NATIONAL ADVISORY COUNCIL FOR HUMAN GENOME RESEARCH
SUMMARY OF MEETING[1]
September 12, 2011

The Open Session of the National Advisory Council for Human Genome Research was convened for its sixty-third meeting at 8:30 A.M. on September 12, 2011 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 2:00 P.M. on September 12, 2011. In accordance with the provisions of Public law 92-463, the meeting was closed to the public from 2:00 P.M. on September 12, 2011 until adjournment for the review, discussion, and evaluation of grant applications.

Council members present:
Michael Boehnke
Carlos Bustamante, *ad hoc*
Mark Chee
Sean Eddy, *ad hoc*
Claire Fraser-Liggett
William Gelbart, *ad hoc*
Geoff Ginsburg
Ross Hardison
David Kingsley
David Malkin, *ad hoc*
Howard McLeod
Deirdre Meldrum
Jill Mesirov
Richard Myers, participated via teleconference
Pearl O'Rourke
Pilar Ossorio
Pamela Sankar
David Valle
David Williams
Richard Wilson

Council members absent:
Rex Chisholm

Ex officio members absent:
None

[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
Maggie Bartlett, OD
Basaric, Sanja, DER
Vivien Bonazzi, DER
Vence Bonham, OD
Ebony Bookman, 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
Chris Darby, DER
Camilla Day, DER
Corina Din-Lovinescu, OD
Elise Feingold, DER
Adam Felsenfeld, DER
Tina Gatlin, DER
Jonathan Gitlin, OD
Peter Good, DER
Bettie Graham, DER
Eric Green, OD
Mark Guyer, DER
Linda Hall, DER
Lucia Hindorff, OD
Dennis Huyhn, DER
Heather Junkins, OD
Cristina Kapustij, OD
Caroline Kelly, DER
Rongling Li, OD
Carson Loomis, DER
Chengetai Mahomva, DER
Ian Marpuri, OD
Jean McEwen, DER
Glenn McFadden, DER
Keith McKenney, DER
Ray Messick, DER
Michelle Milligan, DER
Jeannine Mjoseth, DER
Marcia Morris, 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
Aditi Srivastav, DER
Jeff Struewing, DER
Larry Thompson, OD
Elizabeth Thomson, DER
Susan Vasquez, OD
Simona Volpi, DER
Lu Wang, DER
Kris Wetterstrand, OD
Anastasia Wise, OD
Rosann Wise, OD
Jeff Witherly, DER

Others present for all or a portion of the meeting:
Adam Berger, Institute of Medicine
Joann Boughman, American Society of Human Genetics
Rodney Howell, American College of Medial Genetics
Grier Page, Research Triangle Institute
Karen Rothenberg, University of Maryland School of Law
Rhonda Schonberg, National Society of Genetic Counselors
Marc Williams, Intermountain Healthcare

INTRODUCTION OF NEW MEMBERS AND STAFF, LIASONS AND GUESTS

Dr. Guyer introduced new staff members: Caroline Kelly (Program Analyst), Chengetai Mahomva (Program Analyst), Ian Marpuri (Program Analyst), Glenn McFadden (Program Analyst), Aditi Srivastav (Program Analyst), Tamar Roomian (Program Analyst), Derek Scholes (Chief of Policy and Program Analysis branch in the Office of Policy, Communications, and Education), and Cristina Kapustij (NHGRI Policy Fellow). He also introduced liaisons Rhonda Schonberg (National Society of Genetic Counselors), Joann Boughman (American Society of Human Genetics) and guest, Grier Page (Research Triangle Institute).

Dr. Guyer noted that the following Council members are rotating off Council: Claire Fraser-Liggett, Geoffrey Ginsburg, Pilar Ossorio, and David Valle.

APPROVAL OF MINUTES

The minutes from the May 2011 Council meeting were approved.

FUTURE MEETING DATES

The following dates were proposed for future meetings: February 13-14, 2012; May 21-22, 2012; September 10-11, 2012; February 11-12, 2013; May 20-21, 2013; and September 9-10, 2013.

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

Appointment of NHGRI Deputy Director: Mark Guyer, PhD
Dr. Guyer, the Director of the NHGRI Extramural Research Program and the Acting Deputy Director of NHGRI since December 2009 has been appointed as the Deputy Director of NHGRI. He will serve as the Acting Director of the NHGRI Extramural Research Program until further long-term plans for the Division are formulated.

Appointment of NHGRI Policy and Program Analysis Branch Chief: Derek Scholes, PhD
Dr. Scholes recently joined NHGRI as the new Chief of the Policy and Program Analysis Branch within the NHGRI Office of Policy, Communications, and Education. Dr. Scholes received his doctoral training at the University of Liverpool in the UK before coming to Albany, NY for his post-doctoral work at the Wadsworth Center. Dr. Scholes is an alumnus of the NHGRI-ASHG Public Policy Fellowship program during which he spent a few months with the Policy and Program Analysis Branch followed by a year of working in Senator Edward Kennedy's office. Dr. Scholes comes to NHGRI most directly from the American Heart Association, where he advocated for legislation supporting health and biomedical research, including significant contributions to the efforts to see GINA passed and the implementing

regulations drafted, as well as substantial work on the Family Smoking Prevention and Tobacco Control Act.

Appointment of NHGRI Deputy Scientific Director: P. Paul Liu, MD, PhD
Dr. Liu, a tenured senior investigator who joined NIH in 1993 at the inception of the NHGRI Intramural Program, was named the NHGRI Deputy Scientific Director. Dr. Liu leads the Oncogenesis and Development Section within NHGRI's Genetics and Molecular Biology Branch. This appointment is needed because the previous Deputy Scientific Director, Dr. Andy Baxevanis, accepted a new position within the NIH Office of Intramural Research where he will be providing leadership in the area of bioinformatics and information technology for the entire NIH Intramural Program.

Appointment of NIH Intramural Sequencing Director: Jim Mullikin, PhD
Dr. Mullikin, formerly the Acting Director for the NIH Intramural Sequencing Center (NISC) was named the Director of NISC. Dr. Mullikin brings many years of high-level experience to this position.

Elected Fellow by the American Psychological Association: Vivian Ota Wang, PhD
Dr. Ota Wang, Program Director in the NHGRI Extramural Research Program, was elected to Fellow status by the American Psychological Association (APA). Fellow status is an honor bestowed upon APA Members who have shown evidence of unusual and outstanding contributions or performance and requires evidence of national impact on the field of psychology.

Special Advisors to NHGRI Director: Karen Rothenberg, JD, MPA and Marc Williams, MD
Dr. Rothenberg started serving as a full-time Special Advisor to the Director in the summer of 2011 and will continue in this position until the summer of 2012. Dr. Rothenberg is taking a sabbatical from the University of Maryland and will be working on various projects with NHGRI and the Bioethics Department in the NIH Clinical Center this year. More specifically, she will be leading an effort to take a rigorous examination of the ELSI Program and other NHGRI components that will expand into the vision for the Genomics and Society section of the recently published NHGRI Strategic Plan; co-authoring several papers in areas such as regulation of genomic research and the return of research results and incidental findings encountered in whole-genome sequencing studies; and exploring how theatre vignettes can enhance the understanding of ELSI issues in genetics and innovation in science.

