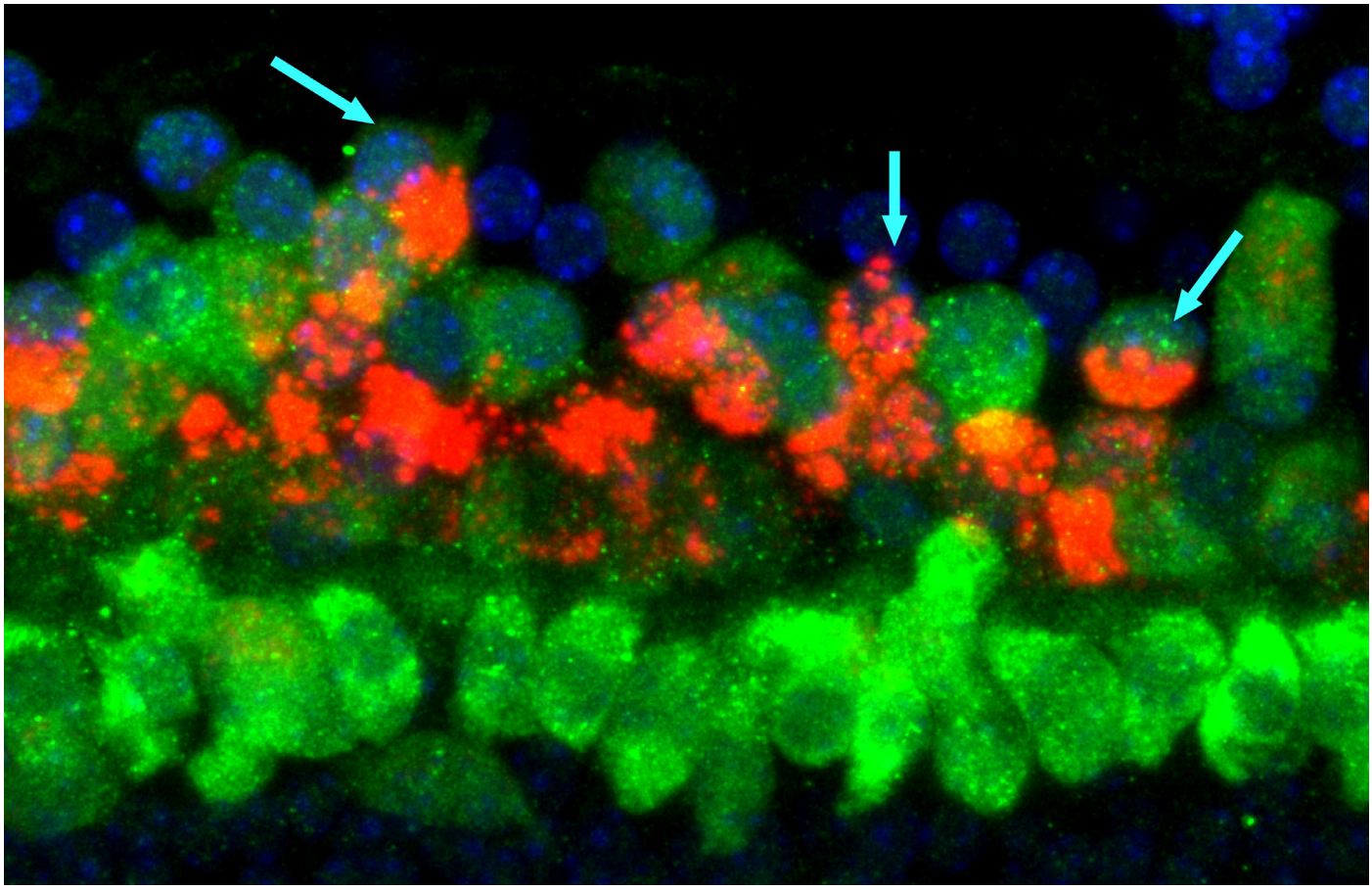
Most cases of hearing loss are caused by damage to hair cells—the tiny sensory organs in the inner ear that convert sound waves into electric signals and to send to the brain. This damage may be age-related or due to exposure to loud noise. Researchers in the Department of Otolaryngology–Head and Neck Surgery at Harvard Medical School, led by geneticist Zheng-Yi Chen, DPhil, are focused on finding ways to regenerate those hair cells. They hope this tactic will eventually lead to pharmaceutical approaches for treating hearing loss.

"Everyone knows someone affected by hearing loss, whether it's themselves or someone close them," says Dr. Chen, an Associate Professor of Otolaryngology at Harvard Medical School and an Associate Scientist in the Eaton-Peabody Laboratories at Mass Eye and Ear. "When you think about how many people are affected by this extremely common condition, it's mind-boggling that there are no drugs approved to treat it."

Dr. Chen first became interested in studying hearing loss as a graduate student, as part of a team that identified one of the first genes responsible for deafness. Since then, he has been involved in cataloguing every gene expressed in the inner ear that contributes to hearing and hearing loss. Some of this work could eventually lead to gene therapies that target deafness caused by mutations in single genes.

However, much of his current research has the potential to be considerably more wide-reaching. His lab is focused on understanding mechanisms that could be harnessed to induce the regeneration and

[continued p. 6]



Hair cell regeneration *in vivo*. Hair cells are regenerated after drug-like cocktail treatment and Ad.ATOH1 infection in adult mouse cochlea *in vivo*. **Green:** hair cells labeled with a marker ESPN. **Red:** Ad.ATOH1 infected cells. **Regenerated Hair cells:** Infected supporting cells that became hair cells (arrows to show examples).

proliferation of inner ear hair cells, thereby restoring hearing. "If we could find ways to treat deafness caused by damaged hair cells, which has much broader implications than treating these rare cases caused by single gene mutations, that would be incredibly rewarding," he says.

Driving the Regeneration of Hair Cells

It has long been known that the hair cells in the inner ear lack the ability to regenerate: Once they're gone, they're gone. But it turns out that holds true only for mammals. In lower vertebrates, including fish and birds, hair cells can be restored—eventually restoring the ability of these animals to hear as well.

Early clues about which genes are key to the regrowth of hair cells came from research Dr. Chen conducted in chickens and zebrafish. This work revealed the role of two molecular signaling pathways vital for this restoration: Notch1 and Myc. The next step was to take these findings in to mammals.

> "Ultimately, if we do show that hearing is restored, it will demonstrate proof of concept all the way from the initial identification of this essential pathway through to hearing rescue. Once we are able to do that, we hope to partner with the pharmaceutical industry to begin developing effective drugs that can be tested in clinical trials."
> – Zheng-Yi Chen, DPhil

A study published in 2019 in *Nature Communications* showed for the first time that when the Notch1 and Myc pathways were activated in adult transgenic mice, cells in the inner ear could divide and be induced to have the characteristics of hair cells. The researchers then confirmed that these newly formed hair cells were able to connect to the auditory neurons, implying that they may be able to send the sound signals to the brain.

But these findings were achieved in transgenic mice and were not directly translatable to humans, in part because there are no known compounds that directly activate Myc. Using RNA sequencing technology, the researchers determined the downstream pathways that are activated by turning on Notch1 and Myc. They found that two other pathways, Wnt and cAMP, played a key role. Fortunately, these were pathways that could be chemically activated. They also found that by small interfering (si) RNAs, they could activate Myc.

