NATIONAL ADVISORY COUNCIL FOR HUMAN GENOME RESEARCH
MEETING SUMMARY
February 6-7, 2017

The Open Session of the 79th meeting of the National Advisory Council for Human Genome Research (NACHGR) was convened at 10:00 AM on Monday, February 6, 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 4:50 PM on February 6, 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 4:50 PM to 6:30 PM on February 6, 2017, and from 8:30 AM until adjournment on February 7, 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
Mark Johnston
Sharon Plon
Jonathan Pritchard
Aviv Regev
Dan Roden
Jay Shendure
Val Sheffield

NHGRI Staff Present

Julia Baker (ERP)
Vence Bonham (OD/DIR)
Joy Boyer (ERP)
Comfort Browne (ERP)
Christine Chang (ERP)
Monica Christman (ERP)
Erin Currey (ERP)
Edith Dehaut Combs (ERP)
Ernesto del Aguila (DPCE)
Valentina di Francesco (ERP)
Carla Easter (DPCE)
Alvaro Encinas (DPCE)
Sheena Faherty (DPCE)
Elise Feingold (ERP)
Adam Felsenfeld (ERP)
Ann Fitzpatrick (DM)
Colin Fletcher (ERP)
Colette Fletcher-Hoppe (ERP)
Tina Gatlin (ERP)
Margaret Ginoza (ERP)
Sarah Gould (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)
Heather Junkins (ERP)
Alexander Katz (DIR)
Jeff Kim (ERP)
Kevin Lee (ERP)
Adam Liebendorfer (DIR)
Nicole Lockhart (ERP)
Jonathan LoTempio, Jr. (ERP)
Ebony Madden (ERP)
Allison Mandich (OD)
Jean McEwen (ERP)
Keith McKenney (ERP)
Donna Messersmith (DPCE)
Ken Nakamura (ERP)
Emily Neveux (DM)

Mukul Nerurkar (DPCE)
Vivian Ota Wang (ERP)
Kiara Palmer (DPCE)
Mike Pazin (ERP)
Ajay Pillai (ERP)
Lita Proctor (ERP)
Teresa Ramirez (DPCE)
Ben Ryan (OD)
Jill Saletta (ERP)
Laura Skow (ERP)
Michael Smith (ERP)
Heidi Sofia (ERP)
Jeff Struewing (ERP)
Jennifer Troyer (ERP)
Beth Tuck (DPCE)
Cara Weismann (DPCE)
Chris Wellington (ERP)
Kris Wetterstrand (OD)
Bob Wildin (DPCE)
Ken Wiley (ERP)
Anastasia Wise (ERP)

Others present for all or a portion of the meeting

Judith Benkendorf (ACMG)
Diana Bianchi (NICHD)
Vivien Bonazzi (NIH OD)
Ashley Lewis (CMS)
Joseph McInerney (ASHG)
Joy Nathan (BETAH Associates Inc.)
Melissa Parisi (NICHD)
Rhonda Schonberg (NSGC)

CALL TO ORDER

INTRODUCTION OF NEW NHGRI STAFF LIAISONS AND GUESTS

FUTURE MEETING DATES

May 8-9, 2017
Sept. 11-12, 2017
Feb. 12-13, 2018
May 21-22, 2018
Sept. 24-25, 2018

APPROVAL OF MINUTES

The minutes from the September 12-13, 2016 Council meeting were approved by unanimous vote of the Council.

DIRECTOR'S REPORT

Dr. Eric Green gave his Director’s Report.

PRESENTATION – *NIH Data Commons* (Vivien Bonazzi)

Dr. Vivien Bonazzi gave a presentation on the NIH Data Commons.

Dr. Bonazzi’s presentation focused on the need for research workspaces that are collaborative and interoperable, such as the NIH Data Commons. She highlighted the FAIR principles of data research, noting that data should be Findable, Accessible, Interoperable, and Re-useable. At

Council’s inquiry, Dr. Bonazzi emphasized that the Data Commons will be a flexible system, in order to accommodate multiple use cases and data types.

