NATIONAL ADVISORY COUNCIL
FOR HUMAN GENOME RESEARCH

MEETING SUMMARY
May 8-9, 2017

The Open Session of the 80th meeting of the National Advisory Council for Human Genome Research (NACHGR) was convened at 10:00 AM on Monday, May 8, 2017, at the Fishers Lane Terrace Level Conference Center in Rockville, Maryland. Dr. Eric Green, Director of the National Human Genome Research Institute (NHGRI), called the meeting to order.

The meeting was open to the public from 10:00 AM until 4:30 PM on May 8, 2017. In accordance with the provisions of Public Law 92-463, the meeting was closed to the public from 8:00 AM to 10:00 AM and 4:30 PM to 6:30 PM on May 8, 2017, and from 8:30 AM until adjournment on May 9, 2017, for the review, discussion, and evaluation of grant applications.

Council Members Present:
Eric Boerwinkle
Jeffrey Botkin
Carol Bult
Brenton Graveley
Jonathan Haines
Gail Henderson
Chanita Hughes-Halbert
Trey Ideker (by phone)
Sharon Plon
Jonathan Pritchard
Aviv Regev (by phone)
Dan Roden
Val Sheffield
Jay Shendure

Staff from the National Human Genome Research Institute:

Julia Baker, ERP
Vence Bonham, IOD and IRP
Joy Boyer, ERP
Larry Brody, ERP and IRP
Comfort Browne, ERP
Christine Chang, ERP
Monika Christman, ERP
Ernesto Del Aguila, DPCE
Valentina Di Francesco, ERP
Carla Easter, DPCE
Alvaro Encinas, DPCE
Elise Feingold, ERP
Adam Felsenfeld, ERP
Kim Ferguson, ERP
Ann Fitzpatrick, DM
Colette Fletcher-Hoppe, ERP
Dan Gilchrist, ERP
Sylvia Garvey, ERP
Tina Gatlin, ERP
Margaret Ginoza, ERP
Kevin Lee, ERP
Jonathan Lotempio, Jr., ERP
Bettie Graham, ERP
Jyoti Gupta, ERP
Linda Hall, ERP
Lucia Hindorff, ERP
Rebecca Hong, DPCE
Ellen Howerton, ERP
Carolyn Hutter, ERP
Deanna Ingersoll, ERP
Sonya Jooma, DPCE
Alexander Katz, ERP
Jonggeol (Jeffrey) Kim, ERP
Ashley Lewis, DPCE

Rongling Li, ERP
Nicole Lockhart, ERP
Ebony Madden, ERP
Allison Mandich, IOD
Teri Manolio, ERP
Jean McEwen, ERP
Keith McKenney, ERP
Donna Messersmith, DPCE
John Ohab, DPCE
Vivian Ota Wang, ERP
Kiara Palmer, DPCE
Mike Pazin, ERP
Ajay Pillai, ERP
Lita Proctor, ERP
Erin Ramos, ERP
Laura Skow, ERP
Michael Smith, ERP
Heidi Sofia, ERP
Jeffery Struewing, ERP
Michelle Tallman, ERP
Elizabeth Tuck, DPCE
Simona Volpi, ERP
Lu Wang, ERP
Cara Weismann, DPCE
Chris Wellington, ERP
Kris Wetterstrand, IOD
Bob Wildin, DPCE

Others Present for All or a Portion of the Meeting:
Peter Kozel, CSR
Rachel Levinson, Arizona State University
Joy Nathan, Bayta Associates
Jacqueline Medina, Booz Allen

INTRODUCTION OF NEW NHGRI COUNCIL MEMBERS, STAFF, LIASONS, AND GUESTS

APPROVAL OF MINUTES FOR THE FEBRUARY 2017 COUNCIL MEETING
The Minutes were approved by a vote of 13 members in favor, none opposed, and no abstentions.

FUTURE MEETING DATES
Sept. 11-12, 2017
Feb. 12-13, 2018
May 21-22, 2018
Sept. 24-25, 2018
Feb. 11-12, 2019
May 20-21, 2019

DIRECTOR'S REPORT

Dr. Eric Green gave his Director's Report.

