NATIONAL ADVISORY COUNCIL FOR HUMAN GENOME RESEARCH
SUMMARY OF MEETING[1]
February 13, 2012

The Open Session of the National Advisory Council for Human Genome Research was convened for its sixty-fourth meeting at 8:30 A.M. on February 13, 2012 at the Fishers Lane Conference Center, Rockville, MD. Eric Green, Director of the National Human Genome Research Institute, called the meeting to order.

The meeting was open to the public from 8:30 A.M. until 6:00 P.M. on February 13, 2012. In accordance with the provisions of Public law 92-463, the meeting was closed to the public from 6:00 P.M. on February 13, 2012 until adjournment for the review, discussion, and evaluation of grant applications.

Council members present:
Michael Boehnke
Carlos Bustamante
Mark Chee
James Evans
Ross Hardison
David Kingsley
Amy McGuire
Howard McLeod
Deirdre Meldrum
Jill Mesirov
Richard Myers
Pearl O'Rourke
Pamela Sankar
David Williams
Richard Wilson

Council members absent:
Anthony Monaco

Ex officio members absent:

[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".

Staff from the National Human Genome Research Institute:

Leslie Adams, DER
Mela Asefa, DER
Jesse Becker, DIR
Maggie Bartlett, OD
Victoria Bishton, DER
Anastasia Bodner, DER
Vivien Bonazzi, DER
Vence Bonham, OD
Joy Boyer, DER
Lisa Brooks, DER
Comfort Browne, DER
Shaila Chhibba, DER
Cheryl Chick, DER
Monika Christman, DER
Nicholas Clemm, DER
Christine Cutillo, DER
Camilla Day, DER
Karen Deleon, OD
Greg Feero, OD
Elise Feingold, DER
Adam Felsenfeld, DER
Ann Fitzpatrick, OD
Colin Fletcher, DER
Tina Gatlin, DER
Jonathan Gitlin, OD
Peter Good, DER
Bettie Graham, DER
Eric Green, OD
Mark Guyer, DER
Lucia Hindorff, OD
Belen Hurle, DIR
Dennis Huyhn, DER
Heather Junkins, OD
Caroline Kelly, DER
Rongling Li, OD
Nicole Lockhart, DER
Carson Loomis, DER
Lindsey Lund, DER
Chengetai Mehomva, DER
Ian Marpuri, OD
Omar McCrimmon, OD
Jean McEwen, DER
Glenn McFadden, DER
Keith McKenney, DER
Michelle Milligan, DER
Jeannine Mjoseth, DER
Janis Mullaney, OD
Ken Nakamura, DER
Cathy Ng, DER
Vivian Ota Wang, DER
Brad Ozenberger, DER
Jacqueline Palchik, DER
Michael Pazin, DER
Jane Peterson, DER
Ajay Pillai, DER
Rudy Pozzatti, DER
Lita Proctor, DER
Erin Ramos, OD
Laura Rodriguez, OD
Ellen Rolfes, OD
Tamar Roomian, DER
Jeff Schloss, DER
Derek Scholes, OD
Heidi Sofia, DER
Jeff Struewing, DER
Larry Thompson, OD
Elizabeth Thomson, DER
Susan Toy, DER
Simona Volpi, DER
Lu Wang, DER
Kris Wetterstrand, OD
Anita Whitehurst, OD
Anastasia Wise, OD
Rosann Wise, OD

Others present for all or a portion of the meeting:
Adam Berger, Institute of Medicine
Juli Bollinger, Johns Hopkins University
Rachel Dvoskin, Johns Hopkins University
Kenton Hasson, Canon US Life Sciences Inc.
David Kaufman, Johns Hopkins University
Rochelle Long, National Institute of General Medical Sciences
Mary Ann Ottinger, University of Maryland
Karen Rothenberg, University of Maryland School of Law
Cary Scheiderer, Presidential Commission for the Study of Bioethical Issues
Rhonda Schonberg, National Society of Genetics Counselors
Joan Scott, National Coalition for Health Professional Education in Genetics
Michael Watson, American College of Medical Genetics
Lonnie Welch, Ohio University

INTRODUCTION OF NEW MEMBERS AND STAFF, LIAISONS, AND GUESTS

Dr. Pozzatti introduced new Council members: Jim Evans and Amy McGuire.

Dr. Pozzatti introduced new Council liaisons Rhonda Schoenberg from the National Society of Genetics Counselors and Ellen Giarelli from the International Society of Nurses in Genetics.

Dr. Pozzatti introduced new staff members: Anastasia Bodner, Nicole Lockhart, Lindsey Lund, Susan Toy, and Allison Mandich,

APPROVAL OF MINUTES

The minutes from the September 2011 Council meeting have not been finalized and will be approved at another time.

FUTURE MEETING DATES

The following dates were proposed for future meetings: May 21-22, 2012; September 10-11, 2012; February 11-12, 2013; May 20-21, 2013; September 9-10, 2013; and February 10-11, 2014.

DIRECTOR'S REPORT

NHGRI staff have created an electronic resource for the Director's Report and associated supplemental material available at http://www.genome.gov/directorsreport. In addition, Dr. Green reminded participants that the Open Session of the Council meeting is Webcast live, with plans to Webcast and Web-archive all future Council meetings.

I. GENERAL NHGRI UPDATES

Proposed NHGRI Reorganization
The most substantive overarching thing to report about NHGRI is that the Institute has moved forward in proposing changes to its organizational structure. The second of two public meetings to provide a forum for feedback about the proposed changes will be held as part of this Open Session of Council.

NHGRI at ICHG/ASHG
At this past fall's joint ICHG/ASHG meeting, NHGRI organized two very successful sessions:

One was an invited session on "Emerging Ethical Issues in Large-Scale International Genomics Research Collaborations" that was moderated by NHGRI staff member Jean McEwen and former Council member Pilar Ossorio. Speakers came from various parts of the world and discussed both general issues and their unique perspectives. These issues are arising more and more frequently, especially for community resource projects that involve plans for broad data release and in situations where different cultural values and norms as well as different legal and regulatory requirements have to be reconciled.

The second session was a tutorial on using 1000 Genomes Project data. This gathering was attended by over 300 people; slides from the presentation have now been downloaded over 350 times from the NHGRI website.

***Cell* commentary on clinical genomics**
Among the many publications emanating from NHGRI since the last Council meeting was an invited commentary published in *Cell*, in which Teri Manolio and Eric Green co-authored a piece that describes some of the clinical implications of genomic advances. Cell asked them to write something about the near-term clinical applications of genomics that provided a bit more detail than what we described in our strategic plan published in *Nature* last February.

II. GENERAL NIH UPDATES

NIH's National Center for Advancing Translational Sciences (NCATS)
The most significant organizational news at NIH in recent months was the creation of a new NIH Center – the National Center for Advancing Translational Sciences (NCATS). As part of the Fiscal Year 2012 Omnibus Appropriations bill, the National Center for Research Resources (NCRR) was dissolved and NCATS was established. NCATS has a budget of $575 million in Fiscal Year 2012.

The Acting Director of NCATS is Thomas Insel (Director NIMH) and the Acting Deputy Director is Kathy Hudson (NIH Deputy Director for Science, Outreach, and Policy). The search for a permanent NCATS Director is ongoing (Eric Green and Tom Insel are co-chairs of that search committee).

Many components are now housed within NCATS; particularly notable ones include the Clinical and Translational Science Awards (CTSA) program, the Cures Acceleration Network, and the newly created Division of Preclinical Innovation (headed by Chris Austin). The latter has mostly been formed from the National Center for Translational Therapeutics (NCTT), an entity was established and operated within the NHGRI Intramural Program for almost a decade. Over 100 NHGRI employees (all under Chris Austin's leadership) departed NHGRI en bloc as part of the creation of NCATS.

Relocation of Programs from the National Center for Research Resources
In addition to the NCRR programs that went to NCATS, other NCRR components were assigned to either the NIH Office of the Director or to one of five Institutes.

There is a fairly lengthy list of the NCRR elements that have now been relocated, available at the website provided in Document 6.

Proposed Merger of Institutes
As previously mentioned in the Director's Report, the NIH Scientific Management and Review Board (SMRB) has recommended the merger of two NIH Institutes involved in research related to addiction and substance use – specifically, the National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA). Abolishing, merging, creating, or even reorganizing NIH Institutes or Centers is a long and complex process.

Last week, the NIH issued a Request for Information (or RFI) seeking input from the public about the scientific strategic plan for the proposed new merged Institute, preliminarily named the National Institute of Substance Use and Addiction Disorders. That input is due by May 11, 2012.

Target Validation Workshop
There was a joint NIH-industry workshop on the subject of target validation this past November. This gathering, including high-level representatives from many of the major pharmaceutical companies, had the goal of exploring how to use various scientific opportunities (particular genomic advances) to improve the process of identifying suitable targets for drug development. The Executive Summary of that workshop is available as Document 7. NHGRI is being asked to help in many of these areas:

- Eric Green is on the overarching steering committee for these efforts.
- Teri Manolio will be co-leading an NIH-industry-academia working group to explore possible genomics-oriented projects that would move from genotype to phenotype and from phenotype to genotype in the pursuit of identifying and validating targets.
- NHGRI has been asked to organize two workshops that will be relevant to these efforts: one on the notion of aggregating genome sequence data in a fashion to accelerate genomic discoveries, and one on exploring the merits of using different types of cohorts in genome sequencing projects.

Fiscal Year 2012 Appropriations Update
At the September, 2011 Advisory Council meeting, Congress was still debating the funding levels for federal agencies for Fiscal Year 2012, and NHGRI's budget for the current Fiscal Year was unclear. Congress was able to complete this just before the holidays with the passage of a 'megabus' bill containing funding for most of the federal government. NHGRI now has a budget through the end of the fiscal year (September 30, 2012).

