NATIONAL ADVISORY COUNCIL FOR HUMAN GENOME RESEARCH
MEETING SUMMARY
May 18-19, 2015

The Open Session of the 74th meeting of the National Advisory Council for Human Genome Research (NACHGR) was convened at 10:00 AM on May 18, 2015, 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 May 18, 2015. 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 18, 2015 and from 8:30 AM until adjournment on May 19, 2015, for the review, discussion, and evaluation of grant applications.

Council members present:
Eric Boerwinkle
Lon Cardon
Joseph Ecker
James Evans
Chanita Hughes Halbert
Howard Jacob
Amy McGuire
Anthony Monaco
Lucila Ohno-Machado
Robert Nussbaum
Arti Rai
Carol Bult, ad hoc
David Page, ad hoc
Dan Roden, ad hoc
Val Sheffield, ad hoc
Jay Shendure, ad hoc

Council members absent:
Carlos Bustamante
Martin Kreitman

Staff from the National Human Genome Research Institute:
Ronit Abramson, DPCE
Ernesto del Aguila, DPCE
Alice Bailey, DPCE
Shannon Biello, ERP
Vence Bonham, IOD and IRP
Gerry Bouffard, IRP
Joy Boyer, ERP
Larry Brody, ERP
Monika Christman, ERP
Deborah Colantuoni, ERP
Julie Coursen, ERP
Cati Crawford, ERP
Priscilla Crockett, DM
Chris Darby, ERP
Jyoti Dayal, ERP
Camilla Day, ERP
Valentina di Francesco, ERP
Carla Easter, DPCE
Alvaro Encinas, DPCE
Jon Lotempio, Jr., ERP
Elise Feingold, ERP
Adam Felsenfeld, ERP
Ann Fitzpatrick, DM
Colin Fletcher, ERP
Tina Gatlin, ERP
Bettie Graham, ERP
Linda Hall, ERP
Carolyn Hutter, ERP

Sonya Jooma, ERP
Heather Junkins, ERP
Rupindei Kahi, ERP
Rongling Li, ERP
Nicole Lockhart, ERP
Ebony Madden, ERP
Allison Mandich, IOD
Casey Martin, ERP
Jean McEwen, ERP
Jeannine Mjoseth, DPCE
Jim Mullikin, IRP
Hannah Naughton, ERP
Anh Quynh Nguyen, ERP
Annie Niehaus, ERP
Jacqueline Odgis, ERP
Kiara Palmer, DPCE
Teri Manolio, ERP
Mike Pazin, ERP
Ajay Pillai, ERP
Lita Proctor, ERP
Erin Ramos, ERP
Laura Rodriguez, DPCE
Jeffrey Schloss, ERP
Michael Smith, ERP
Heidi Sofia, ERP
Jeffery Struewing, ERP
Yekaterina Vaydylevich, ERP
Simona Volpi, ERP
Vivian Ota Wang, ERP
Chris Wellington, ERP
Kris Wetterstrand, IOD
Bob Wildin, DPCE

Others present for all or a portion of the meeting:
Tabitha Hendershot, RTI International
Adam Fagen, Genetics Society of America
Rhonda Schonberg, NSGC
Joseph McInerney, ASHG
James O'Leary, Genetic Alliance

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

APPROVAL OF MINUTES FOR THE FEBRUARY, 2015 MEETING

DIRECTOR'S REPORT

Dr. Eric Green presented the Director's Report to Council. Council had no comments or questions regarding this report.

CONCEPT CLEARANCES

Workshop Report, "From Genome Function to Biomedical Insight: ENCODE and Beyond," presented by Mike Pazin

Dr. Pazin gave a presentation on the NHGRI-sponsored Encyclopedia of DNA Elements (ENCODE) workshop held on March 10-11, 2015, at the Natcher Conference Center on the NIH main campus. Slides and webcast recordings from this meeting are available on the NHGRI website: https://www.genome.gov/27560819.