Dr. Williams is spending one week per month at NHGRI as a special advisor in the area of genomic medicine. Dr. Williams is the Director of the Intermountain Healthcare Clinical Genetics Institute in Salt Lake City, Utah. Among his various efforts, Dr. Williams is particularly active in working to enhance NHGRI programs related to genomics and electronic health records as well as the development of clinical genomics information systems.

II. GENERAL NIH UPDATES

Appointment of Director of the National Institute of Dental and Craniofacial Research: Martha Somerman, DDS, PhD
Dr. Somerman, previously the dean of the University Of Washington School Of Dentistry, has been named the Director of the National Institute of Dental and Craniofacial Research (NIDCR). She began her duties as NIDCR Director on August 29, 2011. Dr. Somerman's research has focused on defining the key regulators controlling development, maintenance, and regeneration of oral-dental-craniofacial tissues.

Appointment of Acting Director of the National Institute of General Medicine Sciences: Judith Greenberg, PhD
Dr. Greenberg has been named Acting Director of the National Institute of General Medical Sciences (NIGMS) to temporarily replace the departing Director, Dr. Jeremy Berg. Dr. Greenberg is a developmental biologist and has been director of the NIGMS Division of Genetics and Development Biology since 1988. Dr. Greenberg was Acting Director of NIGMS from May 2002 to November 2003.

Departing Director of the National Center for Research Resources: Barbara Alving, MD

Dr. Alving, currently the Director of the National Center for Research Resources (NCRR), will be leaving the NIH on September 30, 2011. She became the Director of NCRR in 2007. She also served as Deputy and Acting Director of the National Heart, Lung, and Blood Institute (NHLBI) and headed the Women's Health Initiative before she came to NCRR.

Incoming Acting Director of the National Center for Research Resources: Louise Ramm, PhD
Dr. Ramm, currently the Deputy Director and the Director of Extramural Activities for NCRR, has agreed to be the Acting Director for NCRR starting October 1, 2011. Dr. Ramm received her PhD in microbiology at the University of Virginia in 1974 and was a faculty member at the Johns Hopkins School of Medicine in the Microbiology Department. She joined NCRR in 1987 as a Health Scientist Administrator in the Biological Models and Materials Program and subsequently became the Director of the Program in 1994.

Departing Director of the NIH Center for Scientific Review: Antonio Scarpa, MD, PhD
Dr. Scarpa, currently the Director of the NIH Center for Scientific Review (CSR) is departing in September 2011. Dr. Scarpa came to CSR in July 2005. Throughout his time in this position, he implemented the trans-NIH Enhancing Peer Review changes, which include the new scoring system. He saw NIH through the review of 40,000 American Recovery and Reinvestment Act applications two years ago.

Incoming Acting Director of the NIH Center for Scientific Review: Richard Nakamura, PhD
Dr. Nakamura will serve as the Acting Director of CSR as of September 18, 2011 while NIH conducts a national search for a new Director. Dr. Nakamura has served at the National Institute of Mental Health (NIMH) as both Scientific Director and Deputy Director of the Institute, and he was also Acting Director of the Institute from 2001 to 2002.

New Director of the NIH center for Information Technology: Andrea Norris, MBA
Ms. Norris will be the new Director of the Center for Information Technology (CIT) and Acting Chief Information Officer of NIH as of October 2, 2011. Ms. Norris comes from the National Science Foundation where she was for ten years. Prior to joining NSF, Ms. Norris was the Deputy Chief Information Officer for Management for the National Aeronautics and Space Administration.

Interim Director for NCI Center for Cancer Genomics: Barbara Wold, PhD
Dr. Wold is the Interim Director of NCI's Center for Cancer Genomics and is on sabbatical from Caltech. Dr. Wold is the Bren Professor of Molecular Biology and the director of the Beckman Institute at Caltech. She is well known to NHGRI, where she has served in numerous advisory roles and as a grantee.

Mourning the loss of Bernadine Healey
Dr. Healy, former Director of NIH, passed away in August, 2011. During her tenure as the first female NIH Director she started the Women's Health Initiative, recruited Dr. Francis Collins to lead NHGRI, and created the NHGRI Intramural Program.

Mourning the loss of Senator Mark Hatfield
Senator Mark Hatfield, visionary supporter of medical research, passed away in August, 2011. The NIH Clinical Research Center now bears his name. As chair of the Senate Committee on Appropriations, he served as a strong and principled advocate for the needs of those who are less fortunate. He also consistently defended the importance of NIH-funded research and its importance to our society.

***Science* Articles on Race & Ethnicity Influence on NIH Awards**
NIH has commissioned several studies to examine and improve the diversity of the scientific workforce. One such study by Dr. Raynard Kington was recently published in *Science* and analyzed the probability of securing first-time NIH R01 funding by race/ethnicity. Even after controlling for factors that influence the likelihood of success, such as NIH training, research experience, and institution, Black applicants were still 10 percentage points less likely than White applicants to receive a Type 1 R01 award. In the same issue of *Science*, Drs. Tabak and Collins provide a perspective piece that outlines NIH's commitment to a diverse biomedical workforce and future plans to address this issue.

Revised NIH Regulations of Financial Conflict of Interest

The U.S. Department of Health and Human Services has issued a final rule that amends the Public Health Service (PHS) regulations on Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought and Responsible Prospective Contractors. This is a revision of the 1995 guidelines. The major changes to the previous policies are:

- Lowering the monetary threshold at which significant financial interests (SFIs) require disclosure, generally from $10,000 to $5,000.
- Requiring investigators to disclose to their institutions all of their significant financial interests related to their institutional responsibilities.
- Requiring institutions to report to NIH additional information on identified financial conflicts of interest and how they are being managed.
- Requiring institutions to make certain information accessible to the public concerning identified Significant Financial Interests held by senior/key personnel.
- Requiring investigators to complete training related to the regulations and their institution's financial conflict of interest policy.

Dr. Green encouraged Council members to become familiar with this policy as it will be implemented in August 2012.

NIH's Proposed National Center for Advancing Translational Sciences

The National Center for Advancing Translational Sciences (NCATS) aims to advance the discipline of translational science and catalyze the development and testing of novel diagnostics and therapeutics across a wide range of human diseases and conditions. The blueprint for the proposed NCATS was recently published by Dr. Collins in *Science Translational Medicine*. NCATS was supposed to be created at the beginning of FY2012; however, this plan will most likely be delayed due to budget issues. The search committee to identify an NCATS Director is active; any nominations should be sent to Dr. Green. The implementation of this center has several implications for NHGRI, one of them being that the National Center for Translational Therapeutics (NCTT) will depart en bloc to NCATS and take over 100 NHGRI employees, including its Scientific Director, Chris Austin.