The President had requested an increase of NHGRI's budget to $525M in Fiscal Year 2012 (up from the $511M in Fiscal Year 2011). This was the figure in a bill introduced in the House, while a Senate bill passed by the Appropriations Committee had NHGRI getting a $5M decrease. In the end, NHGRI ended up with a very slight increase over Fiscal Year 2011: $513M, or an increase of just under 0.3%.

Fiscal Year 2013 Appropriations Update
The next uncertainty is the Fiscal Year 2013 budget, which will be proposed and debated against the backdrop of an election year. This is further complicated by the recent failure of the "Supercommittee" to reach an agreement for deficit reduction.

Failure of the Supercommittee triggers an automatic across-the-board $1.2-trillion cut to federal agencies in 2013. In theory, this would amount to an 8%-9% cut to NHGRI's budget starting January 2, 2013 but retroactive to October 1, 2012. NHGRI cannot ignore the possibility of an 8%-9% cut next year, so the staff has been actively developing "what if" budget scenarios to deal with a major budget reductions if FY 2013 should that come to pass.

Alzheimer's Research Initiative
In January 2011, President Obama signed the National Alzheimer's Project Act, which calls for an aggressive and coordinated national Alzheimer's disease plan. As part of that plan, DHHS Secretary Sebelius announced last week that NIH would make available $50 million for Alzheimer's research in Fiscal Year 2012 and an additional $80 million in Fiscal Year 2013.

These efforts will include genomic studies aiming to identify genes that increase risk for the disease, and it is very likely that NHGRI will be involved in this research. The details about how NHGRI will become involved are actively being worked out, and NHGRI will report on any developments at the May, 2012 Council meeting.

NIH Clinical Center Receives Lasker-Bloomberg Public Service Award
A major honor was bestowed upon the NIH this past fall, when the NIH Clinical Center was awarded the 2011 Lasker-Bloomberg Public Service Award. Largely regarded as the 'crown jewel' of the NIH Intramural Research Program, the NIH Clinical Center was given this highly prestigious award for serving as a model institution that has transformed scientific advances into innovative therapies and has provided high-quality care to numerous patients.

Secretary of State Hillary Clinton Visits NIH
In November, Secretary of State Hillary Rodham Clinton visited the NIH to deliver a major policy speech in which she called for a renewed push for an "AIDS-free generation." This speech marked the 30th year in the fight against HIV/AIDS and kicked off preparation for World AIDS Day activities and the international conference "AIDS 2012" (which will be held in Washington, D.C. in June, 2012).

Advisory Committee to the NIH Director Working Group on Data and Informatics
Recognizing the pervasive bottlenecks and challenges related to big data and informatics, Francis Collins established a new working group of his Advisory Committee to the Director. This working group aims to investigate the management, integration, and analysis of large biomedical datasets. Called the NIH Data and Informatics Working Group, this group is co-chaired by David DeMets (University of Wisconsin) and Larry Tabak (NIH Deputy Director) and includes members such as Russ Altman, David Botstein, Dan Masys, and Council member Jill Mesirov.

Recommendations from the working group are due this summer. Meanwhile, NHGRI and NIGMS have been asked to co-lead a trans-NIH working group to take those recommendations forward in the area of molecular data; other NIH working groups will deal with other areas (such as phenotype and imaging data).

Request for Information: NIH Data and Informatics Working Group
As part of their deliberations, the NIH Data and Informatics Working Group has issued a Request for Information (RFI) to solicit input from the community on a broad series of topics relevant to this complex area. A subset of those topics is listed here, while detailed subtopics can be found in the RFI itself.

- Scope of the issues
- Standards development
- Secondary use of data
- Data accessibility
- Incentives for data sharing

- Support needs

The RFI will accept public comment through March 12, 2012.

III. GENOMICS UPDATES

Mourning the Loss of James Crow

The legendary geneticist James Crow died January 4, 2012; he was 95 years old and still actively working at the University of Wisconsin at the beginning of this academic year. James Crow was a leader in the field of population genetics, who helped shape public policy about atomic radiation damage as well as the use of DNA in the courtroom. He was also a highly regarded genetics teacher; his 'Crows Notes' was a textbook widely used at the college level for introduction to genetics courses.

Mourning the Loss of Norton Zinder

Genetics pioneer Norton Zinder died on February 3, 2012; he was 83 years old. Dr. Zinder was involved in some of the early planning of the Human Genome Project. In fact, he served as a member of this Advisory Council when NHGRI was known as the National Center for Human Genome Research. Among his many scientific accomplishments was the discovery of transduction in bacteria. He was a John D. Rockefeller Jr. Professor Emeritus at The Rockefeller University, where he spent his entire research career.

Awards, Recognitions and Prizes to NHGRI-associated Scientists

- **David Altshuler** of the Broad Institute and Harvard University was given the **2011 Curt Stern Award by the ASHG**. He was honored "for his outstanding contributions as a leader in the study of human genetic variation and its application to common, complex diseases using tools and knowledge gained from the Human Genome Project." The Curt Stern Award is given annually by the ASHG in recognition of major scientific achievement in human genetics that has occurred in the last 10 years.
- **Andrew Feinberg** of Johns Hopkins University and NHGRI grantee was given an **NIH Director's Pioneer Award**. This award was based on a proposal entitled "A General Stochastic Epigenetic Model for Evolution, Development, and Disease."
- **Keolu Fox** was a participant in the NHGRI Diversity Action Plan program, spent a couple of years in the NHGRI Intramural Research Program, and is now on an F31 fellowship at the University of Washington. He was recently awarded the **Best Graduate Student Presenter for Genetics** at the **Society for Advancement of Chicanos and Native Americans in Science National Conference**.
- **Manolis Kellis**, Associate Professor in the Department of Electrical Engineering and Computer Science at MIT, was awarded the **2011 Niki Award by the Athens Information Technology Center of Excellence for Research and Education**. The award, which is presented annually, honors prominent Greeks or individuals of Greek descent who are internationally recognized for their contributions to science and technology, and who inspire a new generation of scientists.
- **Harold Shapiro**, will receive the **Public Welfare Medal –** the **National Academy of Science's** most prestigious award. The medal is presented annually to honor someone demonstrating extraordinary use of science for the public good. The Public Welfare Medal will be presented to Shapiro on April 30 during the Academy's 149th annual meeting. Previous recipients of the medal include Neal Lane, Maxine Singer, C. Everett Koop, and Carl Sagan.
- Newly elected leaders of ASHG: **Jeff Murray, President-elect**; **Geoff Duyk, Treasurer**, and **Board of Directors**: **Vivian Cheung, Evan Eichler, and Richard Gibbs**.

- **Martin Blasser, Vivian Cheung, Claire Fraser-Ligget, Richard Gibbs, and David Relman** were elected fellows of the **Institute of Medicine**.
- **Andrew Feinberg, Edward Marcotte, Richard McCombie,** and **Richard Myers** were elected fellows of **AAAS.**

USPTO Study on Genetic Diagnostic Testing
Last fall, Congress passed the Leahy-Smith America Invents Act, reforming U.S. patent law to align it with the systems used by other countries. Contained within this Act is a requirement for the U.S. Patent and Trademark Office to conduct a study on genetic testing. Specifically, the law requires that the PTO prepare a report for Congress on "effective ways to provide independent, confirming genetic diagnostic test activity where gene patents and exclusive licensing for primary genetic diagnostic tests exist." The study is designed to examine the concern that gene patents and exclusive licenses can prevent patient access to genetic testing. The report is due to Congress by June 16, 2012, and the PTO is holding public hearings in February and in March. The public is further invited to submit written comments to the agency by March 26, 2012.

Presidential Commission for the Study of Bioethical Issues Meeting: Whole Genome Sequencing
On February 2, 2012, the Presidential Commission for the Study of Bioethical Issues met in San Francisco to discuss bioethical issues associated with whole-genome sequencing. The Commission heard from a number of experts, including former NHGRI Council members Richard Gibbs and Pilar Ossario. The Commission's focus was mainly on issues of privacy, although the discussions frequently returned to the issue of consent and how to make it meaningfully informed in the light of very low genetic/genomic literacy among clinicians and the general public. The Commission will be publishing a report on the subject later this year, and NHGRI staff members are in close contact with the Commission's staff both to serve as a resource for any information they might need and to provide input on the possible directions the Commission might pursue.

Institute of Medicine Report
This past July, the IOM Roundtable on Translating Genomic-Based Research for Health hosted a workshop to highlight and identify the challenges and opportunities in integrating large-scale genomic information into clinical practice. The main objective of the workshop was to start a discussion on what needs to be done to prepare the necessary infrastructure and to address the various challenges for realizing genomic medicine. There will be a follow-on meeting in July 2012, which will explore the economics of clinical and research applications of whole-genome sequencing, that Greg Feero will be chairing.

National Academies Report
Motivated by the explosion of molecular data on humans— particularly data associated with individual patients— and the sense that there are large, as-yet-untapped opportunities to use these data to improve health outcomes, the National Academies issued a report titled, "Toward Precision Medicine." This report explores the feasibility and need for "a new taxonomy of human disease based on molecular biology" and develops a potential framework for creating one. The report notes that moving toward individualized medicine requires that researchers and healthcare providers have access to very large sets of health-related and disease-related data linked to individual patients. These data are also critical for developing the information commons, the knowledge network of disease, and ultimately the new taxonomy.

Battelle Report on Genomic Clinical Testing Industry

In May of 2011, Battelle Technology Partnership Practice published an economic analysis (supported by Life Technologies) on the economic and functional impacts of the federal investment in genomics R&D through the Human Genome Project and beyond. Recently, they released a related report on behalf of the American Clinical Laboratory Association that examines the economic and functional impacts of genetic and genomic clinical laboratory testing. The study found that the even though it is in its early stage, the genetics and genomics clinical testing sector has been responsible for directly and indirectly employing 116,000 workers, generating nearly $6 billion in personal income, and providing $1.2 billion annually in federal tax revenue.