In a more recent study, published in April 2023 in the *Proceedings of the National Academy of Sciences (PNAS)*, the team reported another big advance: They had formulated a cocktail of drug compounds and small interfering (si) RNAs that had the ability to activate the pathways, Notch, Myc, Wnt and cAMP, and induce the generation of new hair cells in the ears of adult wildtype mice. They tested this new approach in mice that had been treated with the antibiotic gentamicin, which is known to cause hearing loss in patients when given at high doses by destroying the hair cells in the inner ear.

The cocktail works to reprogram the mature cells in the inner ear and revert them to a more stem-like state, the latter of which is a requirement for the precursor cells to be able to generate new hair cells. "The idea is to rejuvenate the adult cochlear cells into a younger state," says Yi-Zhou Quan, PhD, a member of Dr. Chen's lab and a co-author on the paper. The reprogammed mature inner ear cells, like young inner ear cells, can respond to hair cell induction signals such as adenovirus delivered Atoh1.

It worked. When the adenovirus vector and the cocktail were administered to adult wild type mice directly into the inner cochlea, new hair cells grew. Tests confirmed that signal transduction channels were able to uptake a fluorescence dye to indicate that the new hair cell transduction channels were active.

Next Steps to Restoring Hearing Loss

The next challenge is to demonstrate that regrowing the hair cells actually restores hearing. Although the recent work confirmed that the cochlea was able to grow new hair cells and that these cells were capable of sending signals to the auditory nerves, the administration of the cocktail into the ear required cochleostomy surgery, which left the cochlea nonfunctional.

Current studies are looking at ways to administer the cocktail without damaging the cochlea and its connections to the brain. In addition, the adenovirus used to deliver Atoh1 is toxic to the ear, so another delivery method will be needed.

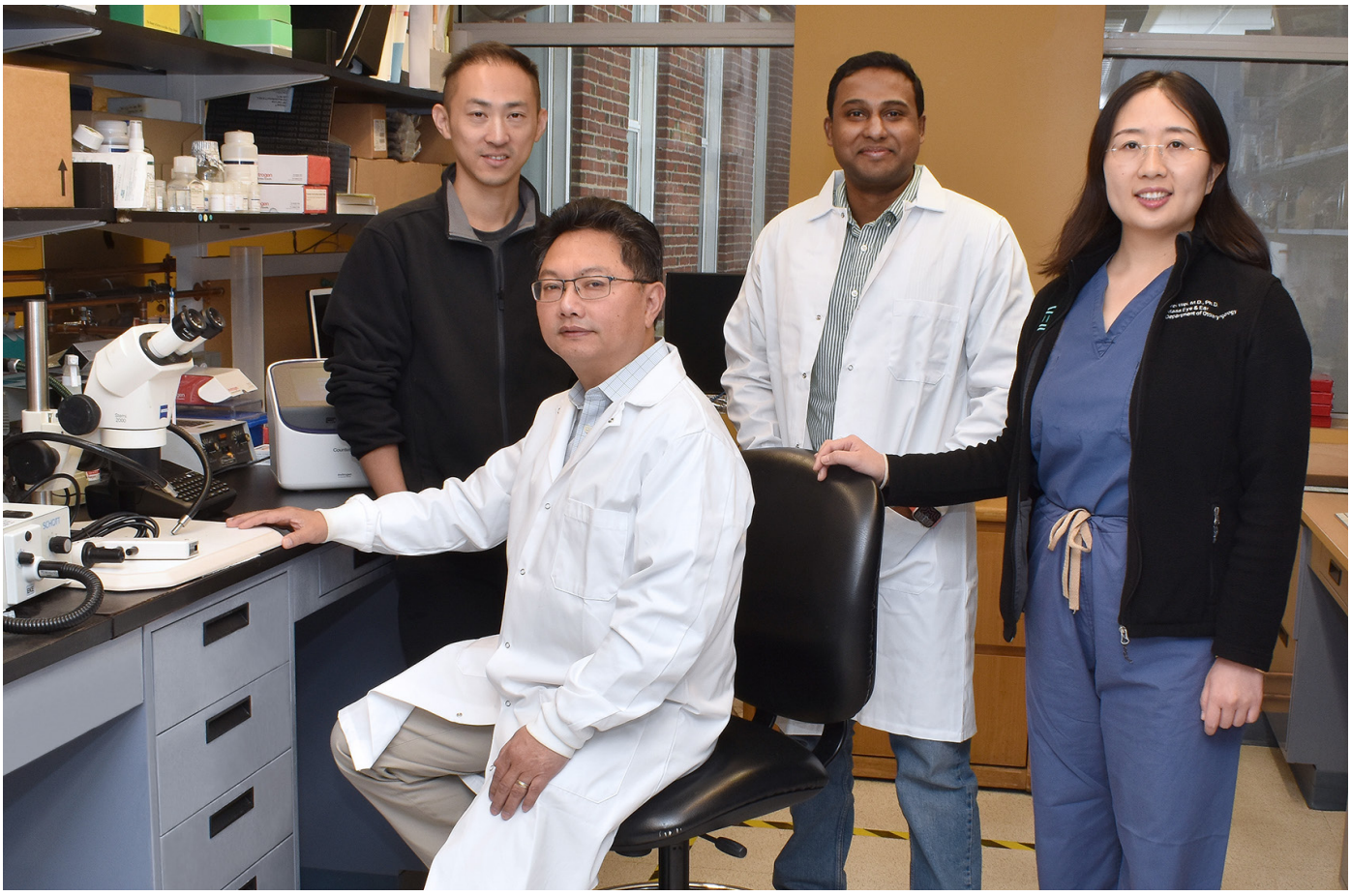
"Ultimately, if we do show that hearing is restored, it will demonstrate proof of concept all the way from the initial identification of this essential pathway through to hearing rescue," Dr. Chen says. "Once we are able to do that, we hope to partner with the pharmaceutical industry to begin developing effective drugs that can be tested in clinical trials."

He hopes to eventually test these drugs in patient populations with many different types of hearing loss. "We will need to develop a system to stratify patients and move them into the most appropriate clinical trials," he says. "We are beginning to step up efforts to be able to do this."

An offshoot of this research has also garnered a lot of interest from other labs studying the workings of the inner ear. In the course of this work, members of Dr. Chen's team found a way to develop explant cochlear systems in culture. This could prove to be a valuable tool for *in vitro* screening of potential drugs in the future.

What drives Dr. Chen and his colleagues is the desire to improve the lives of people with deafness and hearing loss.

"Currently the only treatments available for people with hearing loss are hearing aids and cochlear implants," says physician-scientist Wei Wei, MD, PhD, another member of Dr. Chen's lab and co-author on the PNAS paper. "Although these devices make it easier for people to live their lives, they have a lot of limitations. People don't hear music and sound in the same way, and often still have a hard time hearing properly, especially in noisy backgrounds. There is a real need to find a better way to restore hearing." ■



From left to right: Zheng-Yi Chen, DPhil; Yi-Zhou Quan, PhD; Arun Prabhu Rameshbabu, PhD, and Wei Wei, MD, PhD.