FY2012 Appropriations Update

The Fiscal Year 2011 operating budget was signed by the President in April and funds the NIH at $30.9 billion and the NHGRI at $511 million. This is a 1% reduction compared to last year's budget and the first reduction NIH has seen in many years. The President's FY2012 budget request to Congress for NIH was $32 billion, including $525 million for NHGRI. This is a 2.4% and 1.7% increase for NIH and NHGRI, respectively, compared to the current year, but neither House nor Senate has passed the Labor-HHS bill that funds the NIH yet. At this point, the funding levels for NIH and NHGRI are still unknown and it is likely that a Continuing Resolution will be used to keep the government functioning until a final agreement is reached for the rest of the year. Predictions about NIH funding for next year are quite varied. The best case scenario is assuming a flat budget, the most realistic is a 2% decrease, and worst case would be a 5% decrease. IC Directors are being asked to prepare various scenarios for 2013 that include cuts of 5% and 10%.

A major reason why Congress has not yet completed its Appropriations work is because of the strong disagreements among members regarding the role and size of government programs. This most recently manifested itself as a debate over the size of the government's debt. The debt deal comes in two parts. The first is a cap on the total funds that Congress can appropriate for each year going into the next decade. The Congressional Budget Office estimates that these caps will reduce the federal deficit by $917 billion. This part of the deal only sets a cap on total spending across the government, so there is no reason to assume that all agencies will be equally impacted. Therefore, it is difficult to predict how NIH may fare compared with other agencies throughout the government.

Part two of the Deal established the Joint Select Committee on Deficit Reduction, more commonly referred to as the Super Committee, to identify additional ways to reduce the federal deficit. By November 23, 2011, they are charged with crafting a bill to reduce the deficit by at least $1.2 trillion by 2021, and ideally to identify up to $1.5 trillion in reductions. Each Chamber of Congress is then required, through a simple up-or-down vote, to approve the Super Committee proposal by December 23. The Committee proposal may include reductions in spending, such as further reductions to agency funding or entitlement

programs, as well as ways to increase revenues through changes in the tax code. If the Super Committee fails to agree upon a proposal, or if Congress does not pass their proposal by the end of the year, this will trigger a broad cut to federal agencies in 2013 equal to the $1.2 trillion they were supposed to identify.

Senator Ben Cardin visits NIH
On August 31, 2011, Senator Ben Cardin held a town hall meeting with NIH employees and a group of NIH IC Directors. The senator discussed the state of the economy, the current Federal budget, and its impact on Federal workers. Senator Cardin is a strong NIH supporter and promised a good fight to preserve the NIH budget, but he also stressed the need to be realistic about the likely difficult times over the next 2-5 years.

III. GENOMICS UPDATES

Awards, Recognitions and Prizes to NHGRI-associated Scientists

- **Dr. Ron Davis** was awarded the **2011 Gruber Genetics Prize** from **The Peter and Patricia Gruber Foundation,** which is awarded for pioneering work in biotechnologies that advance the fields of molecular genetics and genomics. Dr. Davis, who has been director of the Stanford Genome Technology Center since 1994, will receive the $500,000 award for his efforts in developing DNA mapping methods, for his studies of ways to sequence genomic variants in humans and other animals, for his contribution in developing the first microarray technologies, and for the work his lab has done in sequencing yeast chromosomes, part of the E. Coli genome, and sequencing of other genomes.
- **Dr. David Haussler** was awarded the **2011 Weldon Memorial Prize** from the **University of Oxford**, which is awarded for contributions to the development of mathematical or statistical methods to be applied to problems in biology. Dr. Haussler is a professor of biomolecular engineering at the University of California, Santa Cruz. He is director of the California Institute for Qualitative Biosciences, and his team's work has focused on using bioinformatics to understand the human genome, for example by analyzing data from the Cancer Genome Atlas, developing the Cancer Genomics Browser, and by founding the Genome 10K project.
- **Dr. Yemi Adesokan** has been recognized by **MIT's Technology Review** magazine as an **Innovator under 35 Honoree for 2011**. The TR35 recognizes the world's top innovators under the age of 35, spanning energy, medicine, computing, communications, nanotechnology, and other emerging fields. He has been honored for his work in the application of next generation sequencing to clinical diagnostics. He founded a company called Pathogenica that aims to develop sequencing technologies to diagnose infectious disease. He is an alumnus of the Diversity Action Plan-supported SMART summer undergraduate research program at the Baylor College of Medicine Genome Sequencing Center.

Dr. Eric Green travels to India on a 'Genomics Tour'
In August, 2011, Dr. Green travelled to India to tour several genomics facilities on behalf of NHGRI. The initial purpose of the trip was to be the Keynote Speaker at a Founder's Day Celebration commemorating the first anniversary of establishing the National Institute for Biomedical Genomics. Dr. Green also toured several other genomics research facilities in Bangalore, Kolkata, and Dehli. The most notable observations he made were: 1) India is making a significant investment in research infrastructure, especially in genomics; 2) Indian researchers are accessing cutting-edge genomic technologies; 3) the research funding situation is improving quickly and does not seem to be the rate-limiting factor for Indian researchers; and 4) India is suffering from the same computational and bioinformatics bottleneck that we have in the U.S., despite training many students in computer science, the majority of which to into the private sector.

Genomics in the News

- The sequence and analysis of the potato genome was recently published. The potato is the world's third most important food crop. Analysis of the genome sequence data has revealed that the potato genome contains at least 39,000 protein coding genes.
- Other notable organisms sequenced recently were the Tasmanian Devil, the branching coral *Acropora digitifera,* and a rabbit-sized species of kangaroo.

- A company called Medicinal Genomics announced in August that it has a draft assembly of the marijuana, *Cannabis sativa.* Company scientists say they were convinced to pursue the research after seeing papers published in academic journals on the plant's tumor-shrinking effects in rats.
- CNN reported that a New Hampshire apartment complex is mandating that residents submit pet DNA samples. The PooPrints program matches samples of unclaimed dog waste to DNA collected through pets' mandatory mouth swabs in the hope of imposing greater responsibility among pet owners.

IV. NHGRI EXTRAMURAL PROGRAM

Large-Scale Sequencing Program Renewal
The large-scale sequencing program is undergoing a renewal. The program represents just over one third of the NHGRI Extramural Program budget. As part of this renewal, NHGRI issued 4 RFAs for: 1) Genome Sequencing & Analysis Centers, 2) Mendelian Disorders Genome Centers, 3) Clinical Sequencing Exploratory Research, and 4) Informatics Tools for High-Throughput Sequence Data Analysis. Dr. Adam Felsenfeld will give a more detailed presentation on this program later in the meeting.

