

National Institute of Dental and Craniofacial Research

National Advisory Dental and
Craniofacial Research Council

Minutes of Meeting
May 16, 2023

Via Videoconference

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

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NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

MINUTES OF THE
NATIONAL ADVISORY DENTAL AND CRANIOFACIAL RESEARCH COUNCIL

May 16, 2023

The 233rd meeting of the National Advisory Dental and Craniofacial Research Council (NADCRC) was convened on May 16, 2023, at 10:00 a.m., via videoconference. The meeting was open to the public from 10:00 a.m. until 2:50 p.m.; it was followed by the closed session for Council business and consideration of grant applications from 3:15 p.m. until adjournment at 4:05 p.m. Dr. Rena D'Souza presided as Chair.

OPEN SESSION

Members Present

Dr. Joel H. Collier
Dr. Frank Ebetino
Dr. Raul I. Garcia
Dr. Jose Moron-Concepcion, *ad hoc member*
Dr. Lee A. Niswander
Dr. Jacques Nor
Dr. Wenyuan Shi
Dr. Amy Smith Slep
Dr. Axel Visel

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. Lillian Shum, Director, Division of Extramural Research (DER)
Dr. Matthew Hoffman, NIDCR Scientific Director, Division of Intramural Research (DIR)
Dr. Marian Young, DIR, Deputy Scientific Director, DIR
Dr. Janice Lee, Clinical Director, DIR
Dr. Sharon Jackson, Deputy Clinical Director, DIR
Mr. John Prue, OD, Director, Office of Information Technology (OIT)

Dr. Shaun Abrams, DIR
Ms. Alexandria Alfarano, DER, Center for Clinical Research (CCR)
Dr. Lorena Baccaglioni, DER, CCR
Ms. Laurie Brenchley, DIR
Dr. Anissa Brown, DEA, Chief, Research Training and Career Development Branch (RTCDB)
Dr. Thomas Bugge, DIR

Dr. Christopher Campbell, DEA, Scientific Review Branch (SRB)
Mr. Gilberto Carmona, DIR
Ms. Dametreea Carr, OD, Office of Clinical Trials Operations & Management (OCTOM)
Mr. Daniel Carter, OD, OIT
Dr. Preethi Chander, DER, Integrative Biology and Infectious Diseases Branch (IBIDB)
Dr. Jingshan Chen, DEA, SRB
Dr. Wanjun Chen, DIR,
Dr. Zhong Chen, DER, IBIDB
Dr. Aiwu Cheng, DEA, SRB
Ms. Jennifer Chi, OD, Deputy Director, OCTOM
Ms. Alicia Chou, DER, Translational Genomics Research Branch (TGRB)
Mr. Kevin Chu, OD, OIT
Dr. Michelle Cortes, DER, IBIDB
Mr. Jimmy Do, OD, Acting Director, Office of Administrative Management (OAM)
Dr. Olga Epifano, DEA, OD
Dr. Dena Fischer, DER, Chief, CCR
Dr. Katarzyna Futrega, DIR
Dr. Rachel Gafni, DIR
Dr. Melissa Ghim, DER, IBIDB
Dr. Ioana Ghita, DIR
Mr. Harry Grant, DIR
Dr. Margaret Grisius, DER, CCR
Mr. Joel Guzman, DER
Dr. Ashleigh Hanner, DIR
Ms. April Harrison, DEA, GMB,
Mr. Gabriel Hidalgo, DEA, GMB, Acting Chief CGMO
Dr. Hiroko Iida, DER, CCR
Dr. Szalayova Ildiko, DIR
Dr. Dara Kessler, OD
Dr. Leila Khaki, DER, Behavioral and Social Sciences Research Branch (BSSRB)
Dr. Zohreh Khavandgar, DIR
Dr. Wendy Knosp, OD, Office of Science Policy & Analysis (OSPA)
Dr. Jamie Kugler, DIR
Dr. Ashok Kulkarni, DIR
Dr. Shuang Li, DER, OD
Dr. Orlando Lopez, DER, IBIDB
Ms. Jayne Lura-Brown, DER, ODHoep
Ms. Alisa Machalek, OD, Office of Communication & Health Education (OCHE)
Dr. Tamara McNealy, DER, IBIDB
Ms. Susan Medve, DEA, GMB
Dr. Yun Mei, DEA, SRB
Dr. Amanda Melillo, DER, Chief, IBIDB
Dr. Eva Mezey, DIR
Ms. Mable Nee, OD, Financial Management Branch (FMB)
Mr. Paul Newgen, DEA, GMB
Ms. Michelle Nguyen, OD, OAM

Ms. Anna Nicholson, OD, OCTOM
Dr. Thomas O'Farrell, DEA, SRB
Dr. Vaishali Patel, DIR, Detailee SRB
Ms. Eileen Pelayo, DIR
Ms. Lisa Peng, OD, OIT
Ms. Debbie Pettitt, DEA, GMB
Mr. Ben Rassuli, OD, OIT
Dr. Melissa Riddle, DER, Chief, BSSRB
Dr. Rachel Sare, DEA, RTCDB
Dr. Yasaman Shirazi, DEA, Chief, SRB
Ms. Ashley Smith, OD, OIT
Dr. Kathryn Stein, DER, TGRB
Dr. Roman Szabo, DIR
Dr. Shoba Thirumangalathu, DEA, RTCDB
Dr. Jason Wan, DER, IBIDB
Dr. Lu Wang, DER, Chief, TGRB
Dr. Blake Warner, DIR
Dr. Achim Werner, DIR
Dr. Hongen Yin, DER, CCR

National Institutes of Health

Dr. Patricia Flatley Brennan, Director, National Library of Medicine

Guests

Dr. Luisa DiPietro, University of Illinois at Chicago College of Dentistry
Mr. Matthew Miller, Neal R. Gross & Co.