American College of Medical Genetics Changes Name to American College of Medical Genetics and Genomics

The American College of Medical Genetics recently decided to change the name of their organization to the American College of Medical Genetics and Genomics. This will take effect in March at their annual meeting; however, they will maintain the same acronym, ACMG. According to ACMG, the name change "recognizes the increasingly central role of medical genomics and its importance alongside genetics in fulfilling the mission of the ACMG."

NHGRI Genome Advance of the Month

NHGRI continues to feature on its website a monthly feature highlighting a genomic advance of the month. Recent topics have included: a genomics approach to the study of trauma, the sequence of the full genome of the bacteria responsible for the Black Death, next-generation sequencing targeted at known tumor suppressor genes, and the use of previously collected GWAS data to uncover new genetic pathways that regulate how our bodies make platelets.

Genomics in the News

- The genome of an aboriginal man who lived in the 1920s was sequenced. An analysis of the resulting sequence data suggests that his ancestors started their migratory journey more than 60,000 years ago, branching off from humans who left Africa.
- Scientists recently sequenced the genome of a Dutch woman who lived to age 115 (Hendrikje van Andel-Schipper, 1890-2004). This woman overcame breast cancer at the age of 100, and never showed signs of dementia or Alzheimer's disease.
- In January, *The Scientist* ran a feature story about Elaine Mardis entitled "High-Tech Choir Master."
- Also in January, the *New York Times* ran a feature article about Eric Lander entitled "Power in Numbers."
- Another *New York Times* article highlighted the genomic data explosion.
- ENCODE was identified by *Nature* magazine as a potential "key finding and event that may emerge in 2012." An accompanying article foreshadows a major update from the project that is expected to be reported in a major publication in 2012.
- The NHGRI Sequencing Technology Development Program was featured in a series of stories reported in the *Wall Street Journal*, Reuters, National Public Radio, *Nature*, and other news outlets. Those reports featured the announcement early last month that two major sequencing technology companies will release new sequencing platforms in 2012 that are predicted to enable sequencing a whole human genome for $1,000.

IV. NHGRI EXTRAMURAL PROGRAM

Large-Scale Genome Sequencing Centers

Following the extensive discussion with Council about the renewal of our Genome Sequencing Program at the September Council meeting, NHGRI made final decisions and announced the new awards in December, 2011. There are four major components of the renewed NHGRI Genome Sequencing Program. The first component is the Large-Scale Genome Sequencing Centers, which was renewed for 4 years at a Year 1 funding level of $86 million. The Large-Scale Genome Sequencing Centers will conduct research into how the human genome works as well as studies of the genetic contributions to common complex diseases and ongoing special projects, such as The Cancer Genome Atlas. The Centers will also be involved in new medical initiatives and will continue to implement technological advances in DNA sequencing; develop new techniques and software to analyze and understand the massive amounts of DNA sequence data now being produced; and continue to train genomic researchers.

Mendelian Disorders Genome Centers

The second component of the renewed Genome Sequencing Program involves the creation of new Mendelian Disorders Genome Centers. For this, NHGRI partnered with the National Heart, Lung, and Blood Institute to invest $48 million over the next 4 years to fund 3 Centers (with NHGRI and NHLBI contributing $40 million and $8 million, respectively). The funded Centers are located at the University of Washington (which will also serve as the Coordination Center for the group), Yale University, and a partnership between Baylor College of Medicine and Johns Hopkins University. These 3 Centers will collaborate with a worldwide network of rare disease experts to sequence the genomes of thousands of patients and their family members to identify the genetic variants responsible for rare genetic disorders.

As the Coordination Center, the University of Washington group will coordinate the center activities that are essential for the program's success and will host the sole web portal for sample solicitation.

Clinical Sequencing Exploratory Research Projects

The third component of the renewed Genome Sequencing Program involves the creation of new Clinical Sequencing Exploratory Research Projects. For this, 6 awards have been made to PIs that will be investigating technical, ethical, and psychosocial questions related to the application of genome sequencing in the clinic. The two awards with particular emphasis on cancer are being co-funded by NCI.

Informatics Tools for High-Throughput Sequence Data Analysis Awards

The fourth and final component of our renewed Genome Sequencing Program involves grants for developing informatics tools for high-throughput sequence data analysis. Six awards have been made for a total of $16M over four years. The goal of this program is to improve access to next-generation DNA sequence analysis software so that independent researchers can analyze their own sequence data. This program builds on previous investments that have led to nascent software tools. The grantees will work to harden such software to make it reliable, robust, easy to install, and user friendly for independent researchers and non-genomicists.

Genome Sequencing Program: Comparative Genomics

One recent highlight from the Genome Sequencing Program is the recent publication in *Nature* reporting the sequencing and comparative analysis of 29 eutherian genomes. The authors generated a high-resolution map of more than 3.5 million evolutionarily constrained elements that encompass about 4% of the human genome. This study further used evolutionary signatures and comparisons with experimental data sets to suggest candidate functions for about 60% of the constrained bases. Overlap with disease-associated variants indicates that these findings will be relevant for future studies of human biology, health, and disease. The data

sets for this study are publicly available at the Broad Institute and at the UCSC Genome Browser.

The Cancer Genome Atlas (TCGA)
The Cancer Genome Atlas (TCGA) program held its first public scientific symposium in November 2011.
All the presentations described research using TCGA data. The meeting was very well attended, and actually "sold out". All of the talks are available on NHGRI's GenomeTV channel of YouTube. Based on the success of the meeting, there will be a second TCGA scientific symposium in November 2012. AACR has agreed to co-sponsor and advertise the meeting with NCI and NHGRI.

TCGA had a goal of analyzing 5,000 tumor samples by end of 2011— and reached it. Another goal is to comprehensively analyze specimens from at least 20 tumor types— today there are 22 active tumor projects in TCGA. Accrual has closed for glioblastoma, ovarian, colorectal, and renal clear cell carcinoma, meaning the goal of qualifying 500 cases for these projects has been achieved. There are active tumor working groups preparing papers for publication for many of the tumor types, including some of the most prevalent cancers. A manuscript describing the full characterization of the colorectal carcinoma genome is under review, and papers for breast, lung, and kidney cancer as well as acute myeloid leukemia are in preparation and are expected to be published by the end of 2012.

1000 Genomes Project
The Phase 1 paper is being written on 1,094 samples from 14 populations, with 40 million SNP, indel, and deletion variants on integrated haplotypes. The Phase 2 data set contains low-coverage and exome sequencing data on 1,600 unrelated samples from 19 populations. The Phase 3 sample collection from 7 more populations should be completed by April. All the sequencing should be completed by fall 2012, on 2500 unrelated individuals plus 161 trio children. Complete Genomics has recently agreed to deeply sequence 500 samples, including 161 trios. In total, there are now 2661 samples being studied by the 1000 Genomes Project.

DNA Sequencing Technology Development
The 8th annual meeting of the Advanced DNA Sequencing Technologies program grantees will be held in April, 2012 in San Diego. As in past years, the last portion of the meeting will be opened to other interested members of the research community. Jeff Schloss will give an update about this program later in the open session.

ENCODE and modENCODE
Three ENCODE RFAs (with U01, U41, and U54 mechanisms) were released this past October, and applications were received in December. These RFAs aim to solicit applications for research projects to apply high-throughput, cost-efficient approaches to extend ENCODE resources toward as complete catalogs as feasible. Applications will be reviewed in March 2012 and discussed by Council in May 2012. Applications received in response to three technology development RFAs will be discussed during the Closed Session. NHGRI is currently in the planning stages for a modENCODE symposium to be held on the NIH campus on June 20-21, 2012. The goal is to broaden community understanding of model organisms and showcase the contributions of the modENCODE Consortium. The meeting is planned to tie in to the upcoming Model Organisms to Human Biology meeting (organized by the Genetics Society of America and scheduled at an adjacent time to our symposium).

At the December GENEVA Steering Committee meeting, there was a joint session including ENCODE and GENEVA investigators. ENCODE investigators analyzed 8 GENEVA/GARNET GWAS datasets, and they were paired up with the GENEVA/GARNET investigators for hands-on demonstrations of how to use ENCODE data to follow up GWAS findings. New collaborations between the consortia were established, and are already resulting in plans for publications and grant applications.

Meanwhile, several integrated analysis papers are the works:

- The ENCODE Consortium has a major integrative paper under revision, along with many companion papers— all of which aim to be published in 2012.
- The modENCODE Consortium is working on a paper that integrates worm, fly, and human modENCODE and ENCODE data.
- The mouse ENCODE Consortium is currently planning a comparison of human and mouse data.

Return of Results Consortium

In the ELSI research program, the new Return of Results Consortium is now active. This is a consortium of investigators conducting either behavioral/social or normative research on ethical, legal, and social issues related to returning genomic results, including incidental findings, to study participants or to patients in the context of clinical care. The consortium includes investigators from seven R01 and R21 grants funded through the recent Return of Results RFAs, the ELSI investigators funded in the six U01 Clinical Sequencing Exploratory Research Project grants, and investigators on two other ELSI grants who are studying related issues. The consortium aims to identify areas of possible consensus that can form the basis for policy development in this complex area. Already, plans are underway among the investigators for sharing outcome measures and instruments, which should facilitate standardization and ultimately make it easier to compare data generated across studies.

Centers of Excellence in Genomic Science (CEGS) & Diversity Action Plan (DAP)

The Centers of Excellence in Genomic Science (CEGS) and Diversity Action Plan (DAP) programs held back-to-back annual meetings this past October at the Dana-Farber Cancer Institute in Boston. This was the largest CEGS meeting to date, with 10 active groups. NHGRI plans to invite the two CEGS groups whose grants are now ending to a future Council meeting, so they can share their experiences and present results with the Council. The most recent round of CEGS applications and their reviews will be discussed during the Closed Session of this Council meeting. The next receipt date for applications to the CEGS program is May 17, 2012 and to the Diversity Action Plan program is May 25, 2012.

