

**NATIONAL ADVISORY COUNCIL FOR HUMAN GENOME RESEARCH**  
**SUMMARY OF MEETING<sup>1</sup>**  
February 7, 2011

The Open Session of the National Advisory Council for Human Genome Research was convened for its sixty-first meeting at 8:40 A.M. on February 7, 2010 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 8:40 A.M. until 5:30 P.M. on February 7, 2011. In accordance with the provisions of Public law 92-463, the meeting was closed to the public from 5:30 P.M. on February 7, 2011 until adjournment for the review, discussion, and evaluation of grant applications.

Council members present:

Michael Boehnke  
Mark Chee  
Rex Chisholm  
Richard Cooper  
Claire Fraser-Liggett  
Geoffrey Ginsburg  
Ross Hardison, *ad hoc*  
Howard McLeod, *ad hoc*  
Deidre Meldrum, *ad hoc*  
Richard Myers  
Pearl O'Rourke  
Pilar Ossorio  
David Valle  
Richard Weinshilboum  
David Williams, *ad hoc*  
Richard Wilson, *ad hoc*

Council members absent:

David Kingsley, *ad hoc*  
Jill Mesirov, *ad hoc*  
Pamela Sankar, *ad hoc*

Ex officio members absent:

None

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<sup>1</sup> 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:

Ajay, DER  
Leslie Adams, DER  
Alice Bailey, OD  
Maggie Bartlett, OD  
Sanja Basaric, OD  
Daphne Bell, DIR  
Barbara Biesecker, DIR  
Vivien Bonazzi, DER  
Ebony Bookman, OD  
Joy Boyer, DER  
Patricia Brown, DER  
Comfort Browne, DER  
Zieanna Chang, DER  
Shaila Chhibba, DER  
Cheryl Chick, DER  
Monika Christman, DER  
Colleen Clark, DIR  
Christine Cutillo, DER  
Chris Darby, DER  
Camilla Day, DER  
Karen Deleon, OD  
Corina Din-Lovinescu, DER  
Jerry Doyle  
Gwen Dudley, DER  
Elise Feingold, DER  
Adam Felsenfeld, DER  
Colin Fletcher, DER  
Jonathan Gitlin, OD  
Peter Good, DER  
Eric Green, OD  
Mark Guyer, DER  
Lin Gyi, OD  
Don Hadley, DIR  
Linda Hall, DER  
Lucia Hindorff, OD  
Jason Hotten, DER  
Sarah Hull, DIR  
Heather Junkins, OD  
Rongling Li, OD  
Carson Loomis, DER  
Rebecca Lowdon, DER  
Raymond MacDougall, OD  
Jean McEwen, DER  
Keith McKenney, DER  
Enrique Michelotti, DER  
Michelle Milligan, DER  
Jeannine Mjoseh, OD  
Anita Nagwani, OD  
Cathy Ng, DER  
Ken Nakamura, DER  
Lisa Oken, DER  
Susan Old, OD

Vivian Ota Wang, DER  
Ken Ow, OD  
Brad Ozenberger, DER  
Jacqueline Palchik, DER  
Mike Pazin, DER  
Dylan Perry, DER  
Susan Persky, DIR  
Jane Peterson, DER  
Rudy Pozzatti, DER  
Ed Ramos, DIR  
Erin Ramos, OD  
Laura Rodriguez, OD  
Anna Rossoshek, DER  
Jeff Schloss, DER  
Heidi Sofia, DER  
Geoff Spencer, OD  
Jeff Struewing, DER  
Larry Thompson, OD  
Christopher Wellington, DER  
Kris Wetterstrand, DER  
Elizabeth Wilder, OD  
Rosann Wise, OD  
Anistasia Wise, OD  
Julia Zhang, DER

Others present for all or a portion of the meeting:

James Anderson, Division of Program Coordination, Planning and Strategic Initiatives, NIH  
Andrea Baruchin, Foundation for the National Institutes of Health  
Adam Berger, Institute of Medicine  
Joann Boughman, American Society of Human Genetics  
Laura Buccini, National Cancer Institute, NIH  
Malia Fullerton, University of Washington, Seattle  
Alan Guttmacher, National Institute of Child Health & Human Development, NIH  
Jane Hammond, RTI International  
Karin Helmers, Center for Scientific Review, NIH  
Rodney Howell, American College of Medical Genetics  
Nicole Lockhart, National Cancer Institute, NIH  
James O'Leary, Genetic Alliance  
Sharon Olsen, International Society of Nurses in Genetics  
Mary Perry, Division of Program Coordination, Planning and Strategic Initiatives, NIH  
Karen Rothenberg, University of Maryland School of Law  
Don Schneider, Center for Scientific Review, NIH  
Rhonda Schonberg, National Society of Genetic Counselors

## **INTRODUCTION OF NEW MEMBERS AND STAFF, LIASONS AND GUESTS**

Dr. Guyer introduced new NHGRI staff: Anastasia Wise, OPG; Mike Pazin, DER; Heidi Sophia, DER; Tina Gatlin, DER; Chris Darby, Grants Management; Jeannine Mjoseh (OPCE); and Lisa Oken, Grants Management.

Dr. Guyer welcomed members of the press and liaisons from professional societies: Joann Boughman, Rodney Howell, James O'Leary, Sharon Olsen, and Rhonda Schonberg.

## **APPROVAL OF MINUTES**

The minutes from the September and May 2010 Council meetings have not been submitted to the group. There will be an e-mail vote to approve them once they are finished.

## **FUTURE MEETING DATES**

The following dates were proposed for future meetings: May 16-17, 2011; September 12-13, 2011; February 13-14, 2012; May 21-22, 2012; September 10-11, 2012

## **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>.

### **I. GENERAL NHGRI UPDATES**

**Strategic Plan published.** The strategic plan for genomics will be published February 10 in *Nature*, culminating the two-year strategic planning process. The issue will commemorate the tenth anniversary of the published human genome sequence. Eric Green emphasized the long-term considerations described in this manuscript as genomics research moves toward translational research and improved healthcare. NHGRI is now beginning to plan how the Institute will implement specific aspects of the strategic plan.

