NATIONAL ADVISORY COUNCIL FOR HUMAN GENOME RESEARCH
SUMMARY OF MEETING
September 9-10, 2013

The Open Session of the 69th meeting of the National Advisory Council for Human Genome Research was convened at 10:00 AM on September 9, 2013 at the Fishers Lane Terrace Level Conference Center in Rockville, MD. 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 September 9, 2013. 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 6:00 PM on September 9, 2013, and from 10:15 AM until adjournment at 3:00 PM on September 10, 2013, for the review, discussion, and evaluation of grant applications.

Council members present:
Carlos Bustamante
Lon R. Cardon, ad hoc
Joseph Ecker, ad hoc
James P. Evans
Ross C. Hardison
Chanita A. Hughes-Halbert, ad hoc
Howard J. Jacob
David M. Kingsley
Amy L. McGuire
Howard L. McLeod
Deirdre R. Meldrum
Jill P. Mesirov
Anthony P. Monaco
Martin E. Kreitman, ad hoc
Robert Nussbaum
Lucila Ohno-Machado
Arti Rai
Pamela L. Sankar
David R. Williams
Richard K. Wilson

Council members absent:
Eric A. Boerwinkle, ad hoc
Igor B. Jouline (Zhulin), ad hoc
David C. Page, ad hoc

Staff from the National Human Genome Research Institute

Ronit Abramson, DPCE
Alexi Archambault, ERP
Alice Bailey, DPCE
Jonathan Bailey, DPCE
Jessica Barry, ERP
Steve Benowitz, DPCE
Shannon Biello, ERP
Vivien Bonazzi, ERP
Vence Bonham, DPCE
Ebony Bookman, ERP
Joy Boyer, ERP
Comfort Browne, ERP
Cheryl Chick, ERP
Monika Christman, ERP
Shane Clark, ERP
Deborah Colantuoni, ERP
Catherine Crawford, ERP
Priscilla Crockett, DM
Camilla Day, ERP
Rachel Dexter, DM
Nicholas Digiacomo, ERP
Carla Easter, DPCE
Alvaro Encinas, DPCE
Elise Feingold, ERP
Adam Felsenfeld, ERP
Leigh Finnegan, ERP
Ann Fitzpatrick, DM
Colin Fletcher, ERP
Brandon Floyd, ERP
Tina Gatlin, ERP
Jonathan Gitlin, DPCE
Zivile Goldner, ERP
Peter Good, ERP
Bettie Graham, ERP
Mark Guyer, IOD
Linda Hall, ERP
Lucia Hindorff, ERP
Heather Junkins, ERP
Rongling Li, ERP
Nicole Lockhart, ERP
Carson Loomis, ERP
Mark Lucano, DM
Allison Mandich, IOD
Teri Manolio, ERP
Jean McEwen, ERP
Keith McKenney, ERP
Preetha Nandi, ERP
Jacqueline Odgis, ERP
Vivian Ota Wang, ERP
Michael Pazin, ERP
Ajay Pillai, ERP
Erin Ramos, ERP
Laura Rodriguez, DPCE
Ellen Rolfes, DM
Leonard Ross, DM
Kate Saylor, DPCE
Jeffery Schloss, ERP
Michael Smith, ERP
Heidi Sofia, ERP
Jeff Struewing, ERP
Kathie Sun, ERP
Larry Thompson, DPCE
Yekaterina Vaydylevich, ERP
Simona Volpi, ERP
Lu Wang, ERP
Chris Wellington, ERP
Kris Wetterstrand, IOD
Anastasia Wise, ERP
Sherry Zhou, ERP

Others present for all or a portion of the meeting:

Rami Alouran, Ohio University
Sarah Beachy, IOM
Judith Benkendorf, ACMG
Joseph McInerney, ASHG
David Kaufman, JHU/GPPC
Lorie Lapierre, Ohio University
Jennie Larkin, NHLBI
Rachel Levinson, Arizona State Univ.
Xiaoyu Liang, Ohio University
Mary Perry, NIH/OD
Rhonda Schonberg, NSGC
Lonnie Welch, Ohio University

INTRODUCTION OF NEW COUNCIL MEMBERS AND STAFF, LIAISONS, AND GUESTS

DIRECTOR'S REPORT

Dr. Eric Green presented the Director's Report to Council.

Council remarked upon the increasing implementation of electronic medical records (EMRs) in clinical care and inquired if NHGRI had plans to engage with some of the industry players, such as Epic Systems, to incorporate genetic and family history information in EMRs.

