U.S. Department of Health and Human Services
National Institutes of Health (NIH)
Office of the Director (OD)
Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)

Council of Councils Meeting
May 17, 2019

Meeting Minutes

I. CALL TO ORDER AND INTRODUCTIONS

James M. Anderson, M.D., Ph.D., Director, DPCPSI, welcomed participants, NIH staff members, and members of the public to the meeting of the Council of Councils. The meeting began at 8:16 a.m. on Friday, May 17, 2019, in Building 60/Cloisters, Lecture Hall/Chapel on the NIH Campus in Bethesda, Maryland. He noted that Dr. Scout was unable to attend. The meeting attendees are identified below.

Following introductions and announcements from Robin Kawazoe, Deputy Director of DPCPSI and Acting Executive Secretary for the NIH Council of Councils, Dr. Anderson reviewed the day's agenda.

A. Attendance

1. Council Members

Council Members Present
Chair: James M. Anderson, M.D., Ph.D., Director, DPCPSI
Acting Executive Secretary: Robin I. Kawazoe, Deputy Director, DPCPSI
Maria L. Acebal, J.D., Food Allergy Research & Education, Inc., Washington, DC
Maria Rosario G. Araneta, Ph.D., M.P.H., University of California, San Diego, La Jolla, CA
Kristin Ardlie, Ph.D., Broad Institute of MIT and Harvard, Cambridge, MA
Jeffrey R. Botkin, M.D., M.P.H., The University of Utah, Salt Lake City, UT
Linda Chang, M.D., FAAN, FANA, University of Maryland School of Medicine, Baltimore, MD
Graham A. Colditz, M.D., Dr.P.H., M.P.H., Washington University School of Medicine, St. Louis, MO
Andrew P. Feinberg, M.D., M.P.H., Johns Hopkins University, Baltimore, MD
Rick Horwitz, Ph.D., Allen Institute for Cell Science, Seattle, WA and University of Virginia School of Medicine, Charlottesville, VA
Patricia D. Hurn, Ph.D., R.N., University of Michigan, Ann Arbor, MI
Kevin B. Johnson, M.D., M.S., Vanderbilt University Medical Center, Nashville, TN
R. Paul Johnson, M.D., Emory University School of Medicine, Atlanta, GA
Paul J. Kenny, Ph.D., Icahn School of Medicine at Mount Sinai, New York, NY
Sachin Kheterpal, M.D., M.B.A., University of Michigan Medical School, Ann Arbor, MI
Gary A. Koretzky, M.D., Ph.D., Weill Cornell Medical College, New York, NY
Michael D. Lairmore, D.V.M., Ph.D., University of California, Davis, Davis, CA
Jian-Dong Li, M.D., Ph.D., Georgia State University, Atlanta, GA
Terry Magnuson, Ph.D., The University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC
Edith P. Mitchell, M.D., FACP, Thomas Jefferson University, Philadelphia, PA
Charles P. Mouton, M.D., M.S., The University of Texas Medical Branch, Galveston, TX

Megan O'Boyle, Phelan-McDermid Syndrome Data Network, Arlington, VA
Bruce Ovbiagele, M.D., M.Sc., M.A.S., University of California, San Francisco, and San Francisco Veterans Healthcare System, San Francisco, CA
Rhonda Robinson-Beale, M.D., Blue Cross of Idaho, Meridian, ID
Susan Sanchez, Ph.D., The University of Georgia, Athens, GA
Jean E. Schaffer, M.D., Washington University School of Medicine, St. Louis, MO
Anna Maria Siega-Riz, Ph.D., M.S., University of Virginia, Charlottesville, VA

Council Members Absent
Scout, Ph.D., The Torvus Group, Beverly Hills, CA

2. Liaisons

Rachel Ballard, M.D., M.P.H., representing **David M. Murray, Ph.D.,** Director, Office of Disease Prevention (ODP), DPCPSI
Michael Chang, Ph.D., representing **Franziska B. Grieder, D.V.M., Ph.D.,** Director, ORIP, DPCPSI
Maureen M. Goodenow, Ph.D., Director, Office of AIDS Research, DPCPSI
Karen L. Parker, Ph.D., M.S.W., Director, Sexual & Gender Minority Research Office (SGMRO), DPCPSI
Wendy Smith, Ph.D., representing **William T. Riley, Ph.D.,** Director, Office of Behavioral and Social Sciences Research (OBSSR), DPCPSI
Elizabeth Spencer, R.N., representing **Janine A. Clayton, M.D.,** Director, Office of Research on Women's Health, DPCPSI
Elizabeth L. Wilder, Ph.D., Director, Office of Strategic Coordination (OSC), DPCPSI
David R. Wilson, Ph.D., Director, Tribal Health Research Office, DPCPSI

3. *Ex Officio* Members Absent

Lawrence A. Tabak, D.D.S., Ph.D., Principal Deputy Director, NIH

4. Presenters

Vivien Bonazzi, Ph.D., Senior Advisor for Data Science Technologies and Innovation, OSC, DPCPSI
Gary H. Gibbons, M.D., Director, National Heart, Lung, and Blood Institute (NHLBI)
Susan Gregurick, Ph.D., Senior Advisor, Office of Data Science Strategy, DPCPSI, and Director, Division of Biomedical Technology, Bioinformatics, and Computational Biosciences, National Institute of General Medical Sciences
Adrienne Hallett, NIH Associate Director for Legislative Policy and Analysis and Director, Office of Legislative Policy and Analysis
Marie Nierras, Ph.D., Program Leader, OSC, DPCPSI
Ananda Roy, Ph.D., Program Leader, OSC, DPCPSI

5. NIH Staff and Guests

In addition to Council members, presenters, and Council Liaisons, others in attendance included NIH staff and interested members of the public.

