

National Institute of Dental and Craniofacial Research

National Advisory Dental and
Craniofacial Research Council

Minutes of Meeting
September 9, 2019

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

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

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NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

MINUTES OF THE
NATIONAL ADVISORY DENTAL AND CRANIOFACIAL RESEARCH COUNCIL

September 9, 2019

The 222nd meeting of the National Advisory Dental and Craniofacial Research Council (NADCRC) was convened on September, 2019, at 8:30 a.m., in Building 50, 1st Floor Conference Room, National Institutes of Health (NIH), Bethesda, Maryland. The meeting was open to the public from 8:30 a.m. until 12:10 p.m.; it was followed by the closed session for Council business and consideration of grant applications from 2:00 p.m. until adjournment at 2:25 p.m. Dr. Martha Somerman presided as Chair.

OPEN SESSION

Members Present

Dr. Kathryn Marie Albers
Dr. Shenda M. Baker
Dr. David J. Couper
Dr. Nisha J. D'Silva
Dr. Lee Niswander
Dr. Daniel Malamud
Dr. Daniel W. McNeil
Dr. Phillip Messersmith
Dr. Sanjay Shete
Dr. Clark M. Stanford
Dr. Joel Strom

Members of the Public

Dr. Styliani Alimperti, Project Leader, American Dental Association (ADA)/National Institute of Standards and Technology (NIST), Gaithersburg, Maryland
Dr. Andy DeSoto, Director of Government Relations, Association for Psychological Science (APS)
Dr. Eun-Jin Lee, ADA, Chicago, IL
Mr. Timothy Leeth, Chief Advocacy Officer, American Dental Education Association (ADEA), Washington, DC
Dr. Ruth Lipman, Director, Scientific Information, ADA, Chicago, IL
Mr. Phil Mauller, Director of State Relations and Advocacy, ADEA

National Institute of Dental and Craniofacial Research

Dr. Martha J. Somerman, Director
Dr. Douglas M. Sheeley, Deputy Director
Dr. Alicia Dombroski, Executive Secretary, and Director, Division of Extramural Activities (DEA)
Dr. Lillian Shum, Director, Division of Extramural Research (DER)
Dr. Matthew P. Hoffman, Scientific Director, Division of Intramural Research (DIR)
Dr. Janice S. Lee, Clinical Director, DIR
Dr. Marion Young, Deputy Scientific Director, DIR
Ms. Kathleen Stephan, OD, Associate Director for Management, Director, Office of Administrative Management (OAM)
Dr. Nisan Bhattacharya, DEA, Scientific Review Branch (SRB)
Dr. Latarsha Carithers, DEA, SRB
Dr. Preethi Chander, DER, Integrative Biology and Infectious Diseases Branch (IBIDB)
Ms. Jennifer Chi, Health Specialist, OD, Office of Clinical Trials Operations and Management (OCTOM)
Ms. Alicia Chou, DER
Dr. Lois K. Cohen, Consultant
Ms. Vicki Contie, OD, Office of Communications and Health Education (OCHE), Science Communication and Digital Outreach Branch (SCDOB)
Ms. Michelle Cortes, DER, IBIDB
Ms. Mary Cutting, DER, Center for Clinical Research (CCR)
Mr. Jimmy Do, OD, OAM, Financial Management Branch (FMB)
Dr. Olga Epifano, DEA
Dr. Catherine Evans, OD, OCHE
Dr. Dena Fischer, DER, CCR
Dr. Leslie Frieden, DEA, Research Training and Career Development Branch (RTCDB)
Dr. Gallya Gannot, DER, CCR
Dr. Nicole Garcia-Quijano, OD, OCHE
Dr. Anna Gillis, OD, OCHE
Dr. Margaret Grisius, DIR
Mr. Joel Guzman, DER
Dr. Ashleigh Hanner, DIR
Ms. Jeannine Helm, DER
Mr. Gabriel Hidalgo, DEA, GMB
Dr. Jonathan Horsford, OD, Office of Science Policy and Analysis (OSPA)
Dr. Emir Khatipov, DER, Translational Genomics Research Branch (TGRB)
Dr. Lynn Mertens King, DEA, RTCDB
Dr. Orlando Lopez, DER, IBIDB
Dr. Nadya Lumelsky, DER, IBIDB
Dr. Dwayne Lunsford, DER, IBIDB
Ms. Jayne Lura-Brown, DER
Dr. Yun Mei, DEA, SRB
Dr. Alissa Meister, OD
Mr. Ricky Moore, DEA, SRB
Ms. Anna Nicholson, OD, OCTOM