Teri Manolio responded that NHGRI has tried to engage Epic through the EMERGE Consortium research program, but the company is waiting to hear from their customers what tools and data types should be adopted and made available through EMRs. Council members noted some progress has been made in the past couple of years to add genetic data, but that activity still represents a relatively small component of the landscape of data and information that the US health system generates and utilizes in providing health care. Council members also noted that NHGRI should pay attention to the issue of interoperability standards for EMR systems. Council acknowledged the overall massive size and scope of the electronic health record business field, which operates in our free enterprise economy, and it may not be possible for NHGRI or NIH to influence outcomes in this field using the traditional research grant process. The NHGRI Division of Policy Communications and Education Genomic Healthcare Branch, which is currently searching for a Chief, is in a position to participate in some of the discussions that address the administrative and policy issues relevant to EMRs.

Council also wondered if NHGRI would consider working with the incoming U.S. Surgeon General to encourage clinical laboratories to share reports. NHGRI DPCE has maintained staff contacts with the Surgeon General's office and will reach out to them once a successor has been named.

PRESENTATION BY ARTI RAI

Arti Rai gave a presentation entitled "Association for Molecular Pathology et al. v Myriad Genetics Inc. et al."

An audience member pointed out inconsistencies in the official Supreme Court ruling and asked Professor Rai why there was such a large misinterpretation between the justices' understanding of cDNA and gDNA that subsequently affected their decision. Professor Rai answered that the issue is not clearly agreed upon, and commented that another difference between the two types of DNAs is that cDNA is more commercially viable. Council members postulated the decision was calibrated to satisfy both the biotechnology industry (upholding cDNA claims) and the scientific community (striking down gDNA claims).

Council expressed concern about the blurred distinction between the terms 'diagnostic' and 'therapeutic,' and the commercial importance of patents in those arenas.

Council wondered about the response of other sequencing companies, (e.g., Ambry Genetics, Genova Diagnostics, etc.), to the ruling and if they are still offering BRCA1/2 tests to the public. Dr. Evans confirmed that other companies are offering BRCA testing, often at much lower cost than Myriad. These companies also dispute the variants of uncertain significance (VUS)

estimates that Myriad has asserted their tests achieve, pointing to evidence that the quality of their tests is actually much higher.

PRESENTATION BY KATHY HUDSON

Kathy Hudson gave a presentation entitled “Data Sharing and the HeLa Genome Sequence.”

Council asked if the group involved in the Lacks family discussions also contemplated developing a scalable privacy policy for family members that could be used in other applications to protect the rights of the relative of individuals who choose to participate in genetics/genomics research. Dr. Hudson noted that the Lacks family’s case was so unique that these discussions did not easily extend to other settings, not even to the families of other cell line donors. Though the Department of Health and Human Services is considering solutions for other cell lines in use, the HeLa cell line is unique because it is widely used and because so much information is widely known about Henrietta Lacks and the extended members of the Lacks family. Regulatory issues for general research participants did not feature as a part of these discussions, though this situation will inform the Department’s proposed revisions to the Common Rule. Dr. Hudson offered the opinion that if an individual participates in genetics research, that decision should not be overridden by family members.

Council noted that large production projects have developed many different types of datasets from HeLa cells. These data are already available in public databases and through dbGaP. The Council wondered if the new Working Group will develop criteria to determine what types of data should be submitted to dbGaP and should have limited access. Dr. Hudson responded that the Working Group was just starting to consider what distinctions will be drawn for different types of HeLa data, and no decisions have been made at this time.

The Council asked what is being done to help the Lacks family interpret the HeLa genome in terms of their own health. Dr. Hudson noted that Francis Collins and a second medical geneticist and a genetic counselor have all met with members of the Lacks family. Some of these discussions have covered basic concepts in human genetics while others have been about specific variants found in the HeLa genome. The family members were also told about existing genetic studies they could enroll in if individual members of the family made the decision to have their own genome studied.

Karen Rothenberg wished to know more about where the stipulation to disclose commercial intentions when using HeLa data came from. Dr. Hudson responded that the Lacks family was concerned about others obtaining financial rewards from the use of HeLa data. Although the NIH cannot prevent investigators from filing patents or seeking to commercialize research findings, NIH is allowed to ask investigators to disclose their intentions. If the Lacks family chooses to contact investigators or companies with a stated interest to pursue commercialization of something derived from the HeLa data, that interaction would take place without NIH involvement. This stipulation was implemented to keep the Lacks family informed; it is not a criterion for data access.