B. Announcements and Updates

Ms. Kawazoe reviewed the following:

- Council members are Special Government Employees during the days of Council meetings and are therefore subject to the rules of conduct governing federal employees.

- Each Council member submitted a financial disclosure form and conflict-of-interest statement in compliance with federal requirements for membership on advisory councils. The financial disclosures are used to assess real and perceived conflicts of interest, and Council members must recuse themselves from the meeting during discussions of any items for which conflicts were identified.

- Time is allotted for discussion between the Council members and presenters, but time for comments from other meeting attendees is limited. The public may submit comments in writing; instructions are available in the *Federal Register* notice for the meeting, which was published on February 8, 2019, and updated on May 13, 2019.

- Minutes from the January 25, 2019, meeting are posted on the DPCPSI website. The minutes from this meeting also will be posted there.

C. Future Meeting Dates

The final Council meeting of the year will be held on September 6, 2019. Additional meeting dates are listed on the Council website and the agenda.

II. NEW NIH CONCEPT CLEARANCE POLICY AND IMPLICATIONS FOR REVIEW BY THE COUNCIL OF COUNCILS

Dr. Anderson provided background for NIH's increased vigilance and transparency regarding concept clearances. Clearances for diverse kinds of programs within DPCPSI have different requirements. For example, ORIP funds projects unlikely to change significantly between issuance of one funding opportunity to the next; in such cases, program reissue and renewal materials are provided to Council members in a standardized format and voted upon *en bloc*. The Common Fund, however, has no fixed portfolio, so every new program must be brought to the Council for discussion and clearance.

The enhanced attention results from irregularities in the Moderate Alcohol and Cardiovascular Health (MACH) Trial. This trial was funded by the National Institute on Alcohol Abuse and Alcoholism and by donations from the alcoholic beverage industry that were channeled through the Foundation for NIH (FNIH), which is intended to reduce conflicts of interest in public partnerships. Details of the program's development, however, were determined to be inappropriate, and the program was terminated. To prevent a recurrence of this type of error, future concept clearances will be conducted in a public format and cleared by a Federal Advisory Committee Act (FACA) group whenever possible. Reissues and renewals are proposed to be voted on *en bloc* from materials provided in advance, and new programs will be brought to the Council for discussion and clearance. Dr. Anderson also proposed a group of approximately five members who would clear concepts prior to Council meetings.

<u>Discussion Highlights</u>

- When asked whether the controversy in the MACH Trial was related to the industry funding component, Dr. Anderson explained that NIH's policy is that staff do not solicit funds from

industry directly. The NIH frequently works with industry, but these collaborations must be transparent. This incident will not fundamentally change the role of the FNIH as an intermediary with industry; the processes in place—if overseen and conducted properly—are sufficient to protect all involved. This situation revealed the need to enforce existing protections more strongly and take extra measures to avoid conflicts of interest.

- In response to a question about NIH's definition of transparency, Dr. Anderson explained that new Common Fund concepts are developed over time with input from workshops and meetings. The Office of Extramural Research is refining guidelines for policies on how to announce and hold workshops; ideally, every workshop will be videocast, or a publicly accessible document of the outcomes and discussions will be made available shortly after the workshop.

- When asked whether any plans are in place to reissue the MACH Trial concept, Dr. Anderson suggested that if there are critical scientific issues to be addressed, it could be possible for a future study to address those issues.

- Council members discussed the ideal size and diversity of the smaller working group that would discuss concepts separately, suggesting a core group for consistency with the addition of ad hoc members for particular clearances if expertise is lacking. Dr. Anderson explained that the Council operating procedures would be updated at the September meeting and could incorporate the guidelines for this group.

- Dr. Anderson clarified, in response to questions, that there has been no move to implement a public comment period in the concept clearance process.

- In response to a question about where in the renewal process innovation can occur, Council members suggested including a requirement in renewals to provide information on how programs have been reviewed for progress, including adaptation.

- When asked about processes to prevent bias in principal investigator (PI) selection, Dr. Anderson explained a policy to ensure that grant applications are not written by investigators involved with workshops to develop the concept.

- Dr. Anderson clarified that renewals that are significantly different from the original are brought for open discussion with the Council.

- Council members recommended including with the materials a list of key highlights of the program's impact on human health, as well as developing a broader consideration of appropriate metrics by which to judge these programs.

III. DPCPSI CONCEPTS FOR FUNDING OPPORTUNITY ANNOUNCEMENT RENEWALS AND REISSUES

ORIP—Primate Centers (P51), Models and Related Materials Programs (R21 and R24), Tools and Devices for Research Facilities (SBIR/STTR), Construction; OSC—Illuminating the Druggable Genome (IDG), Acute to Chronic Pain Signatures (A2CPS)

Elizabeth Wilder, Ph.D., director of OSC, introduced the specific renewal and reissue clearances, explaining that reissued funding opportunity announcements (FOAs), by definition, are minimally changed. Some FOA reissuances are renewals, and others provide the community an additional opportunity to respond to a set of goals. She emphasized that the reasons for reissuance would be made clear to Council members prior to voting.

