NATIONAL DEAFNESS AND OTHER COMMUNICATION DISORDERS

ADVISORY COUNCIL

February 2–3, 2023

National Institutes of Health

Bethesda, Maryland

MINUTES

The National Deafness and Other Communication Disorders Advisory Council (NDCDAC) convened on February 2 and February 3, 2023, via videoconference at the National Institutes of Health (NIH) in Bethesda, MD. Dr. Debara L. Tucci, Director, National Institute on Deafness and Other Communication Disorders (NIDCD), served as Chairperson. In accordance with Public Law 92-463, the meeting was:

Closed: February 2, 2023, 10:00 a.m. to 12:00 p.m. for review of individual grant applications; and

Open: February 2, 2023, 1:00 p.m. to 4:05 p.m. and February 3, 2023, from 11:00 a.m. to 12:52 p.m., for the review and discussion of program development needs and policy.

Council members in attendance[1]:

Dr. Emily Buss
Dr. Nirupa Chaudhari
Ms. Vicki Deal-Williams
Dr. Ruth Anne Eatock
Dr. Carol Espy-Wilson
Dr. Lisa Goffman
Dr. Andy Groves
Dr. Argye Hillis
Ms. Barbara Kelley
Ms. Lynne Murphy Breen
Dr. Dan Sanes
Dr. Ben Strowbridge
Dr. Margaret Wallhagen

Council members absent:
Dr. Anil Lalwani

Ex-officio Council members in attendance:
Dr. Judy Schafer for Dr. Lucille Beck (United States Department of Veterans Affairs)
Ms. Christi Themann (Centers for Disease Control and Prevention)

Ad hoc Council members in attendance:
Ms. Katherine Bouton
Dr. Daniel Merfeld
Dr. Melinda Pettigrew
Dr. Susan Thibeault

The complete Council roster can be found in Appendix 1.
NIDCD staff and other NIH staff in attendance list can be found in Appendix 3.

[1] For the record, it is noted that members absent themselves from the meeting when the Council is discussing applications (a) from their respective institutions or (b) in which a real or apparent conflict of interest might occur. This procedure applies only to individual discussion of an application and not to *en bloc* actions.

CLOSED SESSION February 2, 2023

Call to Order and Opening Remarks ..... Dr. Debara L. Tucci

Dr. Tucci, director of NIDCD, called the meeting to order. She expressed appreciation to the entire Council for their service and advice.

Council Procedures..... Dr. Becky Wagenaar-Miller

Procedural Matters

Dr. Becky Wagenaar-Miller discussed important procedural matters, including requirements imposed by the Government in the Sunshine Act and the Federal Advisory Committee Act. There is a necessity for members to avoid any conflict of interest and they need to maintain confidentiality concerning the proceedings and materials related to the closed portion of the meeting. Dr. Wagenaar-Miller announced that the Council meeting would be closed for consideration of grant applications during the morning session and would be open to the public at approximately 1:00 p.m. via Videocast.

Council Consideration of Pending Applications ..... Dr. Judith Cooper and Staff

Research Project Grant Awards

Consideration of Applications: a total of 102 investigator-initiated R01 grant applications were on the Council's agenda; 87 applications had primary assignment to NIDCD, in the amount of $35.0 million first-year direct costs. It is anticipated that, of the applications competing at this Council, NIDCD will be able to award grants to R01 applications scoring up through the 15th percentile.

Special Program Actions

1. NIH Mentored Patient-Oriented Research Career Development Award (K18): The Council voted to support one application.
2. NIH Mentored Patient-Oriented Research Career Development Award (K23): The Council voted to support one application.
3. NIH Midcareer Investigator Award in Patient-Oriented Research (K24): The Council voted to support one application.
4. NIH Pathway to Independence Award (K99/R00): The Council voted to support two applications.
5. NIH Ruth L. Kirschstein Institutional National Research Service Award (T32): The Council voted to support four applications.
6. NIH Ruth L. Kirschstein National Research Service Award (NRSA) Short-Term Institutional Research Training Grant (Parent T35): The Council voted to support one application.
7. Mentoring Networks to Enhance Diversity in NIDCD's Extramural Research Workforce (R25 Clinical Trial Not Allowed): The Council voted to support one application.
8. NIH Support for Conferences and Scientific Meetings (R13): The Council voted to support three applications.
9. NIH Exploratory/Development Research Grant Award (R21): The Council voted to support six applications.
10. NIDCD Early Career Research (ECR) Award (R21): The Council voted to support seven applications.
11. PAR-22-035 NIDCD Clinical Research Center Grant (P50 Clinical Trial Optional). The Council voted to support applications.
12. NIH Small Business Technology Transfer Grant Applications (STTR): The Council voted to support one (R41) application.

13. NIH Small Business Innovation Research Grant (SBIR): The Council voted to support two (R44) applications.
14. RFA-DC-23-001 NIDCD Research Opportunities for New Investigators to Promote Workforce Diversity (R01): The Council voted to support four applications.
15. PAR-21-064 NIDCD Cooperative Agreement for Clinical Trials in Communication Disorders (U01 - Clinical Trial Required): The Council voted to support one application.

Dr. Tucci adjourned the closed session at 11:54 am.

OPEN SESSION—February 2, 2023

Opening Remarks ..... Dr. Tucci

Dr. Tucci welcomed additional staff and visitors to the open session of the meeting. Videocast of this meeting is available to the public from the NIH Videocast website.

Council Introduction

Dr. Tucci invited each council member to introduce themselves to begin the meeting.

Consideration of Minutes of the Meeting of September 8–9, 2022

Dr. Tucci called the members' attention to the minutes of the September 8–9, 2022, meeting of the NDCDAC. The minutes were approved as written.

Confirmation of Dates for Future Council Meetings

Dates for the Council meetings through September 2024 have been established. A list of these meetings was distributed to the Council members and posted on the NIDCD website before this meeting. The next meeting of the Council will be in person on Thursday, May 18, and Friday, May 19, 2023.

NIDCD Director's Report ..... Dr. Tucci

Dr. Tucci began her Director's Report by introducing two new directors at NIH. Monica M. Bertagnolli, M.D., the director of the National Cancer Institute (NCI), is a surgical oncologist who specializes in treating gastrointestinal disease. Dr. Bertagnolli has advocated for more diversity in patients participating in clinical trials and for patient-focused programs in rural communities. Her leadership in the NCI-funded National Clinical Trials Network has led to the integration of tumor-specific biomarkers and clinical trial protocols. Her research on the adenomatous polyposis coli (*APC*) gene and its role in inflammation has transformed our understanding of how colorectal cancer develops.

Joni L. Rutter, Ph.D., is the new director of the National Center for Advancing Translational Sciences (NCATS). She has championed the use of real-world data, artificial intelligence (AI), and machine learning to rapidly address public health; led an initiative to calculate approximate health care costs for millions of people with rare diseases; and led the National COVID Cohort Collaborative. Before joining NCATS, Dr. Rutter established scientific programs within the NIH *All of Us* Research Program to advance precision medicine.

Dr. Tucci introduced new NIDCD leadership:

- Elyssa Monzack, Ph.D., deputy scientific director of NIDCD, directs the NIDCD Division of Intramural Research training program and serves as a general advisor to the scientific director.
- Nadia M. Biassou, M.D., Ph.D., chief of the Integrative Neuroscience of Communications Unit, holds a joint appointment in Radiology and Imaging Sciences at the NIH Clinical Center, where she has served as a board-certified diagnostic clinical neuroradiologist for 15 years; that position will continue on a part-

time basis while Dr. Biassou participates in the NIDCD Intramural Program.
- Elka Scordalakes-Ferrante, Ph.D., was selected as chief of the Science Policy and Planning Branch.
- Clint Allen, M.D., acting director of the NIH Clinical Center, is a principal investigator (PI) in translational tumor immunology.
- Angela Ballesteros Morcillo, Ph.D., acting chief of the Section on Sensory Physiology and Biophysics in the Division of Intramural Research.

Dr. Tucci said that recruitment for a new NIDCD clinical director is nearing its end. The new clinical director should be announced later this month, with an expected start date of early April.

