NATIONAL ADVISORY COUNCIL FOR HUMAN GENOME RESEARCH
MEETING SUMMARY
September 16-17, 2019

The Open Session of the 87th meeting of the National Advisory Council for Human Genome Research (NACHGR) convened at 10:00 AM on Monday, September 16, 2019 at the 6700B Rockledge Conference Center in Bethesda, 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 – 5:00 PM on September 16, 2019. In accordance with the provisions of Public Law 92-463, the meeting was closed to the public from 8:30 AM – 10:00 AM on September 16, 2019; and from 8:30 AM until adjournment on September 17, 2019 for the review, discussion, and evaluation of grant applications.

COUNCIL MEMBERS PRESENT
Joshua C. Denny (Vanderbilt University Medical Center)
Harry Dietz (Johns Hopkins University School of Medicine)
Jonathan Haines (Case Western Reserve University)
Jonathan Pritchard (Stanford University)
Sharon Plon (Baylor College of Medicine)
Mark Johnston (University of Colorado)
Trey Ideker (University of California, San Diego)
Gail Henderson (University of North Carolina)
Brent Graveley (University of Connecticut)
Jeffrey Botkin (University of Utah)

AD HOC ADVISORS PRESENT
Mark Craven (University of Wisconsin, Madison)
Stephen Fodor (13.8, Inc.)
Rafael Irizarry (Dana-Farber Cancer Institute)
Wendy Kay Chung (Columbia University)
Patricia Deverka (Geisinger Health System)*

**indicates participation by phone*

STAFF PRESENT FROM THE NATIONAL INSTITUTES OF HEALTH
Matthew Arnegard, ORWH
Sarah Bates, DPCE
Joy Boyer, ERP
Comfort Browne, ERP
Eileen Cahill, ERP
Lisa Chadwick, ERP
Joanna Chau, ERP
Monika Christman, ERP
Heather Colley, ERP
Christine Daulton, DPCE
Jyoti Dayal, ERP
Carla Easter, DPCE
Elise Feingold, ERP
Adam Felsenfeld, ERP
Tina Gatlin, ERP
Elena Ghanaim, DPCE
Dan Gilchrist, ERP
Bettie Graham, ERP
Chris Gunter, ERP
Michael Hahn, OD
Linda Hall, ERP
Hwaida Hannoush, ERP
Lucia Hindorff, ERP
Deanna Ingersoll, ERP
Cashell Jaquish, NHLBI
Britny Kish, DPCE
Nicole Lockhart, ERP
Ebony Madden, ERP
Allison Mandich, OD
Donna Messersmith, DPCE

Donna Morris, ERP
Kiara Palmer, DPCE
Mike Pazin, ERP
Natalie Pino, ERP
Jessica Reusch, DPCE
Sarah Robbins, DPCE
Robb Rowley, ERP
Shurjo Sen, ERP
Mike Smith, ERP
Heidi Sofia, ERP
Taylorlyn Stephan, ERP
Tiancheng Sun, ERP
Cecelia Tamburro, ERP
Harry Wedel, ERP
Chris Wellington, ERP
Kris Wetterstrand, OD
Ken Wiley, ERP

OTHERS PRESENT FOR ALL OR A PORTION OF THE MEETING
Austin Booth, Research Triangle Institute
Rich Haspel, Beth Israel Deaconess Medical Center
Samata Katta, American Society of Human Genetics
Catharine Krebs, Physicians Committee for Responsible Medicine
Rachel Levinson, Arizona State University
Mona Miller, American Society of Human Genetics
Derek Scholes, American Society of Human Genetics
Rhonda Schonberg, National Society of Genetic Counselors

INTRODUCTION OF NEW COUNCIL MEMBERS, NHGRI STAFF, LIAISONS, AND GUESTS
Dr. Rudy Pozzatti began the Open Session with the introduction of new members of the NHGRI staff, liaisons, and guests, which can be found at: https://www.youtube.com/watch?v=O9IVocDPiBU.

APPROVAL OF MINUTES
Council members approved the May 2019 minutes by a unanimous vote with no edits, opposition or abstentions.

FUTURE NACHGR MEETING DATES
Dr. Pozzatti mentioned that future NACHGR meetings will take place on the dates listed below with one amendment; the NACHGR meeting originally scheduled for May 17-18, 2021 has been changed to May 22-23, 2021.

- Feb. 10-11, 2020
- May 18-19, 2020
- Sept. 14-15, 2020
- Feb. 22-23, 2021
- May 22-23, 2021
- Sept. 13-14, 2021

DIRECTOR'S REPORT
Dr. Eric Green gave his Director's Report, which included a series of updates on recent activities and awards at NHGRI, NIH, and in the broader genomics research community. The report included a fiscal year 2020 appropriations update, Extramural Research Program overviews and updates, as well as Intramural Research Program updates. A video of his presentation and the slides can be found at: https://www.genome.gov/event-calendar/87th-Meeting-of-National-Advisory-Council-for-Human-Genome-Research.