Dr. Bonazzi indicated that the Data Commons has a two-fold purpose: it will serve as a place to integrate data across NIH research programs, and it will be a workspace for individuals to perform data analyses.

At present, no specific agreement has been reached about how tools should be formatted across the NIH Institutes and Centers (ICs) to enhance interoperability. However, all the ICs participating in the Data Commons agree about the importance of sharing data and analysis tools to minimize redundancy of effort. Dr. Bonazzi also agreed with Council members on the importance of version control. Datasets such as reference genome sequences are not static, and the Data Commons must ensure that new versions are integrated seamlessly across datasets and tools. Council encouraged the Data Commons team to ensure that data and tools are interoperable, and they supported open standards and adequate documentation for the application programming interfaces (APIs).

Council members voiced their concerns about data security (who can access the data) and how sanctions could be enforced against individuals who attempt to access or use the data inappropriately. Solutions can be found in the technology surrounding data access, as well as instituting appropriate policy anticipating potential problems and guiding the way the technology governing data access is developed and implemented. Council also raised the issue of how data sharing is perceived within the medical community, and questioned how these investigators could be encouraged to broadly share phenotypic data. Dr. Bonazzi agreed that changing the culture of data sharing is a difficult task. To approach this challenge, she has been working with individuals from the NIH Clinical Center (CC). The CC has been actively participating in discussions of how they might contribute to the Data Commons, and have identified some datasets they could share. Engaging leaders in the field to participate in the Data Commons is one way to achieve culture change. Dr. Bonazzi identified another important culture change to consider; allowing data to become the “currency of research,” such that raw data are on par with publications as important research products.

Council noted the importance of developing educational materials for many different purposes including: guidance for developing appropriate informed consent documents, and training for users of the Data Commons resources, as well as method developers and software engineers working in the areas of bioinformatics and computational biology.

Lastly, Council members raised the concern that developing a Data Commons on a single cloud platform would allow the cloud provider to achieve a monopoly. Dr. Bonazzi clarified that the Data Commons group is currently operating across three cloud platforms. Although this means that the work must be completed in triplicate (development of three cloud environments), it also fosters competition and innovation.

CONCEPT CLEARANCE – NHGRI Data Sandbox (Valentina di Francesco)

Ms. Valentina di Francesco gave a presentation on the proposed NHGRI Data Sandbox.

Ms. di Francesco highlighted the need for a scaleable, high-performance computing and storage system, and presented the NHGRI Data Sandbox as a solution to this requirement. The Sandbox would initially contain data from the Encyclopedia of DNA Elements (ENCODE) Project, the Electronic Medical Records and Genomics (eMERGE) Network, the Genome

Sequencing Program (GSP), and the 1000 Genomes Project, and it would make these datasets interoperable.

Council questioned what the governance structure would be for the Sandbox, and whether NHGRI would determine what tools and datasets would populate the Sandbox initially, or the applicants would propose the datasets that should be put in the Sandbox. NHGRI staff will determine the data content of the Sandbox, and the governance structure will involve an external scientific advisory board that will advise NHGRI.

Council members inquired how this resource would differ from the NIH Data Commons presented by Dr. Bonazzi. The Sandbox would be part of the NIH Data Commons in the same way that the National Cancer Institute (NCI) Data Commons is part of the NIH Data Commons. Further, this resource would streamline NHGRI-funded resources so that they are all available via a single cloud platform, and would allow NHGRI to harmonize data and analysis tools across its programs. Ms. di Francesco clarified that the concept document would need to be altered to address data storage needs.