Dr. Hudson clarified that the data access category of “biomedical research” is broad and captures research for many topics, though it does exclude ancestry research. An audience member wondered if some of the data restrictions on the Lacks data could be adopted by other investigators for their own dbGaP databases. Dr. Hudson responded that some cohort data in public databases, e.g. the Framingham Heart Study, have similar restrictions on their usage.

RECENT NHGRI-SPONSORED MEETINGS
Genomic Medicine Working Group Meeting

Dr. Teri Manolio gave a report about the activities from the Genomic Medicine Working Group, and the most recent Genomic Medicine meeting, which was held on May 28-29, 2013 in Bethesda, MD.

Dr. Green clarified that other Institutes/Centers (ICs) contribute funding to programs that are administered by the Division of Genomic Medicine (e.g., NCI dollars in CSER, and Common Fund money that supports the UDN). He explained that reaching out to the large number of national and international groups contacted through the Working Group activities has put a strain on NHGRI staff. While the opportunities are expansive and exciting, this larger picture goes beyond what NHGRI can carry out by itself. This topic will be discussed at an upcoming NIH Directors' retreat where there will be a strategic discussion about how NIH can advance the field of genomic medicine.

Council commented that these collaborations are exciting and questioned if there were efforts to centralize genetic data that could potentially be mined to look at health outcome research. In particular, is there a task force that is being organized to examine this or is the discussion still very preliminary? Dr. Manolio responded that the Department of Defense (DoD) is combining all of the military medical services and databases from the different armed services into one system. Though there are many obstacles, including security and privacy issues, this may be an opportunity to galvanize the other federal agencies to participate in some very large-scale health research activities.

Council cautioned that the DoD has a history of funding potentially unorthodox research that goes beyond use in basic medicine (e.g., research in human enhancement or to assist with job screening), and wondered if NHGRI's objectives could fit in with the DoD research agenda. Dr. Manolio acknowledged the concern and responded that NHGRI is more interested in preparing the DoD for research in genetics and introducing them to the field. Thus far, the DoD has expressed interest to continue discussions with NHGRI.

Council asked where the materials from the Inter-Society Coordinating Committee for Practitioner Education in Genetics (ISCC) will be organized and made accessible to the public. Dr. Manolio stated that she hopes the materials will eventually be maintained by the Genetics/Genomics Competency Center (G2C2) and the Global Genetics and Genomics Community (G3C), two NHGRI web-based education and training resources that are available to the public. Dr. Laura Rodriguez clarified that genome.gov will also contain some information tailored to specific professional disciplines. G2C2 will be expanded to include competencies and training for education aimed at four health disciplines. G3C is an interactive case-study resource for different, specific issues in healthcare. Everything will be cross-linked to the NHGRI site so that all of the materials will be easy to find from any given portal. Dr. Manolio also stated that NHGRI is working with consultants to develop a way to make this effort self-sustaining. Dr. Rodriguez offered to send the links for G2C2 http://www.g-2-c-2.org/, G3C http://www.g-3-c.org/en/, and the Institute's educational resources to the Council members. http://www.genome.gov/27527599

Council remarked that the work accomplished by the NHGRI so far is substantial, but that there does not seem to be a structure to guide further development of this research agenda. Dr. Green agreed that the work of the NHGRI as a convener of these activities is reaching the end

of its resources and that the Institute cannot speak on behalf of the NIH, the U.S. Government, or the entire genomic educational effort. Even so, there are unrealistic expectations that NHGRI will find solutions to the manifold problems that confront the implementation of genomic medicine. Additional groups need to partner with the NHGRI to carry this responsibility. Council suggested that from a conceptual point of view, the Accreditation Council for Graduate Medical Education (ACGME) and the Continuing Medical Education (CME) group of the American Medical Association (AMA) are suitable groups to collaborate with on this. Dr. Manolio elaborated that both groups participated in the January meeting and have representatives on the ISCC. The Accreditation Council for Continuing Medical Education (ACCME) in particular has been a very eager participant.

PROJECT/PROGRAM UPDATES
The NHGRI-Smithsonian Genome Exhibition

Vence Bonham gave an update on the activities surrounding the NHGRI-Smithsonian Genome Exhibition that opened in June 2013. Mr. Bonham noted that the exhibition has been identified by museum staff as one where people stay much longer than they do in other parts of the museum. He was also pleased with the presentation of ethical issues in the exhibition.