Dr. Tucci announced the appointment of Ronna Hertzano, M.D., Ph.D., to the Neurotology Branch in the Division of Intramural Research. This new branch will investigate the causes, prevention, diagnosis, and rehabilitation of hearing impairment and balance disorders. Dr. Hertzano will oversee clinical trials of the Neurotology Branch to identify promising new treatment strategies—including pharmacologic, biologic, and gene therapies—and surgical procedures to advance treatments in the NIDCD hearing and balance portfolio. She comes to NIDCD from the University of Maryland where she is a full professor of otolaryngology-head and neck surgery and professor of anatomy and neurobiology. Her research focuses on the molecular basis of hearing loss by examining the regulatory events that lead to the development of the ear and the key regulators of genes involved in hair cell development.

Recruitment is ongoing for four NIDCD health science administrators or program officer positions:

- Voice/speech health science administrator
- Data science health science administrator
- Data science training officer
- Advanced Research Projects Agency for Health (ARPA-H) program manager

Howard Hoffman, M.A., helped assemble a new resource, Population and Clinical Database Resources for NIDCD Mission Areas, which lists different databases across various organizations that are available to NIDCD.

Dr. Tucci reviewed the 2023–2027 Strategic Plan. Developing the plan involved engaging with partners in industry, patient and consumer groups, professional organizations, and the scientific community. The plan identifies significant research areas to advance NIDCD's mission and vision. Dr. Tucci thanked the Council liaisons, Dr. Chaudhari and Dr. Sanes, for their contributions to this process.

Dr. Tucci reviewed the development of steps that were different from previous processes. In 2021, more than 120 ideas were collected from a diverse range of subject matter experts. NIDCD staff reviewed the ideas and created high-level scientific priorities. Baseline metrics have been established to track the plan's implementation.

The future direction of NIDCD research falls into six themes, each with specific goals:

1. Capitalize on advances in basic research to enhance our understanding of normal function and disordered processes.

    Goal 1: Identify and characterize different cell populations in both peripheral and central regions.
    Goal 2: Identify and characterize neural circuits involved in sensory processing.
    Goal 3: Facilitate the utilization of biopsied and postmortem human tissue to advance research.
    Goal 4: Define interactions between immune-mediated networks and the influence of inflammation on normal and disordered function.

2. Develop and improve model systems to inform research.

    Goal 1: Develop robust *in vivo* and preclinical models to study normal and disordered function.

Goal 2: Develop *in vitro* models to accelerate basic studies and high-throughput screening.
Goal 3: Develop *in silico* (computer) models to enable insights into normal and disordered function.

3. Promote a precision medicine approach to prevention, diagnosis, and treatment.

   Goal 1: Accelerate the acquisition and ethical use of genetic and phenotypic data.
   Goal 2: Develop genetic and cellular therapies.
   Goal 3: Identify and develop interventions targeted to specific subpopulations.

4. Translate and implement scientific advances into standard clinical care.

   Goal 1: Accelerate the development of treatments.
   Goal 2: Develop, disseminate, and implement evidence-based practices to improve health-related outcomes.
   Goal 3: Promote health equity and improve access to clinical care.

5. Facilitate use of the best practices in biomedical data science.

   Goal 1: Inform the development and use of standardized outcome measures for basic and clinical research.
   Goal 2: Encourage the use of data repositories to share findable, accessible, interoperable, and reusable (FAIR) data.
   Goal 3: Develop AI and machine learning algorithms that provide novel insights and applications for prevention, diagnosis, and treatment.

6. Harness advanced technology to improve prevention, diagnosis, and treatment.

   Goal 1: Employ rational design principles to engineer novel solutions.
   Goal 2: Enhance augmentative and alternative communication capabilities.
   Goal 3: Develop specialized *in vivo* imaging capabilities to improve diagnosis and treatment.

The strategic plan aligns with NIH-wide cross-cutting priorities:

- Seek innovation through partnerships (e.g., the Brain Research Through Advancing Innovative Neurotechnologies® [BRAIN] Initiative).
- Strengthen research training and career development.
- Reinforce a culture of scientific workforce diversity, equity, inclusion, and accessibility (DEIA).
- Participate in international research to improve global health (e.g., working with the John E. Fogarty International Center).
- Advance research to improve women's health.
- Reduce health disparities.

Three Success Stories from the SBIR/STTR Grant Program.....Dr. Roger Miller
Dr. David Landsberger
Dr. Angelique Johnson
Dr. Rupal Patel

Dr. Miller introduced the three academic PIs who have detoured to commercialization for the betterment of health care:

- David Landsberger, Ph.D., founder of York Sound, Inc.
- Angelique Johnson, Ph.D., founder and CEO of MEMStim
- Rupal Patel, Ph.D., founder and CEO of VocaliD, a Veritone Company

Each awardee was asked to present information about their companies and to answer two questions: What

critical steps would you give other academic researchers who want to pursue funding? How did your team define success for this award?

David Landsberger, Ph.D., founder of York Sound, Inc.

Dr. Landsberger received his Ph.D. from Brown University and is now an assistant professor at the New York University School of Medicine. Dr. Landsberger has received F32, R03, R21, and R01 academic grant awards. He ventured into the SBIR funding world after he and a colleague established York Sound in 2019. They received a Direct Phase II SBIR grant in 2020 and an SB1 Commercialization Readiness Pilot Grant award in 2022.

Dr. Landsberger said that the technology developed in his New York University laboratory is now licensed to York Sound, whose motto is, “Straight talk. No babble.” The company works with hard-of-hearing listeners who have difficulty participating in conversations when other people are talking in the background (babble). Noise reduction has been integrated into other products, but they are not effective at eliminating background talkers. Babble is exhausting and leads to social isolation. Untreated hearing loss is one of the strongest predictors of dementia and cognitive decline.

There is a need to separate a foreground talker from a background talker or speech from speech. Background talkers need to be removed in a computationally simple way, have minimal latency, and be generalizable to novel noises. Dr. Landsberger’s company has developed SEDA (speech enhancement via decomposition approach), a proprietary algorithm to remove babble. SEDA outperformed ClearVoice™ when measuring the normalized percentage of words understood in babble noise, regardless of the noise’s volume.

York Sound will not sell or manufacture any products. Instead, SEDA will be inserted by the hardware manufacturer and licensed non-exclusively by companies in the cochlear implant (CI), hearing aid, telephone, audio/video teleconferencing, and voice recognition industries. Prototypes are currently being evaluated by CI companies.

Dr. Landsberger’s advice to academics thinking about applying for an SBIR is to consider how their technology will be implemented as a product, what the product’s market demand and pain points are, and what the steps to commercialize it are. Earlier in his career, Dr. Landsberger built a new signal processing strategy that improved speech understanding with a CI, but companies did not see it as clinically viable, because it needed too much power and more clinical time to treat a patient with that product. SEDA needed to satisfy two concerns to make itself clinically usable: Was it beneficial in non-babble situations, and could it be implemented in computational and firmware limitations of commercial systems?

SBIR awards are given to companies, so academics need to find a company to work with or create their own company. When starting a company, one must ask who will run it and who will work on the project. A new company will need a lawyer and an accountant and must apply for its own grants.

York Sound defines success as improving the lives of hard-of-hearing patients by helping them hear in difficult situations, commercializing its technology, and transforming its academically generated proof of concept into a viable product.

Angelique Johnson, Ph.D., founder and CEO of MEMStim

Dr. Johnson is the founder and CEO of MEMStim, whose motto is “One pulse over the horizon.” Dr. Johnson received her Ph.D. from the University of Michigan in 2011 and set out to establish her company that year. She was the grand prize winner of both the University of Michigan Business Challenge and the Texas Venture Labs Investment Competition. She received a Phase I SBIR award in 2014, a Phase II SBIR award in 2017, and a Direct Phase II SBIR award in 2020. Dr. Johnson has more than 20 years of experience in medical device innovation and has a second company that provides entrepreneurship training for innovators who are underserved, underseen, and under-spotlighted.

MEMStim is an original equipment manufacturer (OEM) that uses 3D printing to make bio-nerves, sensors, and

stimulators for implantable and wearable medical technology. The new manufacturing process that MEMStim developed for electrode leads in CIs can be used in other implantable applications to treat conditions such as seizures, chronic pain, tremors, and more. The same manufacturing process for stimulators and sensors can be used for wearable applications, such as a bioelectronic nose, electronic skin, biostat sensors, and prosthetic arrays. There is a need for very thin and flexible substrates that mimic the body's nerves, muscles, and tissues. The assembly of electrode leads and sensors is done by hand and is labor-intensive, which slows throughput and restricts future innovations. MEMStim is developing automation solutions to create implantable arrays and wearable sensors. The company does a mix of 3D printing microfabrication that reduces labor to accelerate product development life cycles with rapid prototyping and a toolkit of design options for future innovations. Their technology solutions develop elastic thin leads and miniaturized electrodes that can be body-compliant, durable, long-lasting, and nontoxic.