Drs. Eugene Myers and Herbert Silverstein Establish New Chairs at Mass Eye and Ear

In May 2023, two new Chairs in the Department of Otolaryngology–Head and Neck Surgery at Mass Eye and Ear were established by Eugene Myers, MD, FACS, and Herbert Silverstein, MD, FACS, both of whom are world-renowned surgeons and former trainees of the Harvard Otolaryngology Residency Program.

Drs. Myers and Silverstein shared news of their Chairs at the Combined Otolaryngology Spring Meetings (COSM) in Boston, coinciding with the launch of Mass Eye and Ear's Bicentennial Celebration. Together, their pledges represent a 60-year friendship with one another and with the hospital that played a vital role in the foundation of their extraordinary careers.

After graduating from Temple University Medical School as classmates, Drs. Myers and Silverstein overlapped at Mass Eye and Ear during their subsequent residency training. Dr. Myers, who served as Chair of the Department of Otolaryngology–Head and Neck Surgery at the University of Pittsburgh School of Medicine for more than 30 years, has authored hundreds of publications and served in innumerable leadership positions within the specialty since his residency training. Dr. Silverstein, the President and Founder of the internationally acclaimed Silverstein Institute and the Ear Research Foundation in Sarasota, FL, has authored hundreds of publications and trained more than 50 fellows in otology and neurotology.

As enduring tributes to Drs. Myers and Silverstein, chairholders will be Harvard Medical School faculty at Mass Eye and Ear who embody the same level of commitment and excellence as each Chair's namesake. Daniel G. Deschler, MD, FACS, will be the inaugural Dr. Eugene N. and Barbara L. Myers Chair in Head and Neck Surgery at Mass Eye and Ear, and an incumbent to the Herbert Silverstein Chair in Otology/Neurotology will be announced in the future.

Eugene Myers, MD, FACS, FACE, left and Herbert Silverstein, MD, right, at the COSM reception held in the Harvard Faculty Club, May 2023.

Meet the Inaugural Myers Chair

Dr. Deschler, the Vice Chair of Academic Affairs at Mass Eye and Ear and a Professor of Otolaryngology–Head and Neck Surgery at Harvard Medical School, has dedicated more than two decades of his career to improving cancer care and reconstructive surgical techniques. He has served as Chairman of the Head and Neck Surgery Committee of the American Academy of Otolaryngology–Head and Neck Surgery and former President of the Society of University Otolaryngologist–Head and Neck Surgeons, leaving an indelible mark on the entirety of the field.

"Congratulations to Dr. Deschler, who I am confident will carry forth Dr. Myers' legacy with unparalleled grace and vigor," said Mark A. Varvares, MD, FACS, Chief of Otolaryngology–Head and Neck Surgery at Mass Eye and Ear and Massachusetts General Hospital. "I would also like to sincerely thank Dr. Myers and Dr. Silverstein for their incredible generosity. Their support will not only touch the lives of our faculty, but it will also touch the lives of countless patients, colleagues and trainees who depend on the work of our faculty for a brighter future of otolaryngological care, research and education." ■

Mass General Brigham
Mass Eye and Ear

Mass Eye and Ear's 200th Anniversary:

A Celebration of the Harvard Department of Otolaryngology–Head and Neck Surgery



Join us on Friday, July 19, 2024

Honorary cochairs **Drs. Charles Cummings, Eugene Myers** and **Herbert Silverstein** invite you to join us in Boston for a once-in-a-lifetime celebration of Mass Eye and Ear.

Event highlights include:

- A full day of talks from distinguished alumni
- Presentation of the Mass Eye and Ear Lifetime Achievement Award to Joseph B. Nadol, Jr., MD
- Tour of Mass Eye and Ear
- Black Tie Gala Dinner at the Four Seasons Hotel Boston
- A golf outing at the Belmont Country Club on July 18, 2024

With thanks to our distinguished speakers:

Alessa Colaianni '20
Charles W. Cummings '68
Jeffrey P. Harris '79
KJ Lee '70
M. Charles Liberman '71
Ralph Metson '87
Eugene N. Myers '65
Laxmeesh M. Nayak '03
Jo Shapiro '86
Herbert Silverstein '66
Konstantina M. Stankovic '08
Theodoros N. Teknos '96
Ernest A. Weymuller, Jr. '73
Richard J. Wong '99

To register, scan the QR code or visit **www.masseyeandear.org/events/ohns-200.** Special hotel rates available for alumni visiting Boston. Contact Dana Grider at **dgrider@meei.harvard.edu** with questions.

FAREWELL CLASS OF 2023

Harvard Medical School Celebrates Residents and Fellows Graduating From Combined Otolaryngology Training Program.

Faculty and staff from the Department of Otolaryngology–Head and Neck Surgery (OHNS) at Harvard Medical School (HMS) celebrated the 2023 graduating class of residents and fellows from the Harvard Combined Residency Program in OHNS on Friday, June 16. Graduating residents and fellows were honored inside the Meltzer Auditorium at Mass Eye and Ear, where they were also joined by current and former trainees and immediate family.

Five chief residents graduated from the program, which is led by HMS Otolaryngology Residency Director Stacey T. Gray, MD, Associate Residency Director Kevin S. Emerick, MD, Associate Residency Director Alice Z. Maxfield, MD, and Chair of OHNS Mark A. Varvares, MD, FACS. Seven fellows graduated from the program at Mass Eye and Ear; three clinical fellows from Boston Children's Hospital celebrated their graduation on a separate occasion.

The ceremony began with a surprise visit from Dr. Varvares, who made his first public appearance in several months amid personal health concerns. The auditorium erupted in applause as he welcomed trainees, faculty and families to what he called the pinnacle of the academic year. He expressed his sincere gratitude to the graduating trainees for the amazing work they displayed during their time in the program.

"Thank you for the late nights, the early mornings, the amazing care of our patients, the conversations during cases and the friendships we've developed," said Dr. Varvares. "As faculty, it is so important that we have the opportunity to become mentors, and it is our trainees who give us that opportunity. We couldn't be prouder of the surgeons you are today and can't wait to see the surgeons you will become tomorrow."

Shortly after, Dr. Emerick introduced Jennifer C. Kim, MD, Clinical Professor of Otolaryngology–Head and Neck Surgery Michigan Medicine at the University of Michigan, as the Joseph B. Nadol, Jr., MD, Graduation Lectureship speaker. Dr. Kim and Dr. Emerick met years ago as trainees in the Harvard Combined Residency Program, where they became close friends.

In her speech, Dr. Kim reflected on the personal journey many residents and fellows face after their graduation. Reminiscing on the mentors she met during her own time in the Harvard residency program, she urged each resident to never stop seeking out colleagues who share the same ideals, who collaborate and encourage open and honest dialogue and who value diversity and originality. She also asked each trainee to find time to disconnect and to experience growth and success outside of medicine. The hobbies and relationships they nurture outside of work, she said, will provide the energy needed to avoid burnout in their professional lives.

"Always remember what a gift it is to be a physician," she said. "There are few jobs where you get to interact with so many people with various backgrounds and get to know them on such an intimate level. Your healing touch and words will not only impact your patients but their families and the communities from which they come."

> "Always remember what a gift it is to be a physician. Your healing touch and words will not only impact your patients but their families and the communities from which they come."
>
> –Jennifer C. Kim, MD

Awards and Honors

Jeffrey P. Harris, MD, PhD, Research Award
Presented to the graduating chief resident with the most outstanding FOCUS research project.