Ms. Mable Nee, OD, OAM, FMB
Ms. Lisa Peng, OD, Office of Information Technology (OIT)
Mr. John Prue, OD, OIT
Mr. Ben Rassuli, OD, OIT
Dr. Elise Rice, DER, Behavioral & Social Sciences Research Program (BSSRB)
Dr. Melissa Riddle, DER, BSSRB
Ms. Delores Robinson, DEA
Ms. Diana Rutberg, DEA, GMB
Dr. Yasaman Shirazi, DEA, SRB
Dr. Katie Stein, DER, TGRB
Ms. Allisen Stewart, OD, OCHE
Mr. Joseph Tiano, OD, OSPA
Dr. Kelly Ten Hagen, DIR
Dr. Yolanda Vallejo, DER, IBIDB
Dr. Jason Wan, DER, IBIDB
Dr. Chiayeng Wang, DER, IBIDB
Dr. Lu Wang, DER, TGRB
Dr. Darien Weatherspoon, DER, CCR
Dr. Marian Young, DIR
Dr. Gary Zhang, DEA, SRB

Other Federal Employees

Dr. Helene Langevin, Director, National Center for Complementary and Integrative Health, National Institutes of Health, Bethesda, MD

I. WELCOME AND INTRODUCTIONS

Dr. Martha Somerman, Director, NIDCR, called the open session of the 222nd Advisory Council meeting to order. She welcomed everyone and asked Council members, participants, and guests to introduce themselves. Dr. Somerman welcomed Dr. Lee Niswander to her first meeting as a member of the Advisory Council.

II. APPROVAL OF MINUTES FROM PREVIOUS MEETING

Dr. Dombroski invited the Council to consider and approve the minutes of the May 23rd, 2019 Council meeting. The Council unanimously approved the minutes.

III. REPORT OF THE DIRECTOR, NIDCR

Dr. Somerman's written September 2019 Director's Report to the Council was provided to the Council members and is available on the NIDCR website (<http://www.nidcr.nih.gov>). Her remarks covered NIDCR's budget, a trans-NIH update, an NIDCR update, and selected research highlights. Dr. Somerman began by introducing several new NIDCR employees: Ms. Amber

Lowery, the new Deputy Executive Officer; Dr. Alissa Meister, Presidential Management Fellow; Ms. Mable Nee, Budget Analyst; Dr. Nadine Samara, Stadtman Tenure-Track Investigator and member of the NIH Distinguished Scholars Program; Dr. Denise Stredrick, Chief of the Science Policy and Planning Branch in the Office of Science Policy; Ms. Allisen Stewart, digital content strategist in the Office of Communications and Health Education, Dr. Roxane Tussiwand, Stadtman Tenure-Track Investigator; and Dr. Blake Warner, Assistant Clinical Investigator in the Division of Intramural Research.

Legislative and Budget Updates

Dr. Somerman presented a brief budget overview, including an overview of FY2019 and FY2020 budget events. This summer, the President signed into law the Bipartisan Budget Act of 2019, which sets new spending levels for FY2020 and 2021 and extends the debt limit through July 2021. The House of Representatives has released a draft version of its 2020 Department of Health & Human Services (HHS) appropriations bill. Under this version, the NIH budget would increase by \$2 billion to \$41.1 billion and NIDCR's budget would be set at \$484.4 million. However, the Senate has yet to release any proposed numbers or begin work on related legislation.

Members of Congress' Cancer Survivors Caucus recently visited the NIH campus. Their tour included a stop at NIDCR. Representatives Buddy Carter of Georgia and Mark DeSaulnier of California met with Dr. Jay Chiorini to discuss his gene therapy work, and spoke with Dr. Janice Lee, NIDCR Clinical Director, on the link between oral health and overall health.

NIH Updates

Trans-NIH Activities. Dr. Somerman discussed NIDCR's continued participation in the NIH HEAL (Helping to End Addiction Long-termSM) Initiative, which is a trans-agency effort with the aim of improving prevention and treatment strategies for opioid misuse and addiction, while enhancing pain management. The ultimate goal of the Initiative is to provide lasting, scientific solutions to the national opioid public health crisis. The Initiative is a large-scale partnership that involves coordination with the HHS Secretary, the Surgeon General, federal partners, local government officials, and communities.

Dr. Somerman detailed NIDCR's activities related to the NIH HEAL InitiativeSM. Dr. Somerman thanked Dr. Yolanda Vallejo, NIDCR program officer, who has been spearheading NIDCR's participation in the Initiative. NIDCR's HEAL grants have been focused on temporomandibular disorders (TMD) and identifying and validating novel therapeutic targets for TMD and other types of pain. NIDCR is also involved in discovering and validating TMD biomarkers; specifically, analytical and initial clinical validation of novel cortical biomarker signatures as a predictor of pain severity and duration in TMD. NIDCR has also signed onto a number of other HEAL RFAs on a wide array of topics, including optimization of non-addictive therapies, studies of the use of devices to treat pain, and the Early Phase Pain Investigation Clinical Network (EPPIC-Net), among others.

Dr. Somerman updated the Council on the NIH All of Us Research Program. The program aims to collect and study data over many years from one million or more people living in the United

States. The goal of the program is to speed up health research breakthroughs, enabling new kinds of individualized health care. The program began national enrollment in 2018 and is expected to last at least 10 years. The program has thus far been more successful than many people anticipated, particularly given early concerns about diversity, with over 230,000 participants as of July 2019, 80% of whom are from groups that have been historically underrepresented in biomedical research. Dr. Somerman directed Council members to a special report on the program in the August 15th issue of the New England Journal of Medicine.