MEMStim partners with companies that are interested in low labor costs, miniaturization, and accelerated development. MEMStim will sell components to medical device firms and startups, which will in turn and sell to end users. The market for wearables and implantable stimulators and sensors is $179 billion; the market for initial target implantable simulators is $10.5 billion.

Dr. Johnson advises academics applying for an SBIR award to think like innovators but act like entrepreneurs. Be innovative with an end purpose that may be seen within five years, validate demand, and think about commercialization when initially designing a protype. Dr. Johnson defines success as affecting human lives positively.

Dr. Tucci asked what role the SBIR/STTR funds played in MEMStim. Dr. Johnson did not start with commercialization in mind, so at the end of her dissertation, she learned that the materials she used were not medical-grade for clinical use. This prompted her to redo the manufacturing process and intellectual property, which was funded by the SBIR grants.

Rupal Patel, Ph.D., founder and CEO of VocaliD, a Veritone Company

Dr. Patel received her Ph.D. from the University of Toronto and is now a professor at Northeastern University. Her research funding began with an R03, followed by an R21. In 2015, she received a Boston Globe Game Changer Award and was included in the CloudNOW Award for the Top 10 Women in Cloud Computing. She received her first SBIR Phase I award in 2015, followed by a Phase II SBIR award in 2017.

Dr. Patel presented her company, VocaliD, with the motto "Voice is identity." VocaliD's principle is, "Our voices are not identical, and they are our identities." A voice indicates a person's age, gender, and more. In 2002, Dr. Patel noticed that assistant communication devices had similar synthetic voices that were depersonalized. However, a synthetic voice that is true to a user also should not mimic someone with a disease that severely affects their speech. With her R03 grant and other funding, the company went back to the core basics of speech science to create unique-sounding synthetic voices.

The source theory of speech production involves how the voice is made. To recreate speech, the source characteristics from a person who is unable to speak clearly can be combined with characteristics borrowed from someone with regular speech who also matches the patient's age, gender, height, and other characteristics.

When presenting at a conference, Dr. Patel got an outpouring of volunteers who were willing to contribute their voices to people with speaking challenges. This sparked the idea to commercialize a product by starting VocaliD. The first step was starting the Human Voicebank, an online tool that records people reading sentences out loud.

BeSpoke Voice was an early product from VocaliD. A young girl with cerebral palsy recorded her voice, then a voice donor recorded about 2,000 sentences. Inverse filtering and recombining of the voices were fed to a transformer engine that was taught to speak with clarity.

Patients about to lose their voices started to record them in the Voicebank . For these patients, VocaliD

created Vocal Legacy, where voices do not need to be recombined but instead parts of a person's voice are used.

Dr. Patel offered the following advice to academics:

- Determine whether SBIR or STTR is the appropriate mechanism.
- Assess whether the timing is right for you and the market.
- Be transparent with your department or institution about your plans.
- Be honest about your time allocation and commitment.
- Start with the why, not the how.
- Build a team that understands commercialization, not just research.
- Validate end users' need for and willingness to pay for a product.
- Be ready to be a student again.
- Immerse yourself in an entrepreneurship ecosystem.
- Iteration is "the game." Use your gut, heart, and data to guide decisions.

Dr. Patel's success metrics are about whether the end user can use the product. For the company, success differed at different stages in the journey. Early goals were focused on productization and repeatable process, while later goals were focused on market strategy and positioning. Securing funding and working with the right people and culture were key. The true litmus test is whether value has been created and people want to buy your product.

Discussion

Dr. Patel was asked whether voices needed to be rebuilt for young people as they mature. Dr. Patel said yes, across age bands a voice needs to be updated with a new voice donor. This is done for people of all ages.

Dr. Miller asked Dr. Landsberger how he balances the opportunities in the medical and consumer markets. Dr. Landsberger is focusing on the medical device category because it is straightforward. He does not have the resources to pursue the consumer market.

Dr. Espy-Wilson asked each presenter which mechanism they started with and why they chose it. All three used an SBIR award, due to where their companies or technologies were in development. Dr. Landsberger's technology was more advanced, so they applied for a Direct Phase II grant. Dr. Patel said that there is a large leap between Phase I and Phase II. Letters for commercialization validation really matter, as do market validation pieces. It is challenging to apply for Phase II, so applicants need to be ready for them.

Dr. Miller asked each presenter what is not in the SBIR/STTR programs that they wish could be provided. Dr. Patel would like SBIR funding to cover creation/patenting of intellectual property. Dr. Johnson said it would help to provide support for underserved founders and entrepreneurs with the application process. Dr. Landsberger said that there is a large learning curve with all that is needed to apply for an SBIR grant; he would like a natural network to link applicants' questions. Dr. Miller said that technical and business assistance is available to cover legal costs for a patent, as can the 7% fee, which can be used for anything. NIH's Small business Education and Entrepreneurial Development (SEED) office is trying to reach out to underrepresented applicants and has created a course to assist in SBIR applications.

Dr. Espy-Wilson asked Dr. Landsberger what is available for noise suppression in his CI device. Dr. Landsberger said that it varies among devices, companies, and platforms, so spec ranges are used.

Budget Report .....Mr. Eric Williams

The budget report was given by Mr. Eric Williams, NIDCD chief budget officer. The Fiscal Year (FY) 2022 Operating Plan (Actual Allocations) budget was $514.9 million, all of which except around $5,900 was spent. Growth was seen in Research project grants (RPGs), R25s, and Division of Intramural Research (DIR) for a new neurotology department.

The spending by mission area has remained mostly unchanged over the last few years.

NIDCD recently received an enacted budget that had increased by about $20 million. The enacted budget, in thousands, has been the following over the past years: FY 2020: $490,692; FY 2021: $498,076; FY 2022: $514,882; and FY 2023: $534,330.

NIDCD will continue to grow RPGs, R25 Diversity Grants, U24s, and the DIR budget to bring on new hires and equipment. Some increases to DIR and Research Management and Support (RMS) will fulfill the pay raises that were authorized.

The FY 2023 competing R01/U01 budget pay line is $16 million per council, and the High Program Priority (HPP) budget is $4 million per council.

Report of the Division of Scientific Programs ..... Dr. Judith Cooper

Dr. Judith Cooper, as Division of Scientific Programs director, presented recently published initiatives at NIDCD.

- A Notice of Special Interest (NOSI) titled "Fundamental Science Research on the Neural Circuits Underlying Sensory Processing" (notice number NOT-DC-23-001) is meant to advance a mechanistic understanding of the behavior of neural circuits at cellular and sub-second temporal resolution by integrating cutting-edge technologies and approaches for recording and modulation of cells and circuits. This area is highlighted in the new Strategic Plan, and investigators are encouraged to pursue this area.
- A Request for Information (RFI) titled "Inviting Input Regarding NIDCD's Support of Non-Invasive Imaging in Humans" (notice number NOT-DC-23-004) is inviting input and suggestions on NIDCD's support of noninvasive imaging in humans for the diagnosis, monitoring, and treatment of communication disorders.

The following recent NOSI topics were issued by NIH leadership to enhance the retention of investigators facing critical life events:

- Administrative Supplements to Promote Research Continuity and Retention of NIH Mentored Career Development (K) Award Recipients and Scholars (NOT-OD-23-031): K01, K07, K08, K22, K23, K25, K38, K43, K76, F99/K00, and K99/R00
- Administrative Supplements for Continuity of Biomedical and Behavioral Research Among First Time Recipients of NIH Research Project Grant Awards (NOT-OD-23-032): DP1, DP2, DP5, R01, R00, R15, R21, R35, RF1, and U01

The following are examples of NOSIs that support existing research activities:

- Administrative Supplement for Research and Capacity Building Efforts Related to Bioethical Issues (Admin Supp Clinical Trial Optional) (NOT-OD-23-018). This is for research on bioethical issues to develop or support the development of an evidence base that may inform future policy directions and for certain efforts to develop or augment bioethics research capacity.
- Support for Existing Data Repositories to Align with Findability, Accessibility, Interoperability, and Reusability (FAIR) and Transparency, Responsibility, User focus, Sustainability and Technology (TRUST) Principles and Evaluate Usage, Utility, and Impact (NOT-OD-23-044). This is to improve the adoption of the FAIR and TRUST principles and to develop ways to measure their effectiveness for the research communities they serve.