**Symposium: A Decade with the Human Genome Sequence.** On February 11, NHGRI will host a symposium to celebrate the tenth anniversary of the human genome sequence and the publication of the Institute's new strategic plan for genomics. Speakers will include Francis Collins, James Watson, Eric Lander, among others. The event will be webcast and accompanied by a blog for remote participants to

comment on the event; the webcast will be archived. The evening before the symposium, Eric Green will emcee an event about genomics and science education for middle and high school science educators at the Koshland Museum Science Center in Washington, DC.

Dr. Green also noted that the February 4 issue of *Science* commemorates the 10<sup>th</sup> anniversary of the human genome sequence, and that 2011 is the fourteenth anniversary of the National Human Genome Research Institute.

**FY11 Appropriations Update.** The federal government is operating under a Continuing Resolution until March 2011. The NIH is operating at FY2010 levels until then.

**NHGRI Deputy Director Search.** The search for the NHGRI Deputy Director is ongoing, and Dr. Green encouraged Council to suggest candidates for the position.

**Special NHGRI Visitor.** Karen 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.

## II. GENERAL NIH UPDATES

### Leadership Changes at the NIH

- **Kathy Hudson** was appointed as Deputy Director for Science, Outreach, and Policy, NIH on October 24, 2010. In her new role, Dr. Hudson will oversee and coordinate the work of the Office of Communications & Public Liaison, the Office of Legislative Policy and Analysis, and the Office of Science Policy within the Office of the Director, NIH.
- On October 15, 2010, **Della Hann** was officially appointed as Deputy Director, Office of Extramural Research. Since 2003, she has served as Director, Office of Science Policy, Planning and Communications at NIMH. She has also been serving since 2008 as the Acting Director for the Office of Autism Research Coordination at NIMH, and she also has been acting in the OER Deputy Director position.
- **Richard Woychik**, previously the President and CEO at Jackson Laboratory, has been appointed Deputy Director, National Institute of Environmental and Health Sciences.
- **Jeremy Berg** has resigned as the Director, National Institute for General Medical Sciences, effective June 2011. Dr. Berg will become the Associate Senior Vice chancellor for Science Strategy and Planning in the Health Sciences at the University of Pittsburgh. He will also be a faculty member in the Department of Computational and Systems Biology. Eric Green is on the Search Committee for Dr. Berg's replacement and asked Council for their recommendations for candidates for the position.

**Biennial Report of the NIH Director, 2008-2009.** The NIH Director's report released in September 2010 contains an assessment of the state of biomedical and behavioral research and includes a descriptive report regarding the field of genomics.

### NIH Reorganization

- **Planned Merger of NIAA and NIDA.** The NIH Scientific Management Review Board (SMRB) endorsed the proposal to merge the National Institute on Alcohol Abuse and Alcoholism and the National Institute on Drug Abuse to form a new Institute for Substance Use, Abuse, and Addiction (SUAA). The new Institute will also take on relevant components of other current Institutes that study substance use, abuse, and addiction.
- **Therapeutics and Translational Sciences.** Three translational medicine projects that NHGRI has hosted or helped lead (the NIH Chemical Genomics Center, the Therapeutics for Rare and Neglected Diseases (TRND) Program, and the Rapid Access to Interventional Development (RAID) Project) are being combined within the NIH in the NIH Center for Translational Therapeutics (NCTT). NHGRI will house NCTT for the rest of fiscal year 2011.

The recent NIH SMRB report on translational medicine and therapeutics recommended accelerating the progress of promising therapies from labs and called for consolidating some existing programs, including the Clinical and Translational Science Awards (CTSAs) and NCTT. The SMRB also recommended the creation of a new National Center for Advancing Translational Sciences (NCATS), to be operational by FY12.

- **National Institute on Minority Health and Health Disparities.** The National Center on Minority Health and Health Disparities (NCMHD) has become the National Institute on Minority Health and Health Disparities (NIMHD). The new Institute will have a more defined role in the NIH's research agenda for health disparities.

#### **New Award and Scholars Programs**

- The NIH Early Independence Award (EIA) is a new program that aims to support a small number of qualified individuals to move directly to an independent academic level position at U.S. institutions after completing graduate school, without having to do post-doctoral training.
- The NIH Lasker Clinical Research Scholars Program is a unique intramural-extramural partnership that will encourage young researchers to come to NIH to do clinically oriented research in a tenure-track position. The unique feature of the program is that an individual who is given tenure will be given a grant if s/he decides to take an extramural position instead of remaining in the intramural program. NHGRI will participate in this new program, which is starting recruitment soon.

**Sickle Cell Disease Symposium.** NHGRI co-hosted a Symposium in November to commemorate the 1910 publication of the first description of sickle cell anemia in Western medical literature. All talks from the Symposium are available on the NIH videoarchive.

### **III. GENOMICS UPDATES**

**Mourning the Loss of Paul Miller.** Paul Miller, a lawyer who was born with achondroplasia (dwarfism), overcame discrimination because of his disability, and became a leader in the disability rights movement, passed away on October 20, 2010 from cancer at his home on Mercer Island, Wash. He was 49. Mr. Miller was an adviser to Presidents Bill Clinton and Barack Obama, a law professor, and an expert on the intersection of disability law, employment discrimination and genetic science. A professor at the University of Washington in Seattle, Mr. Miller was director of the university's disabilities studies program. In recent years, Mr. Miller focused on tensions between disability rights and genetic science. In a paper titled "Avoiding Genetic Genocide," Mr. Miller criticized scientists for what he saw as their eagerness to use genetics to produce "perfect" humans.

#### **Awards and Prizes to NHGRI-associated Scientists**

- On September 20, the **American Society of Human Genetics** named Rockefeller University's **Jurg Ott** as the recipient of the 2010 **William Allan Award**. Dr. Ott was honored for his "work as a pioneer in developing the statistical basis and advancing research on linkage analysis and complex disease in humans."
- The **American Society of Human Genetics** named **Charles Epstein** the recipient of the **McKusick Leadership Award**. Dr. Epstein's achievements have fostered and enriched the development of various human genetics disciplines beyond establishing a model medical genetics clinic and enhancing the fields of biochemical and clinical genetics. Dr. Epstein helped establish and legitimize the profession of genetic counseling in the late 1970's.
- **Carlos Bustamante** was awarded a **MacArthur Fellowship**. Dr. Bustamante is funded by NHGRI through the 1000 Genomes Project, and studies admixed populations.
- The **2010 Pearl Meister Greengard Prize** was awarded to **Janet Rowley** and **Mary-Claire King** by the Rockefeller University for their roles as pioneering cancer geneticists. The prize recognizes the accomplishments of outstanding female scientists who have made extraordinary contributions to biomedical science.