Discussions and recommendations from this workshop on genome function formed the basis of four concepts included in Dr. Feingold's concept presentation "Functional Genomics." Council did not have any comments or concerns about the "ENCODE and Beyond" workshop report.

Concept Presentation, "Functional Genomics," presented by Elise Feingold

Dr. Feingold gave a presentation on four concepts for the functional genomics initiatives.

The Council members who attended the March workshop noted that it was outstanding. The workshop summary captured the content of the workshop effectively, and the proposed concepts closely matched the main themes of the workshop.

Council asked whether the emphasis will be on applications that propose to study a particular disease, or projects that make use of a model system that might generalize to broad classes of common diseases or rare diseases. Dr. Feingold stressed that NHGRI is interested in the generalizable knowledge that could be gleaned from studying disorders, but also is open to diseases that would make compelling studies based on existing data. Dr. Pazin stressed that, although selected disorders might be different in terms of their biology and phenotype, there is generalizability with respect to how best to study the genetic causes and important variants for these disorders.

Council asked for clarification on the differences between the Computational Analysis Research Centers and the ENCODE Data Analysis Center (DAC). Dr. Feingold explained that the DAC is focused on creating the encyclopedia, analyzing submitted data, and identifying functional elements. The Computational Analysis Research groups will be selected from the researchers' best ideas about how to derive biological insights to learn about disease and develop new computational and statistical methodologies.

Council noted that the complexity of data will increase due to the functional characterization work, but the current plan calls for the DAC to perform less analysis work; therefore, there is a concern whether the analytical horsepower behind data generation will be sufficient to address the increased complexity. Dr. Feingold noted that budget restrictions limited the scope of the work that could be done by the DAC, but the highest priority is to make the data broadly available so the larger scientific community can analyze it. NHGRI is aware that ENCODE will be handling new data types that may require different kinds of analyses early on.

To uphold the ENCODE philosophy that the data should be widely available as a resource to the entire research community, ENCODE will make these data accessible to researchers to perform their own analyses. ENCODE performs some basic data processing on these data, such as uniformly processing data and calling elements.

Council was enthusiastic about ENCODE's transition from cataloging to the very challenging task of using this information in a translational way. Council thought it would be beneficial for investigators to push the envelope in this area as much as possible. Council emphasized the community engagement component and encouraged ENCODE to convene focus groups to receive feedback and questions from the community to ensure that ENCODE investigators are working on problems that are relevant to the community. NHGRI will be holding an ENCODE User's Meeting from June 29 to July 1, 2015. One objective of this workshop will be to elicit suggestions and input from the research community about the utility of the ENCODE resource. The registration link for this 2.5-day workshop can be found at http://www.ENCODE2015.org.

In reviewing the first concept, the Functional Element Mapping Centers, Council recommended that NHGRI staff remain open to well-justified applications from investigators studying model organisms other than the mouse. However, these proposed new model organisms must enable discovery in the human. Council noted that zebrafish is becoming an increasingly common model as it can be used to rapidly assess functionality. Concerns were also raised about bringing in additional organisms as this would present challenges for the data coordination and analysis centers. Council agreed that any organism should be eligible as long as it is well justified, but applicants should be strongly encouraged to contact program staff to describe their research ideas.

In fiscal year 2012, the data production and mapping centers had devoted $22M to mapping. Currently, it has been reduced to $18.5M. In the current proposal, $20M will be allocated toward mapping activities of the Functional Element Mapping Centers. Recognizing that the field is changing rapidly, NHGRI will be open to new data types or methodologies for mapping that generate better information and are more cost-effective. In the concept document, there is discussion of mapping all transcription factors in at least two cell types, as well as long-range interactions. Council cautioned that mapping resolution, as well as the disease models, may have to be studied at different stages of development, particularly in the mouse.