NIH Videocast

Views <https://videocast.nih.gov/watch=49212>
Total views: 219 (162 Live, 57 On-demand) as of 6/22/2023

I. WELCOME

Dr. Lynn King, Director of Division of Extramural Activities (DEA) and Advisory Council Executive Secretary, called the open session of the 233rd Advisory Council meeting to order at 10:00 a.m. and briefly reviewed the logistics for the virtual meeting. Members of the public have until May 31st to submit comments and questions via email at NIDCRCouncilMail@nidcr.nih.gov.

II. APPROVAL OF MINUTES FROM PREVIOUS MEETING

Dr. King asked Advisory Council members if there were corrections or comments on the minutes of the January 25, 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. 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 began her remarks by announcing that Council members Drs. Raul Garcia, Lee Niswander, and Wenyuan Shi will be retiring from the Council following the May meeting. She thanked them for the exemplary service, noting their important work reviewing NIDCR concepts and Requests for Applications (RFAs) during a critical moment in the Institute's history. Dr. D'Souza also announced that four new members have officially been appointed and will be beginning their terms soon: Drs. Terry Dickinson, Luisa DiPietro, Jose Moron-Concepcion, and Paul Krebsbach. Dr. Moron-Concepcion will be serving as an ad hoc member of the Council for the May meeting before beginning his formal term.

Dr. D'Souza reviewed the agenda for the day's meeting and said that the theme for the day is "creating the future we all seek". To better appreciate where the field is today as NIDCR's 75th anniversary approaches, Dr. Souza presented an overview of the history and the evolution of the oral health sciences over the decades. Dentistry can trace its origins to services provided by barbers and blacksmiths in centuries past. In the early 20th century, efforts by leading individuals, such as William J. Gies, to put science at the forefront of the field led to dentistry being accepted as an honorable member of the health professions. The International Association for Dental Research (IADR) was founded in 1920, and the National Institute of Dental Research (NIDR), as NIDCR was originally called, was established in 1948. Dr. D'Souza briefly mentioned notable scientific advancements in the field that occurred in the 19th century and early 20th century, such as Miller Willoughby's discovery that the formation of caries is a bacterial process and Frederick McKay and G.V. Black's early efforts in fluoride research. Dr. D'Souza noted how the National Institute of Dental Research was founded in part to address high levels of severe dental decay that led to many young men being deemed not fit for service during World War II. NIDR was the third Institute to join the National Institutes of Health. Dr. D'Souza highlighted several scientific advancements made by dentists and dental researchers that influenced medicine and science as a whole, such as Norman Simmons' work on DNA and Robert Ledley's pioneering efforts in medical imagery. Dr. D'Souza also reviewed NIDCR-specific highlights in recent decades, such as the creation of the FaceBase Consortium in 2009 and more recent work on dextromethorphan. As it looks towards the future, NIDCR is committed to aligning itself with the findings of the Oral Health in America report and promoting oral health for all.

Dr. D'Souza briefly updated the Council on the status of NIDCR's budget. NIDCR's appropriations for FY 2023 stand at \$520.2M, representing a 3.8% (\$19M) increase from last year.

78.7% of the Institute's budget goes towards the Extramural Program, which is generally consistent with recent years. Due to ongoing fiscal controversies in Congress, NIH anticipates that its budget will be flat for FY 2024 and remain so for the foreseeable future. Dr. D'Souza noted that a flat budget would amount to a budget reduction due to inflation. However, NIDCR remains committed to supporting dental schools. In FY22, 44% of NIDCR's extramural budget went towards dental schools, which represented 65% of NIH's total funding for those institutions. Dr. D'Souza anticipates the ratio of dental school to non-dental school funding to change in the coming years because of the investment NIDCR has made in the recent past. NIDCR continues to increase its support for early-stage investigators (ESIs) as part of its responsibility to ensure a robust career pathway for a diverse array of scholars.

Dr. D'Souza then discussed NIDCR's plans to commemorate the Institute's 75th anniversary this year. Rather than one big celebration, NIDCR will be holding a series of special events and symposia throughout the year, including sessions at stakeholder conferences and annual meetings. The first event was a session held at the American Association for Dental, Oral, and Craniofacial Research (AADOCR) annual meeting in March in Portland, Oregon. On June 27, NIDCR will host an Anniversary Kickoff Symposium and Awards Ceremony. Dr. D'Souza noted that Dr. Francis Collins, former NIH Director, will be attending this event. On September 11, NIDCR will hold a Seminar to Celebrate 25 Years of Fibrous Dysplasia/McCune-Albright Research. The keynote speaker at this event will be Nobel Laureate Dr. Brian Kobilka. The flagship event of the year will be the NIDCR Training and Career Development Symposium, to be held October 10-11, which will include a keynote address by Nobel Laureate Dr. Ardem Patapoutian, a former NIDCR grantee. The anniversary celebrations will continue into 2024 with a series of symposia at the AADOCR 2024 annual conference. Throughout the year, NIDCR staff will produce monthly vignettes on the Institute's history and specialty areas, highlighted health themes, and working with Congress to pass resolutions to honor the occasion, among other activities.