- **George Church** was awarded the **Bower Award and Prize for Achievement in Science**. Dr. Church is a Professor of Genomics at the Harvard Medical School. He received the award for his innovative and creative contributions to genome sciences, including the development of DNA sequencing technologies, as well as for his subsequent efforts to promote personal genomics and synthetic biology.
- Electees to the **Institute of Medicine** in 2010, include several current and former NHGRI grantees (including David Altshuler and Titia de Lange), two NIH IC Directors (Jeremy Berg and Linda Birnbaum), a former NHGRI Council member (Caryn Lerman), as well as several other investigators prominent in genomics and genetics (Sydney Brenner, Charis Eng, Carol Greider, and Neil Risch).
- **AAAS Newcomb Cleveland Prize** was given to the Neanderthal Genome Study. The award is given annually to the best research article or report published in *Science*. The Neanderthal group leadership includes Svante Paabo, David Reich, Ed Green, and Jim Mullikin and Nancy Hansen from the NISC.

#### Genome Scientists in Leadership Positions

- The **2011 ASHG Board of Directors** includes Les Biesecker of the NHGRI Division of Intramural Research.
- **David Nelson** will serve as the new **Editor of the American Journal of Human Genetics**. Dr. Nelson will be leaving his position at Baylor College of Medicine at begin at AJHG in mid-2011.
- **Tufts University** named **Anthony Monaco**, a physician, neurogeneticist, and vice chancellor at the University of Oxford in England, as the institution's next president. Dr. Monaco will be the first ASHG member ever to serve as a university president.
- **Joan Scott** has become the **Executive Director of the National Coalition for Health Professional Education in Genetics** as of September 2010. Ms. Scott is a certified genetic counselor with more than 30 years of experience in clinical genetics, education, the biotechnology industry, and genetic policy whose career has focused on the application of genomic discoveries to healthcare.

**Genome Research Highlighted in *Science* and *Nature*.** *Science* magazine's annual list of the "Breakthroughs of the Year" includes several accomplishments that are genomics-oriented and supported, managed or enabled by NHGRI (the Neanderthal genome, exome sequencing and the discovery of rare disease genes, and next-generation genomics). *Science* also identified "Insights of the Decade," which included elucidating the dark genome, understanding the microbiome, and ancient DNA. *Nature* recently published a list of key findings and events that could emerge from the research world in 2011. Their list included the continuing genome-sequencing explosion, and a prediction that GWA studies will begin to reveal mechanistic insights about the etiology of medical conditions.

***Nature Proceedings* Marker Papers.** The concept of "marker papers" originated at 2003 Fort Lauderdale meeting. As a pilot project to move this concept forward, each of the 15 HMP demonstration projects has recently published such a marker paper in *Nature Proceedings*. These papers are citable, but currently do not have a PubMed ID.

#### Meeting Reports

- **NHGRI at ASHG.** The American Society of Human Genetics (ASHG) 60th Annual Meeting was held from November 2-6, 2010, at the Walter E. Washington Convention Center in Washington, DC. The meeting attracted a record-breaking number of attendees. In conjunction with the meeting, Eric Green attended ASHG and ACMG Board meetings and several NHGRI staff met with press. The popular 1000 Genomes data tutorial described the 1000 Genomes data, how to find them, and how to use them. Since the meeting, the tutorial website has gotten a lot of hits.
- **4<sup>th</sup> National Conference on Genomics and Public Health.** The 4<sup>th</sup> National Conference on Genomics and Public Health Using Genomic Information to Improve Health Now and in the Future was held in Bethesda Maryland on December 8-10, 2010. NHGRI co-sponsored the meeting, along with CDC, HRSA AHRQ, NICHD, NCI, ORD, OBSSR, and several professional

and advocacy organizations. There were more than 440 attendees from seven countries who presented peer-reviewed presentations and posters. A take-home message of the conference was that public health as a field needs coordinated efforts for evidence review and service delivery supported by those genomic screening tools that have already established benefit. Most notable examples are those presented by newborn screening, family history assessment and population screening to identify those at high risk for familial cancer syndromes.

- **Advances in Genome Biology and Technology.** The AGBT meeting was in Marco Island February 2-5, 2010. There were many exciting presentations, mostly of new applications of recent technology.

**Genomic Advance of the Month.** In January, NHGRI began a “Genomic Advance of the Month” series on its website [www.genome.gov](http://www.genome.gov). The series will an example of outstanding or noteworthy ‘genomic advances’ each month, with features accessible to the general public. A letter of congratulations will be sent to the author of each selected paper.

#### **IV. NHGRI EXTRAMURAL PROGRAM**

**Large-Scale Sequencing Program: RFAs Issued.** NHGRI issued four RFAs related to the large-scale sequencing program. These include solicitations for Genome Sequencing and Analysis Centers, Mendelian Disorders Genome Centers, Clinical Sequencing Exploratory Research, and Informatics Tools for High-Throughput Sequence Data Analysis.

**Large-Scale Sequencing Program: Organisms Update.** The sequencing program has provided support for several recently published or completed genome sequences, including those of *Anopheles gambiae* (*Science* October 22, 2010), the orangutan (*Nature* January 27, 2011), and *Geomyces destructans* (white nose fungus, pathogenic to the Little Brown bats; genome sequence released by the Broad in September 2010).

**1000 Genomes Project.** The 1000 Genomes Project published a paper on its pilot projects in *Nature* in October. The project is now preparing for the phase 1 data release and a paper on 1100 genome samples.

**The Cancer Genome Atlas (TCGA).** A manuscript describing the ovarian genome project, the broadest and deepest tumor genome project to date, has been submitted for publication in a major journal. TCGA is currently analyzing 17 tumor types.