Dr. Wilder outlined the IDG FOA, which is intended to develop information about little-studied genes and proteins within families that are usually druggable. Multiple small projects will be issued over time, allowing multiple PIs to address the function of these understudied genes and proteins. Dr. Wilder also explained that if A2CPS program staff decide during an upcoming review that not enough sufficiently meritorious applications have been received, the FOA would need to be reissued. The Council is being asked to approve the reissue in case it is necessary; if the reissue is not approved and no current applications are supported, this aspect of the program would not proceed. ORIP representatives briefed Council members on the concepts under discussion, which are renewals and programs mandated or appropriated by Congress that ORIP would continue to support with few changes.

Council members suggested several improvements for future iterations of this process, including short introductions for each concept, more information on the individual concept's progress toward larger goals, and separate votes for each Office's concepts to provide specific discussion time for each.

Vote

A motion to approve the OSC and ORIP concepts discussed was forwarded and seconded. The motion passed with no abstentions.

IV. COMMON FUND CONCEPT CLEARANCE FOR ADDITIONAL PRECLINICAL ANIMAL STUDY SITES FOR THE MOLECULAR TRANSDUCERS OF PHYSICAL ACTIVITY CONSORTIUM (MoTrPAC)

Marie Nierras, Program Leader, OSC, explained the concept for an FOA for additional preclinical sites for MoTrPAC, which aims to assemble a molecular map of changes that occur in response to exercise and provide a usable, accessible data set open to the research community. The clinical component includes healthy human volunteers who undergo acute exercise or go on an exercise training program, complemented by preclinical studies in adult rats performing comparable exercises, which allows collection of tissues not accessible in humans. A comprehensive collection of phenotypic data will be assembled, and multi-omic molecular data will be generated for humans and rats. All activities are coordinated by MoTrPAC's consortium coordination center, including the clinical and preclinical activities, chemical analyses, bioinformatics, and data release.

Dr. Nierras explained that a first preclinical data release, covering rats that have undergone acute exercise, is expected in September 2019. The proposed FOA would invite applications that would expand the pool of investigators supported to continue analyzing past animal data and participate in the systems analysis of newly generated data.

Discussion Highlights

- Dr. Nierras clarified that the rat strain used was chosen after extensive consideration of complex factors. This strain was provided by the National Institute on Aging colony; several strains were considered and discarded because insufficient numbers of both males and females were available.

- The discussants, Jean Schaffer, M.D., Washington University School of Medicine in St. Louis, and Graham Colditz, M.D., Dr.P.H., M.P.H., Washington University School of Medicine in St. Louis, provided their comments. Dr. Schaffer commended MoTrPAC's coordination and potential to contribute to the understanding of human health, particularly with the use of animals to expand the range of tissues studied. She asked whether the applications under this FOA will have different protocols than those already in existence, and whether animals beyond rats will be considered. Dr. Nierras explained that additional animals are under discussion, and the FOA has

not yet been written. They are hoping to coordinate the release of the initial animal data with the release of the FOA so that a portion of the animal data is available for generating applications in response to the FOA. They hope to get applications that seek to work with the animal tissues not yet characterized or applications that hypothesize based on the released data set.

- Dr. Colditz questioned MoTrPAC's ability to address health disparities; Dr. Nierras acknowledged that the animal model does not include a way to address disparities, but explained that the clinical centers address the charge to recruit according to the racial and ethnic composition of the U.S. population. MoTrPAC's investigators plan to monitor recruitment and retention closely to ensure that it is appropriate.

- Council members recommended keeping the whole-animal perspective in mind while investigating individual molecules. Dr. Nierras reiterated that they are collecting extensive phenotypic data from the animals and clinical data from human participants. She hoped that responses to this FOA could help with the complex issue of integrating data both vertically and horizontally.

- When asked whether MoTrPAC would include any imaging to study visceral fat accumulation in health disparities populations, Dr. Nierras responded that no imaging studies are planned at present, but MoTrPAC has begun to consider ancillary studies. She emphasized that the project remains at an early stage.

- Council members asked about the rationale for not including children younger than 12 years of age in this minimal-risk study, but Dr. Nierras did not have this information.

- When asked about including rural communities in the studies, Dr. Nierras explained that the clinical centers are located in areas that have rural catchments; she planned to raise this issue with the recruitment and retention committee to ensure that this information is tracked.

- Council members encouraged close, refined monitoring of female and aged rat cohorts from the beginning of the study to ensure that a sufficient number of animals are studied for a sufficient amount of time, regardless of logistical pressures that challenge the inclusion of these populations in animal studies.

- In response to a question about the lack of clarity in what is desired of FOA respondents, Dr. Nierras explained that the data are presently being generated; an early analysis working group is reviewing the data, but the FOA will not be released until the data are ready for release, which will illuminate what the data show, as well as the additional research opportunities.

Vote

A motion to approve the MoTrPAC addition was forwarded and seconded. The motion passed with one abstention.