Alan D. Workman, MD, MTR
Cystatin and Polyp Disease: From a Proteomic Approach to a Murine Model of CRSwNP

Alan D. Workman, MD, MTR, right, was presented the Jeffrey P. Harris, MD, PhD, Research Award by David Jung, MD, left.

Clinical Fellow Teaching Award:
Charles D. Meyer, MD

Chief Resident Teaching Award:
Lauren E. Miller, MD, MBA

William W. Montgomery, MD, Faculty Teaching Award:
Rosh K. Sethi, MD, MPH

Harvard Otolaryngology Resident Life Award:
Adina Gutium, MD

[1] From left to right: Graduating Mass Eye and Ear residents Lauren E. Miller, MD, MBA; Vinay K. Rathi, MD, MBA; Tara E. Mokhtari, MD; Alan D. Workman, MD, MTR; and Ciersten A. Burks, MD. **[2]** Graduating Mass Eye and Ear fellows, seated, Dara R. Adams, MD; Christina M. Yver, MD, MBA; Thad W. Vickery, MD; standing, Charles D. Meyer, MD; Douglas J. Chieffe, MD; and Yew Song Cheng, BM, BCh. Not pictured: Natalia Kyriazidis, MD.

Graduating Residents, Mass Eye and Ear

Ciersten A. Burks, MD
Future Plans: Facial Plastic and Reconstructive Surgery Fellowship, University of Minnesota

Lauren E. Miller, MD, MBA
Future Plans: Head and Neck Oncologic Surgery Fellowship, The Ohio State University

Tara E. Mokhtari, MD
Future Plans: Head and Neck Surgical Oncology and Microvascular Reconstruction Fellowship, Washington University

Vinay K. Rathi, MD, MBA
Future Plans: Rhinology and Endoscopic Sinus/Skull Base Surgery Fellowship, Medical University of South Carolina

Alan D. Workman, MD, MTR
Future Plans: Rhinology and Skull Base Surgery Fellowship, University of Pennsylvania

Graduating Fellows, Mass Eye and Ear

Dara R. Adams, MD
Rhinology
Future Plans: Practicing Otolaryngologist, Chicago, IL

Yew Song Cheng, BM, BCh
Neurotology
Future Plans: Assistant Professor in Neurotology/Otology, University of California, San Francisco

Douglas J. Chieffe, MD
Pediatric Otolaryngology
Future Plans: Pediatric Otolaryngologist, Mary Bridge Children's Hospital

Natalia Kyriazidis, MD
Thyroid and Parathyroid Surgery
Future Plans: Faculty, Mass Eye and Ear, Quincy

Charles D. Meyer, MD
Head and Neck Oncology/ Microvascular Surgery
Future Plans: Head and Neck Surgical Oncology and Microvascular Reconstruction, Portsmouth Naval Hospital, US Navy

Thad W. Vickery, MD
Rhinology
Future Plans: Department of Head and Neck Surgery, Kaiser Permanente South San Francisco Medical Center

Christina M. Yver, MD, MBA
Facial Plastic and Reconstructive Surgery
Future Plans: Division Faculty, University of Pittsburgh Facial Plastic Surgery

Graduating Fellows, Pediatric Otolaryngology, Boston Children's Hospital

Gabrielle French, MD
Future Plans: Faculty, Alberta Children's Hospital, Calgary, Alberta

Ken Kennedy, MD
Future Plans: Faculty, Children's Healthcare of Atlanta/Emory University, Atlanta, GA

Farrukh Virani, MD
Future Plans: Faculty, Texas Children's Hospital/Baylor College of Medicine, Houston, TX

From left to right: Graduating fellows from Boston Children's Hospital Gabrielle French, MD; Ken Kennedy, MD; and Farrukh Virani, MD.

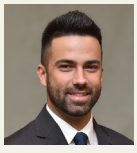
NEW TRAINEES

Meet our PGY-1 Residents

Harvard Combined Residency Program in Otolaryngology–Head and Neck Surgery

Alyssa Suining Chen, MD, grew up in Novi, MI, and studied biomedical engineering at Yale University. She earned her medical degree at the University of Michigan Medical School, where she was inducted into the Alpha Omega Alpha Honor Medical Society and awarded the Charles and Phyllis Lowe Merit Scholarship. At the University of Michigan, she worked on a clinical trial for a new cartilage conduction hearing device and designed a 3D-printed patient education simulator for a novel nasopharyngeal airway device. She also co-led the design of an automatic supplemental oxygen titration device, which is currently the basis of a new start-up company. Dr. Chen's research interests include surgical innovation, medical device development and outcomes-based research.

Originally from Ashland, OR, **Elisabeth "Elise" Hansen, MD,** graduated *cum laude* from Pomona College with degrees in chemistry and French. She received a Fulbright Scholarship to study at Pierre and Marie Curie University in Paris, France, where she graduated summa cum laude with a Master's degree in microbiology. After conducting research at the Pasteur Institute in France and the University of Wuerzburg in Germany, Dr. Hansen matriculated at Harvard Medical School. She graduated *cum laude* and undertook several research projects on equitable delivery of high-volume surgical care and timely access to care for head and neck cancer patients. Her current interests include mentorship, health equity and disparities, health services and global healthcare delivery.



Zachary Kons, MD, grew up in Benicia, CA, and graduated from the University of California, Davis, with a degree in neurobiology, physiology and behavior. He then worked at the University of California, Davis West Coast Metabolomics Center for two years studying small molecule metabolites before matriculating at the Virginia Commonwealth University (VCU) School of Medicine. During medical school, he completed a research fellowship under mentor Mark Richardson, MD, PhD, at the Brain Modulation Lab of Massachusetts General Hospital. His fellowship focused on mapping the human olfactory neural pathway—a collaborative effort between the VCU School of Medicine and Massachusetts General Hospital. Dr. Kons' research interests include clinical outcomes, hearing and olfaction.

Kushi Ranganath, MD, of Potomac, MD, graduated *summa cum laude* from Johns Hopkins University, where she studied neuroscience and public health and completed a Woodrow Wilson Undergraduate Research Fellowship. She subsequently earned her medical degree from Harvard Medical School. At Harvard, Dr. Ranganath researched diagnostic biomarkers of head and neck cancer at the Mike Toth Head and Neck Cancer Research Center and the epidemiology of HPV-relayed oropharyngeal cancer at the Dana-Farber Cancer Institute. She also researched patient-reported outcomes after reconstructive surgery at the Beth Israel Deaconess Medical Center and Mass Eye and Ear. Dr. Ranganath's interests include precision medicine, patient-centered outcomes and surgical innovation. Her work has been featured in national, peer-reviewed journals such as Cancers, Head & Neck and Oral Oncology, among others.

Originally from Ithaca, NY, **Katherine Tashman, MD,** studied theoretical math at Binghamton University. There, she was inducted into the Phi Beta Kappa Honor Society, earned the State University of New York (SUNY) Chancellor's Award for Student Excellence and graduated *summa cum laude.* Prior to medical school, Dr. Tashman performed statistical genetics research at the Broad Institute of the Massachusetts Institute of Technology and Harvard University. She matriculated at Harvard Medical School, where she conducted health equity research among various patient populations within otolaryngology and studied the effects of functional endoscopic sinus surgery on long-term quality of life in patients with chronic rhinosinusitis. Dr. Tashman's interests include harnessing imaging data to improve clinical outcomes within the field.

