

National Institute of Dental and Craniofacial Research

National Advisory Dental and
Craniofacial Research Council

Minutes of Meeting
September 13, 2023

Building 35A
Conference Rooms 620/630
National Institutes of Health
Bethesda, Maryland

U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

MINUTES OF THE
NATIONAL ADVISORY DENTAL AND CRANIOFACIAL RESEARCH COUNCIL

September 13, 2023

The 234th meeting of the National Advisory Dental and Craniofacial Research Council (NADCRC) was convened on September 12 and 13, 2023, at 10:09 a.m., in Building 35A, Conference Rooms 620/630, National Institutes of Health (NIH), Bethesda, Maryland, and via videoconference. The meeting was open to the public from 10:09 a.m. until adjournment at 4:17 p.m.; it was preceded by the closed session for Council business and consideration of grant applications from 9:00 a.m. until 10:02 a.m. Dr. Rena D'Souza presided as Chair.

OPEN SESSION

Members Present

Dr. Joel Collier
Dr. Luisa DiPietro
Dr. Frank Ebetino
Dr. Paul Krebsbach
Dr. Jose Moron-Concepcion
Dr. Jacques Nor
Dr. Amy Smith Slep
Dr. Axel Visel
Dr. Michelle Hamilton

National Institute of Dental and Craniofacial Research

Dr. Rena D'Souza, Director
Dr. Jennifer Webster-Cyriaque, Deputy Director
Dr. Lynn King, Executive Secretary, and Director, Division of Extramural Activities (DEA)
Dr. Indu Ambudkar, Acting Scientific Director, Division of Intramural Research (DIR)
Dr. John (Jay) Chiorini, Acting Associate Scientific Director, DIR
Dr. Sharon Jackson, Deputy Clinical Director, DIR
Dr. Janice Lee, Clinical Director, DIR
Ms. Joy Postell, Chief Diversity Officer, Office of the Director (OD)
Dr. Lillian Shum, Director, Division of Extramural Research (DER)

Dr. Shaun Abrams, DIR
Dr. Mehrnoosh Abshari, DIR

Dr. Azeez Alade, DIR
Ms. Alexandria Alfarano, DER, Center for Clinical Research (CCR)
Dr. Hosam Alraqiq, OD, Office of Science Policy and Analysis (OPSA)
Dr. Lorena Baccaglini, DER, CCR
Dr. Alison Boyce, DIR
Ms. Beth Brillante, DIR
Dr. Anissa Brown, DER, Research Training & Career Development Branch (RTCDB)
Dr. Christopher Brown, DEA, Scientific Review Branch (SRB)
Dr. Thomas Bugge, DIR, Office of the Scientific Director (OSD)
Dr. Christopher Campbell, DEA, SRB
Dr. Preethi Chander, DER, Salivary Biology and Immunology Program
Dr. Jingshan Chen, DEA, SRB
Ms. Tiffany Chen, OD, Office of Communications & Health Education (OCHE)
Mr. Wanjun Chen, DIR, OSD
Dr. Zhong Chen, DER, Integrative Biology & Infectious Diseases Branch (IBIDB)
Dr. Aiwu Cheng, DEA, SRB
Ms. Jennifer Chi, OD, Office of Clinical Trials Operations & Management (OCTOM)
Ms. Alicia Chou, DER, Translational Genomics Research Branch (TGRB)
Mr. Kevin Chu, OD, Office of Information Technology (OIT)
Dr. Michelle Cortes, DER, IBIDB
Mr. Jimmy Do, OD, Financial Management Branch (FMB)
Dr. Bill Elwood, DER, Behavioral & Social Sciences Research Branch (BSSRB)
Dr. Olga Epifano, DEA
Dr. Luis Fernandez de Castro, DIR, OSD
Dr. Dena Fischer, DER, Director, CCR
Dr. David Fraser, DIR, OSD
Dr. Kat Futrega, DIR, OSD
Dr. Rachel Gafni, DIR, OSD
Dr. Melissa Ghim, DER, IBIDB
Dr. Ioana Ghita, DIR, OSD
Mr. Harry Grant, DIR
Dr. Margaret Grisius, DER, CCR
Mr. Joel Guzman, DER
Dr. Kenneth Hargreaves, Chair, NIDCR Board of Scientific Counselors
Ms. April Harrison, DEA, GMB
Mr. Gabriel Hidalgo, DEA, GMB
Dr. Matthew Hoffman, DIR, OSD
Dr. Timothy Iafolla, OD, OSPA
Dr. Hiroko Iida, DER, CCR
Dr. Tomoko Ikeuchi, DIR, OSD
Dr. Dara Kessler, OD
Dr. Leila Khaki, DER, BSSRB
Dr. Zohreh Khavandgar, DIR, OSD
Dr. Wendy Knosp, OD, OSPA
Dr. Taishi Komoro, DIR, OSD
Dr. Jamie Kugler, DIR, OSD

Dr. Ashok Kulkarni, DIR
Dr. Priyam Jani, DIR
Dr. Shuang Li, OD, DER
Dr. Yuanyuan (Kevin) Liu, DIR
Dr. Orlando Lopez, DER, IBIDB
Ms. Jayne Lura-Brown, DER
Ms. Alisa Machalak, OD, OCHE
Dr. Michael Maio, DIR
Dr. Tamara McNealy, DER, IBIDB
Ms. Susan Medve, DEA, GMB
Dr. Yun Mei, DEA, SRB
Dr. Amanda Melillo, DER, IBIDB
Dr. Randy Merling, DIR
Dr. Eva Mezey, DIR
Ms. Amy Mhatre-Owens, OD, OCTOM
Dr. Hitomi Minagi, DIR
Ms. Mable Nee, OD, FMB
Mr. Paul Newgen, DEA, GMB
Ms. Michelle Nguyen, OD, Office of Administrative Management (OAM)
Ms. Anna Nicholson, OD, OCTOM
Mr. Thomas O'Farrell, DEA, SRB
Dr. Noffisat Oki, DER, Data Science, Computational Biology, & Bioinformatics Program
Ms. Marshelle Parker, DEA, GMB
Dr. Vaishali Patel, DIR
Dr. Eileen Pelayo, DIR
Dr. Iriana Pena Manrique, OD
Ms. Lisa Peng, OD, OIT
Dr. Paola Perez, DIR
Ms. Debbie Pettitt, DEA, GMB
Dr. Fatemeh Pour, OD
Mr. John Prue, OD, OIT
Mr. Ben Rassuli, OD, OIT
Dr. Pam Robey, DIR
Ms. Diana Rutberg, DEA, GMB
Dr. Zubaida Saifudeen, DER, TGRB
Dr. Nadine Samara, DIR
Dr. Rachel Sare, DER, RTCDB
Dr. Yasaman Shirazi, DEA, SRB
Dr. Maruska Silveira, OD, OSPA
Ms. Jamie Sim, OD, OSPA
Dr. Ashley Smith, OD, OIT
Dr. Kathryn Stein, DER, TGRB
Mr. Shareef Syed, DIR
Dr. Roman Szabo, DIR
Dr. Ildiko Szalayova, DIR, OSD
Dr. Kelly Ten Hagen, DIR