Council expressed concern about the proposed computing costs that users would face; specifically, the costs may affect the ability of many investigators to use the Sandbox. NHGRI staff acknowledged this concern, and noted that NIH is considering a credit model wherein NIH-funded investigators would be provided with a certain amount of free access to the services available in the NIH Data Commons. NHGRI staff also noted a major objective of the Sandbox concept is to provide an environment where analyses of large datasets can be done, and currently, many investigators cannot even attempt to conduct this type of analysis. Council also enquired what services would be provided by the Sandbox; these decisions will be made in consultation with the advisory board over time, and will be informed by a changing research environment.

Council expressed several concerns about the contract mechanism proposed for this project, including the metrics that will be used to judge the contract's success, particularly because this is such a rapidly moving field. Although metrics have not been finalized, several have been proposed, including the number of users, the level of user engagement with the resources, the number of datasets that populate the Sandbox, and the number of tools created. NHGRI program staff are looking at similar existing infrastructures to help determine appropriate milestones. Milestones may change as the concept moves forward. Council recommended defining what constitutes success of the project and how many people are expected to use the resource before the Sandbox is launched.

Council members raised some concerns that future NHGRI Requests for Applications (RFAs) might require grantees to use the Sandbox, which would ensure its success by defining the number of users. Program staff clarified that grantees will be encouraged, but not required, to use the resource, and may be given funding to innovate within the Sandbox, e.g., create new tools.

Council also inquired about the proposed length of the contract (seven years), as the field of data science could change rapidly within this timeframe. Staff members clarified that if necessary, the contract mechanism will enable them to change the tasks requested of the contractor and the length of the contract after it is awarded, thereby allowing the resource to meet the changing needs of the user community. The Sandbox will be governed by a Scientific Advisory Board (SAB) comprised of members nominated by the contractor and vetted by NHGRI, to avoid conflicts of interest. Council members recommended that the Sandbox undergo an annual review by this committee. After seven years, NHGRI staff will re-assess whether the Sandbox has or has not been an effective resource, how exactly it has been effective, and whether it will continue to meet the evolving needs of the data science community.

Council inquired how the Sandbox might influence opportunities for innovation in data science. Ms. di Francesco clarified that the Sandbox contractors will not be responsible for developing tools; instead, users will upload tools themselves, and the Sandbox will provide investigators with a computational space to use these tools. She also noted that the Sandbox was proposed because data scientists frequently invent similar tools to address the same research questions in different research settings, which is neither innovative nor efficient. However, this resource would not prevent investigators from inventing new tools if the need arises.

Staff members will bear the constructive comments from Council in mind when developing the Request for Proposal (RFP) document. Dr. Pozzatti thanked the Council members for their guidance and asked for a vote to approve the Sandbox Concept. The Council voted: 15 votes for approval, none opposed, and no members abstained.

REPORT – Genomics and Society Working Group (Lisa Parker)

Dr. Lisa Parker gave a presentation on behalf of the Genomics and Society Working Group of the Council, which she chairs.

Dr. Parker reviewed the work of the Genomics and Society Working Group (GSWG) over the past year, including developing metrics for the success of Ethical, Legal, and Social Implications (ELSI) research, re-evaluating the three-year project span of ELSI grants, and promoting ELSI research at other NIH ICs. Council inquired about what metrics were used to support Dr. Parker's assertion that the majority of ELSI research supported by NHGRI has been successful. This analysis was based on traditional metrics including productivity, publications, and in some cases, inducing changes in practice of physician scientists who work with ELSI investigators in so-called imbedded research settings.

Council brought up a manuscript that is currently under development, wherein the GSWG seeks to define the differences between "normative research" and "conceptual research." This document is intended to serve a very broad audience of investigators. Dr. Parker described conceptual research as "meaning-making," whereas normative research involves a "descriptive analysis of values."

PRESENTATION – *Building Bonds between NHGRI and NICHD* (Dr. Diana Bianchi)

Dr. Diana Bianchi, the newly appointed Director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), gave a presentation to the Council.