New Clinical Fellows

Mass Eye and Ear

[1] Noel Ayoub, MD
Rhinology

[2] Abel David, MD
Neurotology

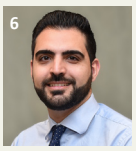
[3] Omar Karadaghy, MD
Head and Neck

[4] Kevin Quinn, MD
Facial Plastics

[5] Marika Russell, MD
Thyroid and Parathyroid

[6] Firas Sbeih, MD
Rhinology

[7] Keith Volner, DO
Pediatric Otolaryngology



Boston Children's Hospital

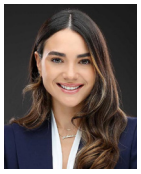
[8] Ghedak Ansari, MD
[9] Thomas Flowers, MD
[10] Zachary Kelly, MD
[11] Sepideh Mohajeri, MD

OHNS Residency Program at Beth Israel Deaconess Medical Center/ Harvard Medical School Hosts End-of-Year Celebration

On Friday, June 16, the Otolaryngology–Head and Neck Surgery (OHNS) Residency Program at Beth Israel Deaconess Medical Center/Harvard Medical School honored its graduating fellows and celebrated its newest class of trainees during its end-of-year celebration. The celebration was led by **Scharukh M. Jalisi, MD, FACS,** Chief of OHNS and OHNS Residency Director at the Beth Israel Deaconess Medical Center; **David S. Caradonna, MD, DMD,** Associate OHNS Residency Director at the Beth Israel Deaconess Medical Center; and James G. Naples, MD, Associate OHNS Residency Director at the Beth Israel Deaconess Medical Center.

Two graduating fellows were honored at the event: **Anton Warshavsky, MD,** the program's Head and Neck Surgical Oncology and Microvascular Reconstruction Fellow, and **Mohamed Aboueisha, MD,** the program's OHNS Fellow. Dr. Warshavsky is a senior physician in the Head and Neck Unit of the Otolaryngology Department at Tel Aviv Sourasky Medical Center in Tel Aviv, Israel. Dr. Aboueisha is pursuing an otolaryngology fellowship at the University of Washington.

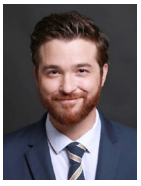
Please join us in welcoming the newest class of trainees to the OHNS Residency Program at Beth Israel Deaconess Medical Center/Harvard Medical School



Residents

Originally from Sarasota, FL, **Gabriella Ojeda-Badillo, MD,** graduated from Boston College with a degree in biology. There, she was actively involved in medical education, working as a teaching assistant for pre-medical education courses and mentoring STEM students. Dr. Ojeda-Badillo spent a year working as a medical assistant in Boston and subsequently matriculated at Tufts University School of Medicine. There, she conducted clinical research in plastic and reconstructive surgery under the mentorship of Alan Lim, MD, and research in pediatric otolaryngology under the guidance of Andrew Scott, MD. She is bilingual in English and Spanish and is interested in improving patient equity and inclusion.

Lauren Schlegel, MD, of Fleetwood, PA, graduated *summa cum laude* from Lehigh University, where she studied biochemistry and completed dual majors in health, medicine and society and religious studies. At Lehigh, she conducted research in the laboratory of Vassie Ware, PhD, studying post-translation modifications of ribosomal protein L22. She was accepted into the International Honors Program and subsequently matriculated at the Sidney Kimmel Medical College at Thomas Jefferson University, where she served as Assistant Director for the Jefferson Vulnerable Community Mobile Vaccine Program amid the COVID-19 pandemic. She also served as the school's Health Design Lab research fellow, developing an expertise in 3D printing techniques.



Fellow

Laurent Ganry, MD
Head and Neck Surgical Oncology and Microvascular Reconstruction Fellow

Ben and Ellen Harvey

Compassionate care lasting a lifetime.

In 2013, Ellen Harvey noticed an ache in her neck that felt similar to a twisted muscle. When the pain did not subside, she received a CT scan from her local doctor. The results did in fact show a twisted muscle, but also a 7x11 cm growth in the middle of her neck.

Reassuringly, the biopsy results were negative, but Ellen still needed surgery to remove the growth. Due to the significant risks associated with the operation, her local surgeon referred her to the "absolute best," Gregory W. Randolph, MD, FACS, Director of the Thyroid and Parathyroid Endocrine Surgical Division at Mass Eye and Ear.

Dr. Randolph determined that the growth, which was narrowing her airway, had been growing for over ten years, and they were lucky to have stumbled upon it.

Gregory W. Randolph, MD, FACS, FACE

"I had complete trust in Dr. Randolph before the surgery," said Ellen. "He was transparent, positive and caring. He was there beside me when I woke up, asking me to speak to him. We both were filled with joy when my voice sounded just as good as it did pre-surgery."

Just five weeks after her surgery, Ellen delivered the speech of her lifetime when she was inducted into the Environmental Industry Association's Hall of Fame, one of only three women ever to receive this prestigious honor. Much to her relief, she spoke effortlessly.

When the Harveys sold their family company in 2021, a philanthropic opportunity presented itself and they chose Dr. Randolph to be the first major recipient of their generosity.

> **"We are profoundly grateful for the unmatched skill and compassion of Dr. Randolph. Our hope is that this gift will make an important impact on the lives of a great many others who face thyroid surgery."**
>
> – Ellen Harvey

"The Harveys' gift was exceptionally touching as it shows how compassionate care will stay with a patient for years after their visit to Mass Eye and Ear," Dr. Randolph said. "I will be using their gift for thyroid surgical research and global teaching. This gift will not only help us lead the fight against thyroid diseases, but gives us the opportunity to teach future leaders of medicine how to care for their patients to make a lifelong impact." ■

The Alumni Giving Society of the Department of Otolaryngology–Head and Neck Surgery at Harvard Medical School

The Department of Otolaryngology–Head and Neck Surgery at Mass Eye and Ear/Harvard Medical School established the Alumni Giving Society in 2015 to recognize faculty and alumni who make gifts of $1,000 or more during the fiscal year (October 1–September 30). Participation is a way to stay connected and to help deliver the finest teaching experience for today's otolaryngology trainees.

Our alumni know from firsthand experience that support of the vital work of our students and faculty in the Department of Otolaryngology–Head and Neck Surgery helps drive continued achievement across all areas of education, research and patient care. In the 2023 fiscal year, we had 45 members who we thanked for their generosity and partnership. Their collective support helped us achieve our department goals and institutional mission.

If you are not a member, please consider joining your colleagues today by making a gift with the enclosed envelope. As a member, you may designate your gift in the way that is most meaningful to you.

To learn more, please contact Julie Dutcher in the Development Office at **617-573-3350**.

HARVARD MEDICAL SCHOOL | Department of Otolaryngology Head and Neck Surgery

Current Alumni Giving Society members for fiscal year 2023, from October 1, 2022, to September 30, 2023, are listed below. With your gift of $1,000 or more, you will be included in the 2024 Alumni Giving Society.

