

National Institute of Dental and Craniofacial Research

National Advisory Dental and
Craniofacial Research Council

Minutes of Meeting
September 10, 2020

Video Teleconference

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 10, 2020

The 225th meeting of the National Advisory Dental and Craniofacial Research Council (NADCRC) was convened on September 10, 2020, at 9:30 a.m., via video teleconference. The meeting was open to the public from 9:30 a.m. until 12:40 a.m.; it was followed by the closed session for Council business and consideration of grant applications from 12:45 p.m. until adjournment at 1:23 p.m. Dr. Lawrence Tabak presided as Chair.

OPEN SESSION

Members Present

Dr. Kathryn Marie Albers
Dr. Patricia Arola, *ex officio*
Dr. Joel Collier
Dr. David J. Couper
Dr. Nisha J. D'Silva
Dr. Frank Ebetino, *ad hoc*
Dr. Raul I. Garcia
Dr. Daniel W. McNeil
Dr. Lee A. Niswander
Dr. Ruth Ruprecht, *ad hoc*
Dr. Wenyuan Shi
Dr. Clark M. Stanford
Dr. Joel Strom
Dr. Axel Visel

National Institute of Dental and Craniofacial Research

Dr. Lawrence Tabak, Acting Director
Dr. Jonathan Horsford, Acting 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
Ms. Mehrnoosh Abshari, DIR, Combined Technical Research Core (CTRC)
Dr. Nisan Bhattacharya, DEA, Scientific Review Branch (SRB)
Dr. Alison Boyce, DIR
Ms. Laurie Brenchley, DIR

Ms. Beth Brillante, DIR
Mr. Brian Brito, OD, Office of Information Technology (OIT)
Dr. Thomas Bugge, DIR
Dr. Peter Burbelo, DIR
Dr. Preethi Chander, DER, Integrative Biology and Infectious Diseases Branch (IBIDB)
Ms. Jennifer Chi, Office of Clinical Trials Operations and Management (OCTOM)
Ms. Alicia Chou, DER
Mr. Kevin Chu, OD, OIT
Ms. Michelle Cortes, DER, IBIDB
Mr. Bret Dean, OD, Office of Administrative Management (OAM), Financial Management Branch (FMB)
Mr. Jimmy Do, OD, OAM, FMB
Mr. Shravan Donthi, OD, OIT
Dr. Olivier Duverger, DIR
Dr. Olga Epifano, DEA
Dr. Catherine Evans, OD, OCHE
Dr. Nardos Fessaha, DIR
Dr. Dena Fischer, DER, Center for Clinical Research (CCR)
Ms. Olivia Fish, DIR
Dr. Leslie Frieden, DEA, Research Training and Career Development Branch (RTCDB)
Mr. Christopher Greco, DIR
Ms. Marsha Greco, DER
Dr. Margaret Grisius, DER, CCR
Ms. Katherine Hall, DIR
Dr. Ashleigh Hanner, DIR
Ms. April Harrison, DEA
Ms. Jeannine Helm, DER
Mr. Gabriel Hidalgo, DEA, GMB
Dr. Minghan Hu, DIR
Mr. Tem Ibidapo, OD, OIT
Dr. Hiroko Iida, DER, CCR
Ms. Jennifer Jackson, DEA
Dr. Shyh-Ing Jang, DIR
Dr. Priyam Jani, DIR
Dr. Wenwen Jin, DIR
Dr. Rajesh Kar, DIR
Dr. Leila Khaki, DER, Behavioral & Social Sciences Research Branch (BSSRB)
Dr. Emir Khatipov, DER, Translational Genomics Research Branch (TGRB)
Dr. Zohreh Khavandgar, DIR
Dr. Fahad Kidwai, DIR
Dr. Jimok Kim, DEA, SRB
Dr. Yeowon Kim, DIR
Dr. Lynn King, DEA, TCDB
Dr. Jamie Kugler, DIR
Dr. Advait Limaye, DIR
Dr. Wei-Yin Lin, DIR