Council asked how ENCODE plans to reduce the very large dimensionality of this project in that many different cell types and data types may be proposed. Bounding this space would be helpful to both the applicants and reviewers. At the "ENCODE and Beyond" workshop, attendees proposed defining boundaries by either: 1) studying the samples that are easiest to study first, and model the bounds of ENCODE research based on what is available, or 2) beginning with a modeling component in which ENCODE imputes some of these areas of the matrix, realize where the model breaks down, and identify areas where additional samples and data are needed. The plan is for applicants to make individual proposals and then come together in the consortium to strategize. The intent is that the applicants will have to justify that what they propose to do has a reasonable bound on it, and this would be judged by the peer review committee. This was judged to be preferable to the approach of having the staff set boundaries when the FOA is written. However, not specifying these dimensions at the outset might be a barrier for new investigators who are not already a part of ENCODE.

Council approved the Functional Element Mapping Center concept by a vote of 15 in favor, none opposed, and no abstentions.

Council reviewed the concept of a new component to ENCODE, the Functional Element Characterization Centers. It was suggested that, in drafting the funding opportunity announcement (FOA), NHGRI should clarify the language describing the purpose and intent of these centers; to enhance the catalog of candidate functional elements by characterizing and validating the functional elements in healthy and disease states. Proposed biochemical assays must demonstrate a connection between an element with a biochemical signature and a functional activity in a healthy state and in the disease state. It should also be encouraged that Functional Element Characterization Center applicants try to connect proposed elements with GWAS. Dr. Pozzatti noted that the concept clearance presentation does not include examples of such research projects, but they will be in the funding opportunity announcement.

Keeping ENCODE data as widely accessible as possible, in an open portal rather than in dbGaP, is critical, even if it means forgoing some good samples.

Council approved the Functional Element Characterization Centers concept by a vote of 15 in favor, none opposed, and no abstentions.

Council asked for justification for separating the Computational Analysis Research Projects and the ENCODE Data Coordination and Analysis Center (EDCAC). Dr. Pazin explained that this structure separates projects that are using the resource for different analyses. ENCODE is currently organized in this way. The Computation Analysis Research Projects will support individual projects that are outside of the scope of the consortium's core mission. The EDCAC will be facilitating activities related to the core mission; for example, defining how the basic data processing is done. Council agreed with the proposed separation of the two activities.

Council praised ENCODE for the accessibility of the data, and the large number of publications by investigators outside of ENCODE using ENCODE data to further their own research

activities. But Council questioned if the data are already being readily used by many investigators, is the proposed Computational Analysis Research Project FOA just an invitation for investigators who are already using ENCODE data to receive funding for analyses they are already doing? Council asked what distinguishes existing users of ENCODE data from the investigators who are expected to respond to this analysis FOA. Staff responded the intent of the FOA is to strike a balance between two goals; to attract the best minds to develop new methods to analyze ENCODE data, and attract new investigators who are currently outside the ENCODE "umbrella" to utilize the data, in the course of which they are developing new analysis methods. Some Council members noted in the current ENCODE consortium there has been a substantial advantage to have investigators with analysis expertise interacting with the production groups early on, and looking at the data in the early stages of the production activities.

Council expressed concern about the development of an investigator-initiated program and the use of the U01 (cooperative agreement) activity code for these grantees. The Computational Analysis Research projects will have a lot of freedom to design and implement their projects as they see fit under the U01 mechanism. The cooperative agreement ensures that consortium members will follow consortium practices and share their software rapidly.

Council noted that not all users of ENCODE data will download the data. ENCODE is trying to give users as much flexibility as possible by giving them the option to download data and also to access the data and compute on the data using the Amazon Cloud. There are also universal processing pipelines available through the Amazon Cloud. Investigators can use the data with any ENCODE tool or with any of their own tools.

Dr. Feingold emphasized that the Computational Analysis Research Projects will focus on developing new methods of analysis, rather than on performing comprehensive analyses on the data produced in the Mapping and Characterization centers (the latter being the task of the EDCAC). Favored methods will be those that are generalizable.

Council approved the Computational Analysis Research Projects concept by a vote of 14 votes for approval, none opposed, and no abstentions.