CHAMPION

Gifts of $25,000 and more

Eugene N. Myers, MD, FACS
Herbert Silverstein, MD, FACS

VISIONARY

Gifts of $10,000 to $24,999

Michael S. Cohen, MD
Michael B. Rho, MD, FACS
Josef Shargorodsky, MD
Mark A. Varvares, MD, FACS

INNOVATOR

Gifts of $5,000 to $9,999

Derrick T. Lin, MD, FACS
Phoebe H. Yager, MD

PIONEER

Gifts of $2,500 to $4,999

Samir M. Bhatt, MD
Neil Bhattacharyya, MD
Daniel G. Deschler, MD, FACS
Richard E. Gliklich, MD
Stacey T. Gray, MD
Eric H. Holbrook, MD
Kasey K. Li, MD, DDS
Leila A. Mankarious, MD
Joseph B. Nadol, Jr., MD
H. Gregory Ota, MD
Sunil Puria, PhD
Jeremy D. Richmon, MD
Mark F. Rounds, MD
Phillip C. Song, MD
Jonathan Y. Ting, MD

FRIEND

Gifts of $1,000 to $2,499

Megan E. Abbott, MD
Carlos Ayala, MD
Barry J. Benjamin, MD
Ruth Anne Eatock, PhD
Kevin S. Emerick, MD
Ramon A. Franco, Jr., MD
Richard R. Gacek, MD
Robert A. Gryboski, MD
Paul E. Hammerschlag, MD, FACS
Wade W. Han, MD
Earl Harley, Jr., MD
Jeffrey P. Harris, MD, PhD
Donald G. Keamy, Jr., MD, MPH
Ely A. Kirschner, MD
John B. Lazor, MD, MBA, FACS
William W. McClerkin, MD
Cliff A. Megerian, MD
Ralph B. Metson, MD
Didier L. Peron, MD
Edward J. Reardon, MD
George A. Scangas, MD
Michael Zoller, MD

HIGHLIGHTS

News from every corner of the Department of Otolaryngology–Head and Neck Surgery at Harvard Medical School.

New Faculty

Introducing the newest clinicians, clinician-scientists, researchers and educators in the Department of Otolaryngology–Head and Neck Surgery.

Anna Chambers, PhD, is an investigator in the Eaton-Peabody Laboratories at Mass Eye and Ear. She earned her PhD in neurobiology from Harvard Medical School under the supervision of Daniel Polley, PhD, and completed postdoctoral fellowships at Johannes Gutenberg University Mainz and the University of Oslo. Her research focus is the role of sleep in shaping the brain's adaptation to a loss of inputs from the ear. She uses optical and electrophysiological techniques to measure and manipulate neural activity in animal models of hearing loss.

Natalia Kyriazidis, MD, is a fellowship-trained thyroid and parathyroid surgeon at Mass Eye and Ear who also provides comprehensive ear, nose and throat care to adult and pediatric patients. She earned her medical degree from the UMass Chan Medical School before completing her residency training in otolaryngology–head and neck surgery at SUNY Upstate Medical University. Dr. Kyriazidis subsequently completed a one-year fellowship in advanced endocrine head and neck surgery at Mass Eye and Ear. Her primary clinical and research interests center upon benign and malignant diseases of the thyroid and parathyroid glands.

Recent Promotions

[1] John B. Lazor, MD, MBA, Assistant Professor of Otolaryngology–Head and Neck Surgery, Part-time

[2] Anne Hseu, MD, Assistant Professor of Otolaryngology–Head and Neck Surgery

[3] Yi-Zhou Quan, PhD, Instructor of Otolaryngology–Head and Neck Surgery

Awards, Grants and Honors

Faculty and trainees from **Mass Eye and Ear, Massachusetts General Hospital, Brigham and Women's Hospital** and the **Dana-Farber Cancer Institute** hosted a *New England Journal of Medicine* clinicalpathological conference (CPC) at Mass Eye and Ear Grand Rounds. The CPC was led by **Rahmatullah Wais Rahmati, MD, MPH, FACS,** who was accompanied by **Rosh K. Sethi, MD, MPH.** Dr. Sethi presented on behalf of **Mark A. Varvares, MD, FACS,** who had led treatment of the examined case.

Giovanni Battistella, PhD, was named the recipient of the 2023 Seth Robbins Mass General Neuroscience Transformative Scholar in Tinnitus Research Award. With the support of his grant, Dr. Battistella aims to uncover objective imaging biomarkers of tinnitus that can ultimately inform the design of novel treatment options for tinnitus.

Ciersten Burks, MD, was awarded the Underrepresented Physician of Tomorrow Award by the Massachusetts Medical Society. The award recognizes an underrepresented-in-medicine student or trainee who demonstrates exceptional advocacy, scholarship and leadership.

Zheng-Yi Chen, DPhil, was named a principal investigator of a three-year Hearing Restoration Research Program grant from the Department of Defense. The grant, worth $1.4 million, will fund a study led by Dr. Chen that will explore a possible treatment for hearing damage from exposure to loud noises.

In June 2023, the newly launched **Global Surgery Scholars Program at Mass Eye and Ear** welcomed Nepalese surgeon Pramila Shakya, MD, as its inaugural scholar. For several weeks, Dr. Shakya of the Nepal Cleft and Burn Center, shadowed surgeons from every subspecialty under the mentorship of **David A. Shaye, MD, MPH, FACS.**

Ernest D. Gomez, MD, MTR, was awarded a R01 grant from the National Institutes of Health to develop a virtual reality-based platform for robotic surgical training and assess the effects of transcranial direct current stimulation on surgical learning.

Andrew Blitzer, MD, FACS

Andrew Blitzer, MD, FACS, Professor Emeritus of Otolaryngology–Head and Neck Surgery at Columbia University College of Physicians and Surgeons, delivered the **Harvard OHNS Grinspoon–Montgomery Visiting Professor Lectureship** inside the Meltzer Auditorium at Mass Eye and Ear Grand Rounds.

Phil Huyett, MD, completed his 400th implantation of the Inspire hypoglossal nerve stimulator device, becoming one of the few surgeons nationwide to reach the impressive milestone. The device is produced by Inspire Medical Systems© and is an alternative option for patients with sleep apnea who are unable to tolerate conventional, gold-standard treatments.

In June 2023, Mass Eye and Ear hosted world-renowned experts on ear-related diseases inside the Meltzer Auditorium for the 16th triennial Meeting of the **International Otopathology Society.** Keynote speakers at the meeting included **M. Charles Liberman, PhD,** of Mass Eye and Ear; Sumit Agrawal, PhD, of Western University in Canada; and Nicolas Verhaert, MD, PhD, of Universitair Ziekenhuis Leuven in Belgium.

Nicole Jiam, MD, was awarded a Doris Duke Physician Scientist Fellowship, which provides an opportunity for subspecialty fellows to conduct extra years of research as a clinician investigator. Dr. Jiam's fellowship will help fund her project on age-specific cochlear implant programming for optimal hearing performance.

Karl Koehler, PhD, was named a collaborator on a R01 National Institutes of Health grant awarded to **Cynthia Morton, PhD,** who is studying gene therapies for hearing loss.

At the 2023 World Congress on Thyroid Cancer in London, **Natalia Kyriazidis, MD,** finished in first place for the Oral Podium Presentation Award. Dr. Kyriazidis earned the award for research she presented from the first thyroid cancer neoadjuvant clinical trial currently underway at Mass Eye and Ear and Massachusetts General Hospital.