Characterizing and Displaying Genetic Variants for Clinical Action Workshop

In December 2011, NHGRI hosted a workshop on characterizing and displaying genetic variants for clinical action – dubbed the ClinAction Workshop. The workshop was a collaboration between NHGRI and the Wellcome Trust, and involved ~80 participants from a wide range of disciplines and organizations, including several NIH Institutes and Centers, the Centers for Medicare and Medicaid Services (CMS), and the Food and Drug Administration (FDA). The goal of the workshop was to consider processes, databases, and other resources needed to identify clinically-relevant variants, decide whether they are actionable and what the action should be, and provide this information for clinical use. Videos, presentations, and recommendations from the workshop are now posted on NHGRI's web site (genome.gov), and a manuscript describing the topics covered in the workshop is in preparation. A Concept Clearance about this area will be presented later today by Teri Manolio.

Genomic Medicine II Meeting
In December 2011, NHGRI hosted the Genomic Medicine II meeting, which built on the June 2011 Genomic Medicine I meeting that was presented at the September 2011 Council meeting. This was the second in at least four planned Genomic Medicine meetings under the auspices of Council's new Genomic Medicine Working Group. The meeting was attended by ~70 people. The goals of the meeting were to develop ideas for multicenter collaborative pilot projects in translational genomic medicine, learn of new projects ongoing at potential partner sites, and identify infrastructure needs and solutions to speed the adoption of genomic medicine. Six subgroups in topical areas were created and are now actively meeting. Videos, presentations, and recommendations from the workshop are now posted on genome.gov. A Concept Clearance about this area will be presented later today by Teri Manolio. The Genomic Medicine III meeting will be held in Chicago in May 2012 and will focus on barriers to implementing genomic medicine programs and discussions with payers, professional organizations, and government regulatory agencies.

V. NIH Common Fund Program

Molecular Libraries Program (MLP)
The Molecular Libraries Program holds back 25% of each Center's annual award for release based on demonstrated progress at the mid-year point toward a set of year-end milestones. The four NHGRI-managed centers demonstrated good to excellent progress toward all milestones this year. At the November Steering Committee meeting, center-driven research projects funded as part of each centers' U54 were presented. Another key topic at this meeting was the development of a "next generation database" to advance chemical biology data analysis beyond that currently provided by PubChem. Development of this Molecular Libraries Biological Database will be supported through grant supplements to several MLP centers.

Knockout Mouse Projects (KOMP)
The KOMP program came to an end in September 2012, but there are some no-cost extensions to cover wind-down activities. The KOMP Finale and KOMP2 Kickoff meeting were combined with an International Mouse Phenotyping Consortium (IMPC) meeting in September 2012. For KOMP2, awards were made in Fiscal Year 2011, with overall funding for the program set at $111M over 5 years. The goal is to produce and phenotype 2,500 mouse strains. Three centers that submitted paired mouse production and mouse phenotyping applications were funded. One award was made to the EBI to fund the Data Coordination Center and Database.

Genotype-Tissue Expression (GTEx)
GTEx investigators had their third in-person meeting in December 2011, at the point when the pilot phase of the project was roughly half completed. There has been excellent progress in meeting the milestones for the pilot phase, especially with respect to donor enrollment. Specifically, the program is averaging 10 donors/month, with the current total number approaching 100. Also, the resulting quality of the purified RNA from the rapid-autopsy tissues has been very good. The External Scientific Panel was very impressed with progress. A proposal for scaling up the project to include an additional 600-800 donors is being developed, and will be submitted to the Common Fund for possible Fiscal Year 2013 funding.

Library of Integrated Network-based Cellular Signatures (LINCS)
The LINCS program held a consortium meeting in October 2011 with members of the production centers as well as newly awarded collaborative supplement, technology development, and computational tool awardees. The External Advisory Panel members for the program were also in attendance and provided several recommendations including: developing

a trans-center project between the U54 and U01 groups, creating a public data release policy, and defining metrics for the program. The LINCS centers have created a public website to inform the community about the LINCS program and describe the data available through the respective center's websites, to discuss current experimental components of the program, and to update users on new developments in LINCS. NIH staff is in the process of developing a plan for bridge funding for LINCS in Fiscal Year 2013. The proposal is being coordinated with the Common Fund and should be finalized shortly. As recommended by the External Advisory Panel, NIH staff is currently developing language for a data release policy for the program, which will include input from the LINCS U54 and U01 production centers.

Protein Capture Reagents Program
The newly funded grantees of the antibody production and technology development centers (which comprise the Protein Capture Consortium) met for a kick-off meeting in December 2011. Accomplishments of the meeting include: the formation of working groups to complete certain tasks and the development of a public portal to access the affinity reagents. In addition, NIH staff put together an External Scientific Panel comprised of five members with appropriate expertise for the program. This panel had a chance to make initial suggestions during the December Meeting, and NIH staff is planning a follow-up conversation in the coming months.

Human Heredity and Health in Africa (H3Africa)
Applications for all four RFAs (centers, research projects, biorepositories, and bioinformatics network) were received in December 2011; the response was excellent. The initial review of these applications will be in March 2012, and the second-level review will be at the May 2012 Council meeting. The biorepository RFA was re-issued for technical reasons; the due date is in February 2012. The Wellcome Trust application process is proceeding well and is on a similar timeline. Finally, an important meeting was held in November 2011 in Nigeria, called Ethics and Genomics Research in Africa (or EAGER-Africa). At this meeting, a group of bioethicists, researchers, policy makers, and representative from various African countries, the U.S., and the U.K. gathered to discuss the ethical conduct of genomics research in Africa. These deliberations will inform some of the broader plans for H3Africa.

Single Cell Analysis RFAs Issued
New RFAs were published since the September 2011 Council meeting. The RFAs were as follows: Studies to Evaluate Cellular Heterogeneity using Transcriptional Profiling of Single Cells (U01), Exceptionally Innovative Tools and Technologies for Single Cell Analysis (R21), Accelerating the Integration and Translation of Technologies to Characterize Biological Processes at the Single Cell Level (R01). Applications were due in January 2012.

Possible New Common Fund Initiative: Disruptive Proteomics Technologies
Among the new areas chosen for a potential future Common Fund initiative is "disruptive proteomics technologies." This potential initiative was proposed during the solicitation for potential new Common Fund programs last summer for funding in Fiscal Year 2013. The Institute and Center Directors endorsed this idea, so the Common Fund is moving forward in developing this program. NIGMS and NHGRI have been asked to co-lead this effort. A trans-NIH working group has been established (including Tina Gatlin and Adam Felsenfeld from NHGRI) and strategic planning is underway, which includes a portfolio analysis and gathering community input. The working group's proposal for the program is due April 27, 2012; if approved for further consideration, then a Concept Clearance will be brought to the Council of Councils at their June 2012 meeting. Meanwhile, early planning for new Common Fund programs that will begin in Fiscal Year 2014 has just started, and Eric Green will discuss these efforts at future Council meetings.

VI. NHGRI Office of the Director

NHGRI Catalog of Published Genome-Wide Association Studies (GWAS)
The NHGRI GWAS catalog team continues to curate GWAS data from the published literature. That catalog now includes 1,615 associations for roughly 250 traits with p values < $5x10^{8}$. As of January 2012, the catalog has reached over 5,600 associated SNPs with p values of $<10^{5}$.

Two new columns of information were added to the GWAS catalog: mapped gene and SNP context. For example, clicking on one of the links under the mapped gene column launches the relevant Entrez gene page. These fields are a result of continued collaborations with NCBI to improve the quality of data that are made available to the scientific community. NHGRI recently began a collaboration with EBI to add curation expertise to the catalog team and make informatics improvements— such as automating the catalog diagram and standardizing trait names to an ontology.

***NEJM* Genomic Medicine Series**
13 articles have now been published as a part of the *NEJM* genomic medicine series edited by Greg Feero and Alan Guttmacher. There are a total of 14 articles planned for this series.

U.S. Science and Engineering Festival
The 2nd USA Science and Engineering Festival will take place on April 28-29, 2012 at the Washington Convention Center. As with the last festival held in October 2010, NHGRI will be heavily represented at booths with hands-on activities. This year NHGRI is partnering with the American Society of Human Genetics to have joint activities.

My Family Health Portrait
Greg Feero chairs a trans-NIH working group charged with exploring collaborations on family history research and My Family Health Portrait-related activities. Meanwhile, Geoff Ginsberg and Lori Orlando co-chair an NHGRI-organized working group on family history as part of our broader extramural genomic medicine planning efforts.

Genomic Medicine Lecture Series
NHGRI is collaborating with Suburban Hospital in Bethesda and the Johns Hopkins University School of Medicine to hold a monthly grand rounds-style seminar covering topics in genomic medicine. Greg Feero is leading the planning committee for this series, which will run from December 2011 to June 2012. All the talks are being videotaped and will be made available on NHGRI's GenomeTV channel of YouTube.

Genomic Opportunities for Studying Sickle Cell Disease Meeting: December 2011
A meeting to explore the genomic opportunities for studying sickle cell disease was held in December 2011 in California. While NHGRI was the lead organizer, we partnered with several other NIH institutes including NHLBI, NICHD, NIDDK, NIMHD, and NINDS for the meeting. The meeting was co-chaired by Micheal DeBaun, Richard Gibbs, and Julie Makani (from Tanzania). Attendees included Council member Rick Wilson. There was general enthusiasm from the participants for accelerating research into sickle cell disease using genomic approaches. The discussion also emphasized the fact that attention needs to be paid to the appropriate selection of samples and to phenotyping. The participating NIH Institutes are continuing discussions to explore future collaborations in this area.