Council asked about the EDCAC's function in engaging the broader community. Council noted that at the American Society of Human Genetics (ASHG) workshop, tutorials were held demonstrating how to use ENCODE data that were very well attended. Council suggested that the EDCAC plan meetings and workshops in other parts of the U.S. Dr. Gilchrest told Council that ENCODE also has plans to videocast the upcoming users meeting and will try to post these sessions online as tutorials.

Council asked why the Data Coordination Center (DCC) and the Data Analysis Center (DAC) will be solicited and funded separately (under the same FOA) and if NHGRI expects to have applications submitted as "pairs." In discussions on this point, NHGRI concluded that the expertise for the DAC and DCC were sufficiently different that separate applications would be an appropriate approach. If a single applicant scores well for the DCC component and not as well for the DAC component, or vice versa, it would be challenging to develop a rational funding plan. The separation between the DAC and DCC activities has worked well for the current ENCODE consortium.

A few Council members suggested that NHGRI consider integrating the DCC and DAC as it may be a coordination challenge to have two different groups setting the data analysis environment. Dr. Feingold has not seen much duplication of effort with the current separation of the DAC and DCC, but ENCODE staff will consider this possibility.

Council approved the EDCAC concept by a vote of 15 votes for approval, none opposed, and no abstentions.

"Data Analysis and Coordinating Center for NHGRI's Research Training and Career Development Programs" by Tina Gatlin

Dr. Gatlin gave a presentation on a proposal to continue a Data Analysis and Coordinating Center (DACC) for NHGRI's Research Training and Career Development programs.

Council strongly supported expanding the Coordinating Center to support PhD and MD/PhD trainees. It was recommended that NHGRI provide more detail on how the trainees who are being tracked could be involved in the reporting process to improve the tracking success rates. Applicants should be asked to describe how they will learn from the trainee tracking information and how they will change and adjust training based on this information.

In the past, the Diversity Action Plan (DAP) annual meetings were tied to the Centers of Excellence in Genomic Science (CEGS) annual meetings. Only training coordinators and T32 program directors were invited to attend. Council agreed that restructuring the annual meetings to allow trainees to attend adds value to the program and facilitates interactions among trainees and training program directors and other researchers in the field. For the purpose of networking, it would be useful to create a database that shows webs of connection between different topic areas and the people who are working in them. The DACC would handle travel for any consultants or individual fellows whose institutional, T32, or DAP grants cannot support the full cost of travel. These individuals would be eligible to apply for a supplement to travel to the annual 1.5-day meetings. The first DAP annual meeting will be held on April 7-8, 2016, in Bethesda, Maryland. Council agreed that the annual meetings would also be a good opportunity to engage trainees on ELSI questions.

Although providing support on informed consent documents is important, the informed consent documents might not be relevant to all past trainees. Council suggested that NHGRI consider providing support to trainees based on what the trainee is working on.

The DAP has supported approximately 1,400 participants since 2002. Much of the missing data on trainees was from before the DAP DACC started in 2009.

Council approved the DAP DACC renewal concept by a vote of 14 for approval, none opposed, and no abstentions.

Workshop Report and Concept Presentation, "Genomic Technology Development," presented by Michael Smith

Dr. Smith presented a report on the Genomic Technology Development (GTD) workshop that was held as two webinars in April, 2015. He also presented a concept to support GTD research projects.

Council asked how NHGRI would ensure that the sequencing technology supported by this initiative would not overlap with technology supported by industry. Dr. Smith commented that, to avoid redundancy, the members of the GTD program and reviewers of applications will be aware of industry products and research. There is also the expectation that companies will likely be working on technologies that are more mature, while the GTD program will support research projects at the proof-of-concept stage of development.