**DNA Sequencing Technology.** The annual meeting of the sequencing technology grantees is scheduled for April 4-6, 2011. This meeting is an integral part of this program, promoting rapid knowledge sharing, and has led to numerous productive collaborations. The back-to-back public meeting, scheduled this year for April 6-7, expands that discussion beyond current grantees to share information with others working in the field and with journalists.

**ENCODE and modENCODE.** On December 24, 2011, the modENCODE Consortium published two integrative analysis papers in *Science* highlighting the project's analysis of functional elements in the *Drosophila melanogaster* and *Caenorhabditis elegans* genomes, respectively. A total of 19 companion papers were published in *Nature*, *Genome Research*, *Genome Biology* and *Database*. There are now plans underway for an integrated analysis of *D. melanogaster* and *C. elegans*, with a longer-term goal of additional integration of human ENCODE data.

In November, the ENCODE Consortium PIs met to discuss integrative analysis of ENCODE data. They agreed on the need for further discussion and scheduled an ENCODE Analysis Workshop for March 7-8, 2011 to begin work on the integrative analysis, for a summer 2011 publication. The ENCODE Users' Guide paper is currently under revision.

The joint mod/ENCODE Consortia Meeting is scheduled for May 23-25, 2011 in the Washington, D.C. area. A joint paper from the ENCODE, modENCODE, and the Common Fund Epigenomics Projects that assessed histone modification antibody quality was recently published in *Nature Structural & Molecular Biology*.

**Knockout Mouse Program (KOMP).** The KOMP project continues to make progress with production of embryonic stem cells, and is on track to meet the project's goal in the Fall of 2011.

**Centers of Excellence in Genome Sciences.** The 2010 CEGS annual grantee meeting was held at Arizona State University in October.

**Diversity Action Plan Meeting.** DAP grantees generated progress reports using common data elements collected from each participant. The results pointed out the need: (1) to collect standard information on all participants and (2) for a centralized database to track participants. Anecdotally, many of the participants have moved on to the next career level -- one past participant is a recent Rhodes Scholar. DAP grantees attended an IRB workshop to discuss issues with preparing IRB packages and responding to IRB questions. The T32 grantees discussed appropriate measures to demonstrate program success and the information that needed to be collected on each participant in order to evaluate program progress.

**ELSI Funding Opportunities.** Three RFAs were issued in December, all closely related to the sequencing RFAs mentioned earlier. Additionally, the standing NIH-wide Funding Opportunities Announcement on research involving human participants is being revised and will be reissued this Spring. This new revision will explicitly incorporate many issues relevant to genomic research.

**ELSI Program Events.** The Centers of Excellence in ELSI Research (CEERS) meeting in October was the sixth meeting of the CEERS investigators. The discussion focused on the emerging synergistic results of the research at each of the Centers. A highlight was a joint UW/CASE/PRIM&R/ASHG study of the issues encountered by IRBs reviewing genomic studies.

In April the UNC CEER will be sponsoring the third international ELSI Congress, which will bring together more than 300 researchers, policy makers, students, and the media. The program will focus on exploration of the latest findings in ELSI research and new directions for the field as we move into an era of personalized genomic medicine.

The Consent & Community Consultation (C&CC) Policy Meeting will be held in April by the ELSI investigators involved in the Electronic Medical Records and Genomics (eMERGE) project. The goal of the meeting is to identify areas of consensus, shared norms and processes that can inform policy and policy makers about the ethical, legal, and regulatory issues involved in data sharing that arise from genomic research using linked electronic health records.

## **V. COMMON FUND PROGRAMS**

**Human Microbiome Project.** The HMP baseline clinical sampling was completed on October 1, 2010, requiring less than two years to complete. Of the 15 Demonstration Projects that were originally supported as UH2 pilots, nine have been ramped up and funded for three more years in the UH3 phase. Members of the HMP are working with other members of the International Human Microbiome Consortium to plan the upcoming International Human Microbiome Congress in Vancouver, British Columbia in March. Following the highly successful and overbooked open HMP meeting in St Louis, plans have been made to accommodate up to 700 attendees at the Vancouver meeting.

**Genotype-Tissue Expression (GTEx).** The contract for the Laboratory Data Analysis and Coordinating Center (LDACC) for the GTEx project was awarded to the Broad Institute. Three Biospecimen Source Sites (BSS) were funded; these are at the National Disease Research Interchange (Philadelphia, PA), the Roswell Park Cancer Institute, and Science Care (Phoenix, AZ). The project team plans to have initial collection started by April or May 2011. A series of PI meetings are scheduled to begin the project, now

that awards have been made. The Project Team has produced a new website and brochure explaining the project to the lay public.

**Library of Integrated Network-based Cellular Signatures (LINCS).** The first meeting of the project's External Scientific Panel with the PIs and staff of the U54 centers plus the NIH Project Team will be in March or April of 2011. The Project Team has begun to engage the non-cancer community to work with LINCS-like data by planning to award 3 to 4 administrative supplements to existing non-cancer NIH grant for collaborative proposals developed with the U54 centers. The External Scientific Panel will be consulted in determining which supplements will be made.

**Protein Capture Reagents.** Protein Capture is a NIH Common Fund effort to develop a renewable resource of capture reagents for human transcription factors. The project, which will be supported with \$10M in FY11, includes three components -- antigen generation, production of reagents against human transcription factors, and development of improved methods to reduce costs and cover the entire proteome. The current project is designed to inform the possibility of a future effort directed at the entire human proteome.

**Human Heredity and Health in Africa (H3Africa).** H3Africa is a NIH Common Fund project to enhance research capabilities in Africa by pursuit of population-based genetic and genomic studies on the African continent by African scientists. The project will hold a meeting in Cape Town in March to discuss a white paper that is now posted on [www.h3africa.org](http://www.h3africa.org). The white paper is authored by the project's two working groups and describes the scientific scope of the project. Issues covered in the white paper include which diseases to study, how to improve research infrastructure in Africa, and how to support appropriate genomic technologies for the studies.

