

**NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE ON AGING**

Summary Minutes

The 143rd Meeting

NATIONAL ADVISORY COUNCIL ON AGING

May 11-12, 2021

**National Institutes of Health
Virtual Meeting
Bethesda, MD 20892**

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Department of Health and Human Services
Public Health Service
National Institutes of Health
National Institute on Aging

**NATIONAL ADVISORY COUNCIL ON AGING
SUMMARY MINUTES
May 11-12, 2021**

The 143rd meeting of the National Advisory Council on Aging (NACA) was convened on Tuesday, May 11, 2021, at 3 p.m. by videoconference. Dr. Richard Hodes, Director, National Institute on Aging (NIA), presided.

In accordance with the provisions of Public Law 92-463, the meeting was closed to the public on Tuesday, May 11, from 3 p.m. to 5 p.m. for the review, discussion, and evaluation of grant applications in accordance with the provisions set forth in Sections 552(b)(c)(4) and 552(b)(c)(6), Title 5, U.S. Code and Section 10(d) of the Public Law 92-463.¹ The meeting was open to the public on Wednesday, May 12, from 10:00 a.m. to 12:58 p.m.

Council Participants:

Mr. James Appleby
Dr. Shalender Bhasin
Dr. Dedra Buchwald
Ms. Meryl Comer
Dr. Monica A. Driscoll
Dr. Terry T. Fulmer
Dr. Alison M. Goate
Dr. Margaret Goodell
Dr. Yadong Huang
Dr. Rev. Cynthia Huling Hummel
Dr. Jennifer J. Manly
Dr. Eric Michael Reiman
Dr. David B. Reuben
Dr. Clifford James Rosen
Dr. Julie A. Schneider
Dr. Amy Jo Wagers
Dr. David Weir
Dr. Keith E. Whitfield

Members of the Public Present:

Ms. Kelly Clayton, Rose Li and Associates, Inc.
Ms. Nancy Tuveson, Rose Li and Associates, Inc.

¹ For the record, it is noted that members absented themselves from the meeting when the Council discussed applications (a) from their respective institutions or (b) in which a conflict of interest may have occurred. This procedure only applied to applications that were discussed individually, not to “en bloc” actions.

I. REVIEW OF APPLICATIONS

This portion of the meeting was closed to the public, in accordance with the determination that it concerned matters exempt from mandatory disclosure under Sections 552(b)(c)(4) and 552(b)(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

A total of 2,279 applications requesting \$5,033,952,881 for all years underwent initial review. The Council recommended 1,206 awards for a total of \$3,043,430,950 for all years. The actual funding of the awards recommended is determined by the availability of funds, percentile ranks, priority scores, and program relevance.

II. CALL TO ORDER

Dr. Hodes welcomed members to the open session of the 143rd NACA meeting and called the meeting to order at 10:00 a.m. on Wednesday, May 12, 2021.

A. Director's Status Report

NIH/NIA Budget Status

Dr. Hodes reported that neither the Senate nor House had yet released draft bills pertaining to the Fiscal Year (FY) 2022 budget. President Biden's "skinny" budget, released in April 2021, proposes a \$51 billion appropriation for NIH, a substantial increase of \$9 billion from the FY 2021 enacted level. The additional \$9 billion includes \$6.5 billion to establish the Advanced Research Projects Agency for Health (ARPA-H), which would initially focus on cancer and other diseases such as diabetes and Alzheimer's disease (AD).

The interim paylines presented during the previous NACA meeting in January remain unchanged. For general applications reviewed by the Center for Scientific Review (CSR) and requesting less than \$500,000 (direct costs) in any one year, paylines are 8% for most applications, 11% for new investigator regular research (R01) applications, and 13% for early-stage investigator R01 applications. For CSR-reviewed applications seeking \$500,000 or more, paylines are 5% for most, 8% for new investigator, and 10% for early-stage investigator applications. Paylines are higher for applications focused on AD and AD-related dementias (AD/ADRD): 28% for most, 31% for new investigator, and 33% for early-stage investigator applications. Dr. Hodes noted that interim paylines for NIA-reviewed applications (e.g., program project, career development, and fellowship awards) were 15% to 21% for general applications and 35% to 40% for AD/ADRD-targeted applications. The payline for general parent career development awards increased to 21% from the 20% reported during the previous meeting.