Funding for Small Businesses Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards will be increased by $1M this year, and similar increases are expected in future years as legislatively mandated. Council suggested that NHGRI encourage (or possibly mandate) applicants to collaborate with companies, thereby allowing at least a percentage of SBIR funds to be used to support these applications in place of other NHGRI funds. Dr. Smith noted that SBIR applicants are permitted to have an academic collaborator and up to 30% of their budget request can be dedicated to the academic partner. The majority of GTD funding to small businesses has been in the SBIR program. For STTR funding, the range for academic partner funds must be between 30% and 60%. However, the STTR program is much smaller, about $1M/year. The distributions for academic collaborator funding cannot be changed as these levels are government mandated.

Dr. Smith noted that the scores voted to SBIR applications in this past year have been comparable to those of the unsolicited R01s and R21s submitted to NHGRI. SBIR scores are now competitive and are expected to continue to be competitive going forward.

It was clarified that the distinction between the Request for Applications (RFA) and Program Announcement reviewed by an institute (PAR) mechanisms is that the funds for PARs are not set aside. In addition, the review for PAR applications is done by the institute and not by the Center for Scientific Review (CSR). The funding levels proposed for the GTD PAR are planning target numbers and are not a set aside of funds.

Dr. Schloss stated that a challenge in supporting the GTD initiative through only SBIR is that applicants are required to have a business plan to be awarded an SBIR grant. Many of the GTD applicants are too early in development to have a business plan as the purpose of this initiative is to explore new technologies. NHGRI will use SBIR to the extent that it can and this will provide additional funding for the initiative, but NHGRI cannot support this initiative mostly by the use of the SBIR set aside. The PAR dollar amount is an aspirational goal, but program staff will discuss whether they would want to set aside funds to support the GTD or have this initiative compete with other unsolicited applications that NHGRI receives.

Council questioned whether the proposed level of funding would be enough to attract competitive applicants, and to move the field forward (compared to the investments that industry will make in this area). At the GTD workshop, panelists thought that this initiative would receive high-quality applications. Council noted that the response to the $1000 Genome RFA was vigorous for a number of years for approximately the same amount of funding proposed here. Staff also described investigators have reported that receiving an initial grant from NHGRI not only allowed them to establish proof-of-concept for their novel technologies, but it gave them enhanced credibility to obtain funds from other sources to pursue their research. For these reasons, Council agreed that $5M of funding every year would be sufficient to assemble a community to try out many exploratory concepts.

An important way that these initiatives fit into the wider NHGRI portfolio is that ideas that may not be ready for a full-scale Center of Excellence in Genome Science (CEGS) project can be pursued under the proposed GTD initiatives.

Council was also concerned that, if these ideas were to take off, NHGRI would not be credited for its small initial investment in the concept. NHGRI also might run the risk of creating a new area of activity that it cannot support as it expands. The role of NHGRI has always been to support new concepts at the earliest stages of development, in order to demonstrate that these ideas are worthy of additional outside investment. Industry is not typically interested in supporting research in the earliest stages of development. Council agreed that the field is stimulated by initial funding from NHGRI.

Council approved the GTD concept for an RFA to support novel sequencing technologies and direct RNA sequencing by a vote of 14 for approval, none opposed, and no abstentions. Approval of the PAR was not required.

PRESENTATIONS

"Clinical Sequencing Exploratory Research Consortium" by Gail Jarvik

"NHGRI ClinSeq Project" by Les Biesecker

Dr. Jarvik gave a presentation on the Clinical Sequencing Exploratory Research (CSER) Consortium. Dr. Biesecker then presented on the NHGRI ClinSeq Project.

Council agreed with Dr. Jarvik and Dr. Biesecker that educating medical students and practicing clinicians on how to approach variants of unknown significance (VUS) will be very important moving forward. Educators should be careful not to educate students on genetic testing to the point where students believe that all the information that they would need about the patient can be found in the genetic test results. Clinical evaluation will always be very important. Dr. Biesecker agreed, but suggested that the test results might help clinicians discover what areas should be studied more carefully during the patient's clinical examination.

Dr. Jarvik reported that CSER recently formed a physician education workgroup that has been collecting Continuing Medical Education (CME) materials across the sites. This workgroup has also begun working with the American College of Medical Genetics (ACMG).