Dr. Somerman briefed the Council on the results of NIH's anti-harassment activities. NIH held a series of workshops and staff meetings in recent months as part of this effort. From these activities, the NIH released a new NIH Policy Statement on Personal Relationships in the Workplace and an updated NIH Anti-Harassment Policy. The policy statement says that "personal relationships (including romantic and/or sexual) between individuals in inherently unequal positions, where one party has real or perceived authority over the other in their professional roles, may be inappropriate in the workplace and are strongly discouraged." The statement describes additional disclosure and remediation requirements. The Anti-Harassment Policy defines harassment and other inappropriate behavior and establishes a centralized framework for reporting, investigation, and adjudication through the NIH Civil Program. Civil will be required to provide annual updates on cases. NIH has also established a hotline and web-based portal for reporting. As part of the overall effort to foster greater inclusivity at NIH and the medical research community, NIH Director Francis Collins has released statements expressing his support for diverse and inclusive scientific meetings and conferences, and has pledged not to participate in any panels or speaking engagements at events that lack diversity of participant backgrounds.

Dr. Somerman provided an update on changes to the NIH requirements regarding human fetal tissue research. A notice was issued in July that places tighter restrictions on applications for the use of human fetal tissue from elective abortions. One of the new restrictions is that early-career scientists may not propose the use of human fetal tissue in fellowship or training award applications.

NIH has also been working on policies to combat foreign influences in medical research. Dr. Somerman emphasized that global partnerships and collaboration are vital to medical research and the purpose of this effort is not to restrict the vast majority of partnerships that are done the right way. However, things like shadow labs, data theft, distorted funding decisions, and other types of corruption are real concerns.

NIDCR Activities

NIDCR 2030 Vision and Our Next Strategic Plan. NIDCR has identified the following areas of focus as it looks ahead to 2030: oral health and overall health, precision health, autotherapies, oral biodevices, and workforce diversity. The 2030 vision imagines a world where dental, oral, and craniofacial health and disease are understood in the context of the whole body.

2020 Surgeon General's Report on Oral Health in America. This report was commissioned by Dr. Jerome Adams, U.S. Surgeon General, to coincide with the 20th anniversary of the first report on oral health in 2000. The Surgeon General's top overall priorities are opioids and addiction,

tobacco, community health, and emerging public health threats, among others. The 2020 report is expected to touch on many of these subjects. NIDCR's project leads on the report are Drs. Bruce Dye and Judith Albino. Dr. Somerman reviewed the proposed structure of the report and its main sections.

National Academies Consensus Study on Temporomandibular Disorders. Dr. Somerman updated the Council on the consensus study, which will be titled "Temporomandibular Disorders (TMD): From Research Discoveries to Clinical Treatment." The National Academies are leading stakeholder activities, including public workshops, and held a webinar on July 31 on TMD professional education, research, and specialization. Dr. Somerman stressed that TMD research is a main priority for NIDCR and the Institute provides support for the consensus study along with the NIH Office of the Director.

Research on Fluoride. Dr. Somerman reviewed several recent fluoride studies. One study using NHANES data suggested increased fluoride exposure may alter kidney and liver function in adolescents. A recent study conducted in Canada found that increased fluoride exposure during pregnancy may be associated with cognitive deficits in children. The NIH Institute of Environmental Health Sciences (NIEHS) is in the process of completing a systematic literature review to evaluate potential neurobehavioral effects of exposure to fluoride during human development. NIDCR is working with NIEHS to develop future research opportunities on this topic.

NIDCR at IADR 2019. Representatives from NIDCR recently attended the International Association of Dental Research (IADR) annual conference in Vancouver, Canada. NIDCR staff gave talks, received awards, and had a booth on the conference floor. Dr. Somerman invited members to attend next year's conference.

NIDCR Workshop of Dental Fear and Anxiety. A workshop on dental fear and anxiety was held on July 15, at which Dr. Somerman provided welcoming remarks. Tools exist to manage dental fear, but more research is needed to help understand how to prevent dental fear and anxiety. Overarching themes of the workshop included public perceptions about dental care, education of dental students and workforce, cultural appropriateness, and other patient considerations.

Intramural Research Highlight. Dr. Somerman presented an overview of Dr. Blake Warner's recent research on sicca and Sjögren's syndrome (SS). Dr. Warner and colleagues recently published a study in *The Oncologist* that attempted to characterize the clinicopathologic features of sicca syndrome associated with immune checkpoint inhibitor (ICI) therapy. Dr. Warner and his team also published an article in the *Journal of Dental Research* called "Profiling Autoantibodies against Salivary Proteins in Sicca Conditions." In this study, autoantibodies were evaluated against Ro52, Ro60, and La, as well as against a panel of 22 proteins derived from the salivary proteome. As expected, a high percentage of autoantibody seropositivity was detected against Ro52, Ro60, and La in SS, but only a few immune checkpoint inhibitor-induced sicca (ICIS) patients were seropositive for these autoantigens. However, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) subjects selectively demonstrated seropositivity against several proteins. These findings highlight the complexity of

humoral responses in different sicca diseases and provide new insights and biomarkers for APECED-associated sicca.