Large-Scale Sequencing Program: Comparative Genomics
- Using the draft genome sequence, researchers at the Baylor College of Medicine published a genome-wide SNP resource for Indian-origin rhesus monkeys, one of the most widely studied nonhuman primate model in biomedical research, and identified many potentially harmful non-synonymous coding SNPs.
- The Broad Institute recently completed analyzing the genome of the North American green anole. They found that the genome contains 17,500 protein-coding genes, 4,000 of which are also found in human. In addition, around 30% of the genome is comprised of mobile elements and contains 12 microchromosomes. The group also identified the lizard's sex chromosomes, which appear to be XX and XY; the X chromosome is one of the lizard's microchromosomes.

Large-Scale Sequencing Program: Mendelian Sequencing
Major projects are now underway for four diseases: diabetes/metabolic syndrome, autism, lipid levels and non-TCGA tumor sequencing.

The Cancer Genome Atlas
After receiving funding from the American Recovery and Reinvestment Act two years ago, The Cancer Genome Atlas (TCGA) was named an NIH Signature Project and announced its intent to initiate 20 new tumor projects following the pilot efforts on glioblastoma and ovarian cancer. TCGA achieved its goal of accruing and characterizing 3000 samples in two years, and accrual is now completed for glioblastoma, ovarian, colorectal, and renal clear cell carcinoma. TCGA published the findings from the ovarian carcinoma project in *Nature*. The study included analyses of copy number, gene expression, and promoter methylation on 489 high grade carcinomas plus exome sequence analysis of 316 of the specimens. *Time Magazine* also features a story titled Cracking Cancer's Code in June 2011, in which TCGA Program Director, Dr. Brad Ozenberger was quoted.

1000 Genomes Project
The first phase of 1000 Genomes has produced low-coverage data for 1094 samples, exome data for 1128 samples, including 39 million SNPs, 100,000 indels, 84,000 Structural Variants. The integrated data set is to be released in October 2011. The Phase 2 sequence data including low-coverage and exome data for 1721 samples is set to be complete this fall. The next 1000 Genomes meeting will be on October 10-11, 2011 before the ICHG in Montréal, Canada. A 1000 Genomes data tutorial will also be held during ICHG.

Possible NIH-Wide Inventory of Genome Sequencing Projects
Stemming from previous discussions about the desire to develop a trans-NIH inventory of ongoing genome-sequencing projects, Dr. Teri Manolio was asked to assemble a trans-NIH committee to perform an initial analysis of ongoing and planned genome-sequencing projects. Preliminary analyses revealed several interesting figures and there are several upcoming meetings and workshops to move this effort

forward. NHGRI was asked to be the lead IC for such an effort, thus there will be more updates on this topic in the future.

DNA Sequencing Technology Development
In NHGRI's program to reduce the cost and increase the rate and quality of DNA sequencing, 9 awards were made for applications discussed at May Council. The commitment over the life of these grants is $14.4 million. These projects will explore a diverse set of approaches outlined on the slide presented by Dr. Green.

Lab to Marketplace: Tools for Biomedical and Behavioral Research
NIH has re-issued a Program Announcement for Small Business (SBIR) grant mechanisms (R43/R44) in the area of developing tools for biomedical and behavioral research. This is an NIH-wide program through which NHGRI could fund relevant applications. The Program Announcement encourages the translation of technologies for biomedical or behavioral research from academic and other non-small business research sectors to the marketplace. Applications are due in early November 2011.

ENCODE and modENCODE
NHGRI is planning a modENCODE symposium to be held on the NIH campus from June 20-21, 2012. The goal is to broaden community understanding of model organisms and showcase the contributions of the modENCODE Consortium. Both the ENCODE and modENCODE consortia are currently in the writing phases for integrated analysis papers. ENCODE will coordinate publications to feature a main integrative paper, multiple high-profile companion papers, and many companion papers. modENCODE is working to integrate worm and fly data and if possible bring in the human ENCODE data. A technology development FOA was released after May Council and the applications were received in early August. Applications will receive peer review in the fall and Council review during the February 2012 Council.

Centers of Excellence in Genomic Science
One new award was made in FY11 to Dr. Aviv Regev from the Broad Institute. Dr. Regev will establish a Center for Cell Circuits and will develop reagents, technologies, algorithms, protocols, and strategies for reconstructing molecular circuits. With the addition of this new CEGS, NHGRI currently has 8 active awards in the program and 2 centers that are phasing out of the program after their 10 years of support.

Knockout Mouse Project (KOMP)/KOMP2
KOMP is winding down at the end of September. As of August 1, 8700 knockouts had been produced. KOMP2 is an effort to phenotype knockout strains produced by KOMP and awards for this program will be made at the end of FY11. The overall funding for the program is $111M over 5 years. There are plans to fund 3 Production centers, 3 Phenotyping Centers and 1 Data Coordinating Center. The goal is to produce and phenotype 2500 strains. There will be a major meeting on September 28-29, 2011 that will reflect the finale of KOMP, the kickoff of KOMP2, and the launching of the International Mouse Phenotyping Consortium.

New ELSI Program Announcement
Three new ELSI program announcements based on the new Strategic Plan were released on July 18, 2011. The R01 is designed for medium to large multi-disciplinary studies. The R03 is targeted to small, self-contained analytical or conceptual projects that can be done in two years for up to $50,000 per year. The R21 is aimed at cutting edge exploratory or developmental grants that are taking on new or rapidly evolving ethical issues or the implications of emerging or anticipated scientific/technological developments. The R21 can request up to two years and a total of $275,000 in direct costs. The announcements focus on the issues raised in the Strategic Plan's Genomics & Society section, and include examples of possible high priority research topics. A number of other NIH IC's are participating, including: NCI, NIA, NICHD, NIDCD, NIEHS and NINDS.

Challenges in Research Ethics and Policy: Perspectives on Data Sharing
In July, NHGRI held a meeting to discuss data sharing as it relates to research ethics and policy. The meeting was organized by the eMERGE Consent and Community Consultation Work Group, and its goal was to explore how social implications research, in partnership with genomic research studies like

eMERGE, can inform the development and implementation of research policy. The meeting focused on the impact of data sharing policies on researchers, research participants, and community partners. The meeting extensively explored how data on these issues can be used to inform the development of research policy. In addition to researchers, bioinformatics, and policy experts and community advisors, meeting participants included NIH, OHRP, CDC, VA, FDA, and IOM program officials, group health, pharmaceutical and biobank representatives, and members of professional societies and patient advocacy groups. A journal article summarizing the workshop discussions is planned.