Dr. Cooper highlighted two NIDCD PIs who have received prestigious NIH-wide awards:

- Dr. Sergey Stavisky from University of California, Davis received the NIH Director's New Innovator Award (DP2) that is part of the NIH Common Fund's High-Risk, High-Reward Research Program. This award is for exceptionally creative early career scientists proposing high-impact, innovative projects. Dr. Stavisky's award is titled "Understanding and Restoring Speech Production Using an Intracortical Brain Computer Interface."
- Dr. Yael Emilie Bensoussan from the University of South Florida received an award from the Bridge to

Artificial Intelligence (2AI) Program that supports projects that build ethical, rigorous, and accessible datasets that can be used to develop AI tools. Dr. Bensoussan's award is titled "Bridge 2AI: Voice as a Biomarker of Health: Building an Ethically Sourced, Bioacoustics Database to Understand Disease Like Never Before."

Lastly, NIDCD sponsored a webinar workshop titled "Minimally Verbal/Non-Speaking Individuals With Autism: Research Directions for Interventions to Promote Language and Communication" that took place on January 24–25, 2023. Dr. Cooper will present more about this at the next Council meeting. She and her co-chairs considered the workshop to be successful at many levels and thought that it gave NIDCD much to consider. More information about the workshop will also be provided on the NIDCD website.

Concept Clearances……Dr. Amy Poremba and Dr. Nancy Freeman

Dr. Cooper introduced the new concept clearance process. Each concept will be presented by program staff, followed by Council discussion led by two assigned members and then a hand-raised vote by the full Council. The purpose of the concept clearances is for NIDCD staff to hear the Council's views and advice. NIDCD plans to proceed with the concepts, but publication and timing not guaranteed and will depend on funding. Council-approved concepts will be posted on the NIDCD website after this meeting.

Concept Clearance 1: Advanced Imaging to Increase Structural, Functional, and Temporal Resolution of Communication Systems…….. Dr. Amy Poremba

Dr. Poremba said that the purpose of this concept is to provide or increase the necessary resolution across structural, functional, and temporal domains to view the structures involved in communication across all NIDCD mission areas for use in the clinical setting. The preferred final techniques would be noninvasive and applicable to conscious patients. Current technologies could be modified and brought to the clinical setting sooner, while new technologies would need to be developed in animal models first.

Dr. Poremba presented this concept on behalf of the Strategic Planning Imaging Committee, which includes members from across all of the NIDCD mission areas. The need for advanced imaging is stated in the NIDCD 2023–2027 Strategic Plan under Theme 6, Goal 3: "Develop specialized *in vivo* imaging capabilities to improve diagnosis and treatment." Imaging covers a wide range of possibilities that have generated great interest.

Much of the diagnostic work in conventional health care clinics uses standard images, far-field physiological recordings, behavioral testing, and symptomatology. In some cases, sensory structures can be researched only in postmortem tissues, so there is a significant need for imaging instruments in living humans. NIDCD has specific needs that are sometimes associated with unique sensory input structures. Hearing and balance disorder research is hampered by the encasement of the inner ear in thick temporal bone, which prevents imaging with sufficient structural resolution and functional and temporal imaging in the clinical setting. Other imaging difficulties include the following:

- Poor differentiation of soft tissue
- Inability to differentiate air from bone with magnetic resonance imaging (MRI)
- Low resolution of microvasculature
- Inability to see cellular and subcellular structures
- Placement of cochlear and vestibular prostheses

With forthcoming genetic treatments, knowing what parts of the body need to be repaired would be helpful.

Chemical senses research has limited technology to visualize chemosensory structures in a clinical setting, and the commonly used endoscope does not resolve olfactory epithelium from respiratory mucosa, diminishing the possibility of accurate diagnoses and potential treatments.

Voice, speech, and language research need finer resolution of structures such as the larynx, palate, and tongue. NIDCD would like dynamic, noninvasive imaging capabilities of voice and speech structures to assess structure, function, and temporal dimensions. Other NIH institutes also study language and want greater resolution across structural, functional, and temporal dimensions for cortical regions.

Advancements in imaging would greatly benefit science and the public in the following ways:

- Differential diagnoses and increased accuracy
- Matching of treatment with diagnoses
- Expedited care
- Better clinical treatment
- Development of treatments from better visualization
- Improved outcomes and quality of life

If the concept is approved, its objective would be to encourage the NIDCD scientific community and stakeholders to participate in collaborative efforts with imaging experts, engineers, other NIH institutes, government entities, and corporate entities, to develop significantly improved and new imaging techniques for use in the clinic to rapidly advance personalized patient care through visualization, identification, diagnosis, and treatment of communication disorders. There would be a sustained, long-term commitment to basic and translational research that would focus on improving current techniques and discovering new ones.

Concept Clearance 1 Discussion

Dr. Sanes and Dr. Eatock were asked to lead the discussion. Dr. Eatock said that she is pleased to see this project being considered. There is an urgent clinical need for information about structure that is intertwined with an understanding of function. This investment would aid in the understanding of basic function. Optical coherence tomography (OCT) is advancing understanding in animal research by allowing visibility through structures without invading the cochlea. Advanced imaging could help study balance dysfunction that is caused by mechanical disturbances inside the inner ear. This concept is an opportunity to work with other NIH institutes that would also benefit from advanced imaging.

Dr. Sanes agreed with Dr. Eatock's comments. This is the right time to leverage this mechanism, which could help diagnose patients who experience dizziness. The imaging measurements would provide basic science researchers with information to make a good model.

Dr. Sanes suggested discussing the following issues:

- The concept statement refers to structural, functional, and temporal domains. Dr. Sanes thought of the technologies as being focused on either structure or function, and he thought of resolution as being either the spatial or temporal domains. He suggested recasting the concept's statement to clarify to investigators the need for technologies that allow views of anatomy and measure physiological properties. Advances are needed for greater spatial and temporal resolution.
- Different laboratories get different single measures when using new or existing technologies. Dr. Sanes suggested encouraging investigators to check new technologies by making a second, simultaneous measurement with an existing technology.
- Clarification is needed regarding how the concept applies to language.
- The concept's new technologies could help study normal function and deficits.

Dr. Poremba said that she appreciated all of the points and will discuss them with the Strategic Planning Imaging Committee.

Dr. Merfeld said that unnatural stimuli are the only way to do functional imaging of the CNS from a vestibular perspective. This concept's new technology could enhance diagnosis and improve the understanding of the central vestibular system. Dr. Poremba mentioned an RFP (request for proposal) that asked for needs like this.

Dr. Wagenaar-Miller took the Council's vote for concept 1, which was approved.

Concept Clearance 2: Organoids and Associated Technologies…… Dr. Nancy Freeman

Dr. Freeman presented information about a workshop, "Improving Ex-vivo Models to Accelerate Therapies to Treat Hearing Loss," at the January 2022 Advisory Council meeting. NIDCD has a long history of supporting stem cell research, which fulfills aspects of the 2023–2027 Strategic Plan's Theme 2: to develop and improve model systems to inform research.

Organoids are mainly derived from embryonic stem cells or by human induced pluripotent stem cell (hiPSC) technology. The stem cells are directed to become organoids, within which are hair cell–like cells. Uses of organoids include the following:

- Development of cells (can be used to answer research questions)
- Regenerative medicine (recapitulate tissues and whole organs)
- Disease modeling (take cells from a patient with a genetic aberration and propagate organoids to fine-tune therapy strategies)
- Gene therapy (improve the efficacy of gene therapy in different cell types)
- Organ on chip (multiple organ systems can be on a chip)
- Otoprotection
- Drug screening (automated, high-throughput volumes allow thousands of organoids to be laid out in a uniform manner, and thousands of molecules can be screened)

Organoids are highly scalable and easily accessible. They have human genes, 3D organization, and multiple cell types. Organoids can complement existing research models, such as non-mammalian vertebrates, rodents, and 2D cell cultures.

The number of organoid research publications peaked in the 1970s and 1980s and has risen again since 2013 with the use of hiPSCs. Some key publications of organoid research include the 2002 NIH tissue chip paper and the 2017 ear organoid paper.