## **VI. NHGRI OFFICE OF THE DIRECTOR**

**Office of Population Genomics.** The Office of Population Genomics remains active in producing genome-wide association data for a number of diseases and populations and depositing the data in dbGaP. To date, the GENEVA consortium has released GWA genotyping data on 15 studies and imputed genotypes on 6 studies. The PhenX Toolkit, a set of standardized measures of phenotypes and exposures in 21 disease and exposure domains, has finalized measures in its final five domains -- Social Environments, Speech and Hearing, Infectious Diseases, Gastrointestinal, and Psychosocial measures -- for a total of 291 standard measures thus far.

Teri Manolio was asked to coordinate DHHS research efforts in the wake of the Deepwater Horizon disaster, particularly in a long-term study of the clean-up workers. The study is now designed and in the field, and Teri has returned to NHGRI. We look forward to valuable research findings from this important cohort.

**New England Journal of Medicine Genomic Medicine Series.** The NEJM series will ultimately contain a total of 14 articles focusing on genomics. Upcoming installments include papers by Charles Rotimi with Lynn Jorde on ancestry and disease, and Mark McCarthy on Genomics and type 2 Diabetes.

**Journal of Nursing Scholarship Special Series.** This series in the premier international journal for nursing highlights the key role of nurse educators in bridging the gap between genomic discoveries and clinical care. It will be published throughout 2011.

**Faculty Champion Initiative.** The Faculty Champion Initiative is a year-long intervention designed to increase genetics and genomics nursing curriculum integration. The program began in September 2009 with a meeting of 20 competitively selected faculties.

**ASHG and NHGRI Policy Fellowship.** The Public Policy Fellowship program is a long-standing joint partnership between NHGRI and the ASHG. The program began in 2002 and the tenth joint fellow will be selected this year. The program is 16 months long, with fellows spending time working in the NHGRI

Policy & Program Analysis Branch and on the Hill; many also spend time in the ASHG office to round out their experience.

**Genomics and Health Education Tools.** In February 2009 Genetics/Genomics Competency Center for Education (G2C2), a web-based repository of curricular resources on genetics and genomics was launched. The goal of the resource is to make freely available an open source repository of curricular materials and resources that is designed to provide nursing and physician assistant educators with tools that can be used to prepare students to meet the discipline-specific competencies in this area of health care. Resources for genetic counselors and pharmacists are planned for the future.

The U.S. Surgeon General's My Family Health Portrait (MFHP) tool had its busiest year since its inception seven years ago, thanks in part to new connection to the Microsoft Health Vault. The MFHP has been formally validated in the ClinSeq population as a method to automate family history collection. As the tool is increasingly used, NHGRI is spearheading planning efforts for long-term governance of the tool.

**NHGRI and the Institute of Medicine Roundtable on Translating Genomic-Based Research for Health.** The IOM recently released three reports of interest, on topics including genomic technologies, newborn screening samples for translation research, and establishing collaborations for genomics-driven product development. These reports are available at the IOM website. Greg Feero has replaced Laura Rodriguez as the NHGRI representative to this body.

**Newborn Screening in the Genomics Era Workshop.** The workshop generated several ideas for pilot studies moving forward, as well as the need to have a follow up meeting specifically on the bioethics issues raised. David Valle discussed this meeting later in the Open Session.

**Genomics and health information technology systems: Exploring the issues.** This meeting in April 2011 will explore the spectrum of issues that must be addressed to ensure that the public derives the maximum benefit from the intersection of genomic discoveries and clinical informatics systems.

**USA Science & Engineering Festival.** NHGRI recently presented some simple and fun DNA-related activities at the inaugural USA Science & Engineering Festival in Washington, D.C. on Saturday, October 23 and Sunday, October 24, 2010. *The Washington Post* estimated that more than 500,000 people visited the festival. Fifty NHGRI staff from all divisions volunteered to guide the activities. A website has been created for those who couldn't attend the festival. Instructions and resources for each activity are available on the website, along with a video of Eric Green doing the strawberry DNA extraction.

## **VII. NHGRI INTRAMURAL PROGRAM**

**NHGRI Intramural Research Highlights.** Eric Green highlighted three recent papers by intramural investigators -- a study by Chuck Venditti using gene therapy in a murine model of lethal propionic academia; a project led by David Bodine that identified a mutation in a barrier insulator element of the ankryin-1 gene associated with hereditary spherocytosis; and continued success by William Gahl in the Undiagnosed Diseases Program, which has continued to be featured in the national media.

**2011 Dr. Nathan Davis Award from the American Medical Association Given to William Gahl.** William Gahl was awarded the Dr. Nathan Davis Award from the AMA for recognition as an outstanding public servant of the federal executive branch. This AMA award is presented to a local, state or federal career or elected government official and is one of the AMA's most prestigious forms of recognition for outstanding public service in the advancement of public health.

**New Joint Hopkins-NHGRI Medical Genetics Training Program.** NHGRI and Johns Hopkins are joining their medical genetics training programs to form the NIH/Johns Hopkins University Medical Genetics and Genomic Medicine Residency Training program, with its first students to begin in the summer of 2012.

**THE NIH COMMON FUND.** Dr. James Anderson presented an overview of the Common Fund, located in the NIH Division for Program Coordination, Planning and Strategic Initiatives. The Common Fund was created in 2006 by the NIH Reform Act. Common Fund programs are temporary efforts, receiving 5-10 years of support, which address specific challenges and catalyze IC-funded work. These are intended to be high-risk, investigator-initiated or large-scale projects that are potentially transformative, should support new ways to foster innovation and accelerate the pace of discovery, and benefit public health. Additionally, the trans-NIH Common Fund programs are synergistic and cross-cutting, and are intended to propel research in a range of scientific fields through the development of resources, technologies, or data sets that can be widely used by investigators at all ICs.

One example of how the Common Fund is accelerating national research priorities is its Global Health Initiative, which is designed to respond to the President's initiative to improve the health of women and children in developing nations. It has two components at present, the Medical Education Partnership Initiative and the Human, Heredity and Health in Africa (H3Africa) Program. The two focus on complementary research efforts to improve healthcare and medical education in Africa, advance understanding of non-communicable diseases, and support the improvement of infrastructure and collaborations to study genetics and genomics in African populations.