Upcoming Extramural Meetings:

- Centers for Excellence in ELSI Research Program Meeting: October 3-5, 2011
- Centers of Excellence in Genomic Science and Diversity Action Plan Program Meeting: October 18-21, 2011
- ELSI Session at the International Congress of Human Genetics: October 13, 2011
- Approaches for Characterizing Genetic Variants for Clinical Use: December 1-2, 2011

V. NIH COMMON FUND PROGRAMS

Molecular Libraries Program

The Molecular Libraries Program (MLP) began the fourth year of its production phase in June 2011. MLP met its goals for year 3, which included having 20 or more new projects per center; 15 or more active chemistry projects per center, and 10-12 approved probes by peer review per year per comprehensive center. To date, MLP has accepted 490 high-throughput screening assays, has completed over 180 chemistry projects, and has produced 229 small-molecule probes. The future of MLP will focus on qualitative milestones including higher-quality probes and better-characterized probes. Dr. Green presented a pie chart of the areas being served by the MLP effort, which showed a diverse and balanced portfolio of projects assigned in the MLP, including probes for cancer, infectious diseases, diabetes, and neurological disorders, among several other areas. Two publications were highlighted for the MLP program. One was about the first IND filing on an MLP probe by Scripps and the other involved NCTT identifying 32 highly active anti-malarial compounds and genetic loci associated with differential responses to those drugs.

Human Microbiome Project

To date, 108 publications in PubMed cite Human Microbiome Project (HMP) support. Two major papers from the HMP Consortium are nearing completion with plans for submission in fall, 2011.

Genotype-Tissue Expression

The pilot phase of the Genotype-Tissue Expression (GTEx) Program is now underway with 2 dozen post-mortem donors already enrolled. A program update on GTEx will be given later in the meeting.

Library of Integrated Network-based Cellular Signatures

The Library of Integrated Network-based Cellular Signatures (LINCS) program will hold a Fall Consortia Meeting on October 27 to 28, 2011. The reviews for U01 applicants in computational tool and advanced technology development were held in the summer. Program Staff expect to fund 8 awards from the applicant pool at NHLBI and NCI's September Councils. The LINCS Production Centers have created public websites to inform the community about released data through its data browser, discuss current experimental components of the program, and update users on new developments in the LINCS program.

Protein Capture Reagents Program

Applications for the production and technology development components of the Protein Capture Regents Program will be discussed later on in the Council agenda. NIH Protein Capture Staff will be coordinating a meeting with all newly funded grantees and current members of the program in the winter of 2011 in the DC/Bethesda area.

Human Heredity and Health in Africa

The June 2011 issue of *Nature* features an article about science in Africa. The Human Heredity and Health in Africa (H3Africa) Program is funded by the NIH Common Fund in partnership with the Wellcome

Trust. NHGRI is the lead IC for this program; a program update for H3Africa will be given later in the meeting.

New Common Fund Initiatives
In May 2011, the NIH held an Innovation Brainstorm Meeting to generate ideas for new Common Fund projects. By design, Common Fund projects scale back over time allowing new projects to be launched. For this meeting, NIH IC directors nominated junior investigators to participate; attendees included Goncalo Abecasis, Brad Bernstein, Manolis Kellis, and Brad Malin. Among the topics discussed at this meeting was the possibility of a new microbiome-oriented program. In addition to the ideas proposed at the meeting, each IC was invited to submit up to 2 new Common Fund ideas for further consideration. NHGRI's 2 proposals are in the area of disruptive proteomic technologies and molecular phenotype for genome function and disease. The proposals are now in a comment period for 2 more days. Council members can look at the proposals and comment on them online.

VI. NHGRI OFFICE OF THE DIRECTOR

Office of Population Genomics – eMERGE Network Recent Publications
The Electronic Medical Records and Genomics (eMERGE) network completed its first phase and entered its second phase with 7 awards: 5 to the phase I sites, 2 to new investigative sites, and 1 to a Coordinating Center. The goals of eMERGE II are to demonstrate that patients' genetic information linked to disease or clinical manifestations in their electronic medical records can be used to improve their care. Because eMERGE II has no pediatric sites, an RFA to solicit pediatric sites was released in July with applications due today.

NHGRI Catalog of Published Genome-wide Association Studies (GWAS)
As of the first quarter of 2011, the NHGRI GWAS Catalog contained 862 publications with 1,319 associations at p<=5x10-8 for 221 traits. The catalog reached 1000 publications in September 2011.

PhenX Program
The PhenX Toolkit design paper was published in the August 2011 issue of *American Journal of Epidemiology*. PhenX also published a paper in the May 2011 issue of *American Journal of Preventive Medicine* on adoption of standard measures in biomedical research. NIDA is providing $730,000 for a one-year project to expand substance use measures in the Toolkit and will convene three working groups to identify additional substance use and addiction measures to promote data harmonization within the NIDA and NIAAA grantee community. The PhenX administrative supplement program, in which investigators are adding a variety of PhenX measures to existing studies, had the kick-off meeting earlier this month. This supplement program will help evaluate the overall usefulness of the PhenX Toolkit and is expected to be completed in the fall of 2012.

NHGRI INTRAMURAL PROGRAM

Blue Ribbon Panel Review of NHGRI Intramural Research Program
Dr. Green is arranging a Blue Ribbon Panel Review for the NHGRI Intramural Research Program in order to provide a high-level assessment of the Intramural Program and to augment quadrennial review of individual investigators. Dr. Michael Gottesman will oversee the review along with Dr. Green. The review panel includes the following investigators: David Page (Chair), Rick Myers, Bruce Korf, Wylie Burke, Nancy Cox, Bob Waterston, and Huda Zoghbi, The review is a 9 month process scheduled to take place between now and next summer. A report and presentation on the review will be brought to Council.

NHGRI Intramural Research Highlights
- NHGRI scientists led by **Dr. Les Biesecker** have found the gene mutation that causes Proteus syndrome. The study describing the *AKT1* gene mutation was published in the online edition of *The New England Journal of Medicine.*
- **Dr. Charles Venditti** and a team from NHGRI's Genetics and Molecular Biology Branch and the Genetic Disease Research Branch published a study in the August 14 issue of *Nature Genetics* in

which whole-exome sequencing led to finding the gene for combined malonic and methylmalonic aciduria.

- NHGRI researchers led by **Dr. Meral Gunay-Aygun** from the Medical Genetics Branch published a study in the July 17 issue of *Nature Genetics* finding that mutations in *NBEAL2* cause the bleeding disorder known as Gray Platelet Syndrome.
- Two studies from the Genome Technology Branch, led by **Dr. Kan Cao**, provided new insights about Hutchinson-Gilford progeria; one was published in the June 29 early online issue of *Science Translational Medicine* and another published on June 13 in the *Journal of Clinical Investigation*.
- A collaboration between researchers from NHGRI and Oxford University, led by **Dr. Grant Belgard** published a study in *Neuron* on August 25 providing a gene expression map of the mouse cerebral cortex.