V. UPDATE FROM THE NHLBI DIRECTOR

Gary Gibbons, director of the NHLBI, remarked on the Institute's recent 70th anniversary and explained the "virtuous cycle" of biomedical research in which observational population science can illuminate potential areas of basic science and clinical research, which then can improve the health of populations. Advances in the understanding of cardiovascular disease, with significant contributions from NIH research, have reduced heart disease deaths by nearly 70 percent over the past 50 years. Additional areas

the NHLBI is studying, in collaboration with other Institutes, Centers, and Offices (ICOs), include hypertension and its relationship to cognitive impairment. Dr. Gibbons also pointed out that advances in pulmonary medicine have the potential to allow clinicians to detect problems and intervene early in a preventive, preemptive, and precise way.

Dr. Gibbons highlighted ongoing projects that show how the NHLBI fulfills the NIH mission of turning basic science discovery into public health improvements. He emphasized that the Institute ensures that the portfolio always maintains a core principle around investigator-initiated discovery research, as well as a balanced spread of basic, translational, clinical, population, and community-based implementation science. He stressed the importance of training a diverse new generation of scientific leaders, who will drive future innovation. His "passion areas" include supporting implementation science that empowers patients and innovating an evidence-based elimination of health inequities. These drivers of NHLBI's philosophy were developed from the Institute's Strategic Vision, which was created with input from more than 4,000 individuals in all 50 states and from 42 countries. Dr. Gibbons particularly emphasized the incremental increase of paylines for R01s in recent years, as well as programs to help early-stage investigators. The NHLBI also invests strongly in pipeline and loan repayment programs as part of the commitment to nurturing the next generation of investigators. The Institute participates in a number of trans-NIH efforts, such as the Helping End Addiction Long-Term (HEAL) and INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE (INCLUDE) initiatives.

Dr. Gibbons provided examples of how the NHLBI is implementing its Strategic Vision. Sickle cell disease, once likely to lead to early death, now has an expanded life expectancy as a result of research discoveries. Additional research is necessary, however, and Dr. Gibbons advocated a "full-court press" across the spectrum of research disciplines. He emphasized that the population most affected by sickle cell disease in the United States—predominately African Americans—has been marginalized, and successful clinical trials have not always been implemented into practice. Innovation is needed to accelerate the uptake and use of hydroxyurea in the United States, and implementation science must be used to reduce the global burden of sickle cell disease. Furthermore, the NHLBI is committed to accelerating curative genetic therapies leveraging lentiviral vectors and CRISPR technology with a goal to push for cures in the next 5 years. Dr. Gibbons emphasized that this effort requires an entire ecosystem of care with critical patient engagement strategies at the center.

Although cardiovascular mortality has improved dramatically, Dr. Gibbons noted that not all communities have benefitted equally from research advances. Distribution of cardiovascular mortality follows similar geographic disparity patterns as chronic lung disease, and Dr. Gibbons speculated that other conditions—such as maternal mortality, HIV incidence, and opioid use—likely follow these patterns as well. He emphasized the need to prioritize implementation and consider social and contextual determinants of health, creating a more multidimensional, multilayered, and multilevel approach. For example, research shows that diets rich in fruits and vegetables can improve cardiovascular, brain, and microbiome health, but lower income areas often do not have access to fresh foods. NHLBI's Coronary Artery Risk Development in Young Adults (CARDIA) study also demonstrated that blood pressure improves for those who move away from racially segregated neighborhoods. The Trans-Omics for Precision Medicine (TOPMed) program leverages a portfolio of cohorts with longitudinal, phenotypic, and whole-genome information, as well as several other 'omic datasets, to provide a rich genomic resource that also is reflective of communities of color. Dr. Gibbons emphasized the opportunity to create a communal space for data, primarily by promoting standardization and interoperability.

<u>Discussion Highlights</u>

- When asked how to ensure hard-to-reach populations receive treatments, Dr. Gibbons acknowledged that this area needs further work. The Sickle Cell Disease Implementation

Consortium has nine sites around the country and has been charged with determining innovative strategies to reach their communities, particularly those who often fall through the cracks of care, such as patients making the adolescent-to-adult transition. Empowering the patient and developing provider systems that can connect care between the clinic and the emergency room will be important components of this effort.

- In response to a question about how the NHLBI is supporting investigators in light of stagnant amounts for K awards and salaries, Dr. Gibbons explained that the K award stipends recently were increased from $75,000 to $100,000, although this amount still is lower than what is needed. He emphasized the responsibility that the NIH and academic leaders have to collaborate; the NIH's seed capital should allow academic institutions to contribute additional support. He emphasized that the NHLBI focuses on other elements of support, such as an initiative that bridges the K award to an R03, reducing barriers to independent funding. He also acknowledged that the cost of R01s is increasing while the use of modular grants is decreasing and emphasized the importance of increasing the overall success rate to maximize the value of R01s.

- When asked about partnerships with the Veterans Administration (VA), Dr. Gibbons responded that the Institute historically has collaborated with the VA but could improve its current efforts.

- In response to a question about digital health technologies, Dr. Gibbons suggested that all ICOs could benefit from input on how to improve in this sphere. He added that the NIH cannot drive this issue alone, and partnerships with technology companies are necessary. He encouraged the planning of a trans-NIH initiative to work with technology companies more efficiently.

- When asked about NHLBI's research on rare diseases other than sickle cell, Dr. Gibbons explained that many blood disorders often are genetic, and early discoveries in heart disease that benefited everyone were related to research into rare disorders of cholesterol metabolism. The NHLBI studies cystic fibrosis because of its effects on the lungs. Dr. Gibbons emphasized that several rare diseases are in the NHLBI portfolio, such as sickle cell, for which the window of opportunity to discover a cure currently is particularly poignant; the application of new technologies to some of these diseases is likely to lead to advances in a number of other rare disorders.