PRESENTATION – *Inter-Society Coordinating Committee for Practitioner Education in Genomics (ISCC-PEG): Promoting Collaboration in Genomics Education* – Dr. Richard Haspel

Dr. Richard Haspel provided an overview of the Inter-Society Coordinating Committee for Practitioner Education in Genomics (ISCC-PEG) effort. The ISCC-PEG is supported by NHGRI and consists of various NIH-affiliated and industry groups for developing genetics curricula and implementing courses. Dr. Haspel reviewed the "compendium" which collects and lists all efforts within ISCC-PEG to allow medical educators to easily access these resources, to collaborate, and to learn more about genetics education. The ISCC-PEG is ultimately interested in developing a collaborative resource, providing the educator community a forum for discussion, and providing input on education funding within NHGRI strategic planning efforts. The group has a diverse membership and welcomes new members.

A video of Dr. Haspel's presentation can be found at: https://www.youtube.com/watch?v=HesHq5LTMMQ.

CONCEPT CLEARANCE – *Genomic Community Resources (PAR)* – Chris Wellington

Chris Wellington presented a renewal of the Genomic Community Resources U24 Program Announcement, which has no significant changes from the previous version. The PAR supports databases and informatics resources, comprehensive collections of genomic resources, and the development of standard data types for central sample collections. Special review considerations for this PAR include: a broad definition of innovation, performing needs assessment and community outreach, emphasizing service and training, providing a resource maintenance plan, and ensuring that all data are findable, accessible, interoperable and reusable.

Council members approved the concept unanimously. A video of Chris Wellington's presentation can be found at: https://www.youtube.com/watch?v=cRWz2_0I1OQ.

CONCEPT CLEARANCE – *ELSI Program Announcements for Unsolicited Applications (PAR)* – Joy Boyer

Joy Boyer presented a concept for the renewal of a set of three ELSI program announcements as PARs for R03, R21 and R01 applications, which now have special receipt, referral, and review considerations. The renewal PARs contain no substantial changes from the current Program Announcements, other than the new PARs invite the submission of clinical trials as an option. The ELSI Program Directors will continue to maintain an online list of research topics reflecting NHGRI's Strategic Plan and emerging issues in ELSI research as additional guidance to applicants.

Council members approved the concept and all three PARs unanimously. A video of Joy Boyer's presentation can be found at: https://www.youtube.com/watch?v=H_C3vkNoETU.

CONCEPT CLEARANCE – *Genomic Technology Development (PAR)* – Michael Smith

Dr. Michael Smith presented a concept to renew the existing Genomic Technology Development Program Announcement. The concept includes three PARs for R01, R21

and R43/R44 applications. Dr. Smith highlighted some examples of technologies that were developed using Genomic Technology Development funding, which have shown a high return on investment, enabling the progression of other projects. In response to NHGRI's current strategic planning efforts, the scope of the proposed PARs will be broad while still aiming to enhance certain areas such as generation of multi-omics datasets and clinical applications. Dr. Smith acknowledged applicants may have some trouble distinguishing between the Genomic Technology Development and Nucleic Acid Sequencing Technology Development funding opportunities. The FOA language will clarify the distinction between the two and applicants are asked to submit letters of intent and specific aims to help identify to which opportunity they should apply.

Council members approved the concept and all three PARs unanimously. A video of Dr. Smith's presentation can be found at: https://www.youtube.com/watch?v=gAVoLw3S77E.

CONCEPT CLEARANCE – *Technology Development (RFAs)* – Michael Smith

Dr. Michael Smith next presented a concept for three RFAs: Nucleic Acid Sequencing, Synthetic Nucleic Acids, and a Coordinating Center RFA. The Nucleic Acid Sequencing RFA is a renewal of the existing RFA with an increase in the level of funding to encourage new sequencing approaches to address the challenges of phasing, telomere to telomere sequencing, and novel clinical applications. The goal of the new Synthetic Nucleic Acids RFA is to produce cheaper, more accurate, and longer oligonucleotides and very large synthetic constructs of double strand DNA with base modifications. The new Coordinating Center (CC) RFA is designed to foster a cohesive technology development community, stimulate advances in DNA synthesis, facilitate technology transfer, and implement a process to quickly distribute opportunity funds to grantees. Council noted adding concrete goals to these RFAs such as a requirement to achieve a specific level of increase over existing technologies would be appropriate. Language that specified how applicants would be expected to interact with the CC would be helpful to the applicants and would help define the roll of the CC.

Council members approved the concept for all three RFS with one member abstaining. A video of Dr. Smith's presentation can be found at: https://www.youtube.com/watch?v=QJPjgi9ugxU.