PROGRAM UPDATES

Update on the NHGRI Office of Policy, Communications, and Education by Laura Lyman Rodriguez

Dr. Laura L. Rodriguez, Director of Office of Policy, Communications, and Education (OPCE), presented an overview of the OPCE structure and activities. OPCE is situated within the NHGRI Office of the Director, but its activities reach across all parts of the institute, including the Intramural and Extramural Programs. The OPCE mission is to promote the integration and utilization of genomic knowledge to advance human health and society. With this mission in mind, OPCE aims to disseminate the knowledge of NHGRI research outside of the institute. They accomplish this aim through their interactions and relationships with various groups, including healthcare practitioners, researchers, government bodies, professional organizations, advocacy groups, teachers, students, the general public, and the media.

OPCE is composed of 4 branches: Policy and Program Analysis, Genomics Healthcare, Education and Community Involvement, and Communications and Public Liaison. The Policy and Program Analysis Branch is lead by Dr. Derek Scholes. This group represents NHGRI to the NIH, HHS, Congress, and other government bodies. They track appropriations and relevant legislations, for example, they were involved in the passing of GINA, and they build relationships with Congress people. In addition, they are involved with current events related to policy and biology, such as the recent court ruling on NIH stem cell research funding, the Appeals Court rule on Myriad Gene Patents for the BRCA1/2 genes, and the updates to the Common Rule that governs human subjects research.

The Genomic Healthcare Branch, staffed by Greg Feero and Jean Jenkins, was created in 2007 with the mission to improve the ability of all providers to apply advances in genomics and improve the outcomes of patient care. Most recently, they developed the *New England Journal of Medicine* Genomic Science Medicine Series and wrote a commentary in the *Journal of American Medicine Association* 2011 Medical Education Issue. They have also developed educational resources, such as the Family Health History project in partnership with the Surgeon General and NCI, and the Genetics and Genomics Competency Center for Education website. In the fall, they are planning a Pharmacist Education in the Era of Genomic Medicine meeting.

The Education and Community Involvement Branch deals with K-12 and undergraduate science education and community engagement. This group is planning the Genomic Opportunities for Studying Sickle Cell Disease workshop on December 8-9, 2011, the 2011 NHGRI Summer Workshop in Genomics, and an NHGRI Genomics Literacy Workshop. They oversee the activities on National DNA Day and created the NHGRI talking glossary, which is now available as an iPhone application. This branch is also involved with various communities, such as the National Congress of American Indians, and has translated family history tools into different languages.

The Communications and Public liaison Branch is tasked with providing the public face of NHGRI and interacting with the media and the general public. They write press releases and articles for the NHGRI website, maintain a presence on social media sites such as Facebook and Twitter, and post NHGRI

videos on YouTube. It was also noted that this group is now using a new green screen room at NHGRI to film high-quality videos.

Council members had several questions after Dr. Rodriguez's presentation. The first asked what will happen to activities such as eGAPP if CDC genomic efforts are being cut back. Dr. Rodriguez's noted that there is an upcoming meeting that will discuss the future of public health genomics and she will know more information shortly. Council also asked if OPCE encourages individual investigators to respond in public comment periods for items such as the Advanced Notice of Proposed Rule Making (ANPRM) for the Common Rule. Dr. Rodriguez noted that OPCE has created several committees and meetings to inform people about the proposed changes, but has not reached out to specific individuals and asked them to comment. In addition, it was noted that OPCE has not commented publicly on the ANPRM, but did comment on the draft before it was publicized. Lastly, Council members voiced concerns that videos created in the new green screen room should not use misleading backdrops. Dr. Larry Thompson, Chief of the Communications and Public Liaison branch, noted that although many news channels use the green screen on a regular basis, he will keep this concern in mind as they move forward.

Human Heredity and Health in Africa (H3Africa) by Jane Peterson

Dr. Jane Peterson presented an overview of the Human Heredity and Health in Africa (H3Africa) Program. H3Africa is a Common Fund project being funded in partnership with the Wellcome Trust (WT). The project grew out of NHGRI interest generated by Dr. Charles Rotimi and Dr. Francis Collins, who recognized the need for a genomic health initiative in Africa. Africa suffers from a disproportionate burden of communicable diseases and an emerging prevalence of non-communicable diseases. Despite this knowledge, HIV/AIDS, tuberculosis, and malaria dominate research on the continent. African scientists have limited collaborations and many successful African researchers leave the continent. Africa also presents new research opportunities; African populations have the most genetic diversity, the continent is a unique place to study gene-environment interactions, and data on Africans are needed to archive better ancestral representation in genomic studies.

H3Africa is intended to encourage a contemporary research approach by African investigators to the study of the genomic and environmental determinants of common diseases, with the goal of improving the health of African populations. The project has 3 goals: 1) to increase the number of African scientists that are internationally competitive in genomics and population-based research, 2) to establish collaborative networks of African investigators pursuing genomics-based, disease-oriented projects, and 3) to create and expand the infrastructure for genomics research, particularly bioinformatics and biorepositories.

H3Africa had its first working group meeting in 2010, followed by a press release in 2010, and a White Paper published in 2011. To date, there have been several site visits by NHGRI Staff to African labs in Nigeria, Tanzania, Mali, and South Africa. Several of these labs receive funding from U.S. institutions and are well equipped, but the conditions are still poor compared to American labs.

H3Africa is structured in 4 initiatives: Collaborative Centers, Bioinformatics Networks, Biorepositories, and Societal Implications Research (SIR). All awards will be made directly to African institutes and Principal Investigators and all funded sites must deposit samples in the H3Africa Biorepository, use the H3Africa Bioinformatics Network, include a training component, and may include societal implications research. The biorepositories will start as a 2 year feasibility study and will be funded as a full-scale biorepositories in FY14 and FY15. There is a strong desire to have African scientists retain ownership of the samples in the biorepository and to build biorepositories that are geographically diverse. The SIR component is not finalized yet, thus no RFAs have been written. However, there will be an SIR meeting in Nigeria in 2011 to discuss the needs for this type of research.

The timeline for upcoming H3Africa activities is as follows:

- August 2011: FOAs Released
- September 2011: Applicant Information Session, Kenya
- November 2011: Ethics & Genomics Research Conference, Nigeria

- December 2011: Applications due
- March 2012: Application review
- July 2012: Awards funded for the first 3 initiatives
- 2012: Societal Implications Research FOAs released

Council discussed several topics related to this presentation. It was first noted that ASHG is bringing several African scientists to the ICHG meeting in Montreal this year where they will have a chance to discuss this initiative with collaborators. Council members asked who is attending the SIR meeting in Nigeria and what efforts are being made to include a variety of scientists. Dr. Peterson replied that the meeting is being broadly advertised and is open to anyone in Africa who is interested. The Fogarty Bioethics Training initiatives have already funded some people to attend this meeting. Any suggestions for additional invitees should be sent to Dr. Peterson. Council also asked how the availability of these grants was publicized, and how NHGRI plans to communicate with less-established investigators in Africa. NHGRI Staff replied that all NIH ICs and the WT used their email lists to contact investigators in Africa. In addition, several meetings have been planned in Africa to help investigators understand the funding process, and 2 websites have been established as resources: the H3Africa website and a social networking site on Nature.com. Lastly, NHGRI hopes that the collaborative nature of the project will encourage more established institutions to partner up with less-known institutions in Africa.