Dr. Bianchi gave a broad overview of her vision for NICHD, highlighting current collaborations with NHGRI including: the Gabriella Miller Kids First initiative, the Clinical Genome Resource (ClinGen), the Undiagnosed Diseases Network (UDN), and the Newborn Sequencing in Genomic Medicine and Public Health (NSIGHT) program, and future opportunities for collaborative work in prenatal genomics, particularly the ELSI issues therein. Next steps for these collaborations include a meeting of extramural staff members from both NHGRI and NICHD.

In response to Dr. Bianchi's presentation, Council discussed several issues surrounding non-invasive prenatal testing (NIPT). Council was primarily concerned that NIPT may not be accessible to diverse communities within the U.S. population. Dr. Bianchi acknowledged that the testing is almost exclusively ordered by expectant parents who have access to health insurance, but some states do cover NIPT via Medicaid and some large HMOs also provide this testing. This area is ripe for future ELSI studies, and Dr. Bianchi mentioned that the new director of the NICHD Office of Health Equity is interested in conducting this type of research in multiple communities in the U.S.

Another ELSI issue surrounding NIPT is the fact that these technologies are being introduced into clinical care before their clinical validity has been adequately established. This fuels concerns that clinicians will be overly-reliant on the information furnished by the providers of the NIPT technology for the interpretation of the test results. Council noted there is a great need to develop evidence-based professional education tools and resources for health care providers. Dr. Bianchi remarked that research in this area is a priority for NICHD.

Council liaisons from professional societies noted that the American Society of Human Genetics (ASHG) has a role to play in educating health care providers about these issues. ASHG's policy statement on the use of non-invasive prenatal screening (NIPS) and non-invasive prenatal testing (NIPT) has recently been revised, and the organization is putting together educational materials.

Council was supportive of non-profit educational efforts to address these issues, including the work of ASHG and the NHGRI Genomic Literacy, Education, and Engagement (GLEE) Initiative. Council members recommended that NICHD invest more resources in patient education and the ELSI issues therein, and noted that the Clinical Sequencing Exploratory Research (CSER) consortium has done a lot of work in this area. There may be areas of shared interest among some of the CSER investigators working in pediatric settings and NICHD's research goals.

COUNCIL-INITIATED DISCUSSION

Dr. Pozzatti asked the Council to propose topics for reports or presentations that they would like to receive at future meetings. Council suggested a discussion about tackling the challenges of developing a program in high-throughput functional genomics. Council noted the National Academy of Sciences' statement on gene editing and the ethical and policy issues related to that topic is set for release on February 14, 2017. Council would welcome a presentation about that report. Council would also be interested to hear a discussion about how biomarkers and datasets of metabolomics and/or proteomics could be compared to genomic data to help infer function of the many variants being discovered from DNA sequencing studies.

STATEMENT OF UNDERSTANDING

Dr. Pozzatti reviewed the Statement of Understanding (SOU) with the Council. The SOU was approved and accepted by the Council without modification by the following vote: 15 members approved, none disapproved, and no members abstained from the vote.

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 189 applications, requesting $191,604,396 (total cost). The applications included: 88 research project applications (R01, R03, R15, R21, or RM1); 34 cooperative agreement applications (U01, U24, or U41); 15 ELSI applications (13 R01, R03, or R21, 1 K01 career development, and 1 T32 institutional training application); 5 research center applications (U41); 2 conference applications (R13); 10 career transition award applications (K99/R00); 1 career development award (K01); 5 institutional training applications (T32); 18 SBIR Phase I applications (R43), 7 SBIR Phase II applications (R44), 2 STTR Phase 1 applications (R41), 1 STTR Phase 2 application (R42), and 1 Research Education application (R25). A total of 124 applications totaling $80,137,025 were recommended by the Council.

This Council Minutes document was prepared by Colette Fletcher-Hoppe, Program Analyst at NHGRI.

5/9/2017 Rudy Pozzatti

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

5/9/2017 Eric Green

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

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[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.