Resident **Obi Nwosu, MD,** was presented the 2023 Patricia & Barry Yellen Young Investigator Award. Named after long-time Mass Eye and Ear Trustee Barry Yellen and his wife Patricia, the award supports trainees who are eager to conduct research within their specialty early in their careers. Dr. Nwosu will use funding from the award to improve the functionality of a proof-of-concept machine-learning tool he helped develop to automatically measure perforations, or holes, in the eardrum.

Resident Obi Nwosu, MD was presented the 2023 Patricia & Barry Yellen Young Investigator Award by Stacey Gray, MD.

New Leadership

Reza Rahbar, MD, DMD, was named president of the American Society of Pediatric Otolaryngology.

David H. Jung, MD, PhD, FACS, was appointed Associate Program Director of Otolaryngology–Head and Neck Surgery Research at Mass Eye and Ear.


1


2

David A. Shaye, MD, MPH, FACS, and **Ciersten Burks, MD,** returned from a surgical trip to Zimbabwe, where they completed more than 60 life-changing surgeries for patients ranging in age from three months to 70 years old. The surgeons performed surgeries free of cost at the Mpilo Hospital in Bulawayo, the nation's second-largest city. They worked with the international non-profit Operation Hope and Wayne Manana, MD, a Zimbabwean cleft surgeon who visited Mass Eye and Ear in 2015.

Residents **Krish Suresh, MD,** and **Phoebe Yu, MD, MPH,** were awarded Centralized Otolaryngology Research Effort (CORE) grants by the American Academy of Otolaryngology–Head and Neck Surgery Foundation to support separate research projects. Dr. Suresh will lead the development of an artificial intelligence model for measuring the tumor volumes of vestibular schwannomas. Dr. Yu will assess changes in sleep and respiratory measures among patients with sleep apnea who undergo sinonasal surgeries.

[continued p. 18]

Dr. Matthew Naunheim honored with prestigious awards

Matthew R. Naunheim, MD, MBA, a fellowship-trained laryngologist at Mass Eye and Ear, was presented the Norman Knight Leadership Development Award at the hospital's Spring Meeting of the Trustees and Medical Staff.

The award was endowed by Norman Knight, a self-made broadcast pioneer and media mogul who has been a passionate champion of Mass Eye and Ear for more than 25 years. Recipients are selected for their exceptional promise as future leaders within their specialty in otolaryngology–head and neck surgery at Mass Eye and Ear.

Dr. Naunheim was also awarded a Cochrane Scholarship by the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS). Cochrane Scholarships are prestigious awards bestowed to AAO-HNS members who wish to undergo specialized training in the methodology and techniques of conducting systematic literature reviews.

Meet the 2023 Gliklich Scholars

In June 2023, Harvard HealthTech Innovation Fellows **Jessica Abreu, Roger Flint, Bridget Slomka** and **Ana Trapero Martin** undertook new roles at Mass Eye and Ear as **Gliklich Innovation Scholars.** Since beginning their Harvard HealthTech fellowships at the hospital in fall 2022, each fellow has immersed themselves in the clinical subspecialties of the Department of Otolaryngology–Head and Neck Surgery and conceptualized innovative solutions to a few of the most pertinent problems observed.

Launched in 2013, the Gliklich Innovation Scholars Program aims to provide a transformative opportunity to those pursuing novel and disruptive ideas and projects that might otherwise be difficult to undertake through traditional funding mechanisms. The program routinely attracts individuals looking for a mentored experience in innovation and the opportunity to make an impact on healthcare treatments, delivery, outcomes or education through a focused project, protected time and a rich collaborative environment.

Jessica Abreu

Roger Flint

Bridget Slomka

Ana Trapero Martin

RESEARCH ADVANCES

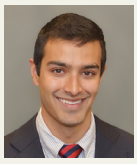
The following are select research advances from the Harvard Medical School Department of Otolaryngology–Head and Neck Surgery.

Millions of patients without full recovery of smell or taste after COVID infection

During the COVID-19 pandemic, millions of patients experienced a loss of taste and smell during and after their SARS-CoV-2 infection. According to a recent study led by **Neil Bhattacharyya, MD, FACS,** of Mass Eye and Ear, a large portion of these patients are still waiting for their missing senses to return.

The study, published in *The Laryngoscope,* is the first to quantify the impact of smell and taste loss related to COVID-19 infection at the national level. Upon assessing tens of thousands of responses to the 2021 National Health Interview Survey, Dr. Bhattacharyya and Mass Eye and Ear residents **Margaret B. Mitchell, MD; Alan D. Workman MD, MTR;** and **Vinay K. Rathi MD, MBA,** estimated





that more than 20 million COVID patients experienced a loss of smell or taste in 2021. Of those who lost their sense of smell to COVID, a little more than a quarter of patients either partially recovered or experienced no recovery whatsoever. Likewise, a little more than a fifth of those who lost their sense of taste have either partially, or have never, recovered the sense.

The researchers also observed a correlation between COVID symptom severity and loss of smell or taste. As symptom severity increased, the percentage of patients with smell or taste loss increased and the likelihood of smell and taste sensory recovery decreased.

Mitchell MB, Workman AD, Rathi VK, Bhattacharyya N. Smell and taste loss associated with COVID-19 infection. The Laryngoscope. 2023; 133: 2357-2361. Doi: 10.1002/lary.30802

Cognitive bias demonstrated in motion perception

Deep inside human ears, a unique set of organs determines how individuals perceive the motion of their body, which, in turn, determines their perception of motion and balance. Analogous to an audiogram, vestibular thresholds measure the minimum amount of movement needed to reliably perceive movement, and can depend on a person's age and disease. Whether past experiences can jeopardize sensitivity and perception to future motion has long been speculated by researchers, but it had not been definitively measured.

Faisal Karmali, PhD, of Mass Eye and Ear, has quantitatively demonstrated the effects of cognitive bias on how humans perceive motion in a recent study published by the *American Journal of Audiology.* According to this study, Dr. Karmali and his team examined how several human subjects perceived a series of motions in a dark, uncertain setting. Their findings suggested that a bias existed among subjects who tended to respond opposite of a perceptual response from a preceding motion. These biases led to the overestimation of the minimum thresholds for detecting motion among subjects, and the magnitude of the biases tended to vary from person to person.

By incorporating an enhanced model accounting for cognitive biases, Dr. Karmali and his team showed they could reduce measurement errors when interpreting vestibular perception data. Such a model would lead to more accurate and reliable results, especially when evaluating vestibular function in clinical medicine, sports science, aviation and space exploration.

Gonzalez ELC, King SA, Karmali F. Your vestibular thresholds may be lower than you think: cognitive biases in vestibular psychophysics. American Journal of Audiology. 2023; April 21. Pages 1-9. Doi: 10.1044/2023_AJA-22-00186

Hearing successfully rescued for first time in aged mouse models

By 2050, one in 10 individuals are expected to live with some form of hearing loss. Of the hundreds of millions of cases of hearing loss affecting individuals worldwide, genetic hearing loss is often the most difficult to treat. While hearing aids and cochlear implants offer limited relief, no available treatment can reverse or prevent this group of genetic conditions, prompting scientists to evaluate gene therapies for alternative solutions.