Pharmacist Education Meeting

Late last year, the Genomic Healthcare Branch in collaboration with Grace Kuo held a meeting on pharmacists' education in the era of genomic medicine that included representatives of major U.S. pharmacy organizations. The meeting discussed pharmacist education in genomics and identified a number of priorities to pursue.

VII. NHGRI Intramural Program

Blue Ribbon Panel Review of NHGRI Intramural Research Program

As was discussed at the last Council meeting, the NHGRI Intramural Research Program is undergoing a Blue Ribbon Panel review. The panel's membership is as follows:

- David Page, M.D. (Chair)
- Rick Myers, Ph.D. (NACHGR)
- Bruce Korf, M.D., Ph.D. (BSC)
- Wylie Burke, M.D. Ph.D.
- Nancy Cox, Ph.D.
- Bob Waterston, M.D., Ph.D.
- Huda Zoghbi, M.D.

The first meeting of the Blue Ribbon Panel occurred in January 2012. Future steps for this review will include a conference call in the spring and then a final in-person meeting in July 2012. At the September 2012 Council meeting, there will be a presentation about the NHGRI Intramural Research Program by Dan Kastner and a presentation about the Report of the Blue Ribbon Panel by Rick Myers.

NHGRI Intramural Research Highlights

Recent highlights from NHGRI's Intramural Research Program include the following:

- Dan Kastner and colleagues published a study in the *NEJM* identifying a genetic mutation that causes cold temperatures to trigger allergic reactions— a condition known as cold urticaria. In addition to providing target for possible therapeutic intervention, this finding provided new insights about immune system function.
- Yardena Samuels and an NIH-led team studying the genetics of melanoma reported in *Nature Genetics* that mutations in a metabotropic glutamate receptor-3 gene are relevant to the pathogenesis of melanoma.
- Les Biesecker and colleagues at the NIH Intramural Sequencing Center, the Children's National Medical Center, and Johns Hopkins University published a paper in the *American Journal of Human Genetics* that reported the use of next-generation genome sequencing method to identify the gene mutated in the pediatric condition known as paroxysmal nocturnal hemoglobinuria.

William Gahl Honored with prestigious Service to America Medal

Bill Gahl, NHGRI's Clinical Director and Founding Director of the NIH Undiagnosed Diseases Program, received the Samuel J. Heyman Service to America Medal from the Partnership for Public Service. He won the award in the category of Science and Environment. The award pays tribute to members of the federal workforce, highlighting those who have made significant contributions to our country. Honorees are chosen based on their commitment and innovation, as well as the impact of their work on addressing the needs of the nation.

Council Comments

Jil Mesirov encouraged everyone to respond to the RFI for big data.

Council members had several comments after the Director's Report. Several Council members noted that they attended the TCGA Symposium in November 2011 and felt that it was tremendously successful. There was a lot of enthusiasm to learn about NHGRI and TCGA from communities like nurses, insurance companies, and disease-specific researchers. Council members also noted that the ENCODE-GENEVA meeting was very valuable and shows the importance of connecting different groups to facilitate collaborative growth.

SCIENTIFIC REPORTS

Genomics and Society: The ELSI Research Program and Beyond by Prof. Karen Rothenberg

Eric Green introduced Karen Rothenberg, reminding Council that she is serving as a special advisor to the NHGRI Director while on sabbatical from the University of Maryland. Professor Rothenberg expressed her appreciation to the staff at NHGRI for being so supportive and helpful during her time at the Institute.

The ELSI research program was established ~20 years ago with a mission to "anticipate and address the ethical, legal, and social implications of genetic and genomic research." The 5% of NHGRI's extramural budget that funds this program makes NHGRI the largest, single funder of bioethics research in the world. Several inherent challenges also exist: the clash of cultures, interdisciplinary trust, clarification of goals and roles, genetic exceptionalism, and measuring impact. At NHGRI the co-existence of ELSI researchers and genomic researchers in the same programs provides opportunities and challenges for advancing science. The vibrancy of the field and robustness of published research in genetics suggest that the ELSI portfolio has helped encourage growth.

This assessment is one of many previous assessments of the ELSI program. Some perceived tensions seem to appear throughout and are not unique to NHGRI's research portfolio. The objectivity and integration of the ELSI program with the rest of the extramural portfolio has helped NHGRI become the envy of other Institute's extramural programs. NHGRI has a strong commitment to basic research and translation which extends to the ELSI program. The ELSI program also has a very strong investigator-initiated portfolio accounting for about 50% of the portfolio. At the same time, the ELSI program has utilized an evolving approach to funding applications. The program started with broad program announcements, moved towards staff-initiated RFAs and parallel ELSI RFAs with genomic projects, and now includes the program for Centers of Excellence in ELSI Research and ELSI components inside genomic RFAs. As the science matured, the funding has evolved to reflect the integrated role of ELSI in many types of genomic research.

The section 'Genomics and Society' from NHGRI's strategic plan highlights how ELSI research looks both at the social implications of genetics research and societal impacts on genetic research. Prof. Rothenberg highlighted the importance of community engagement and the success that programs like eMERGE have had in integrating ELSI into genomic research. At the same time, she noted that philosophers have been successful ELSI grantees, with work focusing on concepts of group identification and free will. Over time the trends in ELSI funding, generated through a rough assessment of the ELSI grant portfolio, showed that the legal and social issues portfolios were larger at the start of the program while the number of studies focusing on ELSI issues in genomic medicine and genomic research increased as the program matured. As the ELSI grants are incorporated into larger research projects (like the Clinical Sequencing Exploratory Research Program) the grants become more expensive and fewer

grants are able to be funded. Nevertheless, the ELSI portfolio incorporates a diversity of methods and continues to include a good number of grants focused on developing regulations or policy.

ELSI work at NHGRI is not limited to the extramural program. The intramural bioethics core and SBRB lead the intramural programs across the NIH in the careful consideration of ELSI issues. The Office of Policy, Communication, and Education (OPCE) also plays a big role in helping promote the growth of the ELSI program. The goal for the future should be to integrate and expand ELSI programs into other Institutes and federal agencies. NHGRI can provide the global leadership and act as a catalyst for promoting consideration of these issues throughout the world.

Council members had several questions after Prof. Rothenberg's presentation. The first asked for clarification about how the portfolio analysis was generated. Prof. Rothenberg noted that the grants were placed into categories based on their primary aim, but this did not mean that grants in one category could not also fall in other areas. When asked, as a follow-up, whether NHGRI has enough coverage of ELSI issues, Prof. Rothenberg mentioned that she personally wishes there could be more normative research looking into topics such as return of results. Council also asked whether Prof. Rothenberg had done a needs assessment about where the ELSI funding should be focused. This type of assessment has only been done within the Centers for Excellence in ELSI Research (CEER) program, and Prof. Rothenberg feels that NHGRI could benefit from an ELSI-specific advisory group, perhaps a working group of Council, to address this question. Council also asked what had been some of the major successes stories from the ELSI program. Prof. Rothenberg highlighted research on informed consent which has led to changes in the Common Rule, as well as the research leading to the Genetic Information Nondiscrimination Act, as highly successful products of the ELSI program. She also noted the high response rate to the clinical sequencing RFA as an indication of the successful collaboration between genomicists and ELSI researchers. Council was also curious whether the ELSI program should fund studies looking at ways that genetics interact with environment, including the social environment. Prof. Rothenberg notes that the CEER at the University of Oregon has a small P20 to look at epigenetics and that these efforts should be a part of the ELSI program. Council also inquired about the 'communication gap' between the research side and the policy side, and whether Prof. Rothenberg looked into how the broader research community views NHGRI with respect to ELSI research. Prof. Rothenberg noted that all past and present ELSI grants are listed on the NHGRI website, but the Institute should do a better job sharing the research it has funded with those working on policy changes. Council agreed that NHGRI should follow-up with research that had the goal to study policy and should determine whether the research actually had an impact on policy. As a final question, Council asked whether the ELSI program should be spun out to some other entity to allow better cross-pollination within NIH. Prof. Rothenberg noted that the ELSI program already attracts a small amount of joint funding from other Institutes. While there is certainly room for improvement, the CEER program has shown that NHGRI's focus on training has been critical in raising the 'ELSI consciousness' of the rest of the scientific community. Ultimately, Prof. Rothenberg feels that the ELSI program should continue to lead the community from within NHGRI.

Sequencing Technology 2012 Dr. Jeffrey Schloss

At end of the Human Genome Project (HGP) it was clear that the scientific community would need more sequencing for the growing number of genomic applications. During HGP, the cost of sequencing decreased due to technology improvements, automation, and economies of scale. As a part of the first "Bookend Meeting" at the conclusion of the HGP, several quantum

leaps were proposed (including the $1000 Genome) which would lead to massive breakthroughs in research and medicine. The initial sequencing technology RFAs had the goal of a 10,000-fold reduction in cost, by 2014, of a high-quality draft genome. The RFAs have been re-issued annually using R21 and R01 activity codes, with some SBIR and STTR FOAs as well. The average annual spending on this program has been ~$20 million, totaling ~$190 million for the total life of program (including ARRA). The program has funded 45 academic groups and 20 companies and resulted in a large number of publications and patents. Some of the research focused on improving existing technology, while other projects looked at techniques for which even the basic physics was not understood. Together many of these grants contributed to the development of sequencing-by-synthesis which has drastically changed the sequencing workflow and improved throughput. In fact, the throughput for today's mainline sequencing machines is so high that many of the companies have developed smaller versions to accommodate lower throughput laboratory uses.

At the same time, the multiple technologies that currently make up the sequencing landscape feature many different innovations generating lots of competition in the marketplace. Right now several new technologies are under development including sequencing-by-synthesis using pH detection instead of light, DNA polymerase as a sequence detector, nanopore sequencing, and sequencing using electron microscopy. Due to NHGRI's investments these technologies are beginning to reach the commercial marketplace.