Another Common Fund initiative, the HMO Collaboratory, addresses the difficulty of creating large cohorts for population studies with the existing, distributed healthcare networks in the U.S. The NIH collaboration with the HMO Research Network seeks to enhance research capacity for multi-disease studies by leveraging existing resources shared in the network of HMOs.

Dr. Anderson then described the new NIH Director's Early Independence Award (EIA), which is an opportunity for exceptional investigators to move directly into a faculty-level position after graduate school. The NIH EIA is modeled on similar programs at Carnegie, Whitehead and other institutions and will propel exceptional candidates into making the most of their research careers.

The Common Fund's strategic planning process involves gathering input from many stakeholders about the current challenges to scientific progress and areas of emerging opportunities. Some of the recommendations go forward to become grant programs managed by trans-NIH working groups. Last year, the planning process yielded concepts for two FY12 funding opportunities, one in metabolomics and one in single-cell analysis.

In the subsequent discussion, some Council members expressed concern about the Early Independence Award and the ability of recent graduate students to run their own labs. It was noted that the ability of students to begin their own labs may be very discipline-specific. Dr. Anderson acknowledged that the program is not for most new graduates, and that the Common Fund will be tracking the progress of awardees. Similar to the Whitehead Fellows Program awardees will be placed in a heavily mentored environment. Dr. Anderson also clarified that this is an individual award, with the goal of providing more flexibility to both the individual and the institution. The Common Fund plans to bring the EIA awardees together each year to discuss their experiences with the program; he also expects that there will be site visits.

When asked how the Common Fund is coordinated with parallel initiatives in other countries, Dr. Anderson responded that they rely primarily on the ICs to help coordinate with international partners. For example, NHGRI Program Staff helps the Common Fund coordinate with protein capture efforts at the Karolinska Institute in Sweden. Council advocated collaborating with researchers in Asia, whose biomedical research capacity is growing. Dr. Guyer noted on the ongoing US-Asia collaborations in the Human Microbiome Project, Epigenomics project, and others.

**CSR REVIEW OF ELSI GRANT APPLICATIONS.** Dr. Rudy Pozzatti updated the Council about changes to the review process for ELSI grant applications. A recent evaluation by the Center for Scientific Review (CSR) recommended merging the ELSI study section (ELS) with the standing Clinical Ethics Research (CRE) Special Emphasis Panel (SEP) because the number of applications assigned to ELS has fallen

significantly over the last 3-4 years. The CRE SEP reviews applications focused on bioethics in the areas of clinical research and the delivery of healthcare. The first meeting for the new review committee, now called "Societal and Ethical Issues in Research," will be on February 15, 2011, and Dr. Karin Helmers will be the Scientific Review Officer for the group.

The biggest difference is that the new committee is not genetics-specific, while the ELS committee was. However, strong representation on the committee from former ELS members will ensure continuity. The staffs of both CSR and the NHGRI ELSI program will follow the outcomes of this new committee and will also gather feedback from applicants and reviewers about this change.

In discussion, Council asked if the ELSI program will still have its own budget; Dr. Pozzatti clarified that the ELSI budget is not affected by this change in review. In response to concerns about the voting behavior of ELSI reviewers, he noted that NHGRI ELSI program staff will monitor the scores assigned to NHGRI ELSI applications to see if there is any systematic difference in scoring relative to the non-ELSI applications. Furthermore, he pointed out that program staff can take voting behavior into account in making funding decisions, even to the point of funding poorly scoring or even unscored applications, if desired. Dr. Pozzatti emphasized that there will be an effort to include reviewers with genetics expertise and the new review committee is assembled.

**SCIENTIFIC PRESENTATION: Panel discussion chaired by Laura Rodriguez, with panel members Pearl O'Rourke, Malia Fullerton, and Sarah Hull.** At the last Council meeting, members had requested a discussion of IRBs and genomics research with human subjects. A challenge for research in genomics with human participants involves resolving the needs of the genomics community (e.g., for rapid access of public data) with those of the research participants (e.g., individual protections and autonomy). This is complicated by the shifting trends of research involving human participants, access to data by many investigators, consent for prospective studies, and the undefined or unbounded timeline for the use of data from research involving human participants. The panel discussed what NHGRI can do, through policy and as a resource for the community, to make progress on these issues.

- **Understanding IRB processes.** Dr. Pearl O'Rourke reviewed the basic principles and procedures that IRBs use for dealing with research involving human participants. The set of basic ethical principles regarding human participants in research is the Belmont Principles, which espouse respect for persons (autonomy), beneficence, and justice in selection of subjects. IRBs must balance these principles with Federal and state laws, which are open to changing interpretation and guidance. Dr. O'Rourke reviewed the IRB's framework for determining if proposed research involving human participants is within the purview of the Common Rule. If the proposed research involves identifiable private information, it is subject to the Common Rule. However, she pointed out that what data are considered to be identifying is an issue that continues to be debated, and that for now, identifiability of data falls into a continuum. The challenge for IRBs then is to reconcile indeterminably identifiable data into a dichotomous model of oversight and regulation. There have been some attempts at creating "indirectly identifiable" data through coded databases, but this has not solved the fundamental problems with the current system.

Dr. O'Rourke then reviewed the current guidance and flowchart that IRBs follow to determine if the proposed research involves human research participants, if they are identifiable and whether informed consent is required. She acknowledged that, in general, no stakeholder in this process is completely satisfied. While the public has a limited understanding of research in general and many misconceptions about genetics research in particular, research participants often would like to be involved in research, regardless of the identifiability of their samples, and they want information about results of the research. They are also concerned about privacy, and addressing these two issues can result in added costs to the research. Consequently, researchers may have to forgo the large, up-to-date, fully phenotyped datasets that they would like to have and they end up working with smaller datasets or de-identified specimens, giving up some potentially valuable clinical information to avoid extra costs and logistics. IRBs may also be uncomfortable defining identifiability, and issues such as large retrospective tissue or data collections, research involving

children and other people with limited decision-making abilities, return of results, and withdrawal of consent of banked samples continue to challenge the system. Moving forward, researchers need to interact with the public to create a community of research participants who are engaged and support biomedical research that advances public health. Key issues will revolve around the prioritization of human and capital resources dedicated to research.