Objectives and possible outcomes of this concept include the following:

- Increase use of both human and animal organoids
- Allow a 3D scalable model system that could be complementary
- Increase understanding of stem cell biology in ear-specific organoids
- Advance knowledge of cell mimicry
- Improve reliability and reproducibility
- Implement use of forefront organoid technologies, such as 3D bioprinting and multiplex screening platforms

Concept Clearance 2 Discussion

Dr. Groves and Dr. Eatock were asked to lead the discussion. Dr. Groves participated in the workshop that Dr. Freeman organized last year. Dr. Groves said that about 3,000 hair cell–like cells can be obtained from a newborn mouse cochlea and about 5 million cerebellar granule cells can be obtained from a newborn mouse cerebellum; the ability to generate large amounts of cells from the inner ear would solve many issues that investigators have and would greatly reduce the number of animals needed. The organoids can be used for screening and to understand genetic abnormalities in the ear's cells, as well as to understand the basic, fundamental mechanisms of how the ear's cells are produced, function, and respond to damage. There is a need for reliable, reproduceable, and quality sourced cell materials. Different stem cell lines used to generate organoids can behave in different ways, and a laboratory can get variable outcomes with different cell lines, so having a way to standardize organoids in a research plan would be important. There is a need to study how to grow and propagate organoids and how to generate different cell types to order. There should not be an exclusive focus on human stem cells to model patient diseases, because human stem cells take much longer to generate organoids. Mouse tissue generates organoids faster and should be included in this model. This project also has the potential to fabricate and model tissues or structures such as the endolymphatic duct and

sac epithelium, stria vascularis, and middle ear epithelium. Dr. Groves said that it is time for NIDCD to support this project.

Dr. Eatock agreed with Dr. Groves' comments. She works with the inner ear and is interested in brain organoids; Dr. Freeman mentioned that she knows investigators doing this work. Organoids are attractive for studying peripheral sensory structures, which are highly ordered structures. This model system can clarify what is and is not known about how structures work. This project brings collaborators together to share their work. She agrees that this project is timely. Cross connections could be made in sharing tissue with other NIH institutes.

Dr. Freeman said that a recent publication describes growing ear organoids innervated into neuron organoids, so piecemeal steps are rapidly advancing, speaking to the timeliness of this project. Perhaps all fabrication devices will be able to replicate a cochlea. There is a need for stability of organoids across laboratories so that all laboratories can start at the same place, without variability.

Dr. Hillis agreed with the need for stability of organoids across laboratories because brain organoid research is growing and is used by researchers at NCATS.

Dr. Wagenaar-Miller took the Council's vote for concept 2, which was approved.

Report of the Division of Extramural Activities ..... Dr. Wagenaar-Miller

Dr. Wagenaar-Miller provided updates for the Division of Extramural Activities (DEA). Eliane Lazar-Wesley, Ph.D., retired from DEA after more than 30 years of service in several NIH offices. The staff appreciated Dr. Lazar-Wesley's enthusiasm and wish her well.

There are three new members of DEA:

- Sonia Nanescu, Ph.D., scientific review officer (replacing Dr. Lazar-Wesley)
- Brook Sydnor, program analyst
- Dawn Walker, grants management specialist

NIH Policy Updates

Dr. Wagenaar-Miller discussed two NIH RFIs.

Update to NOT-OD-05-034: Guidance on Prompt Reporting of Noncompliance to Office of Laboratory Animal Welfare (OLAW) (NOT-OD-23-063) seeks input on updates to the current Guidance on Prompt Reporting to OLAW Under the PHS Policy on Humane Care and Use of Laboratory Animals (NOT-OD-05-034). The goal is to reduce administrative burden by clarifying the reporting requirements without negatively affecting the accountability and transparency of the process. All responses must be submitted electronically on the NOT-OD-23-063 RFI webpage by May 5, 2023, at 11:59 p.m. ET.

Simplified Review Framework for NIH Research Project Grant Applications (NOT-OD-23-034) seeks input about the revised framework for evaluating and scoring peer review criteria for NIH RPG applications. The revised framework reorganizes five major regulatory criteria to three scored categories and reduces the number of non-scores that drive considerations that reviewers evaluate. Responses must be submitted electronically on the NOT-OD-23-034 RFI webpage by March 10, 2023, at 11:59 p.m. ET.

Dr. Wagenaar-Miller reviewed the behavioral codes of conduct for NIH award recipients. The NIH Grants Policy Statement (GPS) update states that institutions receiving NIH support are required to have internal controls to ensure compliance with terms and conditions of an award, including behavioral codes of conduct, to ensure safe and healthful working conditions for their employees and to foster work environments conducive to high-quality research. This applies to all awards issued on or after October 1, 2022. See Mike Lauer's blog for more information.

Dr. Wagenaar-Miller said that DEA is accepting nominations for peer reviewers, who may also be self-nominated. She thanked DEA staff for their hard work.

Closing Comments……Dr. Tucci

Dr. Tucci thanked the Council members and presenters. She adjourned this session of open council at 3:42 pm.

OPEN SESSION—February 3, 2023

Director's Greeting ..... Dr. Tucci

Dr. Tucci welcomed additional staff and visitors to the open session of the meeting, which could be viewed by the public through the NIH Videocast website.

Dr. Tucci reviewed the three presentations that would be given.

NIDCD DEIA Update ..... Dr. Cendrine Robinson

Dr. Tucci introduced Dr. Robinson, the first chief diversity officer at NIDCD. Dr. Robinson shared a key experience she brings to her role. She became aware of the need for DEIA at a bake sale organized by students who disagreed with the university's diversity-focused policies: They priced cookies based on their perception of how hard the buyer had to work to get into the university, so a cookie for a White student was $1.00 and a cookie for a Black student was $0.50. This group felt that Black students were half as competitive for admission to the school. Dr. Robinson recognized that this model ignored the impact of structural racism on educational opportunities. Dr. Robinson aligned herself with students and staff committed to promoting DEIA education and policy, and she learned how policies such as redlining impact health, education, and economic opportunity.

Dr. Robinson has participated in several programs that level the playing field and address systemic racism, such as the Ronald E. McNair Program and the NIH Diversity F31 Predoctoral Fellowship. Through these experiences, she developed expertise in health disparities and a passion for diversifying the biomedical workforce.

NIDCD's spheres of influence for DEIA are the following:

- The internal workforce and its scientists in the extramural program
- The extramural workforce grantee community and its pipeline
- Work toward health equity

Across the three spheres, Dr. Robinson envisioned these DEIA strategies:

- Equity in recruitment and advancement, which means using best practices to reduce biases in recruitment and promoting equal opportunities for advancement in the internal workforce. For the external workforce, equitable opportunities to receive NIDCD funding are needed.
- Transparency and accountability. NIDCD will communicate DEIA activities, efforts, and progress to both internal and extramural workforces. Dr. Robinson will formalize the DEIA strategy into an action plan that will further facilitate accountability.
- Cultural awareness. The internal workforce has regular education and training about topics such as structural racism. The external community may receive mentoring opportunities, such as the R25 Mentorship Award, to improve cultural awareness.

Dr. Robinson plans to enhance DEIA at NIDCD by tracking and monitoring initiatives across the lifecycle of the internal and extramural workforces. DEIA efforts in the internal employee lifecycle include recruitment that will ensure processes are equitable and will diversify staff, retention with cultural awareness training, development to align with NIH's initiative to develop opportunities, and reward by recognizing and promoting staff. DEIA efforts in the extramural workforce lifecycle include development of a pipeline by investing earlier in students,

recruitment using equity and access to apply for funding, retention that provides opportunities, and reward with recognition. The DEIA efforts in the extramural workforce will benefit recruitment for the internal workforce.

One of NIDCD's goals is to have research that is innovative and high-quality, enhances public trust, and involves underserved populations. Dr. Robinson said that the internal and extramural efforts combine to enhance NIDCD's health equity portfolio.

NIDCD's DEIA infrastructure includes Dr. Robinson as Chief Diversity Officer collaborating with NIDCD's Diversity Working Group, Advisory Council Working Group on Diversity and Inclusion, and Implementation Committee. These efforts align with the NIH-wide UNITE initiative and the Anti-Racism Committee's work.

Dr. Robinson has facilitated uptake of the NIDCD Recruiting Guide, search committees for leadership positions, and the training office's postbaccalaureate intramural recruiting initiative.

NIDCD participates in diverse conferences, promotes equity in grant writing resources with a sample grant application on its website, employs diversity scholars, and reaches out to historically Black colleges and universities (HBCUs) and minority-serving institutions (MSIs) to develop a pipeline and recruit for the extramural workforce.