The Sequencing Technology program has done a great job of moving bottlenecks, but there is still work to be done. A key component of the program is the annual meeting where NHGRI grantees gather and share their results. Even though there is a lot of competition, the meetings are successful because the participants are motivated and learn from one another and collaborate. NHGRI's financial commitment combined with Council's willingness to take some risks has allowed this program to foster the development of technologies that cut across many aspects of the Institute's mission.

Council discussed several topics related to Dr. Schloss's presentation. Council noted that it is good that NHGRI supports both companies and academia with this program. Dr. Schloss added that the program works hard to reach a happy medium between intellectual property concerns, which are necessary for commercialization, and collaboration, which is a hallmark of NHGRI programs.

Council also noted that while it is difficult to track all the features of a given technology, such information will be particularly useful as the program matures and issues like quality begin to take on greater importance. As a follow-up, Council asked what kind of quality the new, cheaper technologies are currently able to achieve. Dr. Schloss responded that the next-gen technologies are getting close to the goal of producing a draft assembled genome. Some clever algorithms and mapping schemes are needed to achieve this, but currently, the total cost is in the $5,000 to $10,000 range. While the program is often framed in terms of cost, quality will remain a focus as well.

Council also asked how the fast-tracking of these technologies affects other parts of the NHGRI budget. Dr. Schloss estimated that the centers are investing ~10% of their budgets in the adoption of new technologies. The information feedback provided by these "sophisticated users" is critical for development and commercialization. Council was also curious about how this program supports technologies for targeted sequencing. Dr. Schloss noted that the program mostly focuses on whole-genome sequencing and applications that focus on capture

technologies or targeted sequencing are not disadvantaged in the normal NIH review processes.

PUBLIC HEARING ON REORGANIZATION

Dr. Laura Rodriguez introduced the public hearing on NHGRI's reorganization. According to the Public Health Service Act as amended by the NIH Reform Act, the agency is obliged to have a period of public comment any time it proposes to change its internal structure. The first public meeting was held on January 18, 2012 as a webinar. Over 50 participants from universities, professional societies, and the media joined the webinar. NHGRI has also received several written comments. The questions and comments to date have focused on several issues: the rationale for and potential benefits of the proposed reorganization, the potential affect on funding, the new Division of Genomics and Society and its implications for the ELSI program, the need for attention to computational biology, the relationship between the proposed research divisions and policy division, and the interaction with other Institutes and Centers.

Dr. Eric Green then presented further details about the reorganization. Dr. Green wished to thank the NHGRI staff for their help and support as the reorganization has proceeded. He also thanked Council for taking time from the open session to allow for this public meeting. NHGRI was started as the Office of Human Genome Research to coordinate the NIH's plans for the Human Genome Project (HGP), then the Institute was promoted to National Center for Human Genome Research, and finally became an full-fledged Institute. The current organizational structure contains three divisions: Office of the Director (OD), Division of Extramural Research (DER), and Division on Intramural Research (DIR). The Institute has grown in size and complexity in recent years and the organizational structure of OD and DER has remained relatively unchanged since the HGP. The strategic plan, published last year, highlighted the growth in scope of the Institute's research goals. From having one named project (HGP) at it creation, NHGRI is now responsible for 24 named projects (including those NHGRI manages for the Common Fund).

The proposed changes affect DER, and to a lesser-extend OD. DIR will remain unchanged and already has a sub-structure that serves it quite well. The reorganization will promote the Office of Policy, Communications, and Education (OPCE) and the Office of Administrative Management (OAM) to divisions. DIR will be the third division and DER will be transformed into four new divisions (Genome Sciences, Genomic Medicine, Genomics and Society, Extramural Operations). The Office of Population Genomics will move out of OD and into the Division of Genomic Medicine. Each division will eventually have a division director reporting directly to the NHGRI Director.

Many questions from the first webinar focused on how projects and funding will be allocated within the divisions. NHGRI envisions that projects will draw on expertise across all divisions and the expectation is that the collaborative programmatic operation of the extramural staff will continue relatively unchanged. The funding priorities will continue to be decided based on individual projects, not within a division.

The implementation process is following the conditions of the NIH Reform Act of 2006. All information about these meetings has been posted in the Federal Register. NHGRI has held two public meetings. A packet of information will be submitted to the NIH and the Department of Health and Human Services, and if approved, NHGRI will begin appointing division directors. Dr. Green believes that the new organizational structure effectively reflects the Institute's

research portfolio. He feels confident that the new divisions will improve succession planning and are commensurate with his vision for the Institute's future success,

Dr. Rodriguez, who moderated the discussion, asked for questions or comments from the audience before opening the discussion up to Council members.

Council had several questions regarding the reorganization. At first, they asked whether there are any parts of the organizational structure that are currently broken. Dr. Green responded that nothing is broken, but now is the time for NHGRI to position itself to take advantage of the changing research portfolio. As a follow-up, Council noted that the successful collaboration at NHGRI is unique and the reorganization should not mettle with that spirit. Dr. Green guaranteed that the reorganization will not affect the collaborative operation of the extramural program, but instead will aim to make the internal operation of DER smoother while preserving the collaborative environment of the current structure. Council also asked how the reorganization will affect the way that funded scientists interact with the new extramural program. Dr. Green noted that the while a program officer's (PO) supervisors may be different, the interactions between PIs and POs will remain relatively unchanged. Council was further curious about the roles of the extramural divisions and how they will interact with the other new divisions. Dr. Green explained that the extramural divisions will provide intellectual concentration within the extramural program and should offer more opportunities for mentorship and professional development. The four new divisions of DER will each interact with DIR and the other two divisions. This should increase the collaboration between the extramural program and other parts of the Institute. NHGRI has also begun developing processes for dealing with tightening budgets and managing the consensus-building process across DER. Ultimately, the decision making process is an iterative one that relies on staff, advisors, and others. Dr. Green feels that the extramural funding will remain as before, and that the decisions regarding the funding will not be affected by the new organizational structure.

Council also asked about the Genomics and Society Division and its broadened focus. In particular Council inquired about things that were not a part of the ELSI program but will now be included in the Division of Genomics and Society. Dr. Green responded that NHGRI is looking to build on the past successes of the ELSI program and give it more freedom to operate. Dr. Green plans to leave room for the new division director to structure the division to incorporate initiatives within and outside the ELSI portfolio. This new division is meant to reflect the growth of the ELSI program and the consultative role that is plays within the Institute and the rest of NIH. The ELSI brand will not be extinguished; we will keep it as an important part of Genomics and Society. Furthermore, Dr. Green expects greater interaction between the Division of Genomics and Society and the Division of Policy, Communication, and Education, aided by the fact that the divisions are now on the same level.

CONCEPT CLEARANCES

Centers for Excellence in ELSI Research (CEERs) by Joy Boyer

The CEERs program developed out of the 2003 strategic planning process and has several goals: to encourage trans-disciplinary research, to translate research into healthcare practices and public policies, and to train the next generation of ELSI researchers. The program uses P50 and P20 activity codes. The first CEERs were funded in 2004 and total funding for the CEERs program is limited to 33% of the ELSI set aside. Currently six P50s and two P20s are funded. There have been concerns about the impact the CEERs have on ELSI research outside the centers and on investigator-initiated ELSI research. However, the CEERs have established

productive research teams that support the integration of ELSI and genomic research, provide expertise to policy makers and advisory boards, and train a diverse cadre of future ELSI researchers. Furthermore, the program generates institutional support for ELSI research in the broader genomics community.

The proposed RFA would be released in the spring of 2012 with grants beginning in the spring of 2013. The RFA would require applicants to focus on a clearly defined issue to focus the mission of the center. NHGRI plans to fund $2.75 million in grants (two P50s and two P20s) which will keep the program within the 33% fiscal cap and allow for future year flexibility. The P50s last for 5 years, the P20s last for 3 years, and applicants are limited to 10 total years of funding (or 1 renewal).

In discussion, Council asked for clarification about the P20s and what options applicants have for funding at the end of 3 years. Joy Boyer noted that program tries to time the re-issuing of the RFA for P50s to coincide with the end of the P20s. Grantees coming off of P20s have not always applied for P50s and typically have not had success in bringing together the people at an institution to form a research community that is suitable for P50 funding. However, Council noted that the CEER at the University of North Carolina was able to use it P20 funding to establish a community from across disciplines so that the grantee could hit the ground running with a P50.

Council members also asked why the budget decreased from the last RFA. Joy Boyer noted that the 33% cap for CEERs funding includes active grants so the amount set aside for the new RFA reflects the money available after applications from past RFAs are funded.

Council also asked if there are any lessons learned about what makes a successful program and what criticisms the program has received. Joy Boyer responded that when the CEERs are located within an established department, they have been more successful. The presence of a strong genomics department also makes a huge difference. NHGRI strongly recommends collaboration with genomics departments within a CEER's institution or with outside institutions. The main criticisms seem to center around the perception that the centers' budgets take away from the investigator initiated portfolio and create an elite set of researchers with greater success rates for other funding. The new RFA places a greater emphasis on developing a central idea or issue to try to focus the thinking of potential CEERs.

Council also expressed a desire for the program to consider how to preserve the training infrastructure developed by the P50 centers and track those who have participated as trainees. Joy Boyer noted that the ELSI program staff is working with the CEERs to standardize the tracking of trainees. Preliminary results indicate that CEERs trainees have gone on to receive R01 funding, to secure tenure track positions, and to take positions with the federal government.

The motion to approve this concept clearance was passed.