VI. CONGRESSIONAL UPDATE

Adrienne Hallett, the NIH Associate Director for Legislative Policy and Analysis and the director of the Office of Legislative Policy and Analysis, provided an overview of how the Office educates members of Congress on biomedical research and other NIH-related issues. She noted that the NIH mimics and at times drives federal non-defense research and development spending and has received a $9 billion (30%) increase in its budget over the past 4 years. Ms. Hallett described the series of budget caps in place since 2013 that end in 2021, leaving only one 2-year budget agreement remaining to be negotiated. A failure to reach a bipartisan budget agreement would result in a cut to total government spending which could endanger the NIH's funding, and Ms. Hallett noted that the debt ceiling also will be relevant to budget negotiations this fall.

Ms. Hallett highlighted that the election of 2018 included much turnover and a record number of retirements. Congress lost many senior members who were strong supporters of particular NIH areas of interest, meaning the NIH now needs to develop both general and specific support for important issues in the current Congress. More than 100 of the 535 members of Congress are new, and many of them are unfamiliar with the NIH. Although the NIH has worked to educate new members through their local institutions, NIH representatives also need to get to know the members personally, which many other

groups also are trying to arrange. Ms. Hallett noted that, to an unprecedented extent, voters now want elected officials who share their identities. She emphasized that although longstanding relationships have been lost, many of the new members of Congress have exciting visions that could benefit the NIH.

Ms. Hallett pointed out some national and global issues that affect the NIH, including foreign influence issues shared by the energy sector and the cultural impact of the #MeToo movement, which appropriately includes science along with other fields.

Discussion Highlights

- In response to a question about partnerships, Ms. Hallett described a recent meeting with advocates to discuss ways to provide information about the NIH. She emphasized that her job and that of the advocates overlap but are not completely synonymous, although opportunities to coordinate messages are beneficial. She suggested that advocacy for individual ICOs can create pressure to do well for the whole NIH.

- When asked about the China data issue, she pointed out that a group of 535 people creates many countervailing pressures and opinions. She and her staff have tried to be true to the field by engaging in many sophisticated conversations. Recent issues have led to her talking more frequently with the intelligence community, introducing them to biomedical research, and educating them on the basics so they can apply that knowledge to the world as needed. She noted that biomedical science does not work the same way as other scientific fields that might have worked with the intelligence community, such as the energy field.

- Ms. Hallett recommended accessible personal stories as a way for the patient advocacy community to connect with the NIH and Congress. She explained that personal stories collected by an advocacy group can be effective tools for members who want to speak on the issue with short notice but strong impact.

- Ms. Hallett noted that many previously junior members of Congress now have moved into senior positions, which changes the dynamics she must consider. She also noted that the current Congress is pushing strongly for addressing health disparities.

- When asked what Council members can do to improve collaborations, Ms. Hallett emphasized that her job is to convince Congress to lead the country in the direction suggested by the NIH's biomedical expertise. Members of Congress often do not know much about how the NIH operates, so Ms. Hallett is more successful when she can explain and contextualize the science before members make important decisions.

- When asked how to prioritize time and effort when legislative turnover is frequent, Ms. Hallett noted that balancing the reactive and proactive agendas is a challenge everyone must face, but it is helpful that NIH Director Dr. Francis Collins states his priorities clearly. Ms. Hallett commented on a bill that could require public nominations to FACA committees, which would increase the barriers to speedy scientific progress. Despite the benefits of increasing transparency, the administrative burden associated with this bill would be significant.

- In response to a question about scientific literacy on Capitol Hill, Ms. Hallett explained that her office acts as trusted advisors to provide data and briefings on scientific issues. They also offer their expertise proactively in areas with technology advancements, such as CRISPR/Cas9. Their

job is to ensure that an evidence-based conversation is held about risks and benefits of any scientific issue.

- When asked about support for scientific infrastructure, Ms. Hallett explained that the chair of the Appropriations Committee in the Senate is a strong supporter of extramural research infrastructure; he has been including such appropriations in the Senate bill for several years, but this is the first time it has made it into the final bill. She recommended that attendees talk to her counterpart at their own institutions about issues that are important to them. Ms. Hallett emphasized that because any issue can become a priority during negotiations, Capitol Hill offers many opportunities to raise the profile of important issues.

- In response to a question about whether new members of Congress receive scientific education, Ms. Hallett explained that the new members must learn about many issues very quickly, and their initial education is on parliamentary procedures. She added that many members comment on their enjoyment of NIH briefings, which provide education and explanation without any requests.

- Ms. Hallett encouraged attendees to contact the people in her position at their own institutions, who are legally protected to lobby Congress, which she is unable to do.

VII. REVIEW OF GRANT APPLICATIONS

This portion of the meeting was closed to the public, 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 Federal Advisory Committee Act, as amended (5 U.S.C. Appendix).[1] Members were instructed to exit the room if they deemed that their participation in the deliberation of any matter before the Council would represent a real or perceived conflict of interest. Members were asked to sign a conflict-of-interest/confidentiality certification to this effect. The *en bloc* vote for concurrence with the initial review recommendations was affirmed by all Council members present. During the closed session, the Council concurred with the review of 53 ORIP applications with requested first-year direct costs of $26,025,679 and 1,045 Common Fund applications with requested first-year direct costs of $1,778,417,335.