- **Participant preferences and policy**, Dr. Malia Fullerton noted that current ethical and regulatory standards are predicated on a specific approach to the protection of human research participants that emphasizes risk relative to respect. In modern genomic research involving the subsequent analysis of data from human participants, the participants are effectively absent from the research, which may encourage research participants to believe themselves misled regarding how investigators are handling their samples. This has led to regulators over-emphasizing the mitigation of harm, and underemphasizing how to engage meaningfully with research participants.

Dr. Fullerton shared new data that suggest that research participants have a desire to have control over their information and to be kept informed with how their information is being used. In light of these data, it is worth examining the nature of research oversight and public engagement with science. Because researchers have an ethical responsibility to, as much as possible, keep participants informed of the uses of their data and results, in order to continue open-ended research, the research investigators must maintain quality contact with research participants.

- **Ethics Review of Intramural “Next Generation” Sequencing Research at NIH**, Dr. Sarah Hull noted that, in the current age of genomics, whole exome (WES) or whole genome sequencing (WGS) do not raise novel ethical issues as compared with those related to earlier genetics research. However, WES/WGS magnify and make more concrete concerns that have previously been theoretical. This realization has important implications for how to conduct ethical reviews of proposed research. WES/WGS raise three primary areas of concern: return of incidental findings of individual research results, data sharing, and informed consent.

In the context of whole genome sequencing, it is inevitable that “incidental” findings will arise, likely multiple times for each participant, and the distinction between incidental and non-incidental findings is becoming less meaningful. In response, the NHGRI IRB is implementing new criteria to determine if and which “incidental” results should be returned to individuals. As for data sharing, data from human research participants will increasingly include rare and common variants, which may enhance identifiability. The NHGRI IRB is anticipating future data sharing requirements and encouraging investigators to disclose their data sharing plans to study participants upfront and to give participants choices about how the data will be shared. Informed consent for prospective and retrospective studies continues to raise important questions about re-consent and other issues concerning human research participants. New IRB trends in this area include being more rigorous with designing explicit consent or re-consent documents to ensure that the scope and scale of the project is communicated to participants, as well as to provide choices for how an individual’s results should be handled in the future.

Lastly, the NHGRI Bioethics Core is concerned that WES/WGS research will be performed on de-identified samples without any IRB review, oversight, or plan for how to handle incidental findings. For such samples, the NHGRI IRB is developing policies that will ensure that proper oversight is maintained over such samples, creating guidance documents and model language for investigators to use, and collecting data on the perspectives of research participants regarding re-consent for these samples, and on IRB members’ perspectives regarding return of results.

In discussion after the Panel presentations, one Council member asked how identifiable whole genome sequencing actually is. The panel noted that theoretically and scientifically, identifiability of a whole genome sequence is a real risk, but generally, scientists do follow the rules regarding identified samples and respect controlled access of data. Another question was what an investigator should do when re-consent is needed but a patient is deceased. The panel responded that according to the Common Rule,

a deceased person is no longer a human subject (in most states), and therefore the sample would not need re-consent.

The conversation then turned to the issue of the liability institutions take on when investigators want to deposit data into dbGaP. This issue involves policy from the Office of Civil Rights, which has not ruled whether dbGaP data is deemed identifiable. However, the NIH required the institution's IRB to take on liability for any problems or issues that arise from their investigators' dbGaP-deposited data. As a result, IRBs and investigators are discouraged from depositing their data in dbGaP. Many Council members agreed that in this case, the NIH is asking IRBs and institutions to take on too much liability, especially while not providing clearer guidance on what data are or are not identifiable. Some members expressed the opinion that fear of liability imposed from the NIH is impeding research. David Valle and Pearl O'Rourke suggest that Council recommend to the NIH Director that NIH develop guidelines or best-practices for genomic research involving human participants and informed consent, beyond the single guidance on GWAS policy now available. Other Council members, including Mark Chee, suggested that research participants have their own dbGaP account where they could access all their research information and their data, and change their level of participation on their own. Dr. Fullerton agreed that research participants would really value such a resource, and she noted that there is some interest in the bioinformatics community for developing such a capacity. Others agreed such a resource would engender trust among the research participant community, could be used as a vehicle for return of results, education and "ongoing consent," and possibly save money in the future.

## **CONCEPT CLEARANCES**

### **ENCODE TECHNOLOGY DEVELOPMENT (Dr. Michael Pazin)**

The major long-term goal for ENCODE-type projects is to identify functional elements in a genome, and the development of new technologies that improve the ability to further functional annotation of the genome has been an important component of the ENCODE Program since its outset. Completing the ENCODE and modENCODE catalogs for the *D. melanogaster*, *C. elegans*, and human genomes is a high priority for NHGRI, but current technologies are not adequate. Cheaper, more sensitive assays are needed to achieve that goal, along with better technologies for biological validation. Therefore, NHGRI is proposing two new RFAs to solicit applications for research projects to develop new technologies that go well beyond currently available methods and can be used to comprehensively identify and biologically validate sequence-based functional elements in eukaryotic genomes, with particular emphasis on methods that will enable annotation of the human genome sequence. The goals of these RFAs are (1) to reduce the cost of identifying functional elements by several orders of magnitude; (2) to reduce the amount of biological material required to identify functional elements, moving towards single-cell analysis; and (3) to increase the throughput of biological validation assays.

In the discussion, Dr. Chisholm asked if the RFAs target any particular technological areas. Dr. Pazin responded that NHGRI is interested in anything that will reduce the cost of assays or reduce the sample size for these assays towards single cell samples. Dr. McLeod asked if NHGRI was considering an SBIR approach, instead of an R01. Dr. Feingold and Dr. Schloss responded that in the past, NHGRI has had more success supporting this kind of technology development with R01 awards, but that program staff will consider a SBIR RFA. Council agreed that it would be comfortable adding an SBIR RFA to this concept clearance.

Dr. Feingold and Dr. Schloss clarified that NHGRI is not seeking fundamentally new sequencing methodologies through these RFAs, but that new applications of current sequencing technologies would be responsive. They noted that NHGRI will coordinate with the new Common Fund single-cell technologies initiative to monitor how these two efforts develop in parallel. In response to a question about the preferred species for biological validation, Dr. Pazin clarified that the RFA would be open to the use of any species, but that the proposed technology should be applicable to human biology.