Population Architecture using Genomics and Epidemiology (PAGE) Renewal by Dr. Lucia Hindorff

The goals for Phase I of PAGE were to develop population-based profiles of Genome-wide Association Study (GWAS) variants, modifiers of gene-trait associations, and biological insights. These data were generated by studying different populations with related phenotypes and were disseminated as aggregate allele frequency data through dbGaP. Four participating studies with one coordination center were funded. PAGE quickly realized the importance of GWAS SNPs

that do not generalize to non-European Ancestry (EA) populations. Therefore, PAGE developed the 'metabochip' with 1000 Genomes SNPs. In years 3 and 4 of Phase I, grantees focused on genotyping non-EA samples using the metabochip. PAGE's external scientific panel recommended that PAGE continue to focus on interrogating non-EA populations with a focus on productivity and value-added power. At the February 2011 Council meeting, PAGE was extended for one year, and an increase in productivity and publications resulted. PAGE has allowed NHGRI to leverage large multi-ethnic databases to improve mapping, to detect, refine, and compare the strength of associations, and to consider the ELSI issues relating to the return of results in minority populations.

The proposed goals for PAGE Phase II include the identification of disease-associated regions, the building of a comprehensive population resource for non-EA individuals, and the exploration of variation within the broad range of PAGE phenotypes. The potential trait-specific samples size for this study approaches 100,000 total samples. In Phase II, grantees would work to coordinate selection of ~2,000 samples for whole-genome sequencing (WGS), analysis, and data dissemination. NHGRI expects to improve the centralization of the analyses and improve the role of the coordinating center. The WGS costs will require NHGRI to decide whether to allocate sequencing to grantees or to a central sequencing effort.

In discussion, Council asked whether PAGE planned to collect environment data or additional phenotypes. Dr. Hindorff responded that PAGE has not funded the collection of phenotype data, though the cohorts have more data that could be harmonized in the future.

The bulk of Council discussion centered on Council's concern that the concept clearance's use of WGS limits how many of the 100,000 total samples can be studied. In particular, Council members felt that making use of current genotyping options, like the exome chip, would allow NHGRI to stretch its dollars further. Council members felt that it is important to do this work but to do it right and make sure that uniqueness of PAGE's phenotype data and the racial-distributions are leveraged for the best results. Dr. Hindorff responded that many of the samples in PAGE have already had whole-exome sequencing (WES) or been genotyped with the exome chip, and that a pilot initiative to use WGS on these uniquely phenotyped samples would provide insight about future models for analysis. As a follow-up, Council expressed concern about how to best maximize the power, in terms of the sample numbers and racial-distributions, given limited funds. If only ~2,000 samples are to be studied, a carefully selected group that is more homogenous would yield better results. Furthermore, it is important to get the design correct and build a cohort based on what PAGE has already accomplished. This may mean leaving out the sequencing for now and continuing to genotype samples. Other Council members noted that NHGRI might miss the opportunity to take advantage of sequencing data by spending all the money on non-sequencing methods. In fact, it may be possible to pick out the most used samples in the PAGE cohorts and sequence them to target the benefits of sequencing. In general, Council members noted that PAGE is a great program and critical for bringing basic variation data to these large and deeply phenotyped cohorts.

The motion to approve this concept clearance was passed.

Clinical Sequencing Exploratory Research (CSER) Coordinating Center by Dr. Lucia Hindorff

Last year NHGRI funded the CSER program to investigate the infrastructure, methods, and issues when integrating genomic sequence into clinical care. The CSER program also aims to address the ELSI challenges related to sequencing in the clinic and to disseminate methodology

and best practices to the broader community. Six sites were funded, and NHGRI plans to re-issue the RFA and fund up to two more sites depending on available funding. The coordination center will help the CSER Consortium by collecting sequencing standards, phenotype measures, EMR interactions, actionable variants, psychosocial measures, informed consent standards, policy/practice guidelines, and tools. This coordination center would take on logistical and administrative roles, similar to those performed by current NHGRI coordination centers used by GENEVA, GARNET, and eMERGE. The proposed RFA would use a U01 mechanism, would be funded for 4 years at a cost of $800K total cost/year, and would be released with the additional clinical sequencing RFAs.

Council members found this to be a very straightforward concept clearance. Based on the success of past coordination centers and the enthusiastic response to the CSER RFAs, Council hoped that the coordination center would emphasize coordination and not complexity to achieve the broader goals of the CSER program. Council also felt that there might be some real benefit from interactions between NHGRI's various coordination centers. Dr. Hindorff responded that NHGRI plans to look into possible interactions after the grants are funded and would expect the coordination center to help decrease the administrative burdens of the consortium for everyone involved.

The motion to approve this concept clearance was passed.

Genomic Medicine Pilot Demonstration Project by Dr. Teri Manolio

This genomic medicine demonstration project concept clearance has been created as a part of the implementation of NHGRI's new strategic plan. It was informed by discussions held with the Disease-oriented Genomic Medicine Working Group and attendees of the Genomic Medicine Colloquium in June 2011. Currently, there are many disparate and uncoordinated genomic medicine efforts that focus on detecting highly penetrant germline mutations, integrating genomic data and electronic medical records (EMR) for clinical decision support (CDS), and sequencing patients for diagnosis or treatment. Some common barriers identified in past discussions were skepticism and resistance, varying expectations for mortality/morbidity evidence, needs for CLIA and IRB approval, confusion over consent and counseling, difficulty integrating EMR data, and the burden of following up with the massive number of results**.**

The proposed RFA would demonstrate the feasibility of and methods for incorporating patients' genomic findings into their clinical care. The RFA aims to link early adopter sites to less experienced groups, to expand the number and types of sites at which implementation is being done, to develop best practices, and to provide answers to questions about outcomes. The RFA will fund several 'lead sites' each linked to several 'partner sites' (geographically nearby or institutionally related) and a coordination center to oversee cooperation between the sites. The RFA would encourage applicants to secure institutional support, identify groups of clinicians willing to learn about integrating genomic approaches, locate CLIA-certified facilities for efficient workflows, and integrate results into EMRs and provide CDS. The coordination center would be responsible for collecting and disseminating implementation protocols, organizing open meetings for genomic medicine communities, coordinating with related NIH/NHGRI projects, exploring the potential to expand projects beyond the pilot phase, and convening a group of centers working towards best practices in genomic medicine. The proposed RFA would fund 3-5 lead sites, each with 3-5 partner sites, and a small coordination center. NHGRI anticipates a funding level of $3 million in FY13 and $4.4 million in FY14-15.

Council members commented that it would be best if the RFA were broad enough to attract both experienced and inexperienced sites as well as projects with a 1-2 year horizon and those with a 4-5 year horizon. Dr. Manolio agreed and added that NHGRI recognizes the importance of bringing the challenges faced by inexperienced sites to the discussion. Council was also curious to know how this program would differ from CSER and other similar initiatives, especially since the results generated by programs like CSER will be crucial to the success of genomic medicine. Dr. Manolio noted that these programs are closely related and should interact and provide feedback to each other, but that this RFA looks at technologies outside of sequencing that are already in the clinic. NHGRI feels that the CSER program will drive exploratory efforts to determine what can be done and will not necessarily establish all the necessary clinical infrastructure. Given the institutional barriers and outstanding questions about when projects are ready to translate to the clinic, there is important work that could be done by this RFA to clarify the issues.

Other Council members noted that many people think that the evidence is already in for some genomic medicine applications, and that the technical barriers like EMRs, clinician education, and decision support need to be addressed by an initiative like this. Council also noted that this RFA should look to study whether a given approach improves patient care and not just whether the approach is feasible. In particular, the RFA needs to focus on whether an effort is ready to be translated and whether efforts already underway need to be brought back from the clinic for further research. Dr. Manolio acknowledged the importance of effectiveness, and added that this initiative would also aim to improve workflows, integration of EMRs, and clinician buy-in to lay the groundwork for translation. As a follow-up, several Council members suggested that effectiveness research using cases and controls would be critical. They were skeptical of current implementations and the lack of good feedback from clinicians to researchers. Dr. Manolio noted that the concept clearance is intentionally broad and NHGRI expects applications like this to come in for the RFA. Jean McEwen also noted that the return of results consortium will bring together participants from both CSER and the genomic medicine initiative to address questions about effectiveness.

The motion to approve this concept clearance was passed.

ClinAction: Unifying Efforts to Identify Potentially Actionable Genetic Variants by Dr. Teri Manolio

Genomic studies increasingly identify variants with potential implications for clinical care. Current genomic medicine efforts need paradigm-setting examples to drive ethical deliberations and infrastructure developments. There have been several calls, including from a workshop organized by NHGRI, to pull together a standard or deliberative body to judge variants based on risk and evidence. As the title suggests, this initiative focuses on actionability which NHGRI sees as distinct and different from utility and validity. While utility indicates evidence of improved clinical outcomes and validity indicates confirmed association between a variant and a disease or condition, actionability combines institutional flexibility within a broad policy and ELSI framework to allow clinicians and patients to decide how to interpret and use variant data. ClinAction would fall between identifying what is related (GWAS, ClinVar, EGAPP, etc.) and what actions should be taken (ROR, CSER). This initiative would complement these efforts by focusing on the variants that can be used in the clinic now. Coordination with these related efforts, even looking at the same set of variants and coming to the same conclusions, provides valuable feedback for the creation and dissemination of best practices.

This initiative would develop consensus by inviting groups to interact within a framework for review and evaluation of potentially actionable variants. The grantee would define domains for grouping variants, would apply a process to reach consensus on variants and clinical actions, would develop consensus or address an inability to do so, and would obtain input on draft recommendations. NHGRI is open to distributing curation and consensus efforts to divide rather than duplicate the work, but dissemination and clinical decision support will be the underlying goal.

NHGRI anticipates funding a single awardee to collect and evaluate clinical relevance. The goal would not be to provide screening recommendations but to provide evidence on which clinicians could make screening recommendations. NHGRI anticipates funding levels of $2 million in FY13 and $4 million in FY14-16.