Dr. D'Souza shifted gears to discuss several important, broad-scale research pathways that are being prioritized at NIH. The Accelerated Medicines Partnership (AMP) program has established powerful public-private partnerships to tackle some of the most complex diseases. Dr. D'Souza highlighted the AMP Common Metabolic Diseases program as an example. The program aims to build resources to generate prioritized targets for all metabolic diseases. The program generates new - and leverages existing - genetic, genomic, and biomarker data, and develops analytical and visualization tools to support integrative analysis in order to identify prioritized targets for these diseases. NIH also plays a prominent role in President Biden's National Cancer Plan, which sets a goal of reducing cancer mortality by 50% in the next 25 years. Other prominent NIH-wide initiatives include the Research COVID to Enhance Recovery (RECOVER) Initiative on long-COVID and other post-COVID effects and the Community Engagement Alliance Against COVID-19 Disparities (CEAL) to enhance clinical trial diversity. Another important federal-wide program is the recently established Advanced Research Projects Agency for Health (ARPA-H), which is designed to attempt high-risk, high-reward research that leads to game-changing advances in the field of biomedical research. ARPA-H has four initial mission areas: health science futures, scalable solutions, proactive health, and resilient systems.

At NIDCR, Dr. D'Souza is focused on translating scientific research and discovery into clinical practice. Since the last Council meeting, the Institute has convened think tanks on the topics of oral health disparities, tooth remineralization, dental restoratives, and head and neck cancers. NIDCR continues to strengthen its stakeholder partnerships with industry associations and sister agencies. NIDCR is also working to support efforts to train and retain a diverse cadre of dental, oral, and craniofacial (DOC) researchers and clinicians in order to align with public health demands. Dr. D'Souza and NIDCR leadership maintain a busy public outreach schedule to enhance communication and build new relationships with stakeholders.

A significant proportion of NIDCR's budget over the years has gone to establishing and maintaining research consortia, such as the Dental, Oral, and Craniofacial Tissue Regeneration Consortium (DOCTRC), FaceBase Consortium, the National Dental Practice-Based Research Network, and the Sjogren's Team for Accelerating Medicines Partnership (STAMP). These programs have proven successful, and NIDCR is working to see how these successes can inform future initiatives, particularly as they approach their renewal phase. Dr. D'Souza highlighted three of NIDCR's most recent RFAs, which have all received a strong response: Temporomandibular Disorder (TMD) Collaborative for IMproving PATient-Centered Translational Research (TMD IMPACT), Practice-Based Research Integrating Multidisciplinary Experiences in Dental Schools (PRIMED), and the Advancement of Head and Neck Cancer Early Detection Research (AHEAD).

Dr. D'Souza presented a number of recent highlights from NIDCR-funded research. Examples include the development of mouse model reagents for the study of amelogenesis, the role of retinoic acid in establishing protective antifungal immunity in the context of oropharyngeal candidiasis, the role of early-life microbiome assembly in predicting dental caries, research on molecular subtypes of head and neck cancer in patients of African ancestry, and research on complementary and integrative health approaches to TMD. Dr. D'Souza made the Council aware of several Notices of Funding Opportunities (NOFOs) with approaching application deadlines: NIDCR Prospective Observational or Biomarker Validation Study (PAR-23-162), NIH Science Education Partnership Award SEPA (PAR-23-137), and the Strengthening Research Opportunities for NIH Grants (STRONG) Structured Institutional Needs Assessment and Action Plan Development for Resource-Limited Institutions (PAR-23-144). There is also a soon-to-expire Notice of Special Interest (NOSI) on Change in Funding Opportunity Purpose of NIDCR Small Research Grant Analyses of Existing Genomics Data (PAR-23-132). Dr. D'Souza also briefly noted grants to provide equipment and capacity-building at resource-limited institutions.

Dr. D'Souza updated the Council on congressionally directed NIH policy changes designed to strengthen internal controls over NIH-funded grantees. These policies require recipient institutions to establish codes of conduct governing ethical values and behavioral expectations. Relatedly, NIH has expanded its Harassment Reporting Portal; Dr. D'Souza noted that complaints are investigated by NIH staff, not staff from the funding IC.

Dr. D'Souza highlighted several upcoming NIH workshops of interest. The NIH Helping to End Addiction Long-term (HEAL) Initiative is holding a workshop in July on "Understanding and Restoring Whole Joint Health in Pain Management," which intersects with a number of

NIDCR's focus areas. The FaceBase Consortium is holding its 2023 Community Forum on June 13th at the University of Southern California. The theme of the forum is "Empowering data-driven, translational research." In late August, NIH is convening a Diversity Supplement Professional Development and Networking Workshop. Over 20 ICs, including NIDCR, will be participating.

To conclude her report, Dr. D'Souza reviewed the spectrum of NIDCR's research training programs, which include both intramural and extramural programs and cover the career lifespan. Among these include several research training and career development programs to enhance diversity in the DOC workforce. Dr. D'Souza noted that NIH has increased the stipend for all trainees as of May 1. NIH is also working to improve the review process for National Research Service Award (NRSA) applications to help level the playing field and remove potential biases.