Funding opportunities for the extramural workforce, such as the Administrative Supplements for Small Businesses to Promote Diversity in Research and Development (PA-21-345) and the Mentoring Networks to Enhance Diversity in NIDCD's Extramural Research Workforce (PAR-21-185), will develop a diverse pipeline. More opportunities will be forthcoming through UNITE.

Funding opportunities for achieving health equity, such as Understanding and Addressing the Impact of Structural Racism and Discrimination on Minority Health and Health Disparities (RFA-MD-21-004) and the Transformative Health Disparity Research at Minority Serving Institutions (RFA-RM-21-002), are available. Dr. Robinson would like to get the word out about these opportunities, and she thanked the NIDCD staff involved in DEIA.

UNITE E Update Discussion ..... Dr. Jon Lorsch
Dr. Lisa Goffman

Dr. Tucci introduced Dr. Lorsch, the director of the National Institute of General Medical Sciences (NIGMS) and co-chair of the UNITE E Committee. Dr. Lorsch provided updates on accomplishments and plans in four main areas:

- Underrepresented groups (URG) career pathways
- Inequities at extramural institutions, with a focus on environment and culture
- Inequities at NIH, with a focus on policies and procedures
- Research resources and capacity at MSIs

URG Career Pathways

The expansion of Science Education Partnership Awards (SEPA) supports innovation in science, technology, engineering, and mathematics (STEM) education for pre-K through grade 12 to build the interest of students from diverse backgrounds in biomedical research careers. Sixteen NIH institutes and centers (ICs) have joined NIGMS to potentially fund SEPA awards. All applications will be submitted to NIGMS, then participating ICs may select applications that they are interested in funding. SEPA awardees funded by all ICs will participate in program-wide activities. NIGMS is committed to funding a certain level of SEPA grants, so Dr. Lorsch asked the Council members to promote the program. Institutions may now have more than one SEPA award if the awards are for scientifically distinct programs.

Additional initiatives under development include incorporating more diversity and mentor training language into parent training grant (T32) and fellowship (F) funding opportunity announcements (FOAs); expanding the use of diversity supplements for small business grants (SBIR/STTR); increasing opportunities for entrepreneurial

training for faculty, students, and trainees at MSIs (with the NIH SEED Office); and expanding the use of the Plan to Enhance Diverse Perspectives (PEDP) in NIH FOAs, which was developed by the BRAIN Initiative.

Inequities at Extramural Institutions, with a Focus on Environment and Culture

Dr. Losch made the analogy that a healthy culture at an IC is like the healthy soil needed to grow seeds. A thriving and diverse biomedical research institution must have a healthy culture with inclusivity and diversity. The first step to improving culture is to assess it with climate assessments and self-studies, then to develop action plans for culture change. These steps will be taken with the Institutional Climate Assessment and DEIA Action Plan Development Grants, which will be coordinated by the National Institute of Dental and Craniofacial Research (NIDCR). ICs' needs will be taken into consideration when these awards are made.

Another new program is the Research With Activities Related to Diversity (ReWARD) Program, which provides five-year combined research and mentoring R01 grants to PIs who have demonstrated excellence in promoting DEIA in biomedical research. These grants will provide support for each PI's research program and continued DEIA efforts. These grants' goals are to help offset the diversity tax, promote advances in DEIA, and help the scientific research of investigators committed to advancing DEIA. This program complements the Chief Officer for Scientific Workforce Diversity (COSWD) Office's mentoring administrative supplement program. NIGMS will handle overall coordination of the grants.

The NIGMS Council cleared the concepts of both of the above new programs in February 2022. The FOAs are under development.

A prize program will be launched for ICs that have exceptional DEIA efforts. It will shine a spotlight on and incentivize ICs.

Dr. Tucci led the Institutional Culture Group that is working with professional societies to encourage institutions to revise promotion, tenure, and recognition policies to support DEIA efforts. This will build off of the American Association of Universities (AAU) report on racial equity.

Institutions are now required to have a behavioral code of conduct related to discrimination and hostile work environments. The new NIH GPS states that recipient organizations' internal controls should be in compliance with guidance in "Standards for Internal Control in the Federal Government" (45 CFR 75.303[a]). Recipient organizations are expected to establish codes of conduct that define expectations of integrity and ethical values and criteria of competence of personnel involved in the work supported by NIH grant funds. Codes of conduct should articulate expectations to ensure compliance with terms and conditions of an award, including but not limited to ensuring work environments are free of discriminatory harassment and are safe and conducive to high-quality work (NIH GPS, Chapter 4).

Inequities at NIH, with a Focus on Policies and Procedures

There is an NIH online form where allegations of harassment or discrimination may be filed. Action will be taken if there appears to be sufficient cause.

Additional initiatives under development include the following:

- Program officer and scientific review officer (SRO) training for inclusive and equitable community interactions
- NIH-wide reporting of potential bias in peer review
- Anti-bias training for IC reviewers and SROs (with the Center for Scientific Review [CSR])
- Efforts to reduce potential biases in peer review language and criteria (led by the Extramural Activities Working Group [EAWG])
- Development of guidelines for writing inclusive and culturally appropriate FOAs
- Development of guidelines for ICs to use to enhance portfolio diversity

Research Resources and Capacity at MSIs

An FOA is under development to fund MSIs so that they can assess their needs for enhancing their biomedical research and training capacities and to provide support for the development of action plans based on the results of the assessments. Identified needs might include development or enhancement of sponsored programs' administrative capabilities, new equipment, targeted hiring in specific scientific or administrative areas, and changes in institutional policies or expectations to better support the research mission. The National Institute on Minority Health and Health Disparities (NIMHD) Council cleared this concept in May 2022, and the FOA is under development.

The Instrumentation Grant Program for MSIs is an S10 equipment grant FOA that is meant to target MSIs with limited resources. It can be used to develop biomedical research and education capacity at lower-resourced MSIs. ICs are to participate by signing on and funding awards with overall coordination by NIGMS. The NIGMS Council cleared this concept in May 2022, and the FOA is under development.

The next generation of the Sponsored Programs Administration Development (SPAD) program UNITE Research Capacity Building Program to Enhance Diversity is under development to build administrative and/or research capacity at lower-resourced institutions.

UNITE would like to enhance the NIH Pathways to Excellence and Innovation (PEI) Initiative to increase contracts at HBCUs and enhance communication between NIH and MSIs. Goals include a better understanding of MSI strengths, capabilities, and needs and better publicity about available NIH funding opportunities and services. Yearly or biennial meetings with HBCU leadership may be held, and an "office" of MSI to support this work may be created.

Dr. Tucci asked about the Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) Awards. Dr. Lorsch said that it began two years ago and that 22 ICs participated in it. The goals are to diversify the faculty ranks of research-intense positions with grants and to run mentoring centers. The mentoring centers provide help such as networking opportunities, career-enhancing activities, and laboratory management skills. Dr. Lorsch encouraged getting to know scholars from this program. The applicant pool is made up of 75% women and 70% underrepresented minorities.

Discussion

Dr. Goffman began the discussion. She said that she is impressed by the progress and initiatives underway. Funded researchers serve as ambassadors who can disseminate these opportunities where extramural research is done. Dr. Goffman laid out the following themes and actionable items to discuss:

- The changing NIH policy and culture and how that filters to universities
- Supporting universities that form alliances with MSIs to grow their training and research efforts
- Getting inter-institutional T32, F, and R awards started
- Engaging professional societies
- Inviting diverse students to conferences and to work in laboratories for the summer
- Rewarding scientists who are committed to diverse themes
- Addressing tenure and promotion at universities that are tied to grant progress and receipt of extramural funding

Dr. Espy-Wilson suggested that the hiring bias training for program officers and SROs be posted online. She asked which institutions are applying for the SEPA grants and how many applicants there were for the postbaccalaureate program. Dr. Robinson said that the postbaccalaureate program had 30 names drawn and 3 were selected; 3 of 9 or 10 PIs were selected from the pool.

Dr. Lorsch agreed with Dr. Espy-Wilson's request to disseminate the hiring bias training. SEPA applicants are from public and private schools, science museums, and other places. The pre-K through grade 12 programs usually have dual PIs, with an educator and a university scientist.

Dr. Chaudhari thanked everyone working on DEIA and said she admired how the general climate has changed. Few people were interested in this training 10 years ago.