Extramural Research Highlight. Dr. Somerman next presented a NIDCR-funded research highlight from the extramural community. She discussed the findings of a study titled “HMGB1 and RAGE as Essential Components of Ti Osseointegration Process in Mice” by Garlet et al., published in *Frontiers in Immunology*. The release of the prototypic damage-associated molecular pattern (DAMP) High Mobility Group Box 1 (HMGB1) into extracellular environment and its binding to the Receptor for Advanced Glycation End Products (RAGE) has been described to trigger sterile inflammation and regulate healing outcome. This study looks at their role on host response to Ti-based biomaterials and in the subsequent osseointegration. The study found that HMGB1 and RAGE have a marked role in the osseointegration, evidenced by their influence on host inflammatory immune response, which includes macrophage migration and M1/M2 response, and MSC markers expression, which collectively modulate bone matrix deposition and osseointegration outcomes.

IV. WHOLE PERSON HEALTH

Dr. Somerman introduced Dr. Helene Langevin, Director of the National Center for Complementary and Integrative Health (NCCIH), to deliver the presentation on NCCIH’s purview and potential avenues for collaboration with NIDCR.

Dr. Langevin defined complementary health as the use of complementary therapies and practices that use nutritional, physical, and psychological approaches. These therapies used to be called “alternative medicine,” but these therapies are now seen not as an alternative to conventional medicine, but as a complement to conventional medicine. Integrative health is generally understood to be the integration of complementary treatments with conventional medicine. Another important aspect, however, is exploring how to integrate care across the whole person. A number of practices that NCCIH classifies as mind and body practices have evolved to address this angle of human health, such as meditation, mindfulness, acupuncture, and yoga, among others. Some of these therapies aim for mental effects rather than physical, but recent studies have shown that some of these techniques can have physical implications as well, for example, in pain modulation. Indeed, according to the National Health Interview Survey, pain in general is far and away the most common reason respondents seek out complementary health treatments and mind and body practices.

As an example, Dr. Langevin traced the historical trends in musculoskeletal and chronic pain research. Musculoskeletal pain is one of the most common and debilitating types of chronic pain among humans. In the beginning, the scientific field was focused on the pathology of musculoskeletal tissue, joints, the spine, vertebral discs, etc. The last couple decades have seen a shift in emphasis towards neurological chronic pain components, such as research on descending inhibition of pain and functional and structural alterations in brain networks. This is relevant to a number of conditions NIDCR studies, most notably TMD disorders.

Treatment of musculoskeletal disorders generally focuses on the joint, and when talking about musculoskeletal tissue, one generally is referring to specialized connective tissues, such as tendons, ligaments, and joint capsules. But there are other non-specialized connective tissues that are studied much less, such as the dense fascia or interfascial connective tissue planes. These connective tissues form an interconnected network that spans the entire body across many anatomical levels (e.g., fascia, interstitium, and extracellular matrix), creating a scaffold that determines the shape of the human body. It is also known that connective tissue continuously remodels across the human lifespan in response to mechanical forces, gravity, externally applied forces, habitual movement patterns, and muscle contractions.

Dr. Langevin discussed research on chronic inflammation, myofascial pain, and the impact on connective tissue in mouse studies. Over time, connective tissue stiffening, lack of mobility, and muscle imbalances can lead to abnormal load distribution in the body, which in turn can put at risk vulnerable structures, such as cartilage, joints, and intervertebral discs. Mind-based complementary health practices can assist in enhancing descending pain inhibitory pathways, and research has suggested they might have beneficial effects on emotional pain processing. In addition, mind-based practices can reduce fear of movement and help correct habitual movement patterns. Improved movement changes the mechanical forces on connective tissues and can reduce movement restriction. This process is gradual, however, and if attempted too quickly can cause increased damage.

If behavioral therapies are unsuccessful or not feasible, manual physiotherapy can be attempted. Dr. Langevin discussed the results of studies looking at the effect of manual therapy in repetitive motion rat models and the effect on neural inflammation and perineural fibrosis, and the beneficial effect of stretching on chronic inflammation. She presented other research on pro-inflammatory mediators and pro-resolving mediators that are promoted by stretching.

Dr. Langevin noted that injuries to connective tissues often go undiagnosed because there are no effective imaging techniques to identify this kind of damage. In general, there are few imaging techniques that are capable of capturing myofascial and soft tissue damage or distinguishing between these tissues and, for example, fat. She described a promising new use of ultrasound sonoelastography to identify myofascial trigger points.