Council complimented the development of ancillary programming to engage and educate the public outside of the exhibition. Mr. Bonham explained that the ancillary programming will be videotaped and made available online after the events take place. He hopes that when the exhibition begins traveling across North America (in 2014), it will engage local scientific communities and recruit other scientists to continue the development of additional ancillary programs. The Smithsonian will develop a “toolkit” for other cities to adopt the same sort of interactive activities for other local communities.

Dr. Green explained that the Smithsonian, as a scientific institution, has become very interested in genomics and has started to develop a genome-sequencing infrastructure to conduct comparative biology studies.

In response to a question from Council about negative pushback from members of the public who are not happy about using genomics to study topics such as evolution and ancestry, Mr. Bonham replied that the public response has been generally positive. Part of the ancillary programming will include a panel that will discuss ancestry and genetics in a nuanced way, and the speakers may not all necessarily agree with the use of genetics to explore ancestry.

The NHGRI Bioinformatics Research Portfolio

Dr. Vivien Bonazzi gave a presentation on the Bioinformatics Research Portfolio of NHGRI’s Extramural Research Program and discussed the Institute’s role in NIH’sBig Data to Knowledge (BD2K) initiative.

There have been several trans-NIH informatics initiatives including the Biomedical Information Science and Technology Initiative (BISTI) and now Big Data to Knowledge (BD2K). Council wondered if there was continuity or linking between these bioinformatics efforts undertaken by the NIH in recent years. Dr. Bonazzi and Dr. Mark Guyer explained that BD2K is leveraging progress from prior programs and extending some of the goals that were described in the initial BISTI report. ICs were able to voluntarily opt-in to BISTI, and the program announcements

made use of the R01 activity code. BD2K will be much more actively programmed and will have a more comprehensive and directed focus on big data of multiple types. Dr. Guyer further elaborated that there has been a recent culture change at the NIH to take the challenges of computation and analysis of complex data seriously, and all ICs are more committed to funding research to solve these problems.

Council wondered if there was a relationship between BD2K and the administration-wide directive to develop plans to make publicly-funded data accessible. Dr. Rodriguez explained that there is an NIH group devoted to responding to the memo from the White House Office of Science and Technology Policy (OSTP) that issued the charge. Several of the group members are involved in BD2K, so that the NIH can develop a coherent response across the ICs.

Council expressed a concern that there was not enough usage of the tools developed by funded investigators, and wondered if NHGRI was helping to market those tools to potential users. Dr. Bonazzi answered that NHGRI has a Program Announcement to support genomics resources developed specifically for community usage that make use of the U41 activity code. Grantees must demonstrate the ability to communicate findings and tools to the community and provide outreach to that effect. Right now, the onus is on the tool developers to market their own innovations and to reach out to users. Council suggested that it would be useful for NHGRI to assist in this endeavor since it has greater reach and visibility. This would also help ensure that the Institute's investments are more broadly applied and used. Dr. Bonazzi responded that the data catalog and software catalog being developed by BD2K are examples of resources that help investigators spread knowledge of their tools and data to other users.

Council wondered if there were plans to form more interactions between the NHGRI and the National Science Foundation (NSF), particularly with regard to access to computing infrastructure. Dr. Bonazzi answered that she has been in discussions with NSF to explore potential collaborations between NHGRI investigators and supercomputing facilities as well as cloud providers linked to NSF to support the necessary computing capacity for big data analyses.

Council questioned the balance of the research program between supporting new methodology and facilitating access to existing software, cautioning against bolstering existing technology at the expense of funding new discoveries. Council also wondered if the goal of the bioinformatics research program was to create fully-developed, commercially-marketable tools, or partially fleshed-out ideas that could be adopted by capable analysts who would continue the development of the tool. Dr. Bonazzi answered that there needs to be a balance of tools across the entire spectrum to meet immediate needs, to improve older tools, and to develop innovative ways to address problems. Council remarked that the role of funded entities may just be to support tool development in universities to the point where they can be used by others, though not ready to fully market to non-sophisticated users. Dr. Guyer explained that the software development part of BD2K focuses on underserved areas in informatics (e.g., compression and pre-processing and filtering of data) and provides resources to further develop new, promising tools.

Council remarked that integration with EMRs has been traditionally kept apart from computational biology and that there is a lack of tools to support data in a HIPAA-compliant manner. Dr. Bonazzi responded that these privacy concerns stem from a lack of computational power. She explained that collaborations with providers of supercomputing systems may help move those efforts forward. Investigators have recently been turning to the Amazon cloud to provide vast computing power at low cost. The problem remains to move these systems into

commercial markets and to work out the details of potential private-public partnerships between funded investigators and computing providers.