COVID-19 Updates

Dr. Hodes explained that NIH recently released a Notice of Special Interest (NOT-AG-21-016) regarding Neurological and Neurocognitive Sequelae from SARS-CoV-2 Infection and COVID-19 in Aging and Age-Related Neurodegeneration. NIH also recently announced a \$1.15 billion

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initiative to study post-acute sequelae of SARS-CoV-2 (PASC) infection, also known as “long COVID.” The PASC Initiative will focus on the substantial number of people suffering from a variety of persistent symptoms, including neurological complications. Researchers will target the causes of prolonged illness, as well as prevention and treatment options. Two PASC research opportunity announcements have been released: (1) to establish recovery cohort studies for longitudinal research on individuals suffering from PASC and (2) to create a series of Cores—Clinical Science Core, Data Resource Core, and a PASC Biorepository Core.

Dr. Hodes commented that NIH is very aware of the pandemic’s impact on the career trajectories of early-career scientists, particularly women and those who care for young children. In response, NIH and NIA will support Fellowship (F) and Career Development (K) awardees in the form of no-cost extensions and funded extensions, upon request.

HHS and NIH Updates

Dr. Hodes reported that Xavier Becerra was confirmed to serve as HHS Secretary by the Senate on March 18, 2021. Secretary Becerra’s career as Attorney General of California and a 12-term member of Congress has focused on immigration, access to health care, and equity and inclusion.

Dr. Hodes reaffirmed NIH’s commitment to ending structural racism. NIH continues to explore ways to support diversity, equity, and inclusion and to identify and dismantle policies and practices that could harm the workforce and the science. The Task Force on Minority Aging Research recently engaged in an extensive discussion that covered many fronts, particularly the UNITE Initiative to address structural racism in biomedical research. NIA staff hold a number of prominent UNITE leadership roles: Dr. Marie Bernard as UNITE Co-Chair and I Committee Co-Chair; Melissa Espinosa as I Committee member; Dr. Michele Evans as N Committee Co-Chair; and Dr. Patricia Jones as E Committee member. The primary goals of UNITE are as follows:

- U—Understanding stakeholder experiences through listening and learning
- N—New research on health disparities, minority health, and health equities
- I—Improving NIH culture and structure for equity, inclusion, and excellence
- T—Transparency, communication, and accountability with our internal and external stakeholders
- E—Extramural research ecosystem: changing policy, culture and structure to promote workforce diversity

The Accelerating Medicines Partnership—Alzheimer’s Disease 2.0 (AMP AD 2.0) launched in March 2021. AMP AD 2.0 is designed to further work toward a precision medicine approach by identifying and validating targets for biomarker and intervention studies. The program has several new foci to inform understanding of the heterogeneity of the dementias and their underlying pathologies: (1) expand multi-omic profiling in tissue and blood samples from diverse cohorts, including African American and Latino American; (2) generate longitudinal immunologic profiling data across diverse cohorts, including Caucasian, African American, and Latino American; and (3) expand the existing single nuclei and single cell molecular profiling efforts to multiple brain regions and in samples from diverse cohorts.

The Agency for Healthcare Research & Quality (AHRQ) conducted a rigorous systematic review of the evidence on care and caregiving interventions for people living with dementia (PLWD)

and their caregivers and released its report in July 2020. Subsequently, the National Academies of Sciences, Engineering, and Medicine (NASEM) established an expert committee to develop a report outlining a set of recommendations on the functional readiness of AHRQ's proposed interventions, as well as any research gaps in the field. The key messages of NASEM's report, released in February 2021, are as follows: (1) Most caregiving interventions were not assessed in the AHRQ study because they had small sample sizes, were pilots, or had a high risk of bias. (2) Two types of interventions demonstrated low-strength evidence of benefit in clinical trials: Collaborative Care and Resources for Enhancing Alzheimer's Caregiver Health (REACH) II. (3) These interventions should be more broadly implemented in real-world settings that allow for continual monitoring, evaluation, and quality improvement. The AHRQ and NASEM studies reinforced NIA's commitment to rigorous and inclusive studies.