In conclusion, there are important interactions between the forces produced by the musculoskeletal system and the immune responses that occur in the same connective tissues that transmit the same mechanical forces. A simple change in movement patterns over time can have profound effects by altering the efferent output to muscle, changing the mechanical forces that remodel the connective tissue, and reducing inflammation. This pathway crosses a number of disciplines that are currently too siloed: neuroscience, physical therapy & rehabilitation, rheumatology, and orthopedics. More interdisciplinary collaborations are needed to further explore the mechanistic underpinning of connective tissues, the relation to chronic pain, and how physical therapy works. NCCIH is uniquely positioned to assist in this process. Dr. Langevin listed three potential areas for further development of common interests: mind and body approaches to the treatment and prevention of chronic musculoskeletal pain, mechanisms of reversible connective tissue and muscle contribution to reduced mobility and impaired function following injuries, and structural and dynamic imaging of soft tissues.

Dr. Langevin next discussed NCCIH's mission to address health promotion and restoration, disease prevention, and symptom management. Human wellness can be seen as a spectrum, from wellness to pre-disease to disease. The medical field is very good at controlling illness at the disease stage, via surgery and pharmacology, etc., but there is a gap in the middle precursor stages where behavioral interventions can have a massive impact in disease prevention and health restoration. Health promotion and restoration and whole person health will be two of NCCIH's main areas of focus in the coming years, and Dr. Langevin looked forward on partnering with NIDCR on topics of mutual interest.

Discussion

Dr. Marian Young, NIDCR Deputy Scientific Director, asked whether NCCIH has done any work on nutraceuticals and how CBD oil works in reducing inflammation. Dr. Langevin said NCCIH recently funded a group of studies to look at cannabinoids and pain-mediation. In the past, research has been hampered by regulations, but as those regulations loosen NCCIH will be at the forefront of this topic.

Dr. Daniel McNeil raised the notion of behavioral and social determinants of pain and thanked Dr. Langevin for presenting a broader understanding of the role of pain and human responses to pain.

Dr. Somerman asked whether the rat models Dr. Langevin discussed accounted for differences in sex. Dr. Langevin said that is an important point given the differences in the pathophysiology of pain between males and females, and is a topic NCCIH has planned for future studies.

V. CONCEPT CLEARANCES

Dr. Dombroski, Director, DEA, 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, and proposed concepts are posted to <https://nidcr2030ideascale.com> for public comment. The NIDCR staff presented seven concepts, and designated Council members led the discussion of each, as summarized below.

Institutional Research Training for a Dental, Oral and Craniofacial Research Workforce

Dr. Lynn Mertens King, Chief, Research Training and Career Development Branch, DEA, presented the concept. The goal of this initiative is to strengthen and sustain a robust, diverse, and inclusive biomedical research workforce. Institutional training programs provide an entry into a research career pathway, a full-time research experience under a qualified mentor, a cohort of trainees providing peer mentoring, and a foundation of research and career development experiences to ensure successful research career progression and transition to an independent research career. This concept will re-issue two Funding Opportunity Announcements (FOAs): the T32 Ruth L. Kirschstein National Research Service Award (NRSA) Institutional Training for

a Dental, Oral, and Craniofacial Research Workforce; and the T90/R90 Institutional Training for a Dental, Oral, and Craniofacial Research Workforce, which allows for non-citizen participation. Dr. King provided an overview of the past performance of these grants, highlighting that individuals supported by fellowships have been found to have greater success at in competing for subsequent NIH funding than those supported by training grants alone. Since 2008, NIDCR has been encouraging the transition from T grants to individual fellowships and will attempt to do so more forcefully going forward. Dr. King also reviewed the performance of the R90 program, which has been successful thus far.

The Council's lead discussants, Dr. Nisha D'Silva and Dr. Clark Stanford, expressed strong support for the re-issuance of the concept.

The Council unanimously approved the concept.

NIDCR Predoctoral to Postdoctoral Transition Award for a Diverse Dental, Oral, and Craniofacial Research Workforce

Dr. Leslie Frieden, Extramural Training Officer, Research Training & Career Development Branch, DEA, presented the concept to the Council. The purpose of this grant program is to help NIDCR's goal of enhancing the diversity of dental, oral, and craniofacial research workforce by supporting a structured transition from predoctoral to postdoctoral career stages for individuals from underrepresented groups. The award has two phases: the F99, which covers the final two years of graduate degree training and the search for a postdoctoral mentor; and the K00, which covers three years of mentored postdoctoral research career development. The predoctoral to postdoctoral transition period is crucial to a researcher's career development and can be difficult to navigate, particularly for individuals from historically underrepresented communities. The program will emphasize mentorship to enable these individuals to achieve postdoctoral research positions. Ultimately, it is hoped that this program will position these individuals to achieve independent faculty positions and future research funding.

The Council's lead discussants, Dr. Clark Stanford and Dr. William McNeil, were supportive of the concept. Dr. Stanford noted that studies have shown that half of researchers who have completed the clinical stage of training made their career choice in grade school or high school. This program is crucial to help provide exemplars to underrepresented communities that this career is open to them or their children. Dr. McNeil added that this program is consistent with the diversity and inclusion goals of Director Collins and NIDCR's vision and strategic plan.