Dr. Jeff Schloss noted there is an expectation among investigators that they will obtain bioinformatics tools free of charge and he questioned whether there is a viable market for them.

NHGRI Training and Career Development Program

Heather Junkins provided an overview of the proposed changes to the NHGRI training and career development portfolio.

Council wondered if investigators with a Master's degree in genetic counseling would qualify for any of the proposed programs. Dr. Graham explained that all of the programs were geared toward independence in research for people with doctoral degrees.

Council applauded NHGRI's plan to establish training efforts in genomic medicine; at the same time, Council noted that the scope of the training needed to support the needs in the field of genomic medicine is a big challenge that goes well beyond what NHGRI can support. Genomic medicine is expected to be implemented across many of the research domains of the NIH. Nevertheless, NHGRI's plan to support training in genomic medicine is certainly a step in the right direction. Council also expressed support for continued training in quantitative fields in genomic sciences, noting that it would be premature to decrease training activities in those domains. Finding the appropriate balance of training between genomic sciences and genomic medicine will be a challenge for NHGRI. Council noted the ratio proposed in NHGRI's training plan seems appropriate. Training in genomic sciences needs to be broader than genomic medicine at this time.

Council suggested that the primary focus of the genomic science T32 should still be molecular biology and biochemistry, alongside other key areas of interest that include biostatistics and informatics. Some Council members prefer the 5-year individual career K awards as opposed to the 4-year. The Council did not regard the NIH funding averages for various training mechanisms to be goals that NHGRI should necessarily attempt to match. The NIH funding averages are influenced by the training goals of individual ICs, and other factors should influence NHGRI's level of support for training and career development.

Council cautioned NHGRI to be careful using the term 'clinical PhD' to describe the types of professionals that would be eligible for the genomic medicine postdoctoral fellow T32s. In Council's view, the term clinical PhD has a rather narrow meaning and NHGRI appears to be interested in training a broader spectrum of individuals in this program.

Council asked for clarification about the cross-training objective related to the K01 program. Dr. Graham elaborated that the K01 program will now have two tracks. One is the original K01 tailored to attract people with PhDs in biostatistics, physics, math, and engineering. The new K01 track will provide an opportunity for quantitative training for individuals who already have a PhD in a field of biology, such as genetics.

Council noted the role NHGRI holds as a 'wedge' to drive genomic medicine into the other ICs of NIH and they wondered if there are opportunities to collaborate with other ICs to create genomic medicine training programs. Dr. Green plans to discuss this topic with the Director of NIGMS at an upcoming joint retreat of the two ICs. He also noted that NHGRI would likely have

more success finding Institutes willing to partner on genomic medicine training programs after NHGRI's programs have been launched.

Council asked for clarification about a couple of the slides in the presentation. One implied that a goal of the genomic medicine T32 postdoctoral training program was to train individuals to practice genomic medicine. Staff responded that the goal of this program is to train people to conduct clinical research in the field of genomic medicine. Council also questioned why the entry requirements for the genomic medicine T32 program were restricted to individuals with MD or clinical PhD degrees. Council recommended this should be open to a much wider variety of trainees who have PhD degrees in fields of biology that are not strictly clinical.

Council also questioned why the primary focus of the genomic sciences T32s should be limited to the fields of biostatistics, computational biology, quantitative sciences and technology development. They argued that fields such as genetics, molecular biology, and biochemistry are foundational to genomics and NHGRI must continue to train in these disciplines. NHGRI staff indicated that these areas would not be abandoned, but that given the complexity of biomedical research, more than a working knowledge of biostatistics, computational biology and quantitative sciences would be needed for future researchers to take advantage of all the data being generated.

COUNCIL-INITIATED DISCUSSION

Council thanked NHGRI program staff for their efforts in coding the Institute's grants.

ANNOUNCEMENTS AND ITEMS OF INTEREST

Dr. Pozzatti drew Council's attention to two documents that were sent to NHGRI:

1. American College of Medical Genetics and Genomics Report to September Council
2. National Society of Genetic Counselors Report to September Council

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.

REVIEW OF APPLICATIONS[1]

In closed session, the Council reviewed 74 applications, requesting $72,654,292 (total cost). The applications included: 52 research project grants, 8 ELSI applications, 1 research center applications, 1 conference applications, 3 career transition award applications, 6 SBIR Phase I applications, 1 SBIR Phase II applications, 1 individual training applications, and 1 education project award applications. A total of 73 applications totaling $72,654,292 were recommended.

[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.

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

02/11/2014
Date

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

02/11/2014
Date

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