One of the most promising tools used in these therapies—adeno associated virus (AAV) vectors—has galvanized the hearing-loss community in recent years. Despite having already rescued hearing in neonatal animals with genetic defects, the vectors have yet to demonstrate this ability in fully mature or aged animal models. Since humans are born with fully developed ears, this proof-of-concept is necessary before testing the intervention in humans.

Zheng-Yi Chen, DPhil, of Mass Eye and Ear, recently became the first scientist to successfully demonstrate AAV vector efficacy in aged animal models. As reported in *Molecular Therapy,* Dr. Chen and his colleagues developed a mature mouse model with a mutation equivalent to a defective human gene typically responsible for progressive hearing loss. The researchers observed robust hearing rescue in the aged mice upon injecting the animal with an AAV carrying a healthy version of the human gene. Findings from the study represent a major step toward testing AAV gene therapies for genetic hearing loss in human trials, especially in the aging patient population.

Du W, Ergin V, Loeb C, et al. Rescue of auditory function by a single administration of AAV-TMPRSS3 gene therapy in aged mice of human recessive deafness DFNB8. Molecular Therapy. 2023; May 26. Doi: 10.1016/j.ymthe.2023.05.005

[continued p. 20]

CRISPR-Cas9 model simultaneously targets two mutations in dominant deafness; partially restores hearing

Deafness affects six percent of the world's population, and over 120 genes have been linked to hereditary hearing loss. However, there are no biological treatments for any form of genetic deafness. One type of hereditary hearing loss—dominant hearing loss—is particularly difficult to treat; any intervention requires targeting two mutations simultaneously, instead of just one. The mutations must be abolished to rescue hearing.

A team of researchers led by **Zheng-Yi Chen, DPhil,** of Mass Eye and Ear, used CRISPR-cas9 genome editing to target mouse models of dominant hearing loss. According to a recent study published in *Nature Communications,* Dr. Chen and his team successfully rescued hearing in these models by targeting a single mutation and two mutations simultaneously.

The team evaluated hearing recovery eight and 16 weeks after injection, reporting robust hearing recovery by single mutation intervention and partial hearing recovery by double-mutation intervention.

Tao Y, Lamas V, Du W, et al. Treatment of monogenic and digenic dominant genetic hearing loss by CRISPR-Cas9 ribonucleoprotein delivery in vivo. Nature Communications. 2023; Vol 14: 4928. Doi: 10.1002/hed.27385

Correlation between safety-net hospitals and mortality found among elderly head and neck cancer patients

Safety-net hospitals offer vital services to some of society's most underserved populations. These hospitals provide care to patients regardless of their insurance coverage, financial circumstances or immigration status. While certainly admirable, the services provided can financially strain a hospital asked to pick up the bill for those receiving care. How safety-net status and total case volume might impact outcomes among complex cases such as geriatric patients with head and neck cancer has remained relatively unknown.

In a study published in *Head & Neck,* **Scharukh M. Jalisi, MD, MA, FACS,** of Beth Israel Deaconess Medical Center, found a correlation between the mortality rates of elderly patients with head and neck cancer and the safety-net status of hospitals. Dr. Jalisi and several researchers began their research by performing multilinear regressions to predict different outcome variables among the elderly patient cohort at safety-net and non-safety-net hospitals. These variables included mortality index, intensive care unit stays, 30-day readmission, total direct cost and direct cost index.

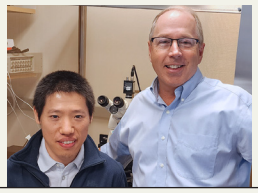
According to the study, the safety-net status of the evaluated hospitals correlated with a higher mortality index and higher costs among elderly patients with head and neck cancer patients.

Tashman K, Noyes EA, Warinner CB, Ogbonna J, Gomez E, Jalisi SM. The relationship between safety-net hospital status and outcomes among elderly head and neck cancer patients. Head & Neck. 2023; Vol. 45 (7): 1741-1752. Doi: 10.1002/hed.27385

Cryoelectron microscopy captures first images of hair cell ion channels

Countless organisms rely on mechano-sensitive ion channels in response to mechanical stimuli. Inside the inner ears of mammals, the auditory organ contains membranes separating high concentrations of potassium ions from high concentrations of sodium ions. When sensory hair cells detect sound waves, potassium ions cross their membranes. Too much stimulation can prompt the hair cells to swell.

A newly identified ion channel relieves the build-up of potassium and prevents the swollen cells from bursting. The exact structure and identity of this channel, however, has long remained a mystery. Drawing on insights from a newly discovered type of ion channel in plants, **Wang Zheng, PhD**, and **Jeffrey R. Holt, PhD,** of Boston Children's Hospital, produced images of the human form of these mechano-sensitive ion channel. The team captured the images using cryoelectron microscopy, or cryo-EM, which generates hi-resolution, 3D images using millions of photos taken under an electron microscope.



Images of the ion channel were published in *Neuron.* From the images, Drs. Holt and Zheng determined that the ion channel is one of the rare channels consisting of a single protein, TMEM63B. The protein has several unique structural features, which contribute to its function in hair cells. Genetic mutations in TMEM63B cause deafness in mice and other disorders in humans, and a better understanding of the protein's structure and function could lead to the development of therapies for these genetic disorders.

Wang Z, Rawson S, Shen Z, et al. TMEM63 proteins function as monomeric high-threshold mechanosensitive ion channels. Neuron. 2023; August 4. Doi: 10.1016/j.neuron.2023.07.006

Revision surgery for recurrent thyroid cancers may help achieve biochemical remission

Nerve monitoring has changed the way surgeons operate on patients with thyroid and parathyroid disease. The technology can pinpoint the exact location of critical nerves in the neck, which allows surgeons to avoid harming nerves that, if injured, can affect a patient's ability to swallow, breathe and speak.

A team of researchers led by **Gregory W. Randolph, MD, FACS, FACE,** of Mass Eye and Ear, sought to study the surgical and biochemical outcomes in nerve monitored reoperation or revision surgery for recurrent thyroid cancers. The team reported the results of 227 patients with recurrent papillary thyroid carcinoma (PTC) who underwent reoperation or revision surgery. As reported in *Otolaryngology–Head & Neck Surgery,* only 12 of the patients experienced permanent hypocalcemia after their procedure and no cases of unexpected vocal cord paralysis.

Findings from the study suggest that reoperation or revision surgery for recurrent PTC may help achieve biochemical remission regardless of age or the number of prior surgeries.

Patel KR, Wang B, Abdelhamid Ahmed AH, et al. Surgical and biochemical outcomes in nerve monitored reoperation surgery for recurrent papillary thyroid carcinoma. Otolaryngology–Head & Neck Surgery. 2023; May 28. Doi: 10.1002/ohn.389

Connect with us on LinkedIn: All former residents and fellows are invited to join the Harvard Otolaryngology–Head and Neck Surgery Alumni Group.

Photo by Garyfallia Pagonis

HARVARD OTOLARYNGOLOGY

News from the Harvard Medical School
Department of Otolaryngology–Head and Neck Surgery
243 Charles Street, Boston, MA 02114

NONPROFIT
U.S. Postage
PAID
N. READING, MA
Permit NO. 121

HARVARD MEDICAL SCHOOL | Department of Otolaryngology Head and Neck Surgery

Beth Israel Deaconess Medical Center
Boston Children's Hospital
Brigham and Women's Hospital
Mass Eye and Ear
Massachusetts General Hospital