The Council unanimously approved the concept.

Administrative Supplement for Collaborative Science (ASCS)

Dr. Jason Wan, Director, Mineralized Tissue Physiology Program, DER, presented the concept re-issuance to the Council. The goal of the supplement is to enhance ongoing research by enabling NIDCR-funded researchers to form a new collaboration that was not anticipated at the time of submission, review, and funding of the parent award. This ability is expected to generate important new opportunities for achieving the goals of the parent project and benefit the research

program of the collaborator. Dr. Wan reviewed the past performance of the program. There were 73 ASCS awarded between 2009 and 2014; 32% of the collaborations continued on with new NIH applications involving the collaborator as co-investigator, and 62% resulted in at least one publication with the collaborator as co-author. This concept encourages collaborative science from Early Stage Investigators, individuals from underrepresented populations, and scientists in different disciplines, new to dental/oral/craniofacial research, or employed in industry or small business.

The Council's lead discussants, Dr. Daniel Malamud and Dr. Kathryn M. Albers, were supportive of the concept reissuance and agreed it filled an important gap in allowing for unforeseen changes in research. Dr. Stanford asked about other outcome measures besides publications. Dr. Wan said there have been some patents created as a result of the supplement, but those can be more difficult to measure and track. Dr. Niswander asked Dr. Wan to explain the application review process. Dr. Wan said the applications are evaluated by NIDCR program officers managing the parent grant.

The Council unanimously approved the concept.

Defining Mechanisms of Disease Recurrence in Dental, Oral and Craniofacial Tissues

Dr. Preethi Chander, Director, Salivary Gland Biology and Immunology Program, DER, presented the concept clearance request to the Council. The purpose of this scientific concept is to encourage studies that examine immune mechanisms of protection against recurrence of infectious and autoimmune diseases of dental, oral, and craniofacial (DOC) tissues, and develop immunomodulatory approaches to protect against episodic recurrence. Ultimately, the program hopes to facilitate development of immunomodulatory therapies to protect against recurrence of DOC diseases. Significant knowledge gaps exist in our understanding of protective mechanisms underlying episodic characteristics of recurrence of DOC disease and disease management. Dr. Chander briefly discussed some areas of interest covered by the concept, such as identifying molecular and cellular processes that contribute to immune memory against recurrence in DOC tissue, deriving approaches and models that allow examination of protective immunity against recurrence, investigating mechanisms of crosstalk between the immune system and other physiological systems, and investigating mechanisms of oral tissue-resident immunity in the context of systemic health and environmental stress.

The Council's lead discussants, Dr. Kathryn M. Albers and Dr. Nisha J. D'Silva, expressed strong support for the concept. Dr. Albers said she was particularly interested in exploring crosstalk between the immune system and other systems in the body. Dr. D'Silva said the program also holds promise for identifying pre-neoplastic lesions and biomarkers.

The Council unanimously approved the concept.

Engaging Dental Health Professionals to "End the HIV Epidemic"

Dr. Melissa Riddle, Chief, Behavioral and Social Sciences Research Branch, DER, presented the concept to the Council. The purpose of this initiative is to support research on how

to optimally engage the dental workforce in meeting the unique needs of individuals living with or at the risk of contracting HIV. The contributions of these and other health providers will be essential for reaching ambitious new goals set by HHS to reduce new HIV infections by 75% in five years and 90% in the next decade. HHS has identified an immense need to maximize the uptake of available biomedical tools and treatments, such as rapid and at-home testing and pre- and post-exposure prophylaxis (PrEP and PEP). Stakeholders have long recognized the potential role of dental care providers, and early research has been supportive of this conclusion. Each step in the HIV care continuum poses opportunities for contributions from the dental community that are ripe for scientific inquiry. Dr. Riddle highlighted patient-provider communication strategies for discussing HIV risk and prevention and coordination with other care providers to support patient medication adherence and engagement in care.

The Council's lead discussants, Dr. Joel Strom and Dr. Daniel McNeil, were supportive of the concept. In previous discussion of the concept, concerns regarding practical implementation were raised. For example, other disciplines or specialties might feel encroached upon or reluctance might be expressed by the dental provider community itself. Dr. McNeil noted that this is a very sensitive topic area for patients and dental care providers will need to be trained on how to handle it with the appropriate sensitivity. Nonetheless, both Council members were in agreement that the value of the program far outweighed implementation concerns. Dr. Niswander asked whether there were instances where an initial HIV infection was diagnosed by a dental care provider. Dr. Gallya Gannot, Director, HIV/AIDS and Oral Health Research Program, DER, said dental providers are not likely to identify HIV, but symptoms of the untreated disease can be visible in oral lesions, for example. She emphasized that this program was more about education, communication, and care coordination than detection and diagnosis by the dental care providers themselves.

The Council unanimously approved the concept.