CONCEPT CLEARANCE – *Mendelian Genomics: Solving the Unsolved (RFAs)* – Lisa Chadwick

Dr. Lisa Chadwick presented a concept for two RFAs that would continue NHGRI's research efforts in the Mendelian Genomics program. One RFA would support Mendelian Genomics Centers as U01 applications, the second would support a Coordinating Center as a U24 application. Dr. Chadwick presented data showing that current whole-exome sequencing approaches identify a genetic variant thought to be strongly associated with a Mendelian phenotype in about half of the cases that have been studied. The new Mendelian Genomics concept places a stronger emphasis on learning how to solve the more complex Mendelian cases by facilitating functional follow-up studies on candidate variants, and data sharing and collaboration within the consortium and broader research community. The novel gene discovery effort will continue to be a strong component in this program.

Council members approved the concept for both RFAs unanimously. A video of Dr. Chadwick's presentation can be found at: https://www.youtube.com/watch?v=AEKVVeMj8ck

CONCEPT CLEARANCE – *Polygenic Risk Scores from Populations of Diverse Ancestry (RFAs)* – Lucia Hindorff

Dr. Lucia Hindorff presented a concept for two Polygenic Risk Score (PRS) RFAs. Both RFAs will support U01 applications. The RFAs are designed to address the problem that PRS developed from datasets largely comprised of samples from individuals of European ancestry tend to show poorer risk prediction in non-European populations. The proposed project structure included PRS Centers (PRSC) that will be required to use sample collections that meet minimum numbers of participants from non-European ancestry. Each PRSC would be expected to contribute to cross-consortium analyses, thereby maximizing sample size and genetic diversity, harmonize health/disease measures for analysis, address data use limitations, integrate ancestry information, and identify metrics for improving PRS prediction. The proposed Coordinating Center would lead analysis efforts, data sharing, genotype imputation, convene appropriate ELSI expertise, and provide limited support for affiliate studies (i.e., to investigators not directly funded by the proposed RFA). Council expressed substantial enthusiasm for the concept overall, but also noted the importance and necessity for methods development to occur in the same timeframe that datasets were being identified, data harmonization would take place, and phenotyping across multiple datasets would be performed. Some Council members noted there were additional important issues to consider about ELSI research questions and the clinical utility of PRS and how they could best be implemented in clinical care.

Council members approved the concept and both RFAs, with 8 votes for approval and 7 votes to oppose the concept. A video of Dr. Hindorff's presentation can be found at: https://www.youtube.com/watch?v=x0-hw7DoOQU. A video of the re-vote taken for the concept can be found at: https://www.youtube.com/watch?v=mxVUKnf7KdM.

COUNCIL-INITIATED DISCUSSION

Council members requested the following topics be presented at a future Council meeting: (1) a presentation and progress report on the Analysis, Visualization and Informatics Lab-space (AnVIL) resource; (2) a presentation from NIH's new Associate Director for Data Science, Dr. Susan Gregurick; (3) a presentation from staff of NHGRI's investment in investigator-initiative research projects versus projects funded by RFAs with set-aside funding, and (4) a more granular presentation of NHGRI's technology development activities, including budget and program delineations. The Council members suggested the R35 grant mechanism may have potential merit in the NHGRI portfolio of grants, but this requires further analysis. Lastly, in response to the genomics community's interest in methods development, Council members recommended NHGRI consider convening a workshop or webinar on the topic of methods development in the context of polygenic risk score and genomic technologies.

A video of the Council-initiated discussion can be found at: https://www.youtube.com/watch?v=pW4TDT07-PM.

CONFIDENTIALITY AND CONFLICT OF INTEREST[1]
Dr. Pozzatti read the Confidentiality and Conflict of Interest Policy to Council members and asked the members to sign the forms provided to them.

DEPARTING COUNCIL MEMBERS
Dr. Pozzatti announced that 4 Council members (Drs. Graveley, Henderson, Johnston and Pritchard) have completed four years of service on Council and will retire following this Council meeting. Dr. Green presented an award to each of the departing members.

REVIEW OF APPLICATIONS

In the Closed Session, the NACHGR reviewed 153 applications, requesting $66,801,511 (direct costs). The applications included: 105 research project applications (R01, R15, or R21); 19 cooperative agreement applications (U01, U24 or U41); 9 career development or career transition applications (K99/R00, K01, or K08); 2 conference applications (R13); 1 education application (R25); 8 SBIR Phase I applications (R43); 4 SBIR Phase II applications (R44), and 5 STTR Phase 1 applications (R41). A total of 95 applications totaling $42,719,982 were recommended for funding by the NACHGR.

This Council Meeting Summary document was prepared by Eileen Cahill, NHGRI Scientific Program Analyst.

02/10/2020 Rudy Pozzatti
Date

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

02/10/2020 Eric D. Green
Date

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

[1] Council members absented themselves from the meeting when the Council discussed applications from their institutions or in which a conflict of interest may occur. Members signed a statement to this effect. This does not apply to “en block” votes.

This report was approved by the NACHGR on February 10, 2020.