Council emphasized their concern about HR 1313 and how it might affect participation in genetics research and accessing clinical genetic testing services. The dual protections have been the Genetic Information Nondiscrimination Act (GINA) and the Affordable Care Act (ACA), and if these were lost, or substantially changed, it might profoundly disrupt the types of research sponsored by NHGRI.

PRESENTATION – Update from the National Institute of Mental Health (NIMH). Dr. Joshua Gordon, Director, National Institute of Mental Health.

Dr. Joshua Gordon gave a presentation on the current and future research activities at NIMH.

Council asked about NIMH's efforts in bioinformatics, including how they plan to establish data standards and integrate data types. Dr. Gordon responded that NIMH wants to use existing tools like PhenX to foster unifiable approaches, and encourage good standards for NIMH-funded databases, such as employing common data elements and consistent phenotyping methods. This will allow easier data harmonization when investigators attempt to analyze results from multiple studies.

Council asked about current collaborations involving NIMH and NHGRI. In addition to large-scale sequencing of DNA samples for neuro-psychiatric disorders, the two Institutes are examining how to maintain disease and model organism databases in ways that make them interoperable and readily accessible to the community. Both Institutes are also developing ideas to ensure long-term sustainability of data resources.

Council inquired if NIMH has engaged the Accelerating Medicine Partnership (AMP) program, and if there is an NIMH-specific effort to turn genetic discoveries into new therapies or possibly even preventive approaches. Dr. Gordon noted that currently most of the genetic-based "leads" for mental health disorders are locus associations, but as specific genes are identified, it should be possible to perform large-scale screens to identify modulators and test these in preclinical models. Council noted that mental health diseases often raise important questions for Ethical, Legal, and Social Implications (ELSI) research, and inquired if NIMH planned to initiate new ELSI research programs. Dr. Gordon replied that through the BRAIN Initiative, NIMH supports a number of neuro-ethics research activities that explore the ethical dilemmas resulting from the application of novel technologies, but an expansion into ELSI-related research topics is not planned at this time.

Dr. Gordon noted that NIMH will continue expanding collaborations with the National Institute on Drug Abuse (NIDA), investigating the relationship between drug abuse and mental health disorders.

Dr. Gordon was asked about NIMH's plans on the application of pharmacogenomic approaches in mental health. He replied there are companies that provide pharmacogenetic direct-to-consumer testing services that are targeted at psychiatric disease. Currently, there is little rigorous evidence that supports the claim that this approach is beneficial to patient care. NIMH has funded pharmacogenomic studies over the past few years, but these studies have not produced ground-breaking results. One drawback to this approach is that the heterogeneity associated with mental health diseases will likely necessitate treatment trials that are prohibitively large in size.

Council asked about the balance of investments at NIMH between investigator-initiated grants versus large program-planned funding opportunities. Dr. Gordon stated the long-standing strength of NIMH has been their portfolio of investigator-initiated grants, but there is a need to stimulate more research in certain areas, including implementation science and computational methods that are applicable to neuroscience research. For large program-planned initiatives at NIMH, one goal is that they should produce resources that will facilitate and support smaller scale investigator-initiated studies.

Dr. Gordon was asked for an update on the BRAIN Initiative. He replied that the initiative received an increase of $100 million in FY2017, bringing the total budget closer to the $400 million that was proposed at the start of the project. The initiative is now focused on building tools that can record brain activities, and identify and characterize different cell types. These tools will be disseminated to the scientific community to help answer basic science questions regarding the neurobiology of the brain. Eleven NIH Institutes and Centers (ICs) are involved in the initiative, and funding is distributed to the participating ICs, who then distribute their allocations to their grantees.

PRESENTATION – Data Science@NIH: Current State, Future Directions. Dr. Patricia Brennan, Director, National Library of Medicine (NLM).

Dr. Patricia Brennan gave a presentation on the current and future research activities of the NLM.