Dr. Orlando Lopez, DER, IBIDB
Ms. Amber Lowery, OD, OAM
Dr. Nadya Lumelsky, DER, IBIDB
Ms. Jayne Lura-Brown, DER
Ms. Susan Macharia, DEA
Dr. Jose Maldonado-Ortiz, DIR
Dr. Jacqueline Mays, DIR
Dr. Kevin McBryde, DER
Dr. George McGrady, DIR
Dr. Tamara McNealy, DER, IBIDB
Ms. Susan Medve, DEA, GMB
Dr. Yun Mei, DEA, SRB
Dr. Alissa Meister, OD
Dr. Amanda Melillo, DER, IBIDB
Ms. Amy Mhatre-Owens, OD, OCTOM
Ms. Yasamin Moghadam, DER, CCR
Mr. Ricky Moore, DEA, SRB
Dr. Shmuel Muallem, DIR
Ms. Mable Nee, OD, OAM, FMB
Ms. Suzanne New, OD
Mr. Paul Newgen, DEA, GMB
Ms. Anna Nicholson, OD, OCTOM
Ms. Pam Orzechowski, DIR
Dr. Vaishali Patel, DIR
Ms. Eileen Pelayo, DIR
Ms. Lisa Peng, OD, OIT
Ms. Liz Perruccio, DEA, SRB
Ms. Debbie Pettitt, DEA, GMB
Ms. Kendra Pope, DIR
Dr. Craig Rhodes, DIR
Dr. Elise Rice, DER, BSSRB
Dr. Melissa Riddle, DER, BSSRB
Dr. Pamela Robey, DIR
Ms. Delores Robinson, DEA
Ms. Diana Rutberg, DEA, GMB
Mr. Oscar Safairad, DIR
Dr. Reut Shainer Melamed, DIR
Dr. Yasaman Shirazi, DEA, SRB
Dr. Ashley Smith, OD, OIT
Dr. Katie Stein, DER, TGRB
Ms. Angela Swann, DIR
Dr. Ildiko Szalayova, DIR
Dr. Kelly Ten Hagen, DIR
Dr. Shoba Thirumangalathu, DEA, RTCDB
Mr. Joseph Tiano, OD, OSPA
Dr. Yolanda Vallejo, DER, IBID

Dr. Jessica Walrath, OD, OSPA
Dr. Jason Wan, DER, IBIDB
Dr. Lu Wang, DER, TGRB
Dr. Yan Wang, DIR
Dr. Blake Warner, DIR
Dr. Darien Weatherspoon, DER, CCR
Dr. Kenneth Yamada, DIR
Dr. Luciana Yamamoto de Almeida, DIR
Dr. Hongen Yin, DIR
Dr. Marian Young, DIR

National Institutes of Health

Mr. Anthony Conoway, Office of the Director
Dr. Karen Frank, Clinical Center
Dr. James Gilman, Clinical Center
Dr. Jordan Gladman, OD
Dr. Helene Langevin, National Center for Complementary & Integrative Health (NCCIH)
Ms. Meghan Rudd, OD
Ms. Kesha Stone, Clinical Center
Dr. Chiayeng Wang, National Cancer Institute (NCI)

Guests

Dr. Rena D'Souza, University of Utah, incoming NIDCR Director

I. WELCOME AND INTRODUCTIONS

Dr. Lawrence Tabak, Acting Director, NIDCR, called the open session of the 225th Advisory Council meeting to order. Dr. Tabak thanked Council members for attending and welcomed four new members to their first meeting. The new members are Dr. Joel Collier, Duke University; Dr. Frank (Hal) Ebetino of BioVinc, LLC; Dr. Axel Visel from the Lawrence Berkeley National Laboratory and Joint Genome Institute; and Dr. Ruth Ruprecht, University of Louisiana at Lafayette. Drs. Visel and Ruprecht have not received final approval for joining the Council and will be serving as ad hoc members for this meeting. Dr. Alicia Dombroski, Executive Secretary to the Advisory Council, reviewed the logistics of holding a virtual meeting and noted that the Council would be accepting questions and comments from the public via email (NIDCRcouncilmail@nidcr.nih.gov) until September 25th.

II. APPROVAL OF MINUTES FROM PREVIOUS MEETING

Dr. Dombroski invited the Council to consider and approve the minutes of the May 19, 2020, Council meeting. The Council unanimously approved the minutes.

III. REPORT OF THE DIRECTOR, NIDCR

Dr. Tabak's written September 2020 Director's Report to the Council was provided to the Council members and is available on the NIDCR website (<http://www.nidcr.nih.gov>). Dr. Tabak introduced Dr. Rena D'Souza, the NIDCR Director selectee, to the Council. Dr. Tabak expressed his excitement that Dr. D'Souza will be bringing her great depth of knowledge and experience to the Institute and to NIH. Dr. D'Souza is the Assistant Vice President for academic affairs and education for health sciences at the University of Utah. She also serves as a Professor of dentistry and Professor of neurobiology and anatomy, pathology, and surgery in the School of Medicine. She is expected to begin her new role as the NIDCR Director later this year. Dr. Tabak invited Dr. D'Souza to deliver remarks to the Council. Dr. D'Souza thanked Dr. Tabak for his leadership as interim director and for helping guide the Institute during these difficult times. She emphasized that Dr. Tabak has modeled the importance of focusing on discovery research and giving back to the community through service and mentorship. Dr. D'Souza underscored the historical role of NIDCR in catalyzing cutting edge research, which continues through to this day. NIDCR's scientific portfolio contains unique biological systems that are often intrinsically multidisciplinary in nature. This presents the Institute with some challenges but also many opportunities to push knowledge forward and ultimately improve human health. Drs. D'Souza and Tabak praised the NIDCR leadership team for their skill in helping the Institute maneuver through the challenges posed by the COVID-19 pandemic.