Defining Lineage Plasticity and Endogenous Regeneration Capacity of Dental, Oral and Craniofacial Tissues

Dr. Nadya Lumelsky, Chief, Integrative Biology and Infectious Disease Branch, DER, presented the concept request to the Council. The long-term goal of the proposed concept is to overcome the shortage of functional cells for regeneration of DOC tissues through in vivo cell lineage reprogramming from alternative cell lineages. This initiative is important because the shortage of functional cells for generation of new tissues significantly impedes progress in regenerative medicine. The immediate goal of this concept is to mechanistically define the capacity of DOC cells to undergo lineage reprogramming in vivo in response to injury and other types of environmental stress. Ultimately, the proposed program expects to help elucidate molecular and cellular control mechanisms of DOC tissue lineage reprogramming in vivo. This work will make use of recent advances in single cell analyses, system biology, bioinformatics, gene transfer, genome editing, bioengineering, and high-resolution imaging.

The Council's lead discussants, Dr. Nisha J. D'Silva and Dr. Phillip Messersmith, were very supportive of the concept. Dr. D'Silva lauded the basic science foundation of the program. Dr. Messersmith was also supportive of the concept. He referred to relevance of the topic to

epimorphic regeneration in lower vertebrates and pointed out that some mechanistic insights into lineage reprogramming in mammals could be obtained from the existing knowledge about epimorphic regeneration.

The Council unanimously approved the concept.

Accelerating Discovery and Characterization of Genetic Variants Underlying Dental, Oral, and Craniofacial Diseases and Conditions

Dr. Lu Wang, Chief, Translational Genomics Research Program, DER, presented the concept to the Council. The purpose of this program is to improve human DOC health by accelerating discovery and characterization of genetic variants underlying a broad range of DOC diseases and conditions. It is hoped the knowledge obtained will shed light on DOC disease etiologies and inform diagnoses, prognoses, and treatments of diseases. In addition, knowledge of shared genes and variants between DOC and other body parts will contribute to understanding the biology of the human body as a whole, which in turn will help improve DOC and overall health.

Over the past decade, genome-wide sequencing and data analysis methods have matured and now allow for the rapid discovery of disease-causing genetic variants. Concurrently, technologies such as CRISPR/Cas9 and iPS cells have made functional characterization and mechanistic study of genes and genetic variants more feasible. This program will prioritize NIDCR's genetics and genomics portfolio for projects that use genome-wide sequencing and otheadvanced technologies for the discovery of DOC genes and variants and characterization and mechanistic study of those genes/variants. This program will also help encourage genome-wide association studies to proceed with investigation of gene function and disease etiology.

The Council's lead discussants, Dr. Sanjay Shete and Dr. David Couper, were strongly supportive of the concept reissuance. Dr. Shete noted the importance of functional studies and the role this program will play in NIDCR's portfolio.

The Council unanimously approved the concept.

VI. GENDER DEMOGRAPHICS OF ORAL HEALTH RESEARCHERS

Dr. Jonathan Horsford, Acting Director, Office of Science Policy & Analysis, OD, presented the findings of his team's analysis of the demographics of oral health researchers. NIH recognizes the need to improve biomedical workforce diversity and has established an Office of Scientific Workforce Diversity as part of those efforts. Women have long been underrepresented among established biomedical researchers. The percentage of male to female workers is about even in the U.S. biological sciences workforce and NIH trainees; women currently make up 61% of U.S. graduate students and postdocs. However, 71% of NIH RPG applicants are men and 73% of NIH intramural PIs are men. Dr. Horsford highlighted two recent papers that studied the gender demographics of the oral health research workforce. One paper showed that women received about one-third of the NIH RPGs awarded from 2008 to 2012. The other paper reviewed 22 oral sciences PhD programs from 2007 to 2016 and found that 60% of the students were women. Data from the American Dental Education Association (ADEA) showed that women

make up about 35% of dental school faculty and that those numbers are larger when only looking at faculty members under 50 years of age.

Dr. Horsford's team conducted an analysis of the NIDCR extramural community across all NIH grant mechanisms. This analysis revealed that NIDCR is similar to the biomedical workforce at large: women are underrepresented, especially at more established career stages, and women comprise only 35% of all NIDCR applicants. In addition, fewer applications are received from established female researchers, in part because they make up a smaller percentage of the pool of available applicants. The analysis also found that funding rates are similar for women and men across the broad range of grant mechanisms assessed, which highlighted the need for more applications from women.

The analysis found a statistically significant difference in the number of applications per applicant, with women submitting fewer than men. In addition, women have been less likely to apply for R01-equivalent awards. That said, Dr. Horsford noted some progress: women are now more represented than men in individual fellowship F awards and are approaching equilibrium for career development K awards.

Dr. Horsford concluded by identifying some potential opportunity areas to help continue to improve gender equity. NIDCR should work closely on this issue with key stakeholders, including the Advisory Council; there needs to be an effort to recruit and retain more female oral health faculty in academia; the oral research community needs to support a safe, inclusive, and respectful workplace culture; there should be a sustained focus on the transition to independent researcher; and NIDCR should do what it can to encourage more R01-equivalent applications from women.