VIII. COMMON FUND CONCEPT CLEARANCE FOR THE 4D NUCLEOME STAGE 2

Ananda Roy, Ph.D., a program leader with OSC, explained the importance of nucleomic research. The Four-Dimensional Nucleome (4DN) project, built on the success of the Human Genome Project and its successors, studies the three-dimensional topology of the genome and adds the fourth dimension of time. Dr. Roy explained that DNA has more than 10,000 loop formations; chromatin is organized into highly heterogeneous nuclear structures of unknown function, and this organization is highly dynamic in both time and space. Understanding this organization is critical because it has implications for health—some cancers, neurological diseases, and developmental disorders are associated with problems in DNA's topical structure.

To understand this organization, it must be studied using multidimensional approached including, imaging, omics, and computational modeling. New tools and technologies must be developed, and it is equally important to ensure that strategies are in place to deliver these methods to the scientific community and ensure their rapid adoption. The program is intended to establish a collaborative effort

[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 applied only to applications that were discussed individually, not to *en bloc* actions.

with other NIH and international initiatives to create a community of practice for rapid data sharing and information exchange. The 4DN program was launched in 2015, and its current success can be attributed largely to the consortium structure it built, leading to development of many omics and imaging technologies and software, publicly available data sets and cell lines, and publications. Dr. Roy provided several examples of successful projects within the 4DN program. Outreach efforts include sharing pre-prints, joining the International Human Epigenome Consortium, participating in joint meetings with the American Society of Cell Biology, and actively collaborating with other institutions and initiatives.

4DN was designed from its inception as a two-phase program; the first phase developed tools and technologies and applied them to a small number of cell lines for proof of concept. For the second phase, program members will use these technologies to probe the function of the genome and the functional implication of its structures. Input on the second phase was gathered from members through webinars, a wide request for information with international responses, and an NIH-wide portfolio analysis. Dr. Roy emphasized that after its initial successes, the 4DN project is now poised to tackle the functional implications of genome topology in physiologically relevant systems.

Functional initiatives in the second phase include applying new and existing tools to studying chromatin dynamics and function in live cells, generating data to integrate modeling and visualization to produce navigable 4DN maps and models of genome organization, and understanding nuclear architecture over the lifespan in human health and disease. The structural initiatives are the same as in the first phase: maintaining the organizational hub and the data coordination center to track and store the data and disseminating the data to the scientific community as rapidly as possible. The project team is requesting a 5-year proposal with a budget nearly identical to that of Phase 1.

Discussion Highlights

- The discussants, Andrew Feinberg, M.D., M.P.H., Johns Hopkins University, and Rick Horwitz, Ph.D., Allen Institute for Cell Science, provided their comments. Dr. Feinberg commended the program for its impact to date but wondered how to define the next transformative event or barrier. He noted that the first two initiatives, as written, overlap with each other and also with the original plan. He expressed excitement for the possibility of combining mathematical modeling and computational genomics in the next stage. He encouraged Dr. Roy and the 4DN team to integrate investigation of the mesoscopic level of organization and noted that the current "big-picture" integration and inclusion of phenotypes were strengths of the program. Dr. Feinberg added that because many tools and methods already have been developed, the focus in the next phase should shift to increasing collaboration on all levels.

- Dr. Horwitz complimented the project on its efforts to integrate with other groups but questioned some of the stated successes. Dr. Anderson clarified that the Council must vote on whether the program can move forward with its initiatives as described or whether rephrasing could be considered.

- Dr. Roy confirmed the cell lines used in the consortium are available to researchers by request or for benchmarking.

- Dr. Roy provided additional examples of how 4DN could improve understanding of disease states—including fragile X syndrome, cancer, and limb development mutations—noting that the main purpose of Phase 2 is to explore these connections and transition from the Phase 1 cell lines to more biologically relevant systems. He noted that further explanation of the initiatives is provided in the written materials, but it was simplified for discussion.

- Council members suggested reviewing the budget proportions for each initiative, and Dr. Roy planned to take that into consideration.

- In response to a question, Dr. Roy confirmed that the initiatives include plans to study Cell Cycle process in addition to disease. Dr. Feinberg recommended to de-emphasize Cell Cycle studies and instead focus more on differentiation/development.

- Dr. Anderson suggested that the Council vote on the concept with the stipulation that the 4DN team use the discussion to change the balance of emphasis among the initiatives to reduce the emphasis on the cell cycle and increase the emphasis on differentiation of disease and integration, as well as reviewing the other areas for work that is duplicative.

Vote

A motion to approve the 4DN project with the stipulations discussed was forwarded and seconded. The motion passed with no abstentions.

IX. COMMON FUND CONCEPT CLEARANCE FOR AWARDS THAT ENCOURAGE USE OF COMMON FUND DATA

Dr. Roy presented on a concept to expand the use of Common Fund data sets, noting that many programs have generated high-value data sets, but many investigators are unaware of this or without the time to learn to use them. If these data are made more available, investigators can use existing computational tools to cross-compare data sets between Common Fund programs. This concept proposes small projects, such as administrative supplements or 1-year projects, to expand the use of Common Fund data sets by encouraging data exploration, hypothesis generation and initial testing, or development of novel computational tools. Projects will be solicited each year for 2 to 3 years as the impact of the initiative is assessed, and direct costs are anticipated to be approximately $100,000 or less, funding 10 to 15 awards. The initiative aims to assess the number of users of and publications derived from each data resource; expand the utility and impact of Common Fund data; support investigators outside the Common Fund consortium; and support the application of data and tools to a wider variety of research topics and diseases. He listed the data sets available and noted that more data sets would be included as they become available.