Council asked about NLM's position on preprints and how they should be handled in PubMed. Dr. Brennan stated that NLM supports preprints, and will record them in PubMed if the preprint exists on a stable external server and has a digital object identifier (DOI) number.

Council asked if the PubMed interface could be modernized, and if NLM is developing better ways to index publications and assist investigators to identify papers relevant to their fields of interests. Dr. Brennan responded that making any change to PubMed must be carefully considered due to the very diverse set of needs of their very broad user base. Furthermore, the majority of access queries coming to PubMed today are machine-based; thus, machine-human and machine-machine interactions need to be successfully transacted.

Council noted that a lot of work relevant to NLM's mission has been done in the private sector, and wondered what NIH is doing to interact and collaborate with the private sector, particularly in the area of data analytics that can improve the way research is performed, and improve healthcare. Dr. Brennan replied that NIH Director, Dr. Francis Collins, has brought together external advisors (many of whom are from industry) to help establish public-private partnerships that will help NLM address the challenges associated with the ever-increasing scale of information and data to be searched and analyzed.

Council asked how NLM can collaborate more with other NIH Institutes regarding data science, and particularly about their plans for providing training for the next generation of data scientists. Dr. Brennan replied that NLM wants to create and encourage standards applicable across the NIH, and help develop roadmaps for more robust data science. NLM will continue BD2K training investments and will work with other Institutes to increase training opportunities in data science. The need for more data scientists in leadership positions at NIH is critical. NLM hopes to add around 50 more data scientists to their staff in the next 18 months.

REPORT – Implementing Genomics in Practice (IGNITE) and Beyond Workshop

Dr. Chanita Hughes-Halbert gave a report on the IGNITE and Beyond Workshop that was held in the summer of 2016.

Council asked if electronic health record (EHR) vendors are willing to conform to standards proposed by IGNITE, thereby improving the ability to share data among investigators. Dr. Hughes-Halbert replied that EHR vendors acknowledged the importance and utility of such standards, but they have not made a commitment to implement them.

Council asked how much interaction there was among the IGNITE projects, since they represent a relatively broad range of research topics. The Council also asked if IGNITE consortium members collaborate with other NHGRI programs, like the Clinical Sequencing Exploratory Research (CSER) Consortium or the Electronic Medical Records and Genomics (eMERGE) Network, and if there are synergies being realized from those interactions? Dr. Hughes-Halbert stated that one of the workshop recommendations was to foster more interactions among the investigators in these consortia. Dr. Ebony Madden added that once the CSER II consortium is established, joint working groups will be developed, and possible interactions and collaborations will be explored with IGNITE projects.

CONCEPT CLEARANCE – Implementing Genomics in Practice Phase II (IGNITE II)

Dr. Ebony Madden gave a presentation on the IGNITE II concept.

Council supported the concept, but did express some concerns and questions about it. One concern was the decision to include a separate Funding Opportunity Announcement (FOA) that would focus on enhanced recruitment of racial/ethnic minorities and individuals from underserved communities. The Council noted that previous genomic medicine FOAs had encouraged recruitment of minorities and people from underserved communities, and the applicants had responded well to this challenge. Thus, publishing a separate FOA for enhanced diversity in some ways appears to undercut the previous success realized in this challenge. Dr. Madden noted the inclusion of a second FOA focused on enhanced diversity had a very successful response in CSER2; thus, staff is optimistic for a similar outcome for IGNITE II. Council also expressed concern that the concept appeared to invite an extremely broad scope of projects. It may be prudent to narrow the field(s) of medicine in which the clinical trials could be proposed (e.g., pediatrics). This would increase the probability that all of the grantees would be able to participate effectively in whatever pragmatic clinical trials are ultimately selected to be carried out.

Council asked how the ELSI research projects would be selected once the pragmatic clinical trials (PCTs) have been identified. ELSI research projects are developed in the context of the clinical study that will be carried out, and Council expressed concern if the selection process would “de-link” ELSI research from the original clinical setting in which they had been designed. Staff noted that ELSI research projects would be selected in the context of the PCTs that are chosen to go forward. The selection process would take into account factors such as: are the ELSI research projects an appropriate fit for the chosen PCTs; do the ELSI investigators have the appropriate expertise to conduct the study; and are the ELSI research goals feasible in the setting of the chosen PCTs?