Discussion

Dr. Shenda Baker asked whether Dr. Horsford's team could analyze the data by cohort over time to see where in the pipeline people are dropping out and which actions have proven successful. Dr. Horsford said that is the type of study he would like to conduct in the near future.

VII. NIH EFFORTS TO COMBAT HARASSMENT

Dr. Kelly Ten Hagen, Senior Investigator, Developmental Glycobiology Section, DIR, briefed the Council on the work of the NIH Anti-Harassment Steering Committee, on which she served. Dr. Ten Hagen is also a member of the NIH Women Scientists Advisors Committee and Advisory Committee to the Director (ACD) Working Group on Changing the Culture to End Sexual Harassment.

As an introduction to the topic, Dr. Ten Hagen presented findings from the 2018 National Academies of Sciences, Engineering, and Medicine's Sexual Harassment report and its recommendations. Among these recommendations were for institutions to confront and address gender harassment; create a diverse, inclusive, and respectful environment; to move beyond legal compliance to address culture and climate; and improve transparency and accountability, among others.

Dr. Ten Hagen next discussed NIH's intramural anti-harassment efforts. The NIH IRP includes 1,100 investigators, over 4,000 postdoctoral, and includes a 240-bed research hospital. In 1993, the NIH Women Scientists Advisors were established, of which Dr. Ten Hagen is a member. The group includes representatives from every IC and meets regularly with NIH IRP leadership to work toward an equal status for women. This group helped take the lead in the recent anti-harassment efforts. As mentioned by Dr. Somerman at the beginning of the meeting, NIH recently released a new Personal Relationship Policy Statement and NIH Anti-Harassment Policy which established norms, guidelines, and adjudication mechanisms for the NIH intramural workforce. Dr. Ten Hagen emphasized the importance of moving beyond a notion of legal compliance towards a broader understanding of inappropriate conduct; expected workplace behavior should exclude all inappropriate behavior, regardless of strict legality.

Regarding the extramural campaign, NIH has conducted a wide-ranging communication and outreach effort to inform the extramural community of NIH policy and ask for the community's assistance in combating sexual harassment. NIH has established a confidential email address (granteeharassment@od.nih.gov) to report concerns about activities at NIH-funded institutions. In addition, NIH has stood up the ACD Working Group on Changing the Culture to End Sexual Harassment to assess the current state of gender equity and provide advice and recommendations on how to improve anti-harassment policies in the extramural community. The Working Group has released interim recommendations:

1. Treat professional misconduct, including sexual harassment, as seriously as research misconduct.
2. Require all PIs to attest, when submitting NIH grant applications and progress reports, that they have not violated and will not violate their institutional code of conduct.
3. Establish mechanisms for restorative justice for survivors and recapture lost talent.
4. Develop novel approaches to support trainee independence and reduce hierarchical relationships between trainees and mentors.

The Working Group will also be tackling other topics, such as supporting research on evidence-based interventions to improve the health and safety of biomedical researchers, developing guidelines to promote safety and inclusivity at NIH-supported conferences, and how to best ask for institutional accountability and action.

Dr. Ten Hagen next discussed findings of a recent IRP internal workplace climate and harassment survey. The survey was sent to all personnel, including trainees and contractors, and focused only on experience in the past 12 months. Most notably, 21.6% of respondents reported experiencing some type of harassment in the past 12 months; among women, the number was 26.9%. Alarming, 44% of respondents of other gender identity reported experiencing harassment in the past year, as did 31.8% of respondents of undisclosed gender. Dr. Ten Hagen also broke down the numbers by sexual orientation and age, with higher percentages among LGBT and younger respondents. Another sobering finding was that 30.7% of trainees reported experiencing harassment of some type over the past 12 months. The survey included follow-up questions which revealed the vast majority of these events took place in NIH buildings and during work hours; 78% of respondents identified the perpetrator as an NIH employee, 71.8% as

a man, and 24.9% as a person who could influence work opportunities at NIH. As for reporting, 54.4% did not report the event, of whom 77.4% did not think their experience was serious enough to report, suggesting much more outreach is needed to the workforce.

Finally, Dr. Ten Hagen highlighted some next steps for NIH and the ICs. ICs should increase leadership engagement with staff, and NIH should provide enhanced training and education throughout the community, support staff in reporting harassment, and conduct ongoing assessments to help ensure penalties are applied consistently. In summary, NIH's efforts to assess the workplace climate and change the culture are ongoing, along with continued efforts to increase diversity in leadership and increase coordination with NIH-funded institutions.

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. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

IX. REVIEW OF APPLICATIONS

X. ADJOURNMENT

CERTIFICATION

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

Martha J.

Somerman -S

Digitally signed by
Martha J. Somerman -S
Date: 2019.11.18
17:17:42 -05'00'

Dr. Martha J. Somerman
Chairperson
National Advisory Dental and
Craniofacial Research Council

/Alicia Dombroski/

Dr. Alicia Dombroski
Executive Secretary
National Advisory Dental and
Craniofacial Research Council

ATTACHMENTS

- I. Roster of Council Members
- II. Table of Council Actions