Council members asked if US-based investigators who want to work in Africa will be funded under H3Africa. Noting that the budget for this program is fairly limited with $8 million for the first year, and $10 per year in the later years, Dr. Peterson explained that grants will only be awarded to African institutions and Principal Investigators; however, these PIs are not precluded from subcontracting back to scientists in the US. Council members voiced concerns that Africans no longer living in Africa might take the funds to other countries. However, it was noted that the grant review process, in which the NHGRI Council will partake, will keep this concern in mind when awarding funds.

Lastly, Council members noted that there has been concern about the sustainability of this project and sending money outside of the US. NHGRI hopes that the Common Fund money will be used to develop a lasting infrastructure and that other ICs will eventually fund specific projects in the future. In addition, it was noted that the WT has committed $12 million over 3 to 5 years. Both NIH and WT will coordinate funding decisions.

Genotype-Tissue Expression (GTEx) Project Update by Jeff Struewing

Dr. Jeff Struewing presented an update on the Genotype-Tissue Expression (GTEx) Project. GTEx is funded by the NIH Common Fund. The project's co-chairs are Drs. Eric Green and Tom Insel. The lead institutes are NHGRI, NIMH, NCI, and NHLBI, and there is also active participation from many other ICs.

The goal of GTEx is to establish a resource database and tissue bank in which to study the relationship between genetic variation and gene expression in reference, non-diseased human samples. The goal is to collect 1000 post-mortem donors with multiple tissues from each donor and measure gene expression in those tissues. Currently, the project is funded as a 2 year pilot project that has 3 specific aims: 1) to enroll 160 post-mortem donors that are unselected for disease status, 2) to obtain high-quality RNA from multiple tissues (30-50 per donor) plus a parallel series of surgery donors (4-5 tissues per donor), and 3) to measure gene expression and high-density genotypes and identify *cis* expression quantitative trait loci (eQTLs).

Dr. Struewing presented the GTEx data flow chart and a schematic diagram for the pilot project. He noted that the eligibility criteria for GTEx are fairly broad; participants are only restricted by age, BMI, and several diseases such as cancer, infectious diseases, and HIV, and there is no restriction on ethnicity. A blood sample will be drawn from each donor that will be used to establish lymphoblastoid cell lines. This blood sample will also undergo genotyping using the Illumina 5M SNP Chip. A skin sample will be obtained from each donor for gene expression analysis, for creating fibroblast cell lines, and for potential iPS cell line establishment. Other peripheral tissues will also be collected along with brain tissues when possible. The goal is to create a community resource with these tissues, although the process for

distributing these tissues has not yet been established. Lastly, one aliquot of the tissue samples will also be fixed for a histopathology review. Although Formalin is the typical tissue preserving component, preliminary experiments in GTEx found that PAXgene produces clearer images of the tissues and is now the only morphologic fixative being used.

GTEx made its first awards at the end of last summer. The Broad Institute serves as the Laboratory, Data Analysis, and Coordinating Center, NCI is coordinating the tissue collection through The Cancer Human Biobank, and 3 awards were made to 3 biospecimen source sites that will obtain the organs and surgery samples. They are the National Disease Research Interchange, Roswell Park Cancer Institute, and Science Care, Inc. Several R01s have also been awarded to a strong group of investigators for statistical methods development. Lastly, GTEx is funding an ELSI sub-study that aims to understand the factors affecting consent to tissue donation for biobanking purposes.

Donor enrollment has gone up since December 2010 and is currently projected to reach 160 donors by September 2012. Dr. Struewing presented figures on the quality of the RNA data for the first 26 donors; the majority of donors have fairly high molecular quality. Most organs collected so far also have high quality RNA. Preliminary gene expression analyses have been completed on several samples from the first 3 donors. Expression analyses showed a good correlation among different methods of preservation and cDNA library preps for the same organs. In addition, preliminary RNA-Sequence analyses look promising for PAXgene preserved tissues. GTEx plans to made quarterly releases to dbGaP with individually identifiable data in controlled access and some data publicly available.

Council members had several questions after the presentation about the tissue samples. Dr. Struewing clarified that there are no pre-deceased tissues from post-mortem donors. This is because most of the organ donors are on life support in the ICU and it is already difficult to receive consent for post-mortem tissue donation, so they did not ask for samples before death. The surgery tissues, however, are not post-mortem. Donors who have been on life support for more than one day usually do not provide brain samples. GTEx is currently not collecting any samples from donors' family members, but they could consider this possibility in the future.

MEETING REPORTS

Genomic Medicine Institutes Colloquium meeting report by Teri Manolio and Geoffrey Ginsburg

Drs. Teri Manolio and Geoff Ginsburg reported on The Genomic Medicine Institutes Colloquium that occurred on June 29, 2011 in Chicago. Drs. Manolio and Ginsburg co-chaired the meeting, which included 40 participants from dozens of universities and institutions nationwide. There were several reasons for holding this meeting, one of which is that the NHGRI Strategic Plan is looking towards genomic medicine, but there are few examples of genomic medicine in clinical applications. The tasks at the meeting were to: 1) identify areas of active translational research across the various groups and determine potential commonalities, 2) define demonstration projects in genomic translation ready for investigation now or in the near future and what is needed to actualize them, and 3) stimulate the development of a consortium for conducting genomic translational research.

As part of pre-work for the meeting, participants were asked to fill out a template about the type of translational work with which their institutions are involved. This was done in order to catalog ongoing genomic medicine efforts. Some examples of current projects included applying whole genome sequencing to undiagnosed genetic diseases, pharmacogenetic work on statins and anti-clotting agents, incorporating genetic risk assessment into cardiac diseases, whole exome sequencing for Mendelian disorders, and integrating whole-genome sequencing into electronic medical records.

Participants were also asked to identify barriers that prevent their institutions from adopting genomics into medicine. The identified barriers were:

- Lack of evidence for benefit/value
- Institution and physician acceptance
- Education of patients, physicians, public

- Availability of testing, licensure, CLIA certification
- EMR integration of genomic results, custom reporting tools and decision support software
- Optimizing turnaround time
- Need for genetic counseling
- Consent
- Improving information for at-risk family members
- Sample availability and biobanking
- Recruitment for genetic studies
- Logistics of follow-up, loss to follow-up
- Research funding and reimbursement
- How do we know a genetic signal applies to our population?