Dr. Shoba Thirumangalathu, DEA, RTCDB
Dr. Jason Wan, DER, IDIDB
Dr. Lu Wang, DER, CCR
Dr. Blake Warner, DIR
Ms. Stacey Warr, OD, OIT
Dr. Drake Williams, DIR
Dr. Ken Yamada, DIR, OSD
Dr. Hongen Yin, DER, CCR

National Institutes of Health

Dr. Melissa Riddle, National Institute on Drug Abuse
Dr. Bruce Tromberg, Director, National Institute of Biomedical Imaging and Bioengineering

Guests

Dr. Makyba Charles-Ayinde, American Association for Dental, Oral, and Craniofacial Research (AADOCR)
Dr. Dana Graves, Penn Dental Medicine; Co-Chair, Council Oral Health Research Workforce Working Group
Ms. Sheri Herron, AADOCR
Dr. Mitsuaki Ono, Okayama University
Dr. Noriaki Ono, University of Texas Health Science Center at Houston (UTHealth) School of Dentistry
Mr. Yehuda Sugarman, AADOCR
Dr. Tongxin Wang, Howard University
Mr. Matthew Miller, Neal R. Gross & Co.

NIH Videocast

N=188 individuals viewed the live videocast

I. WELCOME

Dr. Lynn King, Director of Division of Extramural Activities (DEA) and Advisory Council Executive Secretary, called the open session of the 234th Advisory Council meeting to order at 10:09 a.m. Members of the public may submit written comments and questions until September 28th at NIDCRCouncilMail@nidcr.nih.gov. Dr. King reviewed the meeting logistics and led the Council members and attendees in a round of introductions.

II. APPROVAL OF MINUTES FROM PREVIOUS MEETING

Dr. King asked Advisory Council members if there were corrections or comments on the minutes of the May 16th, 2023, Advisory Council meeting. There were no corrections or comments and the Council voted unanimously to approve the minutes.

III. DIRECTOR'S REPORT AND DISCUSSION

Dr. Rena D'Souza, Director, NIDCR, welcomed Council members, NIH colleagues, and other attendees to the first in-person Council meeting since before the COVID-19 pandemic. Dr. D'Souza led the Council and attendees in a moment of silence to mourn the recent passing of Dr. Henning Birkedal-Hansen, former NIDCR Scientific Director. Dr. D'Souza's written Director's Report was provided to the Council members and is available on the NIDCR website (<http://www.nidcr.nih.gov>).

Dr. D'Souza formally welcomed Drs. Terry Dickinson, Luisa DiPietro, Paul Krebsbach, and Jose Moron-Concepcion to the Council as they formally begin their terms. Dr. D'Souza also announced that Drs. Frank (Hal) Ebetino, Amy Smith Slep, and Axel Visel have agreed to extend their terms on the Council, and Dr. D'Souza thanked them for agreeing to do so. In other personnel news at NIDCR, Dr. Matt Hoffman stepped down as Scientific Director (SD) at the end of August. He will continue to work in his lab for the time being, and Dr. D'Souza thanked him for his leadership during his tenure as SD, particularly his focus on mentoring. Until Dr. Hoffman's permanent successor is identified, Dr. Indu Ambudkar will be serving as acting SD and Dr. John (Jay) Chiorini will fill the role of acting deputy SD.

Dr. D'Souza began her report by underscoring the rapidly evolving scientific and political landscape in the United States in the post-pandemic aftermath and in the face of the continued effects of climate change. At the leadership level, NIH is in a transitional period but remains committed to its mission. The Senate confirmation hearing for President Joseph Biden's nominee for NIH Director, Dr. Monica Bertagnolli, is scheduled to take place in October. Dr. D'Souza sees NIH trending towards the integration of research activities between Institutes and Centers (ICs) in support of the whole person health rubric. Dr. D'Souza's presentation focused on the current state of the NIH, NIDCR's milestone achievements during its 75th anniversary year, and her view looking forward to the next 25 years.

Dr. D'Souza described Dr. Bertagnolli's background in greater detail. Most recently, she served as the presidentially-appointed Director of the National Cancer Institute (NCI), where she was the first female Director. Prior to joining NCI, she was a surgical oncologist at Brigham and Women's Hospital in Boston. During her brief tenure as NCI Director, Dr. Bertagnolli focused on advancing the President's Cancer Moonshot initiative. Elsewhere at NIH, Dr. Jeanne Marrazzo was recently appointed as the new Director of the National Institute of Allergy and Infectious Diseases (NIAID). Prior to arriving at NIH, Dr. Marrazzo was most recently the director of the Division of Infectious Diseases at the University of Alabama-Birmingham.

As noted at the last Council meeting, NIH anticipates that its budget will be flat for FY 2024, with a 1% increase allowable in FY 2025 under the recent debt ceiling legislation. Dr. D'Souza noted that, due to the effects of inflation, a flat budget or even a 1% increase are tantamount to a budget reduction. Given the state of Congress, this state of affairs is likely to continue through the next several budget cycles.

Dr. D'Souza updated the Council on other notable activities at the NIH level over the last several months. The NIH Advisory Committee to the Director (ACD) Working Group on Re-

envisioning NIH-Supported Postdoctoral Training issued a Request for Information (RFI), "Re-envisioning U.S. Postdoctoral Research Training and Career Progression within the Biomedical Research Enterprise," to solicit feedback on issues, challenges, and recommendations to improve recruitment, retention, and quality of life for postdoc trainees in academic research. Responses identified multiple and complex factors, including the effects of the pandemic, lack of opportunities in academia, lengthening time to publish, cost of living, and increased opportunities in industry, among others. In response, the working group issued a series of guiding principles: postdocs should receive a living wage, with regular cost-of-living adjustments and employee-level benefits; working environments should be safe and welcoming; the postdoctoral position should be standardized and clearly defined; improved funding mechanisms are needed to support the postdoc career path; international postdocs should be compensated at the same level as their domestic counterparts; and career development and institutional accountability should be emphasized. NIH has been focused over recent years on improving opportunities for Early-Stage Investigators (ESIs), setting a goal of funding 1,100 ESIs per year. In 2022, NIH funded a recorded number of almost 1,600.