Dr. Biesecker recommended that the field of medicine as a whole should determine which approach, hypothesis generation vs. hypothesis testing (the current standard approach), is applicable in different clinical contexts. Dr. Biesecker does not discourage the hypothesis testing approach, but many clinicians have been desensitized to its limitations. In the case of the newborn sequencing project, investigators reached the consensus that they would prefer a large number of false positives with very high sensitivity. The tradeoff may well be different in adults, and the approach will likely vary for each phenotype.

Council complimented the CSER Consortium on tackling cost-benefit analysis. Council was interested in how CSER is handling issues related to contacting family members who have not been consented for research. Dr. Jarvik responded that, over time, some IRBs of CSER projects have allowed CSER investigators to return VUSs and directly contact relatives. However, it often has been difficult to interest and engage the family members. Dr. Jarvik suggested studying the use of social media tools to engage family members. For instance, websites like Ancestry.com might be able to post genomic information. Dr. Carlos Bustamante has studied how the use of social media can be an important tool for cost-effectiveness research.

Patients are recruited into Dr. Biesecker's ClinSeq project through a diversity of methods, including newspaper ads and word of mouth. About 20% of participants have atherosclerotic heart disease; the other 80% are recruited agnostic to every other phenotype. Approximately half of these participants have reported they were motivated to enter the study for the benefit of themselves or their family members to use the genomic information for their healthcare. The other half entered the study out of altruism and wanted to contribute to the wider knowledge of how genetics contribute to health.

CSER studies are phenotype-based, but the network of sites encompasses populations that are diverse in terms of phenotypes, as well as race and ethnicity. This allows CSER investigators to observe which methods work with different phenotypes and different patient populations. For instance, Dr. Katrina Goddard's site at the Kaiser Foundation Research Institute studies preconception counseling. Participants come in for preconception genetic screening as part of prenatal care and are then asked if they would like to enroll in the study. In Dr. Robert Green's (Brigham and Women's Hospital) study, healthy people are recruited and physicians return the results and record outcomes to see how well this method of returning results is working. Dr. Jim Evans' (University of North Carolina, Chapel Hill) group reaches out to rural communities instead of relying on participants coming in to medical centers.

Dr. Jarvik noted that CSER's biggest contributions to the broader community have been CSER's reaction and push-back to the ACMG's recommendation of mandatory return of incidental findings on 56 target genes. The ELSI workgroup was active in coming together as a community to respond to these recommendations. The impact of CSER's input on the ACMG variant classification criteria also has been substantial. Other significant contributions include the cost-effectiveness studies and activities in creating clear and efficient genomic reports. CSER workgroups and sites have also produced a number of important papers.

The initial focus of ClinSeq was to pilot how to use genomics in a clinical research context. Dr. Biesecker's group also wanted to discover the relationship between genes and atherosclerotic heart disease. The investigators looked at the exomes and then decided to broaden their study to other phenotypes. Dr. Biesecker encouraged NHGRI to support more explorations like this.

To engage the outside community, CSER invites those interested in learning more about how the projects are run to visit the sites and observe their genomic sequencing and return of results (RoR) informatics pipelines.

Dr. Biesecker clarified that the predicted yield for the 56 ACMG recommended actionable genes was 2%-4%. They observed a 3% null variant yield when they looked across the genome. Dr. Biesecker had more Ashkenazi participants represented in his study and this is thought to represent the difference between what was found in ClinSeq and the CSER studies. Dr. Biesecker agreed that the boundary between a disease and a trait is hard to define. Therefore, it was not certain what percentage of the 3% genome-wide null variant yield were linked to traits important to healthcare.

Council asked about the percentage of Mendelian disorders that are currently undiagnosed across the U.S. population. Dr. Biesecker noted that there are significantly more Mendelian disorders that exist than are diagnosed and having patients' genome data can allow investigators to detect disorders in adults.