- The discussants, Kristin Ardlie, Ph.D., Broad Institute of MIT and Harvard, and Kevin Johnson, M.D., M.S., Vanderbilt University Medical Center, provided their comments. Dr. Ardlie commended this idea but cautioned that a different approach might be needed to integrate such disparate data sets. Although she approved of short projects, she suggested that 1 year and $100,000 was insufficient to make significant progress. Dr. Ardlie proposed 2-year projects with a requirement to collaborate with representatives from the data set of interest, which would ensure that the project is realistic and includes a baseline understanding of the data. She also recommended special criteria to ensure that any tools developed are practical. In addition, Dr. Ardlie suggested outreach efforts to increase the use and citation of the data sets.

- Dr. Johnson encouraged further options for collaboration and suggested another timeline option in which a short grant could be followed by a longer grant. He suggested that outreach efforts could begin prior to the launch of the full program to increase visibility. Dr. Johnson also questioned whether these plans used the best data storage locations and expressed his concern about whether access should be managed more strictly, particularly regarding the Genotype-Tissue Expression (GTEx) Program. Dr. Ardlie explained that GTEx has protected access permissions, and Dr. Johnson cautioned that de-accession procedures are not in place.

- When asked whether the program would include other cohorts or other NIH databases, Dr. Roy stressed that this project focuses on existing data sets generated through the Common Fund. Dr. Anderson clarified that this is intended as a pilot to connect disparate data sets; successful methods might not apply in other programs.

Vote

A motion to approve the concept with considerations to increase the funding for individual projects when justified, emphasize collaboration with those already familiar with the data, and conduct outreach was forwarded and seconded. The motion passed unanimously.

X. UPDATE ON THE COMMON FUND DATA ECOSYSTEM

Vivien Bonazzi, Ph.D., the Senior Advisor for Data Science Technologies and Innovation in OSC, explained that the Common Fund's many programs generate large amounts of data and analytical tools at various levels of maturity. In contrast with the pilot program discussed by Dr. Roy, the projects from Dr. Bonazzi's team investigate ways to create connections among programs, as well as biological and computational disciplines, and develop scientific integration points to ask necessary scientific questions of interest.

Data programs at the NIH use cloud services, generally systems provided by Google and AWS (Amazon) in accordance with the Science and Technology Research Infrastructure for Data Experimentation Sustainability (STRIDES) Initiative, a transactional agreement to lower storage and usage costs for the NIH. These services provide both data storage and compute resources, as well as the ability to share information between geographically distributed groups. Although the cloud enables these collaborations, each program is organized differently, and untangling the unique systems created by each project team requires large amounts of time, energy, and resources. If the existing data cannot be reused, they must be regenerated or abandoned, which is wasteful.

The Common Fund Data Ecosystem project leverages results from the NIH Data Commons pilot to make Common Fund data sets more useful and usable within individual programs and between disparate programs. Best practices captured by this project will be made available for new programs to build on. Dr. Bonazzi reminded attendees of the FAIR principle, in which data must be made findable, accessible, interoperable, and reusable to be used successfully. To achieve FAIR standards, the program must develop procedures for consistent on-boarding of data to the cloud, which would ensure interoperability at a project's earliest stages, as well as procedures for version control and maintenance of data stored on the cloud and cost management for the life of the data. Dr. Bonazzi also noted that documentation for planned cloud use is needed, but the level of detail may vary depending on users' familiarity with cloud systems.

The Common Fund Data Ecosystem project aims to ensure that data management plans are created with an understanding of all required elements. Data standards should be created to ensure FAIR principles, but Dr. Bonazzi emphasized that the standards should be driven by the community, rather than mandated by NIH governance. Cross cutting data models are needed in order to be able to query across different program's data. Some potential strategies for increasing usability include creating data dashboards, which can help users less familiar with heavily computational information track the status of a project, and developing platforms that improve and simplify the user experience. Training also must be developed to ensure that researchers approaching data use from disparate levels of expertise and scientific fields are provided with the same ability to use the data.

Dr. Bonazzi pointed out that many Common Fund programs have existing data programs with a set of relevant scientific use cases, and representatives from these programs can provide input and assist in

developing new connections and initiatives. Next steps for Dr. Bonazzi's program include conducting a critical assessment of activities of a small number of Common Fund programs to better understand the issues within those programs and identify additional needs and collaborating with the investigators to build the data dashboards. From these initial steps, appropriate collaborations across ICOs will be identified and pursued.

Discussion Highlights

- Council members discussed the complementary aspects of this program and the concept presented by Dr. Roy. The two programs could eventually merge, or Dr. Bonazzi's program could serve as a preceding structural step to Dr. Roy's. Dr. Bonazzi suggested that Dr. Roy's program could better capture use cases across and between data sets.

- When asked how to avoid siloing work and support data set integration across the NIH, Dr. Bonazzi stressed that this project is a manageable initial step in developing integration strategies. She commented that the social aspect—encouraging investigators to collaborate—is critical to avoiding silos.