Ms. Deal-Williams commended Dr. Robinson and Dr. Lorsch on all they had done. She suggested strategic dissemination plans be made for target audiences in order to avoid great resources going unused.

Dr. Lorsch agreed that outreach is key, citing the MOSAIC program, which did a large amount of outreach, resulting in interest from many more scholars than anticipated. Dr. Robinson said that NIDCD emails professors directly and meets with them to publicize funding opportunities.

Ms. Bouton asked whether HBCUs and MSIs can apply for the exceptional DEIA activities prize. Dr. Lorsch said yes, any institution can apply for it.

Zebrafish: A Complementary Model to Drive Hearing and Balance Research.....Dr. Katie Kindt

Dr. Tucci introduced Dr. Kindt from NIDCD's intramural program. Dr. Kindt said that sensory hair cells, the receptors in the inner ear that are required for hearing and balance, are the main focus of her group's research. Aquatic vertebrates also have these cells to detect movement. The research goal she presented was to understand how hair cells form and function in a living system, work that is clinically significant given the millions of adults in the United States who report hearing loss or balance disorders when hair cells are damaged or die. Understanding more about these cells is important in order to regenerate them after loss.

Studying mammals' sensory hair cells in a native environment is difficult because the inner ear lies within the skull. Hair cells in zebrafish, however, reside in the inner ear and along the surface of the body, called the lateral line, which makes them easier to study. Additionally, zebrafish, mice, and humans have the same genes that disrupt auditory and vestibular function, making the zebrafish a great genetic model. It is easy to create mutant zebrafish to understand gene function and to create transgenic lines to study labeled hair cells and their structures within a living system. With her group's toolkit of transgenic lines, Dr. Kindt has studied *in vivo* hair cell development, function, damage, and death, work that is impossible to do in mammals. The transgenic lines provide a unique and comprehensive understanding of hair cells' role in hearing and balance.

Dr. Kindt presented how hair cells function in a living system in two parts: How do hair cells process sensory information, and what is the cost of synaptic activity?

Part 1: How do hair cells process sensory information?

Mechanosensation triggering synaptic activity is the dogma of hair cell function. Specifically, apical mechanosensory hair bundles respond defectively to a sensory stimulus, opening mechanosensitive ion channels, including calcium channels, that activate the cell and trigger synaptic activity at the base of the hair cell; then, at the base, a calcium influx leads to the release of the neurotransmitter and activation of the downstream neuron. However, human hair cell function is not completely understood. It is predicted that sound activates a collection of hair cells that transmit information to the brain.

Dr. Kindt's group found that not all zebrafish hair cells that detect stimuli transmit sensory information to the brain. Two trainees, Suna Li and Qiuxiang Zhang, studied how hair cells process sensory information with a transgenic line that expressed a calcium sensor; increases in fluorescence corresponded to increases in calcium or activity. A fluorescence indicator placed at the top and bottom membranes of the hair cells was used to read each cell's activity in a live fish while it was stimulated with a fluid jet. When the tops of 12 hair cells were stimulated, a robust calcium influx was detected at the top of all the cells, indicating all experienced mechanosensation and detection of the stimulus. However, at the base of the hair cells, only four had synaptic activity; eight did not, which surprised the researchers. Repeated tests found that only the same four hair cells transmitted information, suggesting that not all hair cells need to simultaneously transmit information, representing a paradigm shift in how hair cells work. Some hair cells seem to be actively silenced. The significance of this is an unexpected complexity that may be preserved in the mammalian auditory and vestibular systems.

The researchers wanted to determine how synapses are silenced and why. One hypothesis was that hair cells are silenced as an important reserve to preserve sensory function. To test whether silenced hair cells could be unsilenced, a laser was used to damage one of the four stimulated hair cells; silenced hair cells soon became synaptically active, proving that silenced cells could be unsilenced as the system needed them. A revised hypothesis—that silent cells could be a way for the system to conserve energy— led to part 2 of Dr. Kindt's presentation.

Part 2: What is the cost of synaptic activity?

Mitochondria provide the energy required to fuel synaptic transmissions, but doing so produces reactive oxygen species (ROS) and oxidative stress that could cause cell death or make the cell vulnerable to insults. This vulnerability to insult is what links mitochondria to hearing loss.

Daria Lukasz, a graduate student, studied whether silent hair cells use less energy and thus have reduced mitochondrial stress. Ms. Lukasz used MitoTimer, which labels young/healthy mitochondria a different color than old/stressed/oxidized mitochondria, to study mitochondrial activity in a mutant hair cell with no synaptic activity. The mutant hair cells showed less cumulative mitochondrial stress over time than the control hair cells did. Ms. Lukasz then studied whether less mitochondrial stress (created by neomycin treatment) protects against ototoxic damage. Significantly more mutant hair cells (that did not have synaptic activity) than control cells survived stress, indicating that synaptic silence offers protection.

Ms. Lukasz tested whether treatment with a calcium channel antagonist would protect normal zebrafish hair cells from stress with neomycin. She found that a short time of treatment with a calcium channel antagonist did not offer protection, but 24 hours did, indicating that the energy demands of synaptic activity accumulate over time. The real cost of synaptic activity is mitochondrial stress, which may be a source of hair cell stress and a mediator of ototoxic stress.

The tests provided three conclusions from the tests:

- There are many silent hair cells.
- Synaptic activity increases mitochondrial stress.
- Silent cells protect against ototoxic insults.

These conclusions translate to the following questions for mammalian hearing imbalance:

- How many sensory cells are required for hearing?
- How many sensory cells must be regenerated to restore lost hearing?
    - Perhaps fewer are needed to restore lost hearing than was originally predicted.
- What are new strategies to protect against ototoxic insults?
    - Acknowledging synaptic stress as a source of hair cell stress helps when considering otoprotective strategies and potential therapeutic development.

Dr. Kindt thanked the members of her group and NIDCD's intramural support.

Discussion

Dr. Strowbridge asked whether failure in vesicle release could explain mitochondrial vulnerability. Dr. Kindt said that silencing was preserved when vesicle release and post-synaptic calcium were studied. Studying another zebrafish mutant that affected both calcium and vesicle release indicated that the vesicle cycle, which creates strong metabolic demands, leaves hair cells vulnerable to insults, a finding consistent with work done in neurons.

Dr. Eatock asked whether efferents or variance of transduction play a role in silencing the hair cells. Dr. Kindt said that neither changed the subset of responding hair cells.

Dr. Groves said that none of this work can be done in mammalian species, underlining the need for alternative model systems. Fish are a good system because they are comparatively inexpensive. He was struck by how fast unsilencing occurred and asked how that happens. Dr. Kindt does not know how unsilencing happens, but she is looking for something, such as surrounding glial cells, that can sense all the hair cells at once.

Dr. Chaudhari asked whether the newly unsilenced or the unsilenced and matured hair cells broaden their sensory profile and how quickly. Dr. Kindt said that jet stimulation is limited but that the same cells respond and the same stay silent with all the types of stimulation tested so far. Different cells respond to different directions of stimulation.

Dr. Wallhagen asked whether Dr. Kindt is differentiating between inner and outer hair cells. Dr. Kindt's system does not have the equivalent of inner and outer hair cells.

Dr. Tucci thanked Dr. Kindt for her presentation and all the Council members for participating in the meeting. She said that Council members can give her topics they would like to discuss at future meetings. The meeting was adjourned by Dr. Tucci at 12:54 pm.

Certification of Minutes

We certify that, to the best of our knowledge, the foregoing minutes and attachments are accurate and correct.