Discussion

Dr. Matthew Hoffman, NIDCR Scientific Director, and Dr. Janice Lee, NIDCR Clinical Director, briefly provided remarks on the activities of their departments. As a preview for later sessions in the meeting, Dr. D'Souza discussed NIDCR's efforts to assess the data science landscape, which led to NIDCR establishing a Data-Driven Solutions Office to propel the Institute's data science-related activities. Dr. Jennifer Webster-Cyriaque, NIDCR Deputy Director, underscored NIDCR's efforts to build belonging at the Institute and throughout the DOC research community.

IV. DIGITAL NIH: A STRATEGIC VISION FOR ADVANCING SCIENCE AND SCIENTIFIC SUPPORT THROUGH INFORMATION TECHNOLOGY

Dr. D'Souza introduced Dr. Patricia Flatley Brennan, Director of the National Library of Medicine, to deliver her presentation on NIH's vision for advancing science through information technology.

Dr. Brennan began by providing a brief overview of the National Library of Medicine (NLM), including the history of the field of biomedical informatics and the NLM itself. The library traces its origins to 1836 as part of the Department of the Army and later the Department of Defense. During the first half of the 20th century, the library was located near the Mall in Washington, D.C., but moved to its current location in Bethesda in 1958. The current building, which opened in 1965, contains over 65 miles of shelving and contains written records dating back 11 centuries. The library became part of the Public Health Service and NIH in 1966. Subsequent decades saw the impact and expansion of the Information Age, and the NLM was an early adopter of computerized methods to track medical publications. During the period until the year 2000, NLM expanded to include research arms, such as the Lister Hill National Center for Biomedical Communications and the National Center for Biotechnology Information. The post-2000 era leading up to NLM's 200th anniversary in 2036 will be characterized by the acceleration of science through data. The library's role has increasingly incorporated the preservation of scientific data along with the preservation of scientific literature. Dr. Brennan briefly noted some of the many important health information tools, databases, repositories, and other resources

created and maintained by the NLM, including PubMed, Medline, ClinicalTrials.gov, RxNorm, as well as genomic resources, health data standards, and consumer health resources for the public. Across these services, NLM receives over 7 million accesses per day.

Dr. Brennan then shifted to the topic of her presentation: advancing science through information technology. She discussed NIH's efforts in recent years to develop the NIH Strategic Plan for Data Science. NIH acknowledges that data technology has become an integral aspect of the biomedical research process. NIH must confront the need for new funding and governance models to harness the power of data science technologies and be agile to account for changing expectations in what these technologies can achieve. This awareness led to the establishment of the Strategic Planning Committee for Digital NIH, which was co-chaired by Dr. Brennan. The committee was tasked with providing strategic guidance on technology decision-making and prioritization at NIH in the coming years. Dr. Brennan defined the Digital NIH initiative's mission as developing "an adaptive governance model that aligns IC-specific technology investments with trans-NIH investments and [NIH's] mission." The year-long effort involved the input of hundreds of NIH employees and over a dozen external stakeholders, which highlighted the need for a more "enterprise-savvy approach to technology governance and decision-making that reflects holistic, integrated planning across NIH." Practical examples would include providing for rapid computational processing, flexible data storage and retrieval, and advanced analytical functions, with the goal of maximizing operational efficiencies for all NIH ICs.

Digital NIH also provides a trans-NIH framework for identifying high-priority capabilities and managing NIH's investments in technology across four functional areas: extramural research management, intramural clinical and basic research, administration and management, and cross-cutting capabilities. In extramural research, new capabilities have the potential to improve grant portfolio management, assist in implementing new policies, streamline protocol planning and tracking, and ultimately reducing researcher and staff burden. For the Intramural Research Program, technology could help improve analysis of large data sets, provide collaboration portals and tools to support clinical trial management, and assist in protocol design. For NIH administration and management, digital capabilities can provide analytic and visualization tools for administrative processes, workflow automation and digitization, and management platforms tailored to IC needs. The cross-cutting capabilities will help set standards for interoperability, foster a technologically competent workforce, strengthen cybersecurity, identify innovative storage and analytic infrastructure, and enable flexible workplace options, among other capabilities.

Implementing Digital NIH will be a multi-year process that will incorporate best practices from the software industry to iteratively explore solutions for the prioritization of capabilities. The initiative is currently in Year 1, and next steps include establishing a capability portfolio, developing a project roadmap and capability proofs of concept, allocation of project funding, and official program launch in September. The aim is to begin integrating successful capabilities into operations by Year 3. To help move the NIH's digital strategy forward, Dr. Brennan asked NIDCR to view technology as a mission-critical resource and apply holistic and collaborative planning to prioritize partnerships and shared solutions to meet the IC's unique technology needs. Finally, Dr. Brennan discussed how the Digital NIH initiative aligns with the 2023-2028 NIH

Strategic Plan for Data Science and supports a future for the NIH that is data-driven and has a robust technological infrastructure.