NIH has also recently announced new Director selectees for four other Institutes: Dr. Michael Chiang at the National Eye Institute, Dr. Lindsey Criswell at the National Institute of Arthritis and Musculoskeletal and Skin Diseases, Dr. Rick Woychik at the National Institute of Environmental Health Sciences, and Dr. Shannon Zenk at the National Institute of Nursing Research.

COVID-19 Update

Dr. Tabak presented the most recent case data on the pandemic. According to the John Hopkins University Coronavirus Resource Center, as of September 8th, 2020, a total of 27,392,203 confirmed cases had been reported globally, of which 6,308,741 were in the United States. A total of 897,713 deaths had been reported globally and the virus remains present in 188 countries. The pandemic continues to deeply disrupt how public health institutions have been focusing their resources and research; the NIH remains no exception.

NIH Response. Dr. Tabak discussed the actions NIH has taken to protect its staff during the pandemic. NIH has been testing symptomatic staff members since mid-March and has recently added asymptomatic staff testing. Occupational Medical Services is responsible for contact tracing for staff members who test positive or are exposed in high risk situations. NIH has also established return-to-work guidelines for recovered staff.

NIH quickly developed a trans-NIH strategic plan for COVID-19 research. The plan provides a framework for accelerating the development of therapeutic interventions, vaccines, and

diagnostics through five cross-cutting strategies: investments to increase fundamental and foundational knowledge; efforts to speed innovation in testing technologies; participation in public-private partnerships (ACTIV & Operation Warp Speed); development and promotion of preventative treatments and community prevention practices; and a focus on increasing accessibility of diagnosis, treatment, and prevention options for underserved and vulnerable populations.

Dr. Tabak described one of the public-private partnerships at the core of NIH's strategic plan. The Accelerating COVID-19 Therapeutic Interventions and Vaccine (ACTIV) partnership comprises 18 pharmaceutical companies, federal health agencies, and the European Medicines Agency, under the auspices of the Foundation for the NIH. The goal is to provide a framework for making recommendations to the FDA on preclinical guidelines, optimal trial design, and approval and consideration prioritization of potential interventions and vaccines. The result is a harmonized approach across multiple vaccine efficacy trials, including the mRNA investigational vaccine developed by Moderna, Inc. and the National Institute of Allergy and Infectious Diseases, which is currently in Phase III clinical trials. Over the last three months, ACTIV has evaluated hundreds of available therapeutic agents with potential application for COVID-19, and prioritized adaptive master protocols for clinical trials of immune modulators, inpatient and outpatient monoclonal antibodies, and anti-thrombotics, among other activities.

Another major component of the strategic plan is the Rapid Acceleration of Diagnostics (RADx) technology initiative. RADx aims to accelerate innovation, development, commercialization, and implementation of COVID-19 testing by funding innovative point-of-care diagnostic technologies, advancing late-stage diagnostic technologies to scale testing infrastructure, identifying effective testing implementation strategies in underserved populations, and working in close concert with other government agencies.

NIH has also established the COVID-19 Prevention Network (CoVPN), which aims to enroll thousands of volunteers in large-scale clinical trials testing a variety of investigational vaccines and monoclonal antibodies intended to protect people from COVID-19. CoVPN is currently involved in the Moderna, Inc. Phase III trial, the AstraZeneca Phase III trial, and two Phase III clinical trials testing whether experimental monoclonal antibodies can prevent SARS-CoV-2 infection.

Dr. Tabak briefly described several other COVID-19-related clinical trials and studies in which NIH is involved. These include a randomized clinical trial evaluating the safety and efficacy of remdesivir plus immunomodulator interferon beta-1a, National Institute of Biomedical Imaging and Bioengineering (NIBIB) efforts to utilize artificial intelligence and medical imaging to create new tools for COVID-19 early detection and personalized therapies, and *Eunice Kennedy Shriver* National Institute of Child Health and Human Development projects related to approaches to identify children at high risk for developing Multisystem Inflammatory Syndrome in Children and a study to track prevalence and impact of SAR-CoV-2 infection among pregnant women in low- and middle-income countries.

Dr. Tabak invited Dr. Jonathan Horsford, NIDCR Acting Deputy Director, to discuss NIDCR-specific activities.