One of the lessons learned from the pandemic was the importance of community engagement to recruit diverse and representative clinical trial populations, which at NIH took the form of the Community Engagement Alliance (CEAL) Against COVID-19 Disparities. NIH has built on that work to develop NIH-wide strategies to improve clinical trial diversity, with current CEAL teams active in 21 states around the country working with partnerships in the regional and local communities. Dr. D'Souza also updated the Council on the Cancer Moonshot and National Cancer Plan, which calls for an integrative, whole-of-government approach with broad societal engagement. Another national health priority is mental health and confronting serious mental illness (SMI), which is experienced by over 14 million Americans, according to 2021 data. The same study found that SMI disproportionately affects underserved populations. Early this year, the White House released a Report on Mental Health Research Priorities and has worked to increase federal mental health-focused funding. A related national public health priority is the effort to combat the opioid crisis and rising overdose rates due to the increased prevalence of fentanyl and other potent substances. Both of these priorities are of particular concern to NIDCR; dental events are the second most common reason for opioid prescriptions, and mental illness is known to lead to increased oral health problems.

Spurred by the efforts of the National Institute of Environmental Health Sciences (NIEHS), the NIH is increasing its focus on the effects of climate change on human health. Climate change and extreme weather patterns can lead to negative health effects and increased prevalence of certain diseases, and research has shown that climate change disproportionately affects under-resourced and marginalized populations, including low-income populations, laborers, the elderly, and people living with chronic conditions. NIEHS has several funding opportunities to support research on climate change and health. NIDCR might have a role to play to explore systemic health effects of climate change.

Dr. D'Souza then discussed NIDCR's recent outreach activities. Communicating NIDCR's mission is ever more vital in the context of the increasing number of new dental schools that do not include a research component. More dental students are needed to address the shortage of dental services in certain areas, but the cost of tuition is skyrocketing and can become prohibitive. NIDCR is also working to support efforts to train, retain, and expand a diverse cadre

of DOC researchers and clinicians in order to align with public health demands. These efforts begin in-house by building a sense of community and belonging for the entire NIDCR workforce. This year, NIDCR leadership convened a gathering of representatives from its stakeholder organizations and professional societies to discuss partnerships to expand the research workforce, where it was agreed the biggest payoff would be gleaned by focusing on the K-12 stage. Dr. D'Souza was thrilled to see that the Senate included language in its Department of Health and Human Services (HHS) appropriations bill that acknowledged the importance of oral health or whole person health and called for additional NIH-funded research "to determine which oral care interventions are most effective for improving medical management and reducing the prevalence of malignant oral cancers, preventing pneumonia in hospitals, and lowering hospitalization and emergency department admission rates for non-traumatic oral conditions." This bill passed in the Senate but has not yet passed in the House.

Dr. D'Souza briefed the Council on NIH's ongoing efforts to strengthen its stewardship of clinical trials by improving the quality, relevance, and transparency of NIH-funded clinical trial research. At NIDCR, the Institute has developed online training modules and resources to help improve understanding of the clinical trial process, clarify NIDCR's expectations, and generally increase efficiencies. These enhanced training offerings for research teams will cover all stages of the clinical trial lifespan.

The rapid uptake and expansion of data science applications has become nothing less than a global societal phenomenon, and no less so in the field of biomedical research. NIH has seen this trend coming for years and published its first NIH Strategic Plan for Data Science back in 2018. NIH recently released an updated strategic plan for the next five years, which prioritizes interoperability and strengthening the data science research workforce.

Dr. D'Souza updated the Council on several of NIDCR's signature initiatives and collaborations. The Practice-Based Research Integrating Multidisciplinary Experiences in Dental Schools (PRIMED) aims to foster a culture of scientific inquiry during dental education by leveraging faculty and student mentorship opportunities and institutional collaborations in patient-oriented clinical research. PRIMED is also designed to stimulate future clinical research activities among program participants. Dr. D'Souza noted that NIDCR's outreach efforts have gone a long way in setting this program up for success. The Advancement of Head and Neck Cancer Early Detection Research (AHEAD) program aims to address the lack of effective early detection methods for head and neck cancers by developing and validating biomarkers. This program emerged from a workshop and think tank series; its first grants will be awarded this month. The Temporomandibular Disorder (TMD) Collaborative for IMproving PATient-Centered Translational Research (TMD IMPACT) is a trans-NIH initiative administered by NIDCR that has its roots in an NIH TMD working group convened in 2020. The goal of the program is to establish an interdisciplinary patient-centered research network to advance TMD basic and clinical research, research training, and translation to treatments and improved clinical care. The first TMD IMPACT awards will also be announced this month. NIDCR is also deeply involved in several programs under the umbrella of the trans-NIH Helping to End Addiction Long-term (HEAL) Initiative, including the Restoring Joint Health and Function to Reduce Pain Consortium (RE-JOIN) and the HEAL buprenorphine program, as well as the Accelerating Medicines

Partnership® in Autoimmune and Immune-Mediated Diseases (AMP® AIM) via the Sjögren's Team for Accelerating Medicines Partnership (STAMP).

Dr. D'Souza highlighted other active NIDCR and NIH grant mechanisms of note, including the Collaborative Science to Achieve Disruptive Innovations in Dental, Oral, and Craniofacial (DOC) Research, Developing Salivary Components as Therapeutics for Oral Health, and the NIH/National Science Foundation Smart Health and Biomedical Research in the Era of Artificial Intelligence and Advanced Data Science. This latter program dovetails with a new office that NIDCR is planning to establish called the Office of Data-Driven Solutions (DDS), which will serve as a liaison between the intramural and extramural communities for the management of research data. The Council will hear more about this new office at the next Council meeting. The Council will also review and vote on a series of exciting new concepts later in this meeting.

Dr. D'Souza briefly remarked on research highlights to emerge from NIDCR-funded studies in recent months, on topics including the mechanical regulation of oral epithelial barrier function, inferring early genetic progression in cancers with unobtainable premalignant disease, the impact of HIV on the oral microbiome of children in Sub-Saharan Africa, and using community engagement principles to develop effective health promotion messages to reduce consumption of sugar-sweetened beverages and food.