Discussion

Dr. Axel Visel noted that there is an ongoing transformation in the way scientific literature is published, such as a shift from closed journal to open access, with concurrent issues around the quality of scientific literature raised by the increasing use of generative AI. He asked Dr. Brennan if she envisioned NLM playing a role in helping researchers assess the quality of the literature. Dr. Brennan said generative AI is a game-changer and represents the biggest technological advance since the internet. In regard to scientific integrity, peer review will remain the gold standard for the near future, although there are challenges for reviewers in terms of time management. NIH now views preprints as valid products of scientific research and an important part of the scientific conversation and has a pilot program allowing preprints to be discoverable in PubMed and PubMed Central. NIH acknowledges that scientific journals must meet certain standards in terms of ethics, transparency, communication, and quality of writing. NLM conducts a rigorous evaluation of each journal that it chooses to add to its Medline index. NLM also publishes guidelines for researchers on how to choose well-regarded journals for publication. Dr. Brennan noted that the International Council of Medical Journal Editors (ICMJE) has stated that generative AI programs, such as ChatGPT, cannot be co-authors on papers, although she acknowledged that some journals have already published a handful of papers that have ChatGPT as a co-author. More work is needed to train reviewers on how to detect the use of such programs when they are not explicitly cited as authors. Other factors to bear in mind on the topic of the use of AI programs in medical research are FDA's guidance on Software as a Medical Device (SaMD) and NIST's AI Risk Management Framework. Dr. Brennan emphasized that this is an extremely fast-moving field with wide-ranging applications that are not yet fully understood.

Dr. Webster-Cyriaque discussed with Dr. Brennan the implications of shifting towards cloud-based computing, which offers increased computational power but has cost and other technical implications for which research teams should be aware. NIH is working to develop a trans-NIH resource to assist researchers in transitioning to cloud-based programs.

V. THE WORK OF PROGRAM OFFICERS

Dr. King and Dr. D'Souza introduced Dr. Lillian Shum, Director, Division of Extramural Research, to deliver her presentation on the work of NIDCR program officers in the DER.

NIDCR DER program staff help achieve the Institute's mission by facilitating the translation of promising scientific and technological discoveries into clinical applications. Via grants and cooperative agreements, program officers develop and manage a broad portfolio of research in DOC health and disease to help improve the health of all people across the lifespan. Program officers also promote a diverse and inclusive research workforce. Dr. Shum reviewed DER's grant portfolio, which funds research in a broad array of DOC disease areas across the disease spectrum. The scientific disciplines represented in NIDCR's grant portfolio run the gamut from cellular and molecular biology and genetics to data science and research workforce

development. Program officers are tasked with providing oversight and management of grant portfolios, implementing, and ensuring compliance with NIH and NIDCR policies and procedures. Using their scientific expertise and broad knowledge of NIDCR's portfolio, program officers develop research priorities and initiatives, and organize think tanks, workshops, and symposia, among other activities.

Dr. Shum described in greater detail the process by which DER develops funding opportunities. At the initial idea stage, program officers identify knowledge gaps and research opportunities via analysis of the current NIDCR and NIH portfolios as well as through literature reviews. Specific concepts are presented, discussed, and vetted in-house to assess feasibility and interest from stakeholders. The concepts are then brought to the NIDCR National Advisory Council for review through the concept clearance process. Council-approved concepts then go through a 30-day public comment period to solicit feedback from the stakeholder community. Finally, the program officers develop the formal Notice of Funding Opportunity (NOFO) in collaboration with Grants Management and Scientific Review staff, which involves determining the mechanism of support, locus of review, and availability of funds.

As an example of one of the ways NIDCR solicits input from the research community, Dr. Shum described four think tanks that NIDCR has convened over the past year. The first was the Head and Neck Cancer Think Tank, which was convened with the awareness that head and neck cancers are the 6th leading type of cancer, with approximately 65,000 new cases per year in the U.S. Individuals with these cancers have a five-year survival rate of approximately 50-60%, a rate that has not seen significant improvement in recent years, and current treatments are often debilitating. The think tank was convened to identify gaps and challenges in the prevention, early detection, patient prognosis, and treatment response of head and neck cancers. Participants also discussed strategies for prognostic biomarker identification and validation for detection and prevention of these cancers. Dr. Shum also described how program officers are responsible for ensuring NIDCR is responsive to relevant federal initiatives, such as, in this case, the National Cancer Plan. The Dental Restoratives Think Tank hoped to confront the current state of limited focus on tissue-material interface and the oral environment, challenges in bringing product innovation to market, and the fact that materials development is siloed from the manufacturing process. The think tank discussed hurdles and solutions to advancing access to currently available restorative materials and accelerating the clinical translation of next-generation dental restorative materials. The Tooth Remineralization Think Tank discussed the limited focus on enamel-biofilm-saliva interfaces and the oral environment and the need for strategic partnerships to address major gaps and challenges to improving delivery of current products. Participants highlighted the need for multidisciplinary approaches and more research on identifying common regulators of biomineralization, among other topics. Lastly, the Oral Health Disparities and Inequities Think Tank confronted the ongoing problem of certain sociodemographic populations remaining underserved when it comes to DOC health. The think tank discussed ways NIDCR can support research to increase the uptake of caries prevention strategies, inform policy to advance population-level oral health goals, and address social determinants of health to close persistent gaps in prevalence and burden of certain DOC conditions.