- Dr. Anderson added that data sets are funded for the duration of individual programs, so programs must be developed quickly rather than taking the time to create an NIH-wide solution. Dr. Bonazzi explained that although a project's funding may end, the data generated will need maintenance and version control as long as they are relevant. The support mechanisms for such maintenance have not yet been developed and must be considered as part of this project. Dr. Bonazzi also suggested mechanisms for non-commercial cloud storage that could be tested. She emphasized the importance of data governance and usage policies, particularly when working with commercial entities.

- Dr. Anderson emphasized that this field is in a period of high evolution, so many questions do not yet have specific solutions. He suggested that Dr. Bonazzi update the Council during the January 2020 session.

XI. INTRODUCTION TO THE OFFICE OF DATA SCIENCE STRATEGY

Susan Gregurick, Ph.D., in her capacity as a senior advisor for the Office of Data Science Strategy, provided an overview of NIH's data science efforts, which involve more than 30 working groups across the NIH working to integrate NIH's data and make it FAIR. Scientific questions crossing fields require connections between data resources at multiple ICOs, but researchers often do not have an efficient way to access data that have been generated for studies but are not stored in a repository. New technologies also could be used to analyze data quickly and improve outcomes for patients in hospitals or clinics.

Dr. Gregurick emphasized that the Office of Data Science Strategy is working to connect data ecosystems, engage the broad community across federal agencies and industry partners, enhance the biomedical workforce, and coordinate in the development of sustainable data policies. The Office provides leadership and coordination on NIH's strategic plan for data science in collaboration with ICOs, including implementing plans for a modernized and integrated biomedical data ecosystem, developing programs for a diverse data science workforce, coordinating with trans-NIH governance committees, and building strategic partnerships to develop and disseminate advanced technologies and methods.

Progress has been made in each area of focus, as well as the overarching goal of making data FAIR. One project involves tagging data with unique, persistent identifiers to make it traceable throughout its lifetime. Data also must be made accessible with the appropriate security protocols. Ensuring that data are

interoperable requires integrating standards across programs. Dr. Gregurick emphasized that those in the Office think about FAIR data holistically and there are no one-size-fits-all strategies.

The data science community is beginning to adopt TRUST principles for data repositories, demonstrating that the repository is transparent, responsible for providing high-quality data and services, focused on the user community, mindful of sustainability, and reliant on modern technologies. Dr. Gregurick noted that the Office plans to issue two FOAs for data repositories and knowledgebase resources as separate programs, which will be a more efficient mechanism than the R01 grants that historically have been used to fund resources. The FOAs will require that the resources have scientific impact, engage the community, focus on data and service quality, and incorporate governance models.

Dr. Gregurick pointed out several models for making data accessible when open-access repositories are not an option, such as attaching data to publications and a pilot program to make data citable, sharable, discoverable, and reusable. She explained that recent community input on data policies suggested that future policies should be coupled with the infrastructure required to implement it. She pointed out that a number of NIH's data investments are ecosystems that require highly connected research communities; a first step toward connection is the development of a single log-on system for controlled-access data. The Office also is partnering with institutions in the broader scientific community to develop ways to enable data science and incorporate new technologies, such as artificial intelligence. These efforts will include codeathons, citizen science, and challenge programs to engage the broader community.

The Office is working to enhance the biomedical workforce through NIH's internal and extramural paths, including through fellowships for undergraduate computer scientists and masters-level laboratory researchers, a national service sabbatical in data science, and expanded language in T programs to incorporate data science. Data-focused training programs also will be launched in specific areas of high need. Additional strategies include providing modules in existing programs to support improvement in rigor and reproducibility, expanding research development programs to include data science, and developing short training programs for a diverse cohort of research trainees. Dr. Gregurick emphasized that this is a highly collaborative sphere, within both the NIH and the broader research community.

Discussion Highlights

- Dr. Gregurick clarified that consent boundaries as defined in patients' initial agreements will be respected when the data are used for other purposes. Future consent agreements will include language to define how the data can be used or shared. A single log-on technological improvement would not change the consent required to use those data, but the Office is working to lower that barrier. Council members suggested a program similar to the Transportation Security Administration's PreCheck to expedite data access for responsible researchers. Dr. Bonazzi added that a central institutional review board also could be explored.

- When asked how training programs would be funded, Dr. Gregurick explained that funding will come from partnerships with ICOs or from individual ICOs.

XII. CLOSING REMARKS

Dr. Anderson thanked the Council members and speakers for their contributions at this meeting. He reminded the members that the next Council meeting is scheduled for September 6, 2019.

XIII. ADJOURNMENT

Dr. Anderson adjourned the meeting at 3:32 p.m. on May 17, 2019.

XIV. CERTIFICATION

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

James M. Anderson -S

Digitally signed by James M. Anderson -S
Date: 2019.06.25 14:33:40 -04'00'

James M. Anderson, M.D., Ph.D.
Chair, NIH Council of Councils
Director, DPCPSI, OD, NIH

Date

Robin I. Kawazoe -S

Digitally signed by Robin I. Kawazoe -S
Date: 2019.06.25 12:22:23 -04'00'

Robin I. Kawazoe
Acting Executive Secretary, NIH Council of Councils
Deputy Director, DPCPSI, OD, NIH

June 25, 2019

Date