NIDCR COVID-19 Initiatives. Dr. Horsford began by describing the Institute's COVID-19-related extramural funding opportunities. NIDCR issued several Notices of Special Interest to catalyze high-priority COVID-19 oral health research via supplements to existing grants in order to fund immediate and high impact research on COVID-19 transmission, pathogenesis, diagnosis, and the protection of dental patients and personnel. The first submission date was June 1st and the second round of applications is due November 2nd. NIDCR also developed a concept clearance to provide funding for investigators that do not hold existing grants. This concept will be presented to the Council later in the meeting. Dr. Horsford encouraged interested parties to visit NIDCR's website (www.nidcr.nih.gov/research/covid19) for further details. To date, NIDCR has funded approximately \$4M of immediate and high impact research related to the COVID-19 pandemic. Dr. Horsford highlighted several research studies that NIDCR has funded through the National Dental Practice-Based Research Network. Study topics include personal protective equipment use in dental settings, aerosol and droplet transmission in dental settings, and acceptance and usability of teledentistry.

Dr. Horsford next discussed NIDCR's involvement in the NIH-wide initiatives mentioned earlier by Dr. Tabak. NIDCR is active in the RADx radical (RADx-rad) program which funds new, non-traditional approaches, including rapid detection devices and home-based testing technologies that address current gaps in COVID-19 testing. NIDCR is co-leading two initiatives under RADx-rad. The first targets the development of novel, non-traditional, safe, and effective COVID-19 biosensing and detection approaches from the skin or oral cavity. The second is determining the utility of chemosensory (i.e., taste and smell) testing as a COVID-19 screening tool. NIDCR participates in two other RADx-rad programs looking at single vesicle or exosome analysis for the detection of SARS-CoV-2 and development and validation studies of COVID-19 surveillance methods for high-risk clustered populations.

NIDCR participates in another RADx initiative called RADx Underserved Populations (RADx-UP). This initiative supports interlinked community-engaged demonstration projects focused on implementation strategies to enable and improve testing of COVID-19 in vulnerable populations. Under RADx-UP, NIDCR is involved in efforts to address social, ethical, and behavioral implications of COVID-19 testing among underserved and/or vulnerable populations. An additional program that NIDCR participates in is focused on community engagement and access. Additional information and a full list of RADx funding opportunities can be found on NIH's website (www.nih.gov/research-training/medical-research-initiatives/radx/funding).

Dr. Horsford noted a number of stakeholder outreach activities NIDCR has conducted in recent months. NIDCR participates in calls led by the Chief Dental Officer of the U.S. Public Health Service, RADM Tim Ricks, between key federal and private stakeholders to discuss the impact of COVID-19 on oral health care in America. On June 11th, Dr. Horsford gave a presentation to the Oral Health Coordinating Committee on NIH & NIDCR COVID-19 initiatives. The Oral Health Coordinating Committee is the primary governmental body responsible for coordinating oral health initiatives across the federal government. On June 15th, NIDCR hosted a meeting with several federal stakeholders to discuss research and training gaps directly impacting the practice of dentistry and dental schools.

Temporomandibular Joint Disorders (TMJD) Multi-Council Working Group. Dr. Horsford updated the Council on the activities of the TMJD Working Group, which was established to respond to the findings of the National Academies consensus study, “Temporomandibular Disorders: Priorities for Research and Care,” which was released in March 2020. This report was supported by NIDCR and the NIH Office of the Director (OD). The Working Group is co-chaired by NIDCR Council member Dr. Clark Stanford, Dr. Bruce Rosen, and Ms. Christin Veasley. Dr. Rosen is on the NIBIB Advisory Council and Ms. Veasley is on the National Institute of Neurological Disorders and Stroke (NINDS) Advisory Council. The TJMD Multi-Council Working Group’s membership reflects the interdisciplinary nature of this disorder, and includes representatives from several NIH Institute, Center, and Office Councils. The Working Group will identify and prioritize research topics described in the consensus study and develop a roadmap to inform research priorities. The Working Group hopes to present its findings to the Advisory Council by May of 2021.

Other Updates. Dr. Horsford briefly updated the Advisory Council on the status of the 2020 Surgeon General’s Report on Oral Health. In addition to the full report, a preview document is under development to showcase some of the findings in a more expedited time frame. Dr. Horsford also updated the Council on the National Toxicology Program’s draft Fluoride Monograph. That draft report is now undergoing a second round of peer review at the National Academies after changes were made in response to the initial peer review. A public meeting of the review committee is scheduled to take place on October 19th. NIDCR looks forward to the release of the final report and potential opportunities to advance this research area.

IV. CONCEPT CLEARANCE

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: <https://www.nidcr.nih.gov/grants-funding/funding-priorities/future-research-initiatives-concept-clearances>. The NIDCR staff presented six concepts, and designated Council members led the discussion, as summarized below.

Dr. Lynn Mertens King, Chief, Research Training and Career Development Branch, provided a background overview for the first two concepts which provide research training support for dentist-scientists during a career transition. The overall goal of both concepts is to help sustain the dentist-scientist research workforce that is vital to identifying important clinical questions that drive basic discoveries, improve diagnostic and therapeutic approaches, and improve dental, oral and craniofacial health. In addition, the concepts will help provide robust research training pathways to build and sustain a well-trained research workforce. The concepts focus on continuity during the transition from predoctoral to postdoctoral and from dental specialty training to research-intensive postdoctoral and junior faculty positions. They are meant to fill gaps that currently exist in the research training pathway.