Dr. Shum then dispelled some myths about NIDCR's Extramural Program. There is a myth that most awards are disbursed through projects solicited by RFAs. In fact, 84% of funding

for new awards goes to investigator-initiated projects. NIDCR also frequently hears that investigators are hesitant to contact program officers too much for fear of bothering them. Dr. Shum stressed that program officers love to hear from study teams and their job involves assisting and supporting researchers, including helping publicize research results after studies are complete. A third myth that Dr. Shum addressed is the belief that diversity supplements are heavily utilized, which is not the case. Dr. Shum briefly noted two diversity supplements that are currently available, Research Supplements to Promote Diversity in Health-Related Research and Administrative Supplements to Promote Diversity in Research and Development Small Businesses-SBIR/STTR, as well as several other administrative supplement opportunities. Dr. Shum then discussed NIDCR's involvement with trans-NIH programs and initiatives, such as the Common Fund, the HEAL Initiative, and the NIH UNITE initiatives. Dr. Shum dispelled the myth that these programs are highly competitive and/or not interested in DOC research and thus not worth the time and effort to apply. She noted that an NIDCR program officer is co-managing the Common Fund's recently approved Human Virome Program that is slated to be launched next year. Dr. Shum also briefly described several award programs that are currently accepting applications under the Common Fund's High-Risk, High-Reward Research Program and other trans-NIH programs that might be of interest to the NIDCR research

Discussion

In response to a question from Dr. D'Souza, Dr. Shum discussed the importance of taking advantage of trans-NIH programs and collaborative opportunities for an Institute of NIDCR's size. As examples, Dr. Shum noted NIDCR's involvement in collaborative initiatives related to HIV/AIDs, adolescent oral health, oral cancer, and TMJ and chronic pain.

VI. ORAL CANCER AND NERVES: MUTUAL BENEFICIARIES

Dr. D'Souza introduced Dr. Nisha D'Silva, Donald A. Kerr Endowed Collegiate Professor of Oral Pathology, University of Michigan School of Dentistry, to deliver her presentation on her research as an NIDCR Sustaining Outstanding Achievement in Research (SOAR) award scholar.

Dr. D'Silva began by noting that the term "oral cancer" is a broad category that encompasses lesions in the oral cavity, oropharynx, hypopharynx, nasopharynx, and larynx. Of these, oropharyngeal cancers are the fastest growing type of oral cancer, but cancers of the oral cavity remain the most common and will be the focus of her presentation. Dr. D'Silva presented an example of an oral cancer that arises from precancerous epithelium and breaches the basement membrane and spreads to the underlying connective tissue through the process of invasion. Invasion allows cancer cells to spread to adjacent and distance sites via nerves and blood vessels and is thus a fundamental process in transforming a lesion from premalignant to malignant. Dr. D'Silva's research focuses on perineural invasion, which is the interaction between cancer cells and nerves.

More than 90% of oral cavity cancer lesions are squamous cell carcinomas. The survival rate of oral cancers is between 50-60%, but the rates are lower for oral cavity cancers specifically. One of the most important factors contributing to these poor survival rates is late

detection. Early detection is complicated by the often asymptomatic nature of early-phase oral cancer lesions. The current treatment modalities for these cancers are surgery, radiation therapy, and, more recently, immunotherapy. These treatments can be debilitating and are not always successful. Treatment is determined by lesion stage; spread of cancer to lymph nodes leads to upstaging of the lesion for more aggressive treatment. Perineural invasion is an important surrogate marker of lymph node involvement in the case of occult metastases and is also an important determinant of treatment selection. Dr. D'Silva briefly described the perineural invasion process, noting that recent research in prostate cancer has shown the involvement of the sympathetic and parasympathetic nervous system in early tumor development, proliferation, invasion, and metastasis.

Dr. D'Silva's research on this topic began with her lab's work looking at signaling pathways involved in oncogenic phenotypes, particularly in the context of galanin receptor 2 (GALR2). Dr. D'Silva noted that GALR2's ligand, galanin, is a neuropeptide. Previous studies indicated a mutual attraction between cancer cells and nerves in *in vivo* models. Dr. D'Silva's team found that galanin released by nerves induces GALR2 on cancer cells, which in turn triggers a signaling pathway that promotes invasion of cancer cells. Another interesting finding was that this biochemical interaction occurs prior to physical contact. Dr. D'Silva next worked to determine the clinical relevance of this research. She noted that perineural invasion has been defined since 2009 as cancer cells in close proximity to a nerve and involving at least 33% of its circumference or present within one of the three layers of the nerve sheath. The requirement of 33% has led to a great deal of discrepancy in the diagnosis of perineural invasion among pathologists. Because such diagnosis determines the treatment approach, correct diagnosis is crucial. Dr. D'Silva's team therefore set out to explore whether perineural invasion should be redefined. Across two studies, the team analyzed samples from 142 patients and performed an analysis of neural parameters using cancer biostatistics. Dr. D'Silva described the study design and process. She noted that the use of immunohistochemistry to detect nerves led to an increase in the number of perineural invasion cases, from 26% to 43%, whereas pathologists typically use H&E stains to assess perineural invasion. The research team confirmed that perineural invasion is an independent predictor of poor prognosis and found that nerve-tumor distance impacts survival rate. Notably, non-perineural invasion tumors in close proximity perform almost as poorly as those that do have perineural invasion, yet these patients do not receive more aggressive treatment under the current definitions. They also found that larger nerve diameter is associated with lower survival rates, even with no perineural invasion.