Council asked if clinicians should be treating patients' genotypes and not phenotypes. Dr. Biesecker answered that this is controversial. There was a report from the IOM called "Towards Precision Medicine: A New Taxonomy of Human Disease" that suggests reorganizing the medical world's understanding of human pathophysiology with a molecular focus, as opposed to the current practice of organizing disease based on a phenotypic focus. Dr. Biesecker suggested taking into account both the genetic test result and the patient presentation.

Council noted the danger in not having either a hypothesis or differential diagnoses in testing an individual is that the clinician will end up with too many VUS and will not know what to pursue. Dr. Biesecker suggested that clinicians use the Bayesian change in probability to direct the care of the patient. Dr. Jarvik also noted that it will be more clinically useful to know the range of implications and penetrance for any particular variant in guiding decisions about patient care.

COUNCIL-INITIATED DISCUSSION

Council expressed an interest to continue discussions about determining research priorities for NHGRI, and what the right balance should be of investigator-initiated grants versus FOAs developed by the staff to implement NHGRI's vision.

Council wanted to know more about the process by which NHGRI programs are determined to end, either by demonstrating success or clear failure. Council requested a list of the projects that NHGRI has set in motion that have acquired their own momentum and have found their own sources of support outside of NHGRI.

Council encouraged NHGRI staff to develop ways to objectively quantify decisions about priorities.

Council liked the demonstration in the CSER and ClinSeq presentations of how whole-exome sequencing can be moved from research into the clinical setting where it is paid for by fee-for-service. In this way, NHGRI could begin offloading research costs into clinical care costs. Council recommended that NHGRI consider moving toward scaling down some sgenome-equencing efforts.

Some Council members encouraged NHGRI to decide how much it will be willing to pay to promote and evaluate uptake and permeation of genomics in the clinic. Council stressed that patient outcomes are very important to assess; but it is also very expensive and it will take a long time to complete such studies. NHGRI will have to struggle with the decision of how much of this the Institute is willing to pay for, and also decide whether outcome results will be done without NHGRI's participation. Since NHGRI lacks expertise in this area, it may be wise to engage in partnerships to conduct patient outcomes research. Other Council members cautioned that haphazard adoption that is not evidence-based could have bad implications in the long term. Council agreed that NHGRI should collect and use hospital data in a more systematic way.

It was agreed that NHGRI should support outcomes research, but NHGRI needs to form the right partnerships with experts in the field and industry. This could include outcomes experts in the NIH and commercial clinical labs, to design long-term experiments that will assess the ethical, legal, and social aspects, as well as political aspects, of clinical implementation. If NHGRI is able to define the research questions and forms the right partnerships, this would help control the costs.

Council encouraged NHGRI to consider how variation validation can be conducted at the "speed of the clinic" and how NHGRI can pre-position basic research to be ready to move into clinical care. There is still much research to be done to examine DNA sequencing at scale, throughput and speed that will maximize its utility and successful implementation in the clinical setting.

At the September 2015 Council Meeting, Council will hear about the sequencing applications for several components of the Genome Sequencing Program. In addition, CSER will be holding a workshop late in September to review the CSER program in a strategic way and stimulate discussion on its future. This will also be presented to Council early in 2016.

ANNOUNCEMENTS AND ITEMS OF INTEREST

Quarterly reports were provided by the American College of Medical Genetic and Genomics, the American Society of Human Genetics, and the National Society of Genetic Counselors.

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 124 applications, requesting $80,014,874 (total cost). The applications included: 58 research project applications, 25 cooperative agreement (U01) applications, 8 ELSI Research Program applications, 2 research center applications, 1 institutional training application, 2 conference applications, 2 career transition award applications, 1 research scientist development award application, 16 SBIR Phase I applications, 4 SBIR Phase II applications, 2 STTR Phase 1 applications, and 3 Research Education applications. A total of 79 applications totaling $44,834,248 were recommended.

9/21/2015
Date

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

9/21/2015
Date

Eric D. Green
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.