In discussion, Council raised several issues related to this concept clearance. Council's first questions focused on how the variants, curated by this program, would be used by patients and clinicians. Would the existence of this resource raise concerns about malpractice claims? Additionally, several Council members noted that this sort of guidance already exists for some pharmacogenomic variants and that those variants followed the traditional route from domain experts to local clinical groups before implementation in specific localities. Nevertheless, Council felt that the goal of providing central guidance on clinical variants is critical and ideally should serve as a starting point for local groups.

Council also asked about the current state of actionable variants. Will this group have the standing needed to attract the respect of other groups working on this? Dr. Manolio acknowledged that getting buy-in from the community will be critical. She noted that clinicians are asking for guidance and are having trouble navigating the current hodgepodge of groups working on this issue.

The bulk of Council's discussion focused on the implementation of this resource. In particular, Council was concerned that an RFA may not be the best mechanism for this initiative. Asking one group to pull together this difficult set of issues may make it impossible to get those who are not funded to agree to the approach of the funded applicant. Furthermore, one group working in this fast moving and disparate field may risk saddling the field with early decisions that prevent the community from advancing. Dr. Manolio noted that this initiative would aim to have the funded group serve as a 'convener' and be expected to solicit input from the community. Ultimately, Dr. Manolio expects this initiative to work like the PhenX project where the groups working on specific domains would take ownership for those domains with the grantee operating like other NHGRI funded resource projects. She also noted that funding multiple groups would require re-working the budget. Council agreed that this is a critical initiative and that a disparate set of similar resources is not a viable solution, but many Council members had trouble seeing how one funded group would be able to accomplish the goal of centralization. Several Council members proposed structuring the initiative as a database with the grantee managing a list of supporting evidence for variants. This model would not provide clinical recommendations or guidelines and helps get around having and NHGRI funded-effort select standards. However, several other Council members noted that clinicians and IRBs want to know what to do and a database of clinical variants might not be good enough. Dr. Manolio noted that NHGRI does not envision this RFA curating a database of 'what should be done,' rather it will provide a resource for others to use to make their decision.

A final question raised by Council dealt with getting the imprimatur of some sort of outside clinical body, like the American College of Medical Genetics. Another option would be for

NHGRI to put out consensus documents based on the data provided by the grantee to form the basis of a position set for use by clinicians. Ideally NHGRI would package the information in a way that would allow other groups to build systems off the data.

In the end, Council felt that while there is an urgent need for this work, a 4-5 month delay to further develop the concept would result in a better final product. A motion to defer this concept clearance to the May 2012 Council meeting was passed.

High Throughput Genomic Analysis in Children with Newborn Screening Disorders
Dr. Anastasia Wise

This concept clearance comes out of the recommendations of a workshop held in December 2010 that had the goal of setting a research agenda for newborn screening in the genomic era. This RFA would focus on pilot studies to determine what sequencing can add to newborn screening for genetic conditions. The RFA would also explore the ethical, legal, and social implications for individuals, parents, and clinicians. The RFA would focus on higher-risk conditions and look to make use of the longitudinal framework of existing newborn screening programs. The funded pilot studies should focus on explicit informed consent for large-scale genome sequencing and look into applicable return of results (RoR). Applicants would be expected to sequence genome-wide or on a large selection of genes, to plan for RoR from a CLIA-certified lab, to deposit sequence data in dbGaP, and to follow subjects longitudinally. These expectations would be combined with programmatic priorities like a varied selection of diseases or traits, ethnically diverse populations, and broad data use to build a portfolio of grants funded by both NHGRI and NICHD. The program anticipates funding 4-5 awards using the U19 mechanism. NHGRI and NICHD would each contribute $2.5 million for 5 years of funding.

In discussion, Council expressed several concerns with this concept clearance. Given that states have a wide variety of laws regarding newborn screening, like excluding retention of data, Council asked if this RFA would exclude researchers in states where deposition is not allowed. This hodgepodge of state laws and advocacy groups also raise ELSI concerns about the public perception of this initiative. Dr. Wise noted that the RFA would be sensitive to state regulations and public perception, and that in states where this is a concern, newborn screening samples would only be used if re-consent was obtained.

Council also asked several questions about the possibility for duplicating efforts given that many of the conditions included in the newborn screening panel are already well-characterized through non-genomic methods. Additionally, newborn screening panels primarily focus on conditions for which there are clinical interventions that can be taken, and this initiative's sequencing is likely to generate many non-actionable results. There was some support from several Council members to modify the RFA to look at actionable conditions or conditions that are not currently tested in newborn screening. Other Council members noted that the RFA seemed to be structured in such a way as to follow-up positives from the newborn screening panel with sequencing. Given these issues and the sensitivity surrounding newborn screening, the ELSI issues would seem to be the most important consideration especially when the sequencing will be used to follow-up with or duplicate results from existing newborn screening panels. Eric Green noted that this is a difficult and somewhat circular discussion and that both NHGRI and NICHD are looking for a way to anticipate the next version of newborn screening while working to address the concerns that are raised when the newborn screening protocol is modified.

Council also had several logistical questions regarding the collection of samples and sequence data. Would the samples be DNA, biospecimens that could be used for future research, or data from newborn autopsies? Dr. Wise noted that while there was some talk about keeping other types of biospecimens the focus would be on DNA.

Dr. Green asked Council for its general view on NHGRI's involvement in this kind of studies. Recognizing the uncertainties about this type of research, how can NHGRI begin to get involved in this research in concert with another Institute? Council strongly agreed that NHGRI should be involved in this important work and raised several issues that merit further discussion. Firstly, it would be helpful to clarify which population will be the focus of this RFA (presumably a population of children where significant benefit to the child is possible). Additionally, it may be worth sequencing children and their parents at the same time or to focus on whole-exome and whole-genome sequencing instead of a panel of 500 genes. Several Council members suggested that the RFA should remain linked to newborn screening so as to avoid simply developing an RFA for children with a suspected medical condition. Council also suggested releasing a broad RFA to attract as many applications as possible and then let the review dictate what gets funded. Dr. Green noted that apart from approving the concept clearance as written and having the review process dictate a portfolio, any other changes to the structure of the RFA would require a working group from Council to engage with experts at NICHD and its Council.

The motion to approve this concept clearance failed to pass. Council will discuss this concept clearance further with the National Institute of Child Health and Human Development.

Development of Genomic Technologies for Non-invasive Sample Collection Methods by Dr. Anastasia Wise

This technology development RFA focuses on developing technologies relevant to analyzing nucleic acids from non-invasive samples. The goal is to encourage research that would refine existing technologies for obtaining data from non-invasive samples. NHGRI expects to fund 3-5 awards for 3 years. This funding, which would come from the SBIR set aside, would total $4.5 million. As a part of the SBIR set aside, this RFA would only be open to commercial grantees.

In discussion, Council asked what sort of samples besides blood spots would be used and what techniques other than genomic analysis could these samples facilitate. Dr. Wise responded that samples could be anything that is not whole blood, for example saliva, and this RFA will be looking for genomic techniques.

The motion to approve this concept clearance was passed.

MEETING REPORT

Genomic Literacy Meeting Report by Vence Bonham

The charge for the Genomic Literacy Meeting in November 201 was to assess the public's current state of genomic literacy and to explore research and programmatic opportunities. Health-related issues were the main focus of the workshop related to genomics. The workshop report recommended integrating patient genomic literacy studies into genomic medicine and ELSI issue, promoting research on best education practices, and studying the use of family health history as clinical tool. Some state departments of public health identified some existing

initiatives related to this effort, but there is a need to study communication of key genomic health messages and how we interpret various concepts that are in the lay literature.

The workshop report also recommended supporting research to define a set of knowledge for the public, conducting a national survey of public understanding, establishing an internet clearing house of tools, and hosting a research meeting of people working on genomic literacy. NHGRI hopes to refocus development of Education and Community Involvement Branch programs to address these issues and work to incorporate these topics into RFAs and PAs.

In discussion, Council asked about funding by the ELSI program for education and how this would interact with and support these efforts. Joy Boyer noted that in 2005, the ELSI received recommendations to discontinue the use of the R25 activity code that was used primarily to develop curricula. Currently, this is mostly incorporated into the research being done by the Clinical Sequencing Exploratory Research centers in patient interaction and education. Council also noted the importance of establishing a clearinghouse so that the community can make use of already completed efforts to address literacy.

COUNCIL Memorandum of Understanding (MOU)

Cheryl Chick presented an overview of the document that details the interaction between Council and NHGRI staff. Council members received a written version of this document. She highlighted the section concerning the Medical Scientist Training Program (MSTP) which has been updated. NHGRI will support up to two total trainees per year, and the grants will be reviewed regularly.

Council unanimously approved the MOU.

CONFIDENTIALITY AND CONFLICT OF INTEREST

Rudy Pozzatti read the Confidentiality and Conflict of Interest policies to Council and asked them to sign the forms provided.

NEW COUNCIL MEMBER

Rudy Pozzatti noted that Anthony Monaco has joined Council but has recently taken a position as President of Tufts University and was therefore unable to join this Council meeting.

REVIEW OF APPLICATIONS

In closed session, the Council reviewed 157 applications, requesting $82,898,497 (total cost). These included: 52 research project grant applications, 19 ELSI applications, 49 applications submitted in response to RFAs, 12 research center grant applications, 2 conference grant applications, 1 career transition award, 1 research scientist development award, 12 SBIR Phase I grant applications, 1 SBIR Phase II application, 1 STTR Phase I applications, 2 individual training grants, and 5 education project awards. A total of 94 applications totaling $46,201,412 were recommended.

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

Date	Rudy Pozzatti, Ph.D. Executive Secretary (Acting) National Advisory Council for Human Genome Research
Date	Eric Green, M.D, Ph.D. Chairman National Advisory Council for Human Genome Research