To confirm the findings related to nerve-tumor distance, Dr. D'Silva's team performed validation studies using spatial transcriptomics, the first such studies of the kind. Among the findings from this effort was that myelin basic protein is reduced in nerves close to tumor, consistent with demyelination and injury response, and that genes linked to neurodegeneration and nerve growth are upregulated. These results suggest that redefining perineural invasion based on nerve-tumor distance could increase patients for adjuvant therapy.

Subsequent studies interrogated the question of whether the number of nerves affected by a cancer plays a role in cancer growth. Using nerve denervation model, the research team found evidence to suggest that reduced nerve density suppresses tumor growth. Dr. D'Silva noted that nerve density and innervation in the oral cavity varies by site, making intratumoral nerve density

an unreliable marker for comparisons across sites. Dr. D'Silva's team proposed a normalized nerve density metric that adjusts intratumoral nerve density for tumor-adjacent nerve density. Analysis of the tongue found a stepwise decrease in survival correlated with increase in normalized nerve density. Dr. D'Silva stressed that nerve-related parameters are interdependent but noted that perineural invasion low nerve-tumor distance/high nerve diameter and high normalized nerve density are associated with the worst outcomes.

In order to making these findings clinically applicable, Dr. D'Silva's team explored the use of machine learning for nerve detection, which produced high accuracy and sensitivity scores. Dr. D'Silva's current work involves mechanistic and biological studies in support of the National Cancer Plan's goal of developing effective treatments and effective diagnoses. One such study is an oral cancer radiation clinical trial that will incorporate the findings of the prior studies on perineural invasion and the importance of nerve distance and density. Dr. D'Silva's group is also working to identify ways to translate molecular findings in a way that is applicable in low-resourced locations around the world.

Discussion

Dr. Hoffman asked whether Dr. D'Silva saw evidence that the tumor cells themselves are producing neurotrophins. Dr. D'Silva said that they do, and they secrete galanin. Dr. Webster-Cyriaque asked if larger diameter nerves are associated with larger blood vessels and if angiogenesis is involved in perineural invasion. Dr. D'Silva said that was an excellent question. Many cancer processes recapitulate the developmental process, so it would seem to follow that the nerves affect the blood vessels as part of this process. However, attempts to quantify the vasculature did not result in any notable findings. Dr. D'Souza asked if there is something about the oropharynx that distinguishes it from the oral mucosa. Dr. D'Silva said that the reticulated epithelium of the tonsillar fossa provides viruses, such as HPV, easier access to the basal layer of the epithelium. More research is needed on perineural invasion and HPV.

VII. 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 an update on the working group's recent activities.

The Data Science Strategy Working Group was established to provide recommendations to inform the development of an NIDCR data science strategy to help the Institute achieve success across its five strategic priority areas. Specific opportunities of interest are advancing the DOC data ecosystem, applications of data science methods, and strengthening research in health disparities. The work group has met regularly since September 2022 and is comprised of 12 regular members who have a diverse array of backgrounds, along with several NIDCR staff as ex officio members. The working group has met twice monthly since its founding and has worked on mapping the DOC data ecosystem and discussed oral health disparities in the context of data science.

As Dr. Visel discussed in greater detail at the last Council meeting, the ecosystem mapping effort has noted several initial findings: complexity and heterogeneity of data resources and repositories, fuzzy boundaries between systems (DOC or non-DOC focused), 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 has begun drafting a report with recommendations related to these findings but is still seeking additional input from the community on how researchers across the translational spectrum interact with data (i.e., needs, gaps, and challenges). The working group has established a subcommittee to develop a Request for Information (RFI) to solicit this feedback, which should be issued soon, and is also planning to hold listening sessions with stakeholders this summer.

The topic of data science and oral health disparities has been a focus of the working group in recent months, and the working group is exploring how data science applications can enhance research in health disparities. Dr. Visel noted that Dr. Hiroko Iida, Program Officer for the NIDCR Oral Health Disparities and Inequities Research Program, has recently joined the working group as an ex officio member. Working group representatives participated in the NIDCR Oral Health Disparities and Inequities Research Think Tank, held in January, which was mentioned earlier by Dr. Shum. Through the think tank, the working group became aware of the National Institute of Minority Health and Health Disparities' (NIMHD) Health Disparities Framework, which attempts to assess the levels and domains of influence of health and health disparities factors across the translational spectrum. The working group is working on mapping the DOC data science ecosystem to the Health Disparities Framework to identify existing resources, as well as gaps and opportunities to address oral health disparities.

Discussion

Dr. D'Souza asked Dr. Visel for his thoughts on Dr. Brennan's presentation earlier in the day. Dr. Visel said he has been struck by the complexity of the endeavor since starting out with the working group, and one of the challenges is finding the right level of detail for the recommendations so that they are actionable for the Institute, a point that he thought was echoed in Dr. Brennan's remarks. In response to a follow-up question from Dr. D'Souza, Dr. Visel noted that the topics of workforce training in data science and ethical use of data science applications are additional areas of interest for the working group down the road.

VIII. ORAL HEALTH RESEARCH WORKFORCE WORKING GROUP UPDATE

Dr. King invited Dr. Luisa DiPietro, Oral Health Research Workforce Working Group Co-Chair, to deliver the update on the working group's activities since the last Council meeting.