Dr. Hodes noted several NIA staffing updates, including the selection of Andy Singleton as Director of the Center for Alzheimer's and Related Dementias (CARD). CARD is a new intramural laboratory focused on expanding knowledge of the biological mechanisms of AD/ADRD and exploring methods of treatment and prevention. Dr. Ron Kohanski was selected as Director of the Division of Aging Biology (DAB), where he has served as the interim director since last year. Further, 11 NIA OD/ERP professional staff were hired since the January meeting.

Since the January meeting, NIA has released 22 research highlights, featuring one or more NIA-supported publications; 17 new blog posts; 11 news announcements; and three press releases. Furthermore, Dr. Hodes, Dr. Bernard, and/or senior NIA staff have participated in six stakeholder/advocacy group meetings and three congressional briefings. Dr. Hodes introduced the new [Alzheimers.gov](https://www.alzheimers.gov) website as the destination for information about dementia, people living with dementia, their caregivers, and NIA and other federal agencies involved in AD/ADRD research. NIA welcomes feedback on ways to improve the value of the site. The 2021 NIH Alzheimer's Disease Research Summit, "Path to Precision Medicine for Treatment and Prevention," was held in April, and the archived presentations are now available. Dr. Hodes expressed thanks to all of the NIA and NIH staff who worked on the summit, as well as the many investigators and other participants who were instrumental to its success.

B. Future Meeting Dates

September 14-15, 2021 (Tuesday and Wednesday), Virtual
January 25-26, 2022 (Tuesday and Wednesday), Building 45
May 5-6, 2022 (Thursday and Friday), Building 45
September 7-8, 2022 (Wednesday and Thursday), Building 45

C. Consideration of Minutes of the Last Meeting

The minutes of the January 2021 Council meeting were considered. A motion was made, seconded, and passed unanimously to approve the minutes.

III. REPORT: TASK FORCE ON MINORITY AGING RESEARCH

Co-chairs Drs. Cliff Rosen and Keith Whitfield presented an update on the Task Force meeting on May 11, including a summary of Dr. Bernard's presentation on the UNITE Initiative and Diversity Catalysts. Dr. Rosen began by acknowledging the substantial efforts of the former co-

chairs, Drs. David Bennett and J Taylor Harden, who disseminated information about the Task Force’s mission and NIA’s efforts to improve diversity, inclusion, and equity.

The UNITE Initiative was a main topic of the Task Force’s May 11 meeting. UNITE recognizes the need for NIH to ensure that biomedical research, and the administrative system that supports it, are devoid of hostility grounded in race, sex, and other federally protected characteristics and to proactively work toward eradicating existing structural racism. Programs are in place, in various stages of implementation, to achieve UNITE’s goals:

- Current and future efforts to promote “Understanding” include refining and expanding a qualitative data collection plan; obtaining information from the various Institutes and their directors regarding current or past activities to inform future UNITE activities; and publishing a request for information seeking input and effective ways to improve diversity and inclusion in research institutions.
- “New research” either in progress or the planning stages includes analyzing the current investments in minority health, health diversity, and health equity (MH/HD/HE) research with key intramural and extramural stakeholders; developing and testing of budget and portfolio tracking and an analytic budget tool for use across NIH to transparently and accurately report funding for MH/HD/HE-focused research; proposing a Common Fund initiative on interventional research in HD for FY 2023; creating an initiative on translation of multi-level interventions to reduce HD; and issuing a Common Fund Funding Opportunity Announcement (FOA) to drive innovation and transformation in reducing health disparities and increasing health equity nationwide.
- Current and future “Improving” efforts include expanding NIH policies to explicitly address racial discrimination and making staff aware of options for reporting racist actions; expanding recruitment of NIH investigators to include members of underrepresented groups; establishing an anti-racism steering committee and coordinating action plans across Institutes; and appointing a diversity, equity, and inclusion officer in every IC who has direct access to the IC director.
- Current and future efforts to create “Transparency” include publicly committing to identifying and correcting any NIH policies or practices that may have helped to perpetuate structural racism; launching a new webpage that provides information about NIH anti-racism policies and efforts; launching both external and internal facing awareness campaigns; and diversifying the portraiture around NIH.
- Current and Future “Extramural” efforts include focusing on stakeholder engagement; reporting grantee demographics in the NIH Databook; and developing possible programmatic proposals encompassing career pathways, institutional culture, evaluation of NIH processes, and expanded assistance to minority-serving institutions.