NIDCR Dual Degree Dentist Scientist Predoctoral to Postdoctoral Transition Award

Dr. Leslie Frieden, from the Research Training and Career Development Branch, presented the first research training pathway concept. The goal of the concept is to support the transition of individuals in integrated dental DDS/DMD and PhD programs from predoctoral student to postdoctoral position. The concept has two phases. The award Phase I (F99) grant covers the final two years of dual degree training and postdoctoral mentorship search. The award Phase II (K00) provides support for three years of mentored postdoctoral research career development. The programs are available to students enrolled in integrated clinical dental DDS/DMD and PhD programs in the United States. F30 and T32/T90 trainees are also eligible. This F99/K00 program is designed to complement existing research training grants currently offered by NIDCR and NIH. Dr. Frieden noted that the K00 allows for up to 25% of effort to be used for clinical or specialty training. NIDCR sees the F99/K00 awards as stepping-stones to promote continuance in the research pathway and future independent awards.

The Council's lead discussants were Dr. Nisha D'Silva and Dr. Clark Stanford. Dr. D'Silva expressed enthusiasm for the concept and agreed that it fills important gaps in the research training pathway. Studies have shown that up to 40% of dual degree research scientists left the research pathway for private practice, which highlights the importance of filling any existing gaps of support. Regarding the 25% clinical effort allowance in the K00, Dr. D'Silva suggested allowing for more flexibility in the percentage to provide some leeway for dentist-scientists involved in offsite rotations, which can vary in length based on the residency. She also recommended extending the length of the K00 to account for variation in lengths of residencies. Dr. Stanford also expressed support for the concept. He noted that many dual degree programs operate on a compressed timeline, which can result in dentist-scientists that emerge from the program in need of further research maturity. This concept provides the mentored guidance necessary to provide that maturity. Dr. Stanford seconded Dr. D'Silva's points about the importance of flexibility to account for the different types of specialty residency requirements and programs. In response to questions from the Council, Dr. Frieden confirmed that K00 awardees will be eligible for the NIH Loan Repayment Program.

The Council unanimously approved the concept.

NIDCR Administrative Supplements to Support Short-Term Dentist-Scientist Research Training

Dr. King presented the concept. This initiative will support short-term, mentored research training for outstanding early career dentist-scientists who have demonstrated high potential and strong interest in pursuing careers as clinician-biomedical scientists. This initiative aims to retain dentist-scientists in the biomedical research workforce and addresses the need to foster the transition of dentist-scientists from dental specialty or residency training to faculty positions with independent NIH/NIDCR grant support. The source of the funding will be through administrative supplements to active NIDCR research grants led by experienced investigators who will serve as research career mentors. Progress towards research career development and research independence will be guided by a structured plan of activities that includes the preparation of a competitive grant application for an individual NIDCR mentored career development award, or an independent research award. The supplement award will provide salary and research development costs for up to 12 months of support and will require a minimum of 75% research

effort. Up to 12 months of additional support will be considered for individuals who have demonstrated substantial progress in research and in submission of a grant application.

The Council's lead discussants were Dr. Raul Garcia and Dr. Clark Stanford. Dr. Garcia expressed enthusiasm about the concept and felt it ably addressed the current gaps in the research training pathway. He praised the inclusion of the option to apply for an extra 12 months of support as a way to provide flexibility to researchers in residency or specialty training. Both discussants felt it was important that the concept was linked to the R01 pathway. Dr. Stanford thought the availability for a second year of support might be crucial for some applicants, particularly those transitioning from clinical studies to research.

The Council unanimously approved the concept.

COVID-19 Research

Dr. Lillian Shum, Director, Division of Extramural Research, presented the new concept. The overall objectives are to encourage research that informs the prevention, detection, diagnosis, and treatment of COVID-19 and COVID-19-related illnesses and stimulate innovations in health surveillance and care delivery during the pandemic environment. Potential outcomes of funded research would be to strengthen the knowledge base of mechanisms of infection and transmission through oral/nasal routes, expand the spectrum of detection and diagnosis through oral/nasal cavities, transform the practice of oral health care, close the gap in oral health disparities and inequities, and inform management of the next pandemics. Given the ongoing state of the pandemic, longer term solutions are needed in disease management, health surveillance, and care delivery. Trans-NIH initiatives have provided many research opportunities for NIDCR-funded investigators, but there are still unfunded avenues to address the full spectrum of NIDCR's priorities. The NOSIs issued by NIDCR, described earlier by Dr. Horsford, represent initial steps to provide this additional support. NIDCR views these as initial seed grants that will lead to supporting research of greater breadth and depth. This concept has a number of areas of interest, including:

- Transmissibility of SARS-CoV-2 and mitigation strategies
- Approaches to minimize aerosolization during dental procedures
- Strategies to triage and manage patients
- Impact of dental care delivery delays, especially in underserved populations
- Impact on dental practitioners, their risk of infections, and chronic occupational health issues
- Oral mucosal immune responses
- Contribution of oral/nasal microbiota and ACE2 receptor on SARS-CoV-2 infectivity and related therapeutics
- Oral biomolecular signatures and oral biosensing technologies

The Council's lead discussants were Dr. Joel Strom, Dr. Wenyuan Shi, and Dr. David Couper. Dr. Strom said the decision to write the concept broadly was a good decision given the uncertain and fast-changing nature of the pandemic. He emphasized the importance of conducting research on the state of dental care during the pandemic and its toll on the dental

workforce. Dr. Shi said the concept is very timely in light of emerging evidence regarding SARS-CoV-2's unique role in the oral cavity, saliva, and salivary glands. Dr. Couper concurred with his colleagues' remarks and emphasized the need to shape research targets and findings in a way that can help prepare for future pandemics. Dr. McNeil said delays in care caused by the pandemic and patients avoiding care during the pandemic would be specific topic areas of importance that he hopes will be covered by this concept.

The Council unanimously approved the concept.

Targeting Upstream Social Determinants of Health

Dr. Darien Weatherspoon, Oral Health Disparities and Inequities Research Program, presented the concept. Social determinants of health (SDOH) are often defined as the conditions in the places where people live, learn, work, and play that can affect a wide range of health risks and outcomes. Examples of SDOH include availability and access to healthy foods, access to quality health care, the availability of reliable transportation, stable housing, and overall economic stability. SDOH can be influenced by larger societal-level influences, such as structural racism, discrimination, and certain policies, which can contribute to inequities related to these health determinants. Within the oral health research community there has been limited research on complex associations between SDOH and oral health and how to integrate SDOH in comprehensive interventions. The primary goals of this concept are two-fold: 1) to support research on how to optimally address SDOH that can be a barrier to optimal oral health and impede the effectiveness of preventive research interventions, particularly in vulnerable and underserved communities; and 2) generate scientific evidence to help inform policies and practices related to SDOH, in order to reduce and eliminate oral health disparities. This concept builds upon research currently funded through the Oral Health Disparities in Children Consortium. It also addresses a 2019 National Academies report recommendation that called for advancing research on SDOH.

The Council's lead discussants were Dr. Raul Garcia and Dr. Daniel McNeil. Dr. Garcia expressed strong support for the concept. In addition to responding to the National Academies report, it is also in alignment with Healthy People 2030 and recent National Institute on Minority Health and Health Disparities (NIMHD) NOSIs related to utilizing systems science in the study of SDOH. Dr. Garcia recommended that NIDCR consult the NIMHD NOSI to see how it can help inform its own efforts in this area. Dr. McNeil also expressed enthusiasm and urged support of this concept.

The Council unanimously approved the concept.

Understanding Oral Human Papillomavirus (HPV) Infection Acquisition and Persistence in People Living with HIV (PLWH)

Dr. Hiroko Iida, Director, HIV/AIDS & Oral Health Research Program, presented the concept. Oral HPV infection is an established risk factor for oral diseases, most notably oropharyngeal squamous cell carcinomas. The incidence of HPV-related oropharyngeal squamous cell carcinomas is on the rise over the last decade. People living with HIV are at two-

to four-fold increased risk for HPV-associated oropharyngeal squamous cell carcinomas as compared to people without HIV. The goal of this concept is to better understand the epidemiology and biology of oral HPV infection, its acquisition and persistence in people living with HIV, and the interrelationships between oral HPV infection and oral diseases in the context of HIV. The concept will attempt to address broad knowledge gaps related to our understanding of the epidemiology of oral HPV infection in people living with HIV and the impact of HIV on oral HPV acquisition and persistence. The concept builds upon two recent clinical and translational research initiatives: Oral Health in People Living with HIV and Additional Non-Communicable Diseases and Engaging Dental Professionals to End the HIV Endemic.

The Council's lead discussants were Dr. Nisha D'Silva and Dr. Ruth Ruprecht. Dr. D'Silva expressed strong support for the concept and expressed enthusiasm regarding the breadth of the concept. There are a number of unanswered questions and a wide range of topics of interest related to oral HPV and people living with HPV. Dr. Ruprecht also praised the timeliness and importance of this concept at the intersection of two major virus-related populations. She also lauded NIDCR's promise to issue future concepts related to prevention and the possibility of recruiting a dentist to assist in Gardasil vaccine administration efforts. She also thanked NIDCR for their continued support of research on "the other pandemic," HIV. Dr. Garcia asked what the barriers are to dentists prompting HPV vaccination. Dr. Iida said the states have different guidelines and laws related to the scope of work of dental professionals. There are other barriers related to reimbursement, coordination of follow-up care, and acceptance from the patient population. Dr. Stanford said orthodontists could be a good place for vaccination efforts given that repeated appointments are common through orthodontal care. Dr. Garcia asked if there was an NIDCR effort that could be mounted to address those barriers. Dr. Iida said the Engaging Dental Professionals to End the HIV Endemic initiative will attempt to address similar barriers from the HIV perspective. Building off that effort on the topic of HPV could be a good addition to NIDCR's research agenda.