The charge of the Oral Health Research Workforce Working Group 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." The working group has held numerous listening sessions and panel discussions with stakeholders, reviewed an analysis of NIDCR training program outcomes, and NIDCR Research Training, and

Career Development funding opportunities. The work group issued an RFI to solicit additional feedback from the community, which received 29 responses. The working group has also spoken with several trainees who left science, held listening sessions with potential partners from academia, professional organizations, and industry, and has conducted a literature review on research training. In total, the working group has engaged over 85 stakeholders in face-to-face discussion and is currently in the process of discussing draft recommendations. The working group anticipates presenting its recommendations to the Council this fall.

Dr. DiPietro presented a summary of the analysis of the responses to the RFI. There were several assumptions that appeared to underlie the comments, including that NIDCR and dental schools are expected to play a major role in workforce development, increased interactions of students with DOC researchers and research institutes will generate interest in DOC research careers; and that students should be engaged in various settings and levels of education, among other beliefs. There were several recommendations in the responses, which Dr. DiPietro stressed do not represent the working group's recommendations. These were that NIDCR should establish DOC research consortia/networks, dental schools should provide DOC research experience to all students, more communication and outreach is needed on the importance of DOC research and career opportunities, and evaluation of research training outcomes needs to be improved via enhanced data collection and incorporation of qualitative measures.

Dr. DiPietro also noted themes that emerged from the working group's conversations with dual degree trainees who left science, with the caveat that the work group identified 12 former trainees but were only able to engage with three of them. While the trainees found their training to be excellent and felt well-supported during the program itself, they identified a lack of guidance after leaving the program. They also found the job market to be lacking for dual degree science-focused trainees.

Dr. DiPietro also reviewed themes and comments that emerged from the work group's listening session with dental school deans and oral health leaders and professional societies. Participants were invited to comment on potential partnerships to promote diversity and early career success of DOC researchers. Ideas offered by the deans include to create partnerships between NIDCR and dental schools to help match early career faculty with research positions in dental schools; the need for dental schools to establish tenure track positions with more flexible/less intense allowances for research time; develop new training programs and partnerships with industry to develop competency in product development and regulatory processes; and foster programs that enhance cross-institution collaboration and networking opportunities. The discussion with professional societies raised the possibility that these groups could work with NIDCR to connect high school students and trainees from groups underrepresented in biomedical research as role models, as well as support research internships that support dental students from underrepresented populations. Professional societies also have a role to play in enhancing mentorship opportunities and providing additional awards and research support.

Discussion

Dr. Webster-Cyriaque asked if the working group reached out to dual degree trainees who stayed in science. Dr. DiPietro said they met with seven such individuals and gleaned a great deal from those conversations. She noted that they echoed the comments from the three dual degree trainees who left science regarding lack of guidance during the transition period after leaving the training program. The working group also heard that postdoc specialty training had the unintended consequence of pushing individuals further into clinical work as opposed to research. Dr. Nor emphasized the importance of new faculty researchers being allowed protected time to receive specialty training. Dr. DiPietro said financial constraints are the most cited reasons for why this type of setup is rare.

IX. CONCEPT CLEARANCE

Dr. King stated that NIDCR is required to present 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 one concept, and designated Council members led the discussion, as summarized below.

Reissuance: FaceBase

Dr. Lu Wang, Chief, Translational Genomics Research Branch and FaceBase Program Director, presented the renewal concept. FaceBase is a state-of-the-art public repository of dental, oral, and craniofacial (DOC) scientific data from the full spectrum of DOC research areas. The goal of the program is to enable and accelerate data-driven efforts in knowledge discovery, translation, and delivery. Dr. Wang provided an overview of the history of the program, which dates to 2009 and has expanded and improved greatly over the years in both data coverage and tools for data contributors and users. Today, FaceBase is the central repository of DOC data sets generated using a variety of molecular, cellular, genomic, imaging, and other technologies from humans and various model organisms. Dr. Wang reviewed some of the many improvements that have been made to FaceBase over the years to streamline and enhance data entry and use of FaceBase data sets. The program conducts frequent outreach and has seen increased use in recent years. Dr. Wang briefly reviewed some examples of how FaceBase has been used in published scientific articles. FaceBase aligns with NIDCR's Strategic Plan and the efforts of the Council's Data Science Strategy Working Group, as well as NIH-wide data science efforts. Dr. Wang proposed criteria that will guide the program renewal and oversight of the renewal program to ensure future success.

The Council's lead discussants for the concept were Drs. Visel, Slep, and Niswander. Dr. Visel expressed strong support for the concept and noted his own research experience as a FaceBase data user and contributor and user. FaceBase ably fulfills its goal of providing a comprehensive DOC research database. Dr. Visel noted that collecting and successfully maintaining such diverse data types is a challenging endeavor, but FaceBase has overcome this hurdle to become a critical resource for the community. He emphasized that FaceBase is more than a database but represents a research community that brings together researchers who might

not normally interact. Drs. Slep and Niswander concurred with Dr. Visel's comments and expressed strong support for the concept renewal.

The Council unanimously approved the concept.

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	696	444
Dollars	\$ 382,228,048	\$299,256,091

XI. ADJOURNMENT

CERTIFICATION

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

Rena N.

D'souza -S

Dr. Rena D'Souza

Chairperson

National Advisory Dental and
Craniofacial Research Council

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Date: 2023.06.29
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Lynn M. King -S

Dr. Lynn King

Executive Secretary

National Advisory Dental and
Craniofacial Research Council

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ATTACHMENTS

I. Roster of Council Members



NADRC 5.16.23
Meeting Roster.pdf