Diversity Catalysts were nominated by senior leadership of their respective Institutes and Centers (ICs) to bring a fresh perspective and new approaches to make significant progress toward achieving scientific workforce diversity (SWD). Diversity Catalysts are charged with contributing to meeting UNITE’s goals; facilitating adoption of SWD resources and tools in their IC; supporting and amplifying SWD communications; and creating channels of clear, consistent communication with IC leadership and Diversity Catalyst committees regarding intramural and extramural activities.

To conclude his comments, Dr. Rosen noted that the Butler-Williams Scholars Program will meet virtually on August 24-26.

Dr. Whitfield summarized the second part of the May 11 Task Force meeting, during which members discussed three manuscripts on the grant submission success rates of African Americans. Members noted that the analyses seemed to oversimplify the problem by identifying a “silver bullet” that overlooks the possibility of more than one causal factor. Members emphasized the need for additional feedback on triaged proposals to enhance the review process and the need to understand whether the low success rates among African Americans extends to other minority groups.

Members then raised the “pipeline issue,” which must be addressed to increase the diversity of grant applicants. Some members commented that minority supplements may be underutilized at the undergraduate and high school levels; Dr. Whitfield emphasized the need for more data to substantiate this claim. Other underutilized efforts to increase the numbers of minority applicants and their success rate include summer programs such as the Butler-Williams Scholars Program and the MOSAIC funding opportunity. Members suggested that NIH should cultivate relationships with historically Black colleges and universities (HBCUs) and other minority serving institutions. Further, the UNITE Initiative should advance equity in grant submissions, and social media advertisements could broadcast grant opportunities to a wider and more diverse group of researchers.

Dr. Bernard commented that UNITE is garnering a lot of energy and enthusiasm about its potential. She appreciates feedback from the Task Force members and NACA members. Dr. Bernard noted that NIA is committed to providing updates to the NIH Advisory Committee to the Director every June and December, and she extended the offer to update NACA at that time, as well.

Dr. Manley commented that Dr. Bernard’s May 11 presentation was inspiring. She considers UNITE’s activities to dismantle structural racism at NIH to be comprehensive and encouraging. Referring to the pipeline issue, she emphasized the critical needs to invest in scholars at all stages of science and to engage with underrepresented people in science and medicine. She added that the cultures of training in science and medicine, academia, and grant funding is often taxing and stressful for minority scientists, so tying funding to authentic efforts at the institutional and team levels would leverage UNITE’s efforts to achieve its mission.

IV. REPORT: WORKING GROUP ON PROGRAM

A. Recommendations from Past Meetings and Planned Meetings—None

B. FOA Concept Clearances

Dr. Monica Driscoll, Chair of the Working Group on Program (WGOP), invited the primary reviewers to summarize the four concepts submitted from three NIA units: Division of Aging Biology, Division of Neuroscience, and Office of Small Business Research. The primary reviewers had provided detailed summaries of the concepts, requested amendments or changes, and documented the WGOP decision. Although the WGOP suggested minor changes to some

concepts, it approved all concepts for full Council consideration. The Council members unanimously concurred with approval of the four concepts seeking clearance.