The Council unanimously approved the concept.

Research Enhancement Award Program (REAP) for Health Professional Schools and Graduate Schools

Dr. Alicia Dombroski, Director, Division of Extramural Activities, presented the concept. Dr. Dombroski noted that this is an NIH-wide concept, rather than an NIDCR concept. Since NIDCR took the lead on development of the concept, its Council is tasked with approval on behalf of NIH. This concept is for reissuance of a previously published program.

Beginning in fiscal year 1985, congressional appropriations for the NIH have included funds for the Academic Research Enhancement Award (AREA) R15 program with the intention of supporting research at primarily undergraduate institutions. Over time, the AREA program expanded to include institutions that focus on health professional and graduate student education. In 2018, NIH decided to return to the original intent of the program to support institutions with majority undergraduate enrollment. The overall goal of this concept is to stimulate research in educational institutions that offer baccalaureate or advanced degrees but have not traditionally been major recipients of NIH support. REAP grants create opportunities for scientists and

institutions otherwise unlikely to participate extensively in NIH research programs to contribute to the nation's biomedical and behavioral research effort. REAP grants are intended to support small-scale research projects proposed by faculty members at eligible domestic health professional schools or graduate schools to engage undergraduate and/or graduate students in meritorious projects in biomedical or behavioral research, and to strengthen the research environment of the applicant institutions. Eligible institutions must award baccalaureate or advanced degrees in health professions and have received no more than \$6 million per year in NIH funding in four of the past seven fiscal years. PIs must have their primary appointment at eligible institutions and cannot be the current recipient of NIH funding. Among other requirements, the application should describe how undergraduate/graduate students will be engaged in and supervised conducting hands-on research, including how students will participate in research activities such as planning, execution, and/or analysis of data and results. However, this is not a training program and applicants do not have to provide descriptions of training. The award will provide up to \$300,000 for direct costs across a project period of up to three years. The award can be competitively renewed.

The Council's lead discussants were Dr. Kathryn Albers and Dr. Lee Niswander. Dr. Albers expressed support for the concept, which she believes should advance the research environment at smaller institutions. Dr. Niswander concurred and added that, while this is a young program without much outcome data, she has seen similar AREA programs bear fruit in improving the research environment at underserved institutions. She expressed a concern that the past NIH funding requirement applies to the parent medical school or health center rather than specific dental school within that parent organization, which could limit the number of eligible or deserving institutions. Dr. Dombroski said she would pass that concern on to the NIH-wide committee that governs the program.

The Council unanimously approved the concept.

V. INTRAMURAL COVID-19 UPDATE – THE ROLE OF SALIVA IN TRANSMISSION OF SARS-CoV-2

Dr. Tabak began the session on the NIDCR intramural activities by remarking that one of the unique traits of NIH intramural research is its ability to quickly pivot in response to developing public health emergencies. This has been the case during the COVID-19 pandemic, where NIH intramural researchers have been able to make some important initial contributions while the funding and coordination necessary for large scale extramural activities were being marshaled. The studies that will be discussed today are just a few of the rapidly initiated COVID-19 protocols that NIH intramural researchers developed within weeks of the initial pandemic outbreak. Dr. Janice Lee, NIDCR Clinical Director, introduced the session. Based on initial findings on asymptomatic transmission of SARS-CoV-2 and reports of loss of taste and smell in infected individuals, the NIH COVID-19 Response Team, led by Dr. Tabak, pushed early on for studies on oral-related phenomena and SARS-CoV-2. Dr. Lee, with Dr. Blake Warner, Chief of the Salivary Disorders Unit, and the research team were able to conceive, develop, initiate, and enroll initial subjects in this saliva study by April. It was the second NIH study to begin enrolling subjects, second to the remdesivir trial. This was a remarkable achievement given the uncertainty of the pandemic at the time and the state of Maryland stay-at-home policy. Dr. Peter Burbelo and

Dr. Karen Frank will also present their work on antibodies and validation of saliva testing, respectively.