All of the initiatives and activities described by Dr. D'Souza are in support of NIDCR's strategic plan and the Institute is constantly evaluating the performance of its grant programs. NIDCR strives to translate what we know into what we do, with the overall mission of enhancing oral health for all. This mission has been at the forefront of NIDCR's 75th anniversary celebrations, which included a series of scientific-focused sessions and remarks by past NIDCR directors at the American Association for Dental, Oral, and Craniofacial Research (AADOCR) General Session in March. NIDCR held a 75th Anniversary Symposium on July 27th on the NIH Campus, which included remarks by Acting NIH Director (and former NIDCR Director) Dr. Lawrence Tabak, former NIH Director Dr. Francis Collins, and Dr. Laurie McCauley, Provost of the University of Michigan. On September 11th, NIDCR held a symposium to celebrate NIDCR's 25-year legacy of research to understand and treat fibrous dysplasia/McCune-Albright syndrome. The symposium was held in the NIH Clinical Center and included a keynote presentation by Nobel Laureate Dr. Brian Kobilka. On October 10-11, NIDCR will hold a Virtual Trainee Symposium titled "Celebrating NIDCR Trainees: Past, Present, and Future," with a keynote address by Nobel Laureate Dr. Ardem Patapoutian.

IV. NIBIB: ENGINEERING THE FUTURE OF HEALTH

Dr. D'Souza introduced Dr. Bruce Tromberg, Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB), to deliver his remarks on the work of his Institute and avenues for future collaboration between NIBIB and NIDCR.

Dr. Tromberg first provided a short history of NIBIB, which was created in 2000 by an act of Congress. After each attempting individually to lobby for an NIH institute for their field,

the imaging and biomedical engineering communities joined forces to advocate for their common goal. Over the 20-plus years of NIBIB's existence, the country has seen a rapid growth of biomedical engineering as a discipline and in the number of biomedical engineering-related academic programs. This period has also seen a shift in the larger engineering community to place human health at the forefront and an accompanying increase in focus on bioengineering in medical schools. NIBIB has played an important part in this paradigm shift, but so have nongovernmental organizations such as the Whitaker Foundation. NIBIB focuses on emerging technologies and innovation in the fields of imaging technologies, therapeutic systems, engineered biology, and sensors and point-of-care tools. Data science, modeling, and computation lie at the center of all these activities at the Institute. Dr. Tromberg has observed an increased emphasis on bioengineering at NIH in terms of funding: approximately 14% of the FY 2022 NIH budget was devoted to bioengineering-related programs. Dr. Tromberg noted that NIBIB is unique at NIH in that it has no specific disease area focus, and NIBIB-funded research does not require a biological hypothesis.

There is significant shared interest between NIBIB and NIDCR. Dr. Tromberg presented a graph that showed, over the past decade, that NIDCR has devoted approximately 20% of its funding to bioengineering-related initiatives, which ranks 5th amongst NIH ICs. Over that period, NIDCR and NIBIB have co-funded 173 projects together, with NIDCR serving as administrative IC for approximately 80% of the projects. Around 60% of these projects have been Research Project Grants (RPGs) and approximately a quarter have been Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs.

Dr. Tromberg provided an overview of NIBIB's signature programs and its pandemic response initiatives. Examples of NIBIB's core programs include its U01 Bioengineering Partnerships with Industry, the U54 Point-of-Care Technologies Research Network (POCTRN), and its P41 Bioimaging and Bioengineering Centers. NIBIB's pandemic response fell into three domains: artificial intelligence (AI) and imaging, in vitro diagnostics, and digital health platforms. Early in the pandemic, prior to the availability of point-of-care diagnostics, there was an urgent need to handle large amounts of imaging data in order to properly diagnose and assess patients and monitor therapies. To help address this need, NIBIB created the Medical Imaging and Data Resource Center (MIDRC), which harnesses machine learning (ML) innovation for the rapid and flexible collection, analysis, and dissemination of imaging and associated clinical data. Since its creation, MIDRC has released over 100,000 medical images, developed effective AI/ML models, and has over 400 collaborative users. MIDRC uses crowdsourcing practices to generate unique database algorithms and includes a pathway for validation of the algorithms with the FDA. MIDRC is also working to prioritize interoperability of its data sets, which has been achieved with the National COVID Cohort Collaborative and BioData Catalyst. Dr. Tromberg noted that MIDRC also provides a comprehensive AI/ML bias assessment tool for researchers.

Another major NIBIB pandemic response initiative is the Rapid Acceleration of Diagnostics Tech (RADx Tech) which aims to rapidly increase the availability of point-of-care and over-the-counter COVID-19 diagnostics. In April 2020, NIBIB received \$500M for this effort, which at the time was over \$100M larger than the entire annual budget of the Institute. The ultimate goal for the project is for point-of-care testing to take the place of laboratory testing for diagnostic testing. POCTRN ended up being the recipient for a large amount of funding for

this effort, and the component institutions agreed to shift the entirety of their work towards COVID-19. POCTRN expanded greatly during this time period, adding a validation core, a clinical studies core, and a deployment core. RADx Tech created a program called the Innovation Funnel to process and evaluate the large number of applications it received and established the Independent Test Assessment Program (ITAP) with the FDA to facilitate more efficient regulatory evaluation and approval. Since its inception, RADx Tech has received over 1,000 applications, of which 50 have gone on to receive Phase 2 funding and increased total testing capacity to almost 8 billion. In order to assist efforts to record and track the results of over-the-counter testing, NIBIB developed the RADx Mobile Application Reporting Standards (MARS), which support the distributing of test results into public-facing digital health platforms, such as MakeMyTestCount.org. Dr. Tromberg also discussed NIBIB's efforts to evaluate the efficacy of antigen tests in order to enhance FDA's evaluation of rapid tests for COVID-19 for regulatory authorization. These efforts significantly shortened the time to authorization, which is vital in the context of pandemic surges. NIBIB is now extending the RADx model to a number of its non-pandemic programs, including its neurotechnologies projects on which NIDCR is a partner IC.

Along these lines, Dr. D'Souza said that salivary diagnostics is another field ripe for partnership for the two Institutes. Dr. Tromberg agreed and added that he sees several other avenues by which NIDCR and NIBIB can work together using the design-build-test-deploy model and the regulatory know-how that NIBIB has learned through the RADx program. Other areas of common interest include biomaterials, tissue engineering, regenerative medicine, and medical devices.

Dr. Tromberg also touched on the activities of NIBIB's intramural program. In March, NIBIB launched the Biomedical Engineering and Technology Acceleration (BETA) Center, which is an NIH-wide center for technology-driven interdisciplinary research, training, and clinical translation. Led by Dr. Manu Platt, previously of Georgia Tech, the Center ultimately aims to accelerate the development, validation, and dissemination of high-impact biomedical technologies and expand partnerships with the biomedical engineering and technology community. Dr. Tromberg added that the BETA Center will have significant focuses on training and retention, provide a makerspace that will include additive engineering tools, and he ultimately hopes the Center will serve as a hub to attract engineers and technology developers who might not have previously considered NIH as a destination.