Limited Competition: Renewal of the Caenorhabditis Intervention Testing Program (U01) and Its Data Coordinating Center (U24)

The proposed concept would expand the Testing Program to include a specific effort to test compounds for their effects on aging hallmarks and models related to AD/ADRD. Testing compounds under the same conditions across three laboratories allows for precise assessment of their efficacy in moderating age-related health declines across diverse species.

Diversifying the Therapeutic Pipeline for AD/ADRD: Drug Discovery for Novel Targets

The proposed concept would help to clarify which candidate targets identified by other projects are potentially druggable. The initiative would improve, diversify, and reinvigorate the AD/ADRD drug development pipeline by leveraging the work done by AMP-AD and other initiatives aimed at discovering nascent, candidate therapeutic targets.

Reissue of the Alzheimer's Drug Development Program (ADDP)

Since 2006, the ADDP has provided funding to academic and biotech researchers to develop AD therapeutics in their own laboratories. AD drug development is one of the top research priorities for NIA. Researchers are learning more about the multifactorial and heterogeneous makeup of AD and seek to develop multitarget therapeutics to address the manifold nature of AD. A web viewer emphasized the importance of continuing to fund these projects to treat and, hopefully, eventually cure AD.

Small Business Innovation Research (SBIR) Research Contract Topics

SBIR attempts to stimulate innovation and address unmet scientific needs through the private sector. This proposal adds three NIA topics to the NIH Parent SBIR contract solicitation: (1) Geroscience-based Chronic Wound Treatment Product Development, (2) The Development of Mechanism-based Adult Stem Cell Treatments to Combat Aging Pathologies, and (3) Improving CNS Gene Delivery Systems for AD/ADRD Therapy Development. SBIR has been a successful program, and Council members noted that application numbers have doubled from FY 2019 to FY 2020.

V. PROGRAM HIGHLIGHTS (DAB)

Long-term Studies of Wild Animal Systems Yield Insights and Advances in the Biology of Aging

Anne Bronikowski, Ph.D., Professor, Department of Ecology, Evolution, and Organismal Biology, Iowa State University

Laboratory studies on model genetic species have revealed candidate phenotypes and molecular networks that underlie aging. They have also identified allelic variants that alter aging rates and life expectancy. These revelations have coalesced into seven pillars, or hallmarks, of aging: Macromolecule Damage, Proteostasis, Inflammation, Metabolism, Stress Adaptation, Stem Cells and Regeneration, and Epigenetics. Although these pillars create a complex system, they provide an organizing principle for research focused on the biology of aging. Dr. Bronikowski sees

comparative biology as offering a complementary approach to querying these pillars across diverse animal species in order to discover evolutionary adaptations. Further, comparative biology, within a specific phylogenetic context, can reveal conserved and flexible (evolving) nodes in aging networks, which are prime targets for interventions in human aging, as well as the evolutionary history of variants as adaptive or single-species anomalies.

Reptiles have several features that recommend them for comparison to mammalian aging, including protective phenotypes, such as shells, venom, and armor. They also possess biological features that recommend them to specific pillars of aging, such as metabolic plasticity and stress adaptation that provide resistance to heat and cold stress and hypoxia; regenerative abilities; and both environmental and genotypic sex determination systems. Dr. Bronikowski and her colleagues have identified flexible nodes across mammals and reptiles. As one example, they have found that, across amniotes, the P53 gene and its regulator (MDM2) are the fastest evolving genes across mammals and reptiles. Further, in P53, specific amino acids are underdiversifying selection in reptiles. The researchers are now taking some of these variants and using CRISPR/Cas to knock-in reptile P53 alleles in cell culture and then test their phenotypes related to DNA repair efficiency to a battery of genotoxic treatments.

Turtles are excellent candidates for genome-wide research, because they have slow molecular evolutionary rates relative to other major lineages in the amniotes and they have slow demographic aging relative to other tetrapods (amniotes and amphibians). The painted turtle is a particularly appropriate model for aging research for several reasons. First, painted turtles exhibit extraordinary hypoxia resistance, especially in the brain, and are a current model for brain research. Second, hatchlings can supercool to as low as -14 degrees Celsius and are a current model for cryogenics research. And third, painted turtles' sex determination is temperature dependent; there are no sex chromosomes, no sex-linked genes, and no genomic architecture differences between female and male at conception.