Update on the COVID-19 Saliva Study at the NIH

Dr. Warner presented preliminary findings from his study looking at the role of saliva in transmission and infection of SARS-CoV-2. As Dr. Lee said, it was early hypothesized that the SARS-CoV-2 was present in saliva. This fact was quickly confirmed, but there remained a great deal of open questions about SARS-CoV-2 in saliva, such as its source and infectiousness, potential for asymptomatic droplet transmission, use in diagnostics, and the effectiveness of masks to reduce transmission. This study was designed to answer some of these questions. Other speakers will talk about saliva-based diagnostics, so Dr. Warner focused on the study's two other primary aims: estimating the probability of asymptomatic transmission from saliva droplet ejection/aerosolization and the reduction in risk due to mask use, and identifying the cellular source of SARS-CoV-2 in saliva. Dr. Warner first presented a brief overview of the distribution of salivary glands within the oral cavity, the state of knowledge on the virus, and then walked through a series of experiments his team conducted to identify the cellular source. In particular, the experiments focused on the minor salivary glands. Dr. Walker walked through the testing procedure at NIH and how the team enrolled its cohort of asymptomatic subjects. He then described the speaking test that the team conducted to assess the effectiveness of standard surgical masks in preventing asymptomatic transmission. That test showed an eight-fold reduction in PCR-detectable saliva, showing strong support for the effectiveness of masks for the reduction of saliva-based transmission. Dr. Warner next discussed single cell sequencing his team conducted on cells procured from healthy human salivary gland biopsies. The team used this data to create SARS-CoV-2 entry factor expression maps to identify putative target cells for infection across diverse tissues with heterogeneous composition. Dr. Warner's team utilized fluorescent in situ hybridization (FISH) to confirm single cell sequencing findings that the ACE2 enzyme and TMPRSS2 protease, the principal entry factors for SARS-CoV-2, are restricted to the epithelial structures of the glands. The team also found that the salivary gland ducts and acini express these principal SARS-CoV-2 entry factors, with the ducts appearing to have higher co-expression of both factors. In collaboration with the NIH COVID-19 Autopsy Consortium, Dr. Warner's team then conducted studies of salivary glands collected from deceased COVID-19 victims to see if the virus itself could be found in the minor salivary glands. Analysis found that ACE2+ cells in the salivary gland ducts and acini harbor SARS-CoV-2 and Digital Droplet PCR detected SARS-CoV-2 in 7 out of 13 salivary glands analyzed. Other parts of the study found ACE2 expression of SARS-CoV-2 genomes in sloughed epithelial cells in saliva from COVID-19-positive subjects.

The Role of Saliva and Antibodies during the COVID-19 Pandemic

Dr. Peter Burbelo, Staff Scientist, Division of Intramural Research, presented his work on SARS-CoV-2 antibodies in blood and saliva. One of Dr. Burbelo's main research interests is the role of antibodies and autoantibodies in Sjogren's syndrome. As part of this work, Dr. Burbelo developed a technique called the luciferase immunoprecipitation system (LIPS), which is a liquid phase immunoassay allowing high-throughput serological screening of antigen-specific antibodies. The immunoassay involves quantitating serum antibodies by measuring luminescence emitted by the reporter enzyme Renilla luciferase (Rluc) fused to an antigen of interest. As the

pandemic emerged, Dr. Burbelo began to design tests that would leverage this system for research on SARS-CoV-2. His team analyzed SARS-CoV-2 nucleocapsid and spike antibodies in serum. Dr. Burbelo also discussed the results of similar studies of saliva samples collected by Dr. Warner's team.

Update on Saliva Validation at NIH

Dr. Karen Frank, Chief, Department of Laboratory Medicine, NIH Clinical Center, presented on COVID-19 diagnostics research at the Clinical Center. After the virus was first identified and sequenced, multiple PCR assays were developed which use different combinations of SARS-CoV-2 gene targets. NIH started with the WHO assay and then moved to the CDC assay once it became available. Dr. Frank briefly discussed the testing and validation systems that have been used at NIH over the course of the pandemic, and then described the saliva testing validation study conducted at the Clinical Center. The study began in April, in collaboration with the Maryland Department of Health, and samples were initially to be collected from Maryland nursing homes. The collection process was not as efficient or as comprehensive as the team had hoped, so a new IRB protocol was started at NIH with samples collected at the testing car line on campus, similar in method to the Warner saliva study. Over 400 subjects were consented into the protocol and over 30 SARS-CoV-2 positive subjects were identified, which was a number sufficient for the purposes of validation. Saliva collected was compared to nasopharyngeal (NP) swabs in paired specimens. The study found 95% concordance for positivity when NP swab Ct value was less than or equal to 30. The overall finding was that saliva is slightly less sensitive than NP swabs, primarily for so-called "weak" positives, but has good performance in general. For context, Dr. Frank compared the saliva testing sensitivity to the sensitivities of NP testing from other studies conducted by the research community.

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).

VII. REVIEW OF APPLICATIONS

VIII. ADJOURNMENT

CERTIFICATION

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

Lawrence A. Tabak -S
Digitally signed by
Lawrence A. Tabak -S
Date: 2020.11.03
18:27:38 -05'00'

Dr. Lawrence A. Tabak
Acting 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