Discussion

Dr. Paul Krebsbach said the field of immunology is another area where NIDCR and NIBIB could form impactful collaborations. Dr. Tromberg concurred. Possible areas for partnership could be in the standardization of microphysiological systems that emulate particular subsystems of the immune system. Dr. Janice Lee, NIDCR Clinical Director, said the NIDCR Dental Clinic could have many synergies with the BETA Center makerspace and asked Dr. Tromberg if NIBIB had selected a location for it yet. Dr. Tromberg said they have procured space in the basement of the Clinical Center for the primary interactive design and collaborative location, while the additive engineering "garage" space will be located on the top floor of Building 13.

V. DATA SCIENCE STRATEGY WORKING GROUP UPDATE

Dr. King invited Council member Dr. Visel, co-chair of the Advisory Council's Data Science Strategy Working Group, to provide his update on the Working Group's recent activities.

Dr. Visel reminded the Council that the Data Science Strategy Working Group has been charged with developing recommendations on the development of an NIDCR data science strategic plan to enable the Institute to leverage data science to advance the full translational spectrum of DOC research, reducing health disparities, and improving overall health. Dr. Visel noted that data science touches on all of NIDCR's strategic pillars, and that another purpose of this effort is to help align the Institute with the NIH Strategic Plan for Data Science. Dr. Visel reviewed the Working Group membership and noted that members have expertise across the translational spectrum.

Since its establishment a year ago, the Working Group has held a series of meetings, issued an RFI to solicit feedback from the community, and has held a series of listening sessions to gather additional input from the stakeholder community on how individuals from across the translational research spectrum interact with data. As the Working Group first met, it conducted an initial ecosystem mapping effort and identified five preliminary observations: the complexity and heterogeneity of data resources and repositories, fuzzy boundaries between systems, lack of connectivity between resources and systems, lack of sustained and dedicated financial support, and hurdles for compliance with FAIR (Findable, Accessible, Interoperable, and Reusable) data principles.

The Working Group's listening sessions took the form of sessions with 10-20 members of the NIDCR community, with focused questions for data generators, data users, individuals with experience sharing data, and broader questions about data standards. The sessions highlighted the fact that DOC researchers produce a large and diverse range of data types, that the size and complexity of data can present challenges, concerns regarding the persistence of stored data over time, and underscored the need for further standardization and alignment with the NIH-wide data ecosystem, among other issues. The RFI was issued in June and remains open. Dr. Visel encouraged members of the community to submit responses. The Working Group will take in all of these responses as it prepares its final report to the Council. Dr. Visel reviewed an outline for the report, which will include background on the need for an NIDCR data science strategy, the current state of the DOC data ecosystem, challenges and opportunities, data science in the context of health disparities, and specific recommendations.

Discussion

Dr. Visel discussed with the Council the importance of standardization and integration beyond the borders of the NIH, which will involve the use of common data standards and designing new systems with interoperability in mind. Funding agencies can play an important role in the adoption of new standards. Dr. Moron-Concepcion raised the topic of NIH's new data sharing and management policy and said additional resources to assist applicants in complying

with the new policy would be helpful. Dr. Nor emphasized the importance of developing a pipeline of data scientists in the DOC research field.

VI. ORAL HEALTH RESEARCH WORKFORCE WORKING GROUP UPDATE

Dr. King invited Dr. Dana Graves, co-chair of the Oral Health Research Workforce Working Group, to deliver the update on the working group's activities.

Dr. Graves reminded the Council of the Working Group's charge, which is to "develop and recommend evidence-based approaches to sustainably recruit, train, and retain researchers who have knowledge to build a diverse DOC scientist and clinician-scientist research workforce." He briefly discussed the history and findings of several workforce-related working groups in 2012, 2014, and an evaluation of the NIGMS National Research Service Awards (NRSA) T32 grant program in 2018. The 2012 Biomedical Research Workforce Working Group's recommendations focused on broadening career opportunities, shortening the time it takes to train scientists, and enriching and diversifying postdoctoral training. The working group commented on the lack of data for evaluating training program outcomes and the need to increase diversity. The 2014 Physician-Scientist Workforce Working Group recommended an increase in individual training grants, programs to support new investigators, and tools to track physician-scientist career development, among other recommendations. The 2018 NIGMS reporter highlighted the need to assess financial challenges for clinician-scientists and to define goals and metrics for clinically-focused research training.

The current Working Group has issued an RFI to solicit community input, conducted an analysis of current NIDCR programs, convened listening sessions and panel discussions with key stakeholders, and discussed potential collaborations between NIDCR and DOC professional societies and foundations. The Working Group has identified some key problems, including lack of mentoring during the transition to independence, scientific isolation, culture and diversity, career opportunities, and financial challenges. To address the mentoring issue, professional societies have agreed to encourage their members to serve as mentors during this key phase for clinician-scientists. NIDCR could also design multi-PI grants to partner established researchers with ESIs. To confront isolation, NIDCR and the professional societies could convene local, regional, and national satellite meetings for ESIs and trainees to encourage networking and foster peer relationships. Professional societies and NIDCR could likewise partner to enhance outreach to improve the diversity of the DOC research workforce, and Dr. Graves noted that programs of this type are already underway. The Working Group has also heard feedback about the lack of opportunities for dual degree clinician-scientists. NIDCR could play a role in matching trainees with existing programs in academia and in industry, and could work with the larger stakeholder community to encourage hybrid academic positions that allow for teaching and research. The Working Group also identified interests among stakeholders to expand loan repayment programs to help mitigate the financial burdens associated with advanced dental education. The Working Group believes that there is continued need for a comprehensive assessment of factors associated with training program success, including both quantitative and qualitative measures. Overall, the Working Group has found the professional societies and foundations to be enthusiastically in support of increased collaboration on these topics.

The Working Group intends to submit its recommendations to the Council in November.

Discussion

Dr. Moron-Concepcion cautioned the Working Group to be wary that researchers may feel discouraged to participate in multi-PI grants due to tenure requirements. Dr. Graves said the Working Group is aware of that concern. He believes academia is shifting towards a more pro-collaboration perspective in this regard. Dr. Graves believes participation in collaborative research projects can go a long way towards helping ESIs prepare for their independent careers, as opposed to the traditional "sink or swim" approach. Additionally, participation in a multi-PI does not preclude that investigator from seeking an R01 grant later on.