Council asked if the IGNITE II PCTs will include an economic analysis, and if the costs for genetic testing and intervention will be covered by the clinical trial or by insurance companies. Staff noted that cost-effectiveness is a question the applicants are expected to address. The applicants may request funds to cover the cost of the genetic testing they propose for their clinical trial in the event that the tests are not covered by payers. Council asked if there will be a planned effort to coordinate with the Trial Innovation Network developed by the National Center for Advancing Translational Sciences (NCATS). Dr. Madden noted that IGNITE will make use of a central Institutional Review Board (IRB) structure. Plans to interact with NCATS trials resources will be explored.

Council asked if staff planned to conduct any comparisons between observational data and the PCTs in IGNITE II to see if biases can be detected in the clinical trials. Staff noted this is planned for the IGNITE II studies.

Another concern expressed by the Council was the extremely ambitious timeline outlined for the IGNITE II projects. The applicants and collaborating sites must achieve rapid ramp-ups to meet the recruitment and trial objectives, and staff should have alternative timelines in mind if the proposed timelines cannot be met by the applicants. Staff noted that the plan to provide funding for the clinical trial work via supplements would enable NHGRI to withhold that funding until the applicants are truly ready to initiate the trial. Council also expressed concern that the budget cap proposed for the PCTs is too low. The number of trials to be funded could be reduced to ensure that adequate funding is available to complete the trials that go forward.

The Council approved the IGNITE II concept by a vote of 12 in favor, none opposed, and no abstentions.

CONCEPT CLEARANCE – Centers of Excellence in ELSI Research (CEER)

Dr. Jean McEwen gave a presentation on the CEER concept.

Council expressed strong support for the concept, but had several questions. Council noted that past and current CEER grants have served as important loci of training and career development for young investigators and trainees, and they questioned why only two awards are contemplated for the re-issued CEER FOA. Dr. McEwen replied this was simply a budget-driven decision based on past advice from the Council that awards made to CEER grants should not exceed one third of the total ELSI research budget, so as not to limit the number of investigator-initiated awards that can be made.

Council also asked if efforts will continue to be made to involve past CEER investigators with the current consortium of CEER grantees, including their involvement in activities like annual meetings. Staff noted the intention to do so, but how this will be achieved has not been determined. “CEERs Central” is the term that has been given to the informal CEER Coordinating Center (CC), which is currently run by investigators at the University of North Carolina. The CC has performed several important tasks, including managing monthly teleconferences as well as planning and coordinating periodic face-to-face meetings of the CEER investigators. The CC has also managed opportunities for individual trainees to visit different CEER sites to learn new methods or to be exposed to new fields of study in ELSI research.

The Council approved the CEER concept by a vote of 12 in favor, none opposed, and no abstentions.

REPORT – Computational Genomics and Data Science Program Workshop

Dr. Ajay Pillai gave a report on the Computational Genomics and Data Science Program Workshop that was held in September 2016.

Council asked about the scope of the portfolio analysis tool iSearch, and whether it is able to survey awards made by other funding agencies, such as the Wellcome Trust or the Global Alliance. Dr. Pillai responded that the tool is able to identify awards that have been made by some funders, but it cannot identify applications submitted to other funding agencies that did not receive an award.

Council noted the critical importance of sponsoring research in the field of data science, and asked if the workshop participants discussed how to set priorities, and in particular, what NHGRI should be supporting in this space. Council members Drs. Aviv Regev and Carol Bult, who participated in the workshop, said that there was not adequate time at the workshop to set priorities among the 13 recommendations that came from the workshop participants. Council noted setting priorities among these recommendations could serve as a good starting point for the new Genomic Data Science Working Group of Council. Council emphasized the importance for NHGRI to show leadership in this area, and noted the entire biomedical research enterprise is in danger of falling far behind the challenges associated with data science. Therefore, we cannot afford to wait too long by continuing to study the problem.