One of the main outcomes of the meeting was an appreciation and understanding of ongoing genomic medicine efforts within the US and internationally. The meeting participants identified the need to establish writing groups to develop perspective papers and best practices, and planning groups for workshops and conferences, in addition to the establishment of a consortium for collaborative studies. The latter suggestion was made because there is a significant overlap among studies. For example, there are over 20 genomic medicine centers at varying stages of implementation supported through multiple NIH and institutional mechanisms. These similar and overlapping efforts could benefit from collaboration, or periodic interactions and consensus building.

As NHGRI looks towards the implementation of genomic medicine, a proposed collaborative Genomic Medicine Effort could identify research directors and priorities, promote collaboration among existing groups, stimulate investigator-initiated efforts and issue funding solicitations as needed, learn more about genomic medicine centers at NHGRI/NIH by visiting those centers, and establish a Genomic Medicine Working Group as a subgroup of Council where members could rotate periodically and report back to Council regularly. The Genomic Medicine Working Group could be tasked to identify topics for subsequent meetings of genomic medicine groups and plan those meetings, identify topics for separate working groups or workshops, monitor the production of white papers and assist production of papers as needed, review progress in specific areas and readiness for moving into working subgroups, review progress overall in genomic medicine implementation and identify gaps, and identify related efforts such as ClinVar, eMERGE, or the Clinical Sequencing Exploratory program, and integrate them as appropriate.

Several current efforts were identified that could benefit from the infrastructure that a Genomic Medicine Working Group could provide. These are:

- Databases and actionable variants; this effort is already going forward in the form of a workshop on December 1-2, 2011.
- Collaborative demonstration projects; in November or December of 2011, the group that met in Chicago in June is meeting again to come up with new initiatives.
- Standardization and quality control of clinical genomic testing and reporting; Dr. Manolio proposed a meeting to tackle this issue in spring of 2012.
- Policy needs (consent, CLIA requirements, reimbursement issues), education, and training.
- Research needed on evidence development for actionable variants, effectiveness of genomic medicine, and tool development for genomic medicine (CDS, clinical algorithms).

Although it will be important to avoid an overburden of meetings, there is value in collaboration among the various genomic medicine groups. The next step in this effort is the Genomic Medicine II meeting that is set for the fall of 2011. This meeting proposes to broaden involvement of relevant groups, identify low-cost pilot projects to build on similar efforts across sites, convene working groups and workshop planning to address obstacles and opportunities from the first meeting, identify additional groups to participate, consider funding through administrative supplement(s) to relevant grant(s), and coordinate with the Clinical Sequencing Exploration Centers.

Council asked if there are other organizations within HHS that should be involved in this effort. Dr. Manolio replied that there are several government organizations that have already been involved, such as CDC and FDA, and others that should be involved, such as CMS the Office of the National Coordinator for Health Information Technology.

Current Status of the NHGRI Large-Scale Sequencing Program by Adam Felsenfeld

Dr. Adam Felsenfeld presented an overview of the recent history and future of the NHGRI Large-Scale Sequencing Program. Recent history shows the decreasing cost of sequencing DNA over the past few years. This has allowed for a reduction of funding dedicated to this program, while at the same time increasing the capacity to produce sequencing data. Accomplishments of this program over the past 5 years include new projects in cancer sequencing (i.e. glioblastoma, ovarian, and 20 other cancers), complex disease studies (i.e. diabetes, autism, and cardiovascular disease), Mendelian diseases, variation resources (i.e. 1000 Genomes), many different organisms (i.e. insect, fungal, and pathogens), and metagenomics. Dr. Felsenfeld noted that all of these projects evolved over time from genotyping several SNPs to whole genome sequencing. The current breakdown by projects shows that 57% of projects are in cancer, 19% in medical sequencing, 13% in other, 7% in organismal sequencing, and 4% in 1000 Genomes.

Other than papers and research results, benefits of the program include building community resources, disseminating tools and technical expertise, promoting a data sharing ethic for genomics, leading standards for formats and quality, creating templates for project design, pioneering new project types (i.e. whole-exome capture) that involves developing new analysis methods and adapting them to new platforms, improving and maintaining the reference sequence, maintaining a commitment to very high quality data, and developing new high quality platforms.

In the context of NHGRI's Strategic Plan for Genomics for the next 10-20 years, the next steps for this program are to reduce large scale centers and to add 3 new activities: the Mendelian disease sequencing program, Clinical Sequencing Exploration, and Sequencing Informatics Tools development. $110 million per year will be spent on the new programs. Four RFAs have been issued to date:

1. **Large-Scale Centers**: This program is meant to continue the benefits of large-scale sequencing and resource development and will involve major projects that require scale or other unique features. $90 million per year will go to this program.
2. **Mendelian Centers**: This program will focus on identifying all variants underlying Mendelian disease. $10 million per year will go to this program.
3. **Clinical Sequencing Exploration Centers**: This program plans to identify requirements for routine clinical sequencing. $5.5 million per year will go to this program.
4. **Sequencing Informatics Tools**: This program will speed up dissemination of sequencing by encouraging the build-up of critical informatics tools. $4 million per year will go to this program. plus SBIR.

After the presentation, Council members asked if there are any data on the cost of analyzing sequencing data. Dr. Felsenfeld replied that he has a vague idea of the costs of analysis, but it is difficult to track these costs because the program has not yet identified consensus end-points to track the costs over time. However, it was noted that this is a priority moving forward. Council also asked about the challenges that NHGRI Staff will face in overseeing this growing program. Dr. Felsenfeld noted that the tracking of these programs is a challenge. In addition, as the program is disseminated and broken down into smaller pieces, it will be increasingly difficult for NHGRI to set standards. Lastly, Council asked how the total sequencing budget for NIH has changed. It was noted that the budget is being maintained, but much of the funding is being directed at specific disease areas.

COUNCIL-INITIATED DISCUSSION

At the Council meeting in February 2012, Dr. Jeff Schloss will give a presentation on the status of sequencing technology and development. In addition, there will be an update on the sequencing inventory project from Dr. Teri Manolio, and a presentation from Dr. Dan Kastner, the Scientific Director of NHGRI, in order to introduce him to Council. Council members also suggested an update from Dr. Karen Rothenberg's work with the ELSI program; however, it was noted that this presentation may be more suitable for the May 2012 Council meeting.

CONFLICT OF INTEREST

Mark Guyer read the Conflict of Interest policy to Council and asked them to sign the forms provided.

REVIEW OF APPLICATIONS

In closed session, the Council reviewed 243 applications, requesting $466,903,915 (total cost). The applications included 70 research project grants, 41 ELSI grants, 78 RFAs, 18 research center grants, 2 conference grants, 2 career transition awards, 14 SBIR Phase I grants, 4 SBIR Phase II grant, 2 STTR Phase I grant, 5 individual training grants, 6 education project awards, and 1 mentored quantitative research center award. A total of 149 applications totaling $329,432,962 were recommended.

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

02/13/2012
Date

Mark S. Guyer
Mark Guyer, Ph.D.
Executive Secretary
National Advisory Council for Human Genome Research

02/13/2012
Date

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