On the topic of lack of career opportunities for clinician-scientists, Dr. Krebsbach observed that fewer than 20 of the dental schools in the country are interested in hiring this kind of faculty, which constrains the market. Dr. D'Souza said NIDCR is aware of this situation and working to find ways to move the needle in the right direction is a priority for the Institute. NIDCR's T32 program has been successful in creating PhD specialists, but these individuals often find themselves in positions where research time is highly limited because their skills are so valuable in the clinic. Dr. Lee emphasized the importance of finding and developing collaborative communities that support and prioritize research; individual investigators cannot develop those connections alone. Dr. Nor said this topic will be on the agenda of AADOCR's Dental, Oral, and Craniofacial Research Summit that is being held in Bethesda, Maryland in October.

VII. CONCEPT CLEARANCES

Dr. King stated that NIDCR is required to document the clearance of concepts by presenting the purpose, scope, and objectives of proposed concepts for research initiatives to the Council in a public forum for the Council's review, discussion, and approval, and for public comment. Concepts approved by the Council are published on the NIDCR website (future research initiatives). NIDCR staff presented seven concepts, and designated Council members led the discussion, as summarized below.

Organs-on-a-Chip in Dental, Oral, and Craniofacial Research (DOC-OoCs)

Dr. Preethi Chander, Program Officer, Integrative Biology and Infectious Diseases Branch, and Director, Salivary Biology and Immunology Program, presented the concept. The goal of the concept is to advance the validation of organ-on-a-chip (OoCs) for disease modeling and preclinical efficacy studies, complement and reduce animal testing, and accelerate the use of 3D microfluidic systems in clinical trials. Dr. Chander noted several gaps and opportunities addressed by the concept, including the inadequacy of 2D cell culture models, variability in preclinical animal models, the need for more human-relevant testing models, and leveraging NIH and trans-agency OoC projects already underway. Dr. Chander noted some examples of how OoCs are being used in other areas of biomedical research and in DOC research, such as the

tooth-on-a-chip platform. Going forward, validation of OoCs that are under development as functional models that better capture the dynamic nature of the DOC environment, interfaces of the oral environment, and inter-organ crosstalk of DOC tissues in the context of the whole body, are avenues for further of research. This concept could also be levered to advance the preclinical foundation for use of OoCs to inform clinical trial design.

The Council's lead discussants for the concept were Drs. Collier and DiPietro. Dr. Collier expressed strong support for the concept, noting the need to develop more non-animal models that better mimic the human context. OoCs also provide potential for the development of patient-specific models, the ability to accelerate the screening process for therapeutics, and ultimately reduce the need for animal models entirely. Dr. DiPietro agreed, adding that OoCs also have the potential to model normal tissue which can be used to assess toxicity, and overall could help reduce the cost of clinical trials.

The Council unanimously approved the concept.

Bacteriophage Therapy: Tipping the Balance to Oral Health

Dr. Amanda Melillo, Chief, Integrative Biology and Infectious Diseases Branch, and Director, Oral Opportunistic Pathogens and Viral Disease Program, presented the concept. The goal of the concept is "to encourage research to better understand bacteriophage biology in the oral cavity to support eventual development of therapeutics." Bacteriophages are viruses that can neutralize or kill specific bacteria. Dr. Melillo provided a brief history of bacteriophage research, which dates back to the early 20th century, during which phage therapy was overshadowed by the prominence of antibiotic treatments, especially in the U.S. However, interest in bacteriophage therapy is reemerging in recent years in light of the growing problem of antibiotic resistance. Many oral cavity bacteria bacteriophages have been identified, but their role in the bacterial population is poorly understood, which this concept hopes to address. The concept might also support research into the antibacterial anti-biofilm properties of bacteriophages, their effects on bacterial virulence, and the therapeutic potential of bacteriophages, among other areas of interest.

The Council's lead discussants for the concept were Drs. DiPietro and Nor. Dr. DiPietro said she believes the concept is timely and important. Given the lack of basic knowledge, she advised the Institute to emphasize the need for fundamental understanding of the biology of bacteriophages, especially in the context of the oral cavity, before considering their therapeutic uses. Dr. Nor concurred with Dr. DiPietro's comments.

The Council unanimously approved the concept.

Advancing HIV/AIDS and Oral Health Research

Dr. Hongen Yin, Director, HIV/AIDS and Oral Health Research Program, presented the concept. The goal of the concept is to support "innovative and multidisciplinary basic, translational, and clinical research on HIV/AIDS that is relevant to DOC health." Despite significant therapeutic advances, HIV/AIDS remains one of the most serious global public health challenges, and DOC tissues are a prominent source of HIV-related comorbidities, coinfections,

and complications (CCCs). This concept hopes to encourage research that advances understanding of the mechanisms and progression of oral HIV transmission and CCCs, and solicit studies that attempt to translate research findings into clinical applications. Potential studies could identify biomarkers for HIV-related oral coinfection, develop strategies to prevent and treat HIV oral transmission and/or CCCs, and explore the biologic mechanisms of transmission and latency within the oropharyngeal tissue, among other topics. Dr. Yin noted that this concept aligns with the NIDCR Strategic Plan and the NIH Strategic Plan for HIV and HIV-Related Research.

The Council's lead discussants for the concept were Drs. Krebsbach and Collier. Dr. Collier expressed enthusiastic support for the concept and said that the oral transmission route is understudied. He noted that the pre-exposure prophylaxis (PrEP) does not prevent oral transmission and oral health is important to protect against opportunistic infection. This concept also helps confront known health disparities in HIV/AIDS. Dr. Krebsbach expressed support for the concept and suggested that NIDCR consider more explicitly including research on the social determinants of health in the context of HIV/AIDS as a topic of interest. Dr. D'Souza opined that that topic might merit its own concept given its complexity.

The Council unanimously approved the concept.

Determining the Tri-directional Relationship Between Oral Health, Nutrition, and Comprehensive Health

Dr. Margaret Grisius, Director, Oral and Comprehensive Health Program and Clinical Technologies Research Program, presented the concept. The goal of the concept is "to better understand the mechanisms of the tri-directional relationship between nutrition, systemic health, and DOC health and to develop nutritional interventions for the dental setting." It is understood that diet-related metabolic and cardiovascular diseases are associated with poor health outcomes, that oral health impacts dietary intake choices, and that sweetened beverages increase childhood caries and tooth loss. It is also known that rural, minority, and lower socioeconomic status populations have a higher incidence of oral disease, which influences food intake and nutrition. Further research is needed to enhance scientific knowledge regarding the interplay of oral health, nutrition and comprehensive health. Knowledge gained may identify preventative, diagnostic, and therapeutic interventions to improve oral, nutritional, and comprehensive health across the lifespan. Areas of interest under this concept include research on oral health conditions that impact the ability to maintain healthy diets, dietary influences affecting comprehensive health through effects on oral microbiome, and the feasibility of medical, behavioral, pharmaceutical, and/or community-level interventions, among other topics. Dr. Grisius noted that this concept aligns with the White House's National Strategy on Hunger, Nutrition, and Health.