PRESENTATION – NHGRI History of Genomics Program

Dr. Green introduced the session with a story of Dr. Francis Collins' wish to preserve NHGRI records before he left as NHGRI Director in September 2008. As NHGRI has matured, the Institute needed a more concrete plan to archive its history. Dr. Green formed the NHGRI History of Genomics Program to address this goal. Dr. Chris Donohue is the historian for this program.

Dr. Donohue gave a presentation on the NHGRI History of Genomics Program.

Council expressed their support for the program, and asked for more information about what is being stored in the archive. Dr. Donohue mentioned that records describing the formation of the Institute were thoroughly captured, especially the international collaboration of the Human Genome Project. This activity could help to encourage the development of genomic history archives around the world. The program has also collected a significant amount of ELSI research records, which represent about 24% of the archive. The archive can collect almost all forms of records – from email, to video, and even handwritten notes. The paper copies of documents are stored in the National Archives in compliance with federal law. The archive is machine searchable, and significant manual curation has also been done on the records.

Council asked why there are restrictions in place to access the archive. Drs. Donohue and Green replied that individuals can access the archive after going through an approval process that documents that the individual is a researcher formally engaged in a research project, and has valid institutional support to accomplish the project. Some information in the archive may be considered confidential, so NHGRI prefers to control access to the entire archive until the program matures enough to adopt a more open approach.

Council inquired if additional sources of documents and information from outside of NHGRI (such as from NHGRI grantees) can be provided to the archive. Accepting information from outside sources has been under consideration for some time; the problem is the small number of staff involved in this program limits the scope of what can be taken on.

COUNCIL-INITIATED DISCUSSION

Council requested updates on the following topics for future Council meetings: the All of Us program; changes at the Food and Drug Administration; an update on the Newborn Sequencing in Genomic Medicine and Public Health (NSIGHT) program; and a report from the new Genomic Data Science Working Group of Council. Council also noted the Institute of Medicine has just released a report on genetic evidence, and what studies are recommended to develop sufficient evidence to support the validity and utility of genetic tests; a presentation from someone who was on that committee would be of interest to the Council.

Council asked if presentations from some of the scientists involved in the very large NHGRI research programs could be made to the Council approximately one year in advance of when those programs would come before the Council for consideration of being renewed. Dr. Green agreed. He added that NHGRI is beginning to plan the process of developing a new strategic plan, and the consideration of the renewal of those large research projects will have to be integrated into the timeline of that process.

CONFIDENTIALITY AND CONFLICT OF INTEREST

Dr. Pozzatti read the Confidentiality and Conflict of Interest Policy to Council, and asked the members to sign the forms provided to them.

REVIEW OF APPLICATIONS[1]

In the Closed Session, the Council reviewed 231 applications, requesting $129,844,539 (total cost). The applications included: 108 research project applications (R01, R03, R21, or DP2); 39 cooperative agreement applications (U01 or U24); 20 ELSI applications (9 R01, 3 R21, 1 K01, 6 U01, 1 U54); 21 research center applications (U41 or U54); 1 conference application (R13); 7 career transition award applications (K99/R00); 10 SBIR Phase I applications (R43); 15 SBIR Phase II applications (R44); 3 STTR Phase 1 applications (R41); 7 Research Education applications (R25). A total of 142 applications totaling $64,874,128 were recommended by the Council.

This Council Minutes document was prepared by Kevin Lee, Program Analyst at NHGRI.

09/12/2017 Rudy Pozzatti

Date

Rudy Pozzatti, Ph.D.
Executive Secretary
National Advisory Council for Human Genome Research

09/12/2017 Eric Green

Date

Eric Green, M.D, Ph.D.
Chairman
National Advisory Council for Human Genome Research

[1] For the record, it is noted that to avoid a conflict of interest, Council members absent themselves from the meeting when the Council discusses applications from their respective institutions or in which a conflict of interest may occur. Members are asked to sign a statement to this effect. This does not apply to “en bloc” votes.