Dr. Bronikowski summarized the field's findings about the painted turtle. Turtles age slowly relative to other tetrapod lineages. At a genome-wide level, their molecular evolution is slow; however, in candidate aging networks, they exhibit rapid evolution in key aging genes. They also have a heritable, sexually dimorphic lifespan despite identical genomes among males and females. Methylation levels and OxPhos decline as turtles age, and age-related gene expression changes are overwhelmingly downregulated with advancing age. Laboratory studies have revealed phenotypes and loci that underlie aging. Yet, gaps in knowledge persist because there are relatively few animal species models, any species' homology to humans is imperfect, and the sample is incomplete. Dr. Bronikowski suggests that studies of wild non-model species can help address these gaps. These wild-dwelling species are amenable to genetic manipulation, and because they are wild, they reflect the natural context in which human aging evolved, enabling comparisons and contrasts among solutions to the problem of aging.

In response to questions posed by Council members, Dr. Bronikowski noted that female and male turtles remain fertile their entire life; however, female fitness declines at the very end of life. Many long-term studies have examined the painted turtle lifespan and demographic features. Dr. Bronikowski is developing a proposal to study the genetics and epigenetics of turtles in different regions to better understand lifespan changes among different populations. To account for different lifespans across species in preserved and non-preserved loci, Dr. Bronikowski

includes a variant in her statistical analysis. However, a whole host of environmental factors could cause variations in turtle lifespan, which requires additional study of different populations and their environmental features.

Dr. Bronikowski agreed with a Council member that hormones are likely even more important in the turtle system than other systems because turtles do not have sex chromosomes. She also noted that where researchers look for binding proteins in turtles, they find them. Finally, researchers are just starting to scratch the surface of expression and RNA and hope to more deeply study epigenomic data in the future.

VI. COUNCIL SPEAKER

Update from NINDS

Walter Koroshetz, M.D., Director, National Institute of Neurological Disorders and Stroke (NINDS)

Neurological disorders, substance abuse, and mental and behavioral disorders comprise 30% of the burden of disease in the United States. Stroke victims are captured in the 12% of disease burden caused by cardiovascular and circulatory diseases. NINDS' mission is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease. The strategies to achieve this mission include investing in basic, translational, and clinical research; identifying any gaps in research and public health needs; communicating and collaborating with all stakeholders, including the public; evaluating and continuously improving all NINDS programs; and training a talented and increasingly diverse research workforce.

The pre-COVID-19 NIH budget included \$9.47 billion for neuroscience research. The majority of these funds were dedicated to NINDS, NIA, and the National Institute of Mental Health (NIMH)—the primary supporters of such research in the United States. NINDS' funds were divided among the base budget and three main targeted NINDS programs: the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, the 21st Century Cures Act, and the HEAL Initiative. NINDS consists of three major divisions: (1) the Division of Neuroscience focuses on fundamental neuroscience and is disease agnostic, (2) the Division of Translational Research focuses on accelerating basic research findings through the research pipeline, and (3) the Division of Clinical Research runs clinical trials. About 75% of the NINDS budget is dedicated to basic research, and the remaining 25% is divided between the Translational Research and Clinical Research divisions.

Researchers from NINDS and NIA explore dementia treatments, prevention, and risk reduction, as well as ways to improve care management. Dr. Koroshetz believes that NINDS' greatest contribution to Alzheimer's research lies in understanding the vascular contributions to cognitive impairment and dementia (VCID). The majority of dementia cases in the elderly population are mixed dementia (MED), mainly Alzheimer's pathology with cerebrovascular disease and/or Lewy bodies, and understanding the intersections of the ADRDs is important to both NINDS and NIA.