The Council's lead discussants for the concept were Drs. Slep and Dickinson. Dr. Dickinson was not in attendance and his comments were reported by Dr. Slep on his behalf. Dr. Dickinson expressed support for the concept and expressed the opinion that the nutritional and behavioral aspects of diet are too often separated from the dental clinical setting. Dr. Slep was also supportive of the concept and believes this more holistic approach to oral and comprehensive health is long overdue.

The Council unanimously approved the concept.

Community-Based Participatory Research Consortium: Advancing Data and Practice Transformation (ADAPT) for Caries Equity

Dr. Hiroko Iida, Director, Oral Health Disparities and Inequities Research Program, presented the concept. The goal of the concept is to "accelerate progress toward reducing dental caries disparities and systemic inequities through collaborative community-based intervention projects and data mining." The concept calls for community-based participatory research (CBPR) approaches towards the design, implementation, and evaluation of population-based intervention strategies. ADAPT will support two research hubs and a research consortium that will leverage NIH's Science Collaborative for Health disparities and Artificial intelligence bias Reduction (ScHARe) data platform. As has been alluded to, there has been halting progress towards reducing oral health-related disparities. The concept will encourage meaningful community engagement, recruitment of populations historically underrepresented in clinical research, and prioritize data sharing and the training of members of the community as part of the research teams. The concept was also informed by discussions that took place at NIDCR's Oral Health Disparities and Inequities Research Think Tank earlier this year. Areas of interest include interventions to address structural discrimination and/or bias, testing of implementation strategies for integrated care, and the testing of evidence-based, culturally-attuned strategies for addressing multi-level common risk factors that influence negative oral health outcomes.

The Council's lead discussants for the concept were Drs. Slep and Dickinson. Dr. Slep again reported Dr. Dickinson's comments in absentia. Both Council members expressed support for the proposal. Dr. Slep said the concept is very ambitious and will likely be challenging to manage. For example, the broad scope of areas of interest might present hurdles to the use of common data elements. Nevertheless, Dr. Slep is excited by the concept and hopes it will move the needle on caries disparities. Dr. Iida spoke with the Council members about the importance of identifying and monitoring metrics by which to assess the effectiveness and impact of community engagement strategies.

The Council unanimously approved the concept.

Accelerating Product Excellence in Innovation and for Clinical Adoption (APEX)

Dr. Lillian Shum, Director, Division of Extramural Research, presented the concept. The objective of the concept is "to accelerate preclinical product development through innovation, commercialization, and clinical adoption, with potential extension to diagnostic products or therapeutics beyond tissue regeneration, and/or products outside the DOC complex." APEX is a follow-on concept to the Dental, Oral, and Craniofacial Tissue Regeneration Consortium (DOCTRC), which supports late-stage preclinical new drug/device studies by engaging scientific, industrial, and regulatory expertise to ultimately facilitate clinical trials for the most promising tissue regeneration technologies. DOCTRC has funded 40 projects, of which 20 remain active; 65% of the current projects have had interactions with the FDA to-date and 95% of the projects have resulted in new patents or pending applications. Specific areas of interest for the APEX

concept include interdisciplinary expertise and core services, systems beyond the DOC complex, development of affordable products that can be used as point-of-care diagnostics, and mentoring, training, and career development opportunities.

The Council's lead discussants for the concept were Drs. DiPietro and Ebetino. Dr. DiPietro expressed enthusiasm for this concept and said that it fills the need to support the advancement of projects from academia to commercialization. She cautioned that successfully bringing products to market is difficult, with low success rates, and failure should be expected. She suggested that NIDCR encourage applicants to seek support partners in their own communities who have expertise in commercialization. She also noted that commercialization can be extremely expensive and additional investors should be sought where possible. Dr. Ebetino was also supportive and commented that concepts like this that integrate basic and translational science can help fully realize the benefits of NIH investments.

The Council unanimously approved the concept.

Reissuance: NIDCR Mentoring Network to Support a Diverse Dental, Oral, and Craniofacial Research Workforce

Dr. Anissa Brown, Chief, Research Training and Career Development Branch, presented the concept reissuance. The goal of the concept is to "facilitate and provide structured interactions among investigators (mentors) and postdoctoral fellows and junior faculty (mentees) who are underrepresented in the biomedical, behavioral, and social sciences to enhance mentees' grantsmanship, professional development, and successful pursuit of DOC research careers." Ultimately, the NIDCR Mentoring Network aims to expand and enhance the DOC research workforce while addressing the unique career development needs of ESIs, in alignment with the priorities of the NIDCR Strategic Plan. Dr. Brown discussed how this concept was first designed in response to NIH-wide initiatives to advance diversity in the biomedical research workforce to foster increased scientific innovation and increase the quality of, and access to, clinical research. The first round of this concept resulted in the AAODCR Mentoring Network to Support a Diverse Dental, Oral, and Craniofacial Research Workforce of the Future (MIND the Future) grant program. The first three cohorts included 25 mentors and 42 mentees. Eighty-six percent of the mentees were female and 30% identified as being from underrepresented minority background. Thus far, 17 mentees have gone on to receive subsequent NIH awards, 12 of whom received Research Project Grants (RPGs).

The Council's lead discussants for the concept were Drs. Visel and Krebsbach. Dr. Visel expressed strong support for the concept renewal, and noted that the first cycle was highly successful and continues to align with NIDCR's Strategic Plan. He suggested that NIDCR consider incorporating outreach to minority-serving institutions, Historically Black Colleges and Universities, and institutions in geographically underrepresented locations. Dr. Krebsbach also expressed support for the concept. He recommended that NIDCR look into including an institution-focused aspect so that home institutions develop the support mechanisms to foster mentoring communities, rather than relying solely on NIH funding.

The Council unanimously approved the concept.

VIII. NOVEL PATHWAYS IN PAIN MODULATION

Dr. King invited Dr. Yuanyuan (Kevin) Liu, Stadtman Tenure Track Investigator, Division of Intramural Research, to deliver the presentation on his laboratory's work on pain modulation and the underlying mechanisms by which the brain controls the perception of pain.