6/20/2023

/Rebecca A. Wagenaar-Miller/
Rebecca A. Wagenaar-Miller, Ph.D.
Executive Secretary
National Deafness and Other Communication Disorders Advisory Council

6/20/2023

/Debara L. Tucci/
Debara L. Tucci, M.D., M.S., M.B.A.
Chairperson
National Deafness and Other Communication Disorders Advisory Council

Director
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Brooke Sydnor
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Appendices

Roster

National Deafness and Other Communication Disorders Advisory Council

(Terms end on 5/31 of the designated year)

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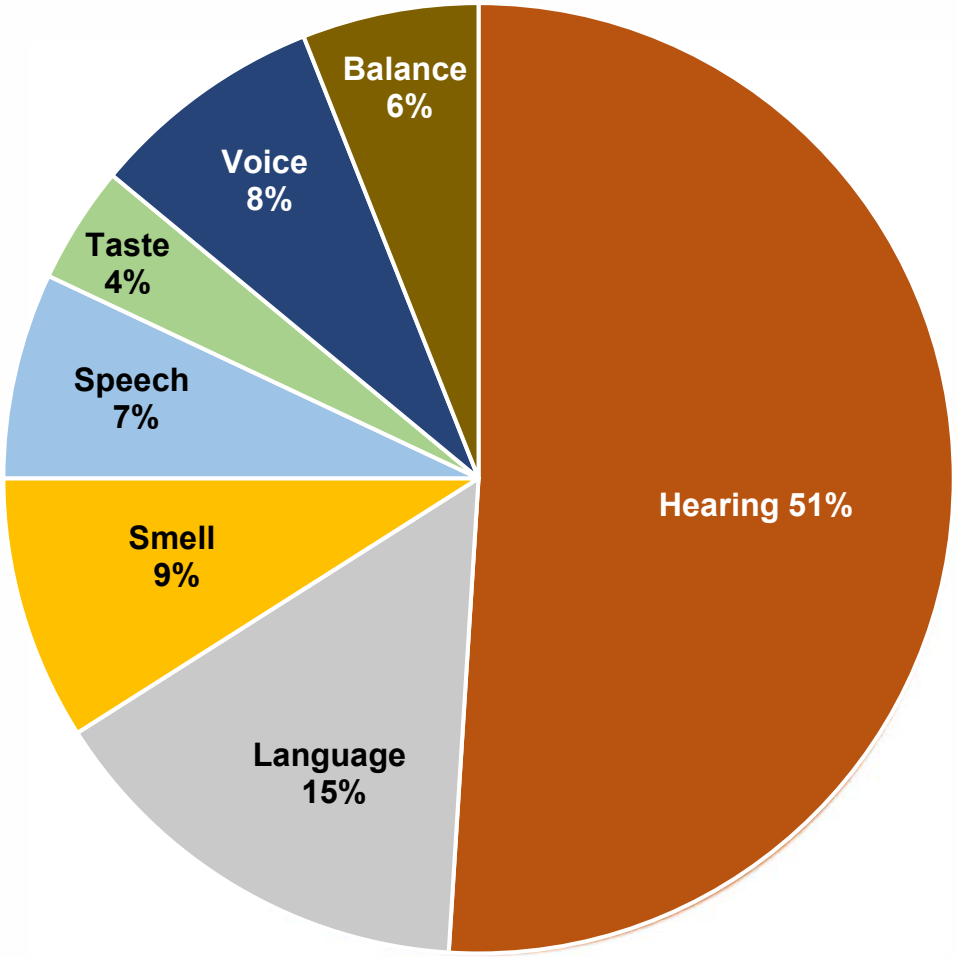
National Institute on Deafness and Other Communication Disorders (NIDCD)

FY 2022 Operating Plan (Actual Allocations)

(Dollars in thousands)

Mechanism	FY22	
	Number	Amount
Research Projects		
Noncompeting	581	$264,766
Administrative Supplements	*(71)*	$5,560
Renewal	38	$20,486
New	153	$59,857
Supplements	0	$0
Competing	191	$80,343
Subtotal, RPGs	772	$350,669
SBIR/STTR	27	$16,015
Research Project Grants	799	$366,683
Research Centers		
Specialized/Comprehensive	6	$15,318
Clinical Research	0	$0
Biotechnology	0	$0
Comparative Medicine	0	$0
Res. Centers in Minority Instit.	0	$0
Subtotal, Centers	6	$15,318
Other Research		
Research Careers	58	$8,884
Cancer Education	0	$0
Cooperative Clinical Research	0	$0
Biomedical Research Support	0	$0
Minority Biomed. Res. Support	0	$0
Other	33	$7,298
Subtotal, Other Research	91	$16,182
Total Research Grants	896	$398,183
Training	FTTPs	
Individual	142	$6,997
Institutional	153	$9,631
Total, Training (FTTPs and Award Amount)	295	$16,628
Research & Develop. Contracts	44	$23,229
SBIR/STTR (non-add)	*(0)*	*($204)*
Intramural Research	56	$52,588
Res. Management & Support	74	$24,248
Total, Program Level		**$514,876**

National Institute on Deafness and Other Communication Disorders (NIDCD)
FY22 Spending by Mission Area



Includes Intramural and Extramural

National Institute on Deafness and Other Communication Disorders (NIDCD)

FY2023 Budget Outlook

(Dollars in Thousands)

- FY 2020 Enacted: $490,692
- FY 2021 Enacted: $498,076
- FY 2022 Enacted: $514,882
- FY 2023 Enacted: $534,330

FY 2023 Competing R01/U01 Budget

Payline: $16,000 per Council

HPP: $4,000 per Council

Appendix 3

NIH Staff Present
Closed Session

Christopher Adams	Trinh Ly	Nanette Stephenson
Kathy Bainbridge	Castilla McNamara	Melissa Stick
May Chiu	Roger Miller	Holly Storkel
Laura Cole	Christopher Myers	Susan Sullivan
Judith Cooper	Edward Myrbeck	Brooke Sydnor
Janet Cyr	Stephanie Nagle Emmens (CSR)	Debara Tucci
Hoai Doan	Sonia Nanescu	Jean Verheyden
Nancy Freeman	Eric Nunn	Becky Wagenaar-Miller
Maria Garcia	Matthew Oh (CSR)	Bracie Watson
Rochelle Henteges (CSR)	Amy Poremba	Tim Wheeles
Howard Hoffman	Kausik (Bobby) Ray	Shiguang Yang
Tanya Holmes	Alberto Rivera-Rentas	
Roger Janz (CSR)	Cathy Rowe	**Other NIH Staff:**
Nichelle Johnson	Merav Sabri	Felice Harper (CIT)
Andrea Kelly	Elka Scordalakes-Ferrante	Tina Baker (Captioner)
Kelly King	Brian Scott (CSR)	
Mimi Lee	Lana Shekim	
Chuan-Ming Li	Katherine Shim	

NIH Staff Present
Open Session Day 1 - February 2, 2023

Christopher Adams	Castilla McNamara	Nanette Stephenson
Kathy Bainbridge	Roger Miller	Melissa Stick
May Chiu	Christopher Myers	Holly Storkel
Laura Cole	Edward Myrbeck	Brooke Sydnor
Judith Cooper	Sonia Nanescu	Susan Sullivan
Janet Cyr	Eric Nunn	Debara Tucci
Hoai Doan	Amy Poremba	Jean Verheyden
Nancy Freeman	Lisa Portnoy	Becky Wagenaar-Miller
Maria Garcia	Kausik (Bobby) Ray	Bracie Watson
Howard Hoffman	Alberto Rivera-Rentas	Eric Willams
Tanya Holmes	Cathy Rowe	Tim Wheeles
Nichelle Johnson	Merav Sabri	Shiguang Yang
Joanne Karimbakas	Elka Scordalakes-Ferrante	**Other NIH Staff:**
Andrea Kelly	Lana Shekim	Felice Harper (CIT)
Kelly King	Katherine Shim	CART Captioner—Edith
Chuan-Ming Li	Shirley Simson	ASL Interpreter Sarah

NIH Staff Present
Open Session Day 2 - February 3, 2023

Christopher Adams	Chuan-Ming Li	Shirley Simson
Kathy Bainbridge	Jon Lorsch	Nanette Stephenson
May Chiu	Castilla McNamara	Melissa Stick
Laura Cole	Christopher Myers	Holly Storkel
Judith Cooper	Edward Myrbeck	Brooke Sydnor
Janet Cyr	Sonia Nanescu	Susan Sullivan
Hoai Doan	Eric Nunn	Debara Tucci
Nancy Freeman	Hua Ou	Jean Verheyden
Maria Garcia	Amy Poremba	Becky Wagenaar-Miller
Howard Hoffman	Kausik (Bobby) Ray	Bracie Watson
Tanya Holmes	Alberto Rivera-Rentas	Tim Wheeles
Nichelle Johnson	Cendrine Robinson	Shiguang Yang
Joanne Karimbakas	Heidi Rosvold-Brenholtz	
Andrea Kelly	Cathy Rowe	**Other NIH Staff:**
Katie Kindt	Merav Sabri	Felice Harper (CIT)
Kelly King	Elka Scordalakes-Ferrante	CART Captioner—Tina Baker
Connie Latzko	Lana Shekim	ASL Interpreter David
Mimi Lee	Katherine Shim	TOC Bob Hamer