NINDS is working to address the recommendations that emerged from the most recent ADRD Summit related to multiple etymology dementias (MED), health disparities (HD), development of a common nomenclature among disease-related groups, VCID, Lewy body dementia (LBD), frontotemporal dementia (FTD), TDP 43 proteinopathy, and traumatic brain injury (TBI). Investment in these areas have increased significantly over the past five years, and with funding received from NIA, NINDS' work to decrease the burden of dementia continues.

The NIH Blueprint for Neuroscience Research aims to accelerate transformative discoveries in brain function in health, aging, and disease. By pooling resources and expertise, the 15 NIH ICs that support research on the nervous system confront challenges in neuroscience that are too large for any single IC to address. To date, the Blueprint has invested more than \$540 million to support the neuroscience community. NIA and NINDS conduct many training activities together, as well as successful outreach programs to connect undergraduates with medical schools or research institutions.

The BRAIN Initiative seeks to develop knowledge of the brain's circuitry and integrate it with neurobiology in order to better understand how the brain processes information. BRAIN researchers look for new and revolutionary tools to explain how the brain functions, how the brain's neuropathology disturbs circuit function to cause patients' symptoms, and how to reverse this disruption in the circuitry. The BRAIN Initiative Cell Census Consortium (BICCC) and the BRAIN Initiative Cell Census Network (BICCN) are developing technology to examine and cell-type millions of cells at a time. Because of this revolutionizing work, neuroscience research is now driven by single-cell analysis to understand the pathology underlying various brain conditions. Furthermore, precision technologies enable the manipulation of specific brain cell-types; however, computational methods and mathematical models that show network changes over time and under differing conditions must still be developed to enable clear understanding of the brain's circuitry. Translating technologies that have been tested in the mouse to humans raises complicated neuroethical concerns. The BRAIN Initiative intends to emphasize proactive, ongoing assessment of the neuroethical implications of the development and application of BRAIN-funded tools and neurotechnologies.

NIH has been very active in developing vaccines and therapeutics for COVID-19, and researchers are now focusing on Post-Acute Sequelae of SARS-CoV-2 Infection (PASC). Poor memory function, fatigue, and difficulty concentrating are the most disabling effects of so-called "long COVID." There is evidence of inflammation and damage in the brains of people with COVID, but researchers do not definitively know whether these changes are responsible for the disease's long-term effects. Congress has appropriated \$1.15 billion to NIH to explore the biological reasons why some people do not recover from the infection, to develop interventions to improve recovery, and to conduct long-term surveillance of COVID-19. Although PASC studies might focus on a particular area affected by SARS-CoV-2, researchers will work together to share and compare data across study cohorts.

Council members expressed concern about the effect that the short timeline for submitting PASC-related applications might have on researchers working with underrepresented groups. Dr. Koroshetz acknowledged the short timeline, but he emphasized that the research is just beginning, and NIH is committed to representing all Americans. In response to a query about

glial cell research, Dr. Koroshetz confirmed that the BRAIN Initiative is looking at glial cells, as well as neurons.

In response to a question from Dr. Hodes, Dr. Koroshetz explained that the program exploring biracial VCID and stroke dementia has learned the value of incorporating people living with dementia, as well as their caregivers, into clinical trials. Dr. Hodes noted the value of locating research centers in the communities where the studied population lives. The REGARDS study cohort could provide a valuable resource for NIA and NINDS to collaborate on a community-based ADRD study.

VII. REVIEW OF INTRAMURAL RESEARCH PROGRAM

This portion of the meeting was closed to the public in accordance with the provisions set forth in section 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).

VIII. ADJOURNMENT

The open session of the 143rd meeting of the National Advisory Council on Aging adjourned at 12:58 p.m. on May 12, 2021. The next meeting is scheduled for September 14-15, 2021.

IX. CERTIFICATION

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.³

Richard J. Hodes, M.D.
Chairman, National Advisory Council on Aging
Director, National Institute on Aging

Prepared by Kenneth Santora, Ph.D.
With assistance by Rose Li and Associates, Inc.

³ These minutes will be approved formally by Council at the next meeting on September 14-15, 2021, and corrections or notations will be stated in the minutes of that meeting.