Dr. Liu began by briefly describing the descending pain modulation pathway, noting the important role of the rostral ventromedial medulla within the brainstem. Dr. Liu and his colleagues wanted to explore whether descending neurons from other regions of the brain, such as the cortex, can play a role in the perception of pain. They found that a subset of corticospinal tract (CST) neurons originating in the primary and secondary somatosensory cortex directly innervate the spinal dorsal horn via CST axons. Dr. Liu discussed further experiments in mice that found that reducing neuronal activity or transecting the CST selectively impairs behavioral responses to light touch without altering responses to noxious stimuli.

Dr. Liu's team also found that such manipulation can significantly reduce the symptoms of tactile allodynia, which is a pathological condition in which normally innocuous touches can cause pain and a prominent feature of peripheral neuropathic pain with limited treatments. Dr. Liu described how tactile stimulation activates somatosensory corticospinal neurons, which in turn facilitate light-touch-evoked activity of interneurons in the deep dorsal horn. The touch-driven feed-forward spinal-cortical-spinal sensitization loop described in these experiments indicates the direct cortical modulation of normal and pathological tactile sensory processing in the spinal cord, suggesting opportunities for new treatments for neuropathic pain. These experiments are detailed in a 2018 article in *Nature*, "Touch and tactile neuropathic pain sensitivity are set by corticospinal projections."

Dr. Liu and colleagues' more recent work on how the mind controls pain perception has focused on the phenomenon of sound-induced analgesia, culminating in a 2022 article in *Science*, "Sound induces analgesia through corticothalamic circuits." This work builds on previous studies that showed that music can promote relaxation and directly suppress pain. In their experiments in mice models, Dr. Liu's team found that sound-induced analgesia depends on the signal-to-noise (SNR) ratio, particularly a low SNR, rather than music or consonant sound *per se*. Dr. Liu presented findings that indicate that low SNR sound inhibits activity of certain glutamatergic auditory cortex neurons to relieve pain. The question remains how the auditory cortex is involved in somatosensory analgesia. Additional research suggests that the thalamus might function as a bridge for audio-somatosensory processing. Dr. Liu's team found that low-SNR sound inhibits the activity of thalamic posterior nucleus (Po) neurons and that optogenetic inhibition of the auditory cortex-Po circuit decreases Po neuronal activity and induces analgesia. Conversely, optogenetic activation of the auditory cortex-Po circuit blocks sound-induced analgesia.

Discussion

Dr. Moron-Concepcion noted the nascent use of virtual reality modalities for pain management, which includes both auditory and visual aspects. He asked whether similar mechanisms could exist for the visual pathway. Dr. Liu said that was likely given the thalamus' role as a sensory information hub.

IX. ESSENTIAL ROLES OF SKELETAL STEM CELLS IN DEVELOPMENT, DISEASES, AND REGENERATION

Dr. King welcomed Noriaki Ono, Associate Professor, UTHealth School of Dentistry, to deliver his presentation on his work on skeletal stem cells. Dr. Ono opened his remarks by thanking NIDCR for helping foster and supporting his unique career trajectory. He received his DDS and PhD in orthodontics in Japan, and then moved to the U.S. to begin a research career in bone biology and eventually received the NIDCR Dual Degree Dentist Scientist Pathway to Independence Award (K99/R00). The award ultimately helped Dr. Ono achieve a tenure-track position at the University of Michigan, where he conducted his first R01 study, before he was recruited to UTHealth in 2021.

Dr. Ono's research is primarily focused on skeletal stem cells (SSCs), which are bone-making stem cells that regulate bone formation in both health and disease. SSCs hold significant potential for cell-based therapies that apply stem cells for augmented regeneration, which would likely involve technologies such as tissue engineering and smart materials, etc. SSCs might also be leveraged via autotherapies that activate native stem cells for inherent regeneration. This would likely require the development of specific stem cells/cell lineages. However, in order to achieve this potential, better knowledge is needed about how SSCs form and develop.

Dr. Ono described how his team performed single-cell RNA-sequencing (scRNA-seq) analyses of the chondrocyte-perichondrial cell lineage in mice to discover the putative cellular origins of the fetal cartilage. This work is detailed in a 2022 *Nature Communications* article titled, "The fate of early perichondrial cells in developing bones." They found that *Dlx5*⁺ early perichondrial cells directly regulate the formation of the marrow space, whereas fibroblast growth factor receptor 3 (*Fgfr3*)-positive fetal chondrocytes regulate bone formation within the marrow space via chondrocyte-to-osteoblast transition, among other findings.

Subsequent research resulted in the publication of another article in *Nature Communications* this year, titled "Bone marrow endosteal stem cells dictate active osteogenesis and aggressive tumorigenesis." These experiments showed that bone marrow endosteal SSCs are defined by *Fgfr3* and osteoblast-chondrocyte transitional (OCT) identities with some characteristics of bone osteoblasts and chondrocytes. They also showed that loss of p53 tumor suppressor through unregulated self-renewal and aberrant osteogenic fates can cause *Fgfr3*⁺ endosteal stromal cells to give rise to aggressive osteosarcoma-like lesions. *Fgfr3*⁺ endosteal SSCs are abundant in young bone marrow and provide a robust source of osteoblasts, contributing to both normal and aberrant osteogenesis. Dr. Ono believes endosteal SSCs could be a good target for autotherapies down the road.

Discussion

Dr. D'Souza asked Dr. Ono to comment on how these findings relate to what is known about intramembranous ossification and the Wnt pathway. Dr. Ono said many cells in the intramembranous pathway carry chondrocyte-like identities and expression patterns. It is not fully understood why that is. Dr. Ono believes cell identity is fuzzy between the intramembranous and endochondral processes.

CLOSED SESSION

This portion of the meeting was closed to the public in accordance with the determination that it was concerned with matters exempt from mandatory disclosure under sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., and Section 1009(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. §§ 1001-1014).

X. REVIEW OF APPLICATIONS

National Institute of Dental & Craniofacial Research
Council Applications Recommended for Further Consideration

Total	Requested	Approved
Number	530	329
Dollars	\$ 216,104,014	\$ 142,842,698

XI. ADJOURNMENT

CERTIFICATION

I hereby certify that the foregoing minutes are accurate and complete.

Dr. Rena D'Souza
Chairperson
National Advisory Dental and
Craniofacial Research Council

Dr. Lynn King
Executive Secretary
National Advisory Dental and
Craniofacial Research Council

ATTACHMENTS

- I. Roster of Council Members