The concept clearance was approved unanimously.

## PROGRAM UPDATES

**THE CANCER GENOME ATLAS (TCGA).** Brad Ozenberger presented an update of the TCGA project. He began by reporting recent changes in the staffing of TCGA. Joe Vockley has departed as the director of NCI's TCGA Office, and Paul Spellman of the Lawrence Berkeley Lab has been appointed as Acting Director until September 2011. Each institute has hired an additional TCGA Program Director for TCGA, Ram Iyer at NCI and Heidi Sofia at NHGRI.

Dr. Ozenberger noted that the completion of the pilot phase of TCGA in 2009 coincided with the beginning of ARRA. TCGA was named a signature project and received an input of ARRA funds, which have been used to increase biospecimen acquisition and sequencing capacity. The goal for ARRA is to complete by September 2011 the characterization and sequencing of 3000 cases, representing 10 tumor types at 200 cases each and an additional 10 tumor types at 100 cases each. TCGA will then continue in years 2011-2014, but the funding levels have not been determined beyond 2011.

Progress towards ARRA goals is promising. The sample accrual goals are nearly on target. The exome sequencing goals have been lagging but have started to catch up. The lag time between sample receipt at the Centers and primary exome data deposition at NCBI is about four months. At present, comprehensive data are currently available for three tumor types – glioblastoma, ovarian, and acute myeloid leukemia. Another six projects have partial data sets – colorectal, lung adenocarcinoma, lung squamous cell carcinoma, breast, gastric, and renal clear cell. In addition, there are nine projects that have recently begun or are upcoming – bladder, cervical, head and neck, liver, melanoma, prostate, sarcoma, thyroid, and uterine.

TCGA has been a major driver of technology, especially for genomic analysis. The scale of growth of data deposition from TCGA is unprecedented; currently, the project is submitting over 8 Tbases/month to NCI, representing 18 Terabytes submitted, in total. To facilitate analysis of the TCGA data, NCI has funded several Genome Data Analysis Centers to provide standardized analysis pipeline reports on all available data.

The first TCGA publication, on GBM, has been cited in 225 publications, showing the reach of the project. The second manuscript, covering ovarian cancer, is under review. This paper will include characterization of 488 cases and exome sequencing on 316 of those cases. Findings in the paper include no novel somatic mutations in ovarian tumors, but support for the view that ovarian cancer is the result of p53-mediated genomic instability. The paper also shows that nearly 70 putative oncogenes that may be involved in ovarian cancer are known to be targets or putative targets of drugs or inhibitors in development.

TCGA is working to collaborate more closely with the International Cancer Genome Consortium (ICGC), including making data types compatible.

Council asked whether TCGA can follow patients over time. Dr. Ozenberger noted that the tissue source sites are incentivized to provide follow-up clinical data. There are also other cancer genomics projects underway at the TCGA Genome Sequencing Centers with separate funding that are looking at clinical trials and longer-term follow-up, as well as pre- and post- therapy analyses. Council also suggested for a 1000 Genomes-like tutorial on accessing TCGA data, and Dr. Ozenberger replied that one has already been planned for Spring 2011.

**LIBRARY OF INTEGRATED NETWORK-BASED CELLULAR SIGNATURES (LINCS).** Dr. Ajay Pillai presented an update on the Common Fund LINCS project, the goal of which is to facilitate a mechanistic understanding of disease in support of drug and biomarker development through the creation of a library of perturbation-induced cellular signals that relate cellular responses to genetic variation, environmental exposures and clinical phenotypes. The Phase I objectives of the project are to correlate phospho-proteome data and gene expression patterns with other biological events. U54 awards for LINCS Phase I have been made to the Broad Institute and Harvard Medical School. Two other RFAs are currently open,

one for technology development and one for computational tool development; the U54 centers have released sample datasets that can be used by investigators in developing their proposals. Program staff anticipates awarding 3-4 grants for each of these RFAs.

The LINCS program has established an External Scientific Panel. The program is also interacting with the Molecular Libraries Program and plans to use some of the MLP's probes in LINCS perturbation experiments. Several working groups have been put together to address issues such as better facilitate collaboration between the U54 centers, data generation, and further outreach to the scientific community. Data production and release metrics for FY11 have been established for each of the centers, and the Broad and Harvard Medical School groups have begun a collaborative project to establish a common portal for querying LINCS data. Two upcoming in-person meetings of the Consortium are planned in March and October 2011 to discuss further organization of the scope and utility of LINCS-produced data.

**MOLECULAR LIBRARIES PROGRAM (MLP).** Dr. Carson Loomis presented an update on the MLP, a Common Fund initiative composed of a nationwide consortium of centers funded to develop small molecule probes to be used as research tools for interrogating existing and novel biological targets and pathways. The program successfully completed its pilot phase in 2008 and is now in the third year of the production phase. One of the strengths of the program is in the integration of biology and medicinal chemistry. The MLP has a portfolio of targets that is quite diverse compared to large pharmaceutical companies' research & development efforts. MLP also has a program of continual improvement that is focused on probe quality. Each probe is evaluated by an external committee, and so far the year-three probes have shown improvement compared to those from year two. Of the 165 probes developed by the end of 2010, 95 have been further developed beyond the MLP and have been taken further along the drug discovery pipeline under other funding. The MLP is also celebrating the first successful Investigational New Drug application (IND) originating from an MLP probe. The compound has started a Phase I clinical trial for the treatment of multiple sclerosis.

Dr. Loomis was asked about the future of probes moving on to drugs and about clear pathways for partnering with drug companies. He noted that 60% of novel drugs originate in academic institutions and that pharmaceutical and biotechnology companies are willing to license these probes as long as they have been "de-risked" by being pushed further down the drug discovery pipeline to become drug leads. Many of the MLP centers actually have the capacity to take probes further into the drug development phase themselves.

## MEETING REPORTS

- **PROTEIN CAPTURE WORKSHOP.** Dr. Adam Felsenfeld presented an update on the Protein Capture Common Fund Initiative. The overall goal of the Initiative is to develop a community resource of renewable high quality protein capture reagents for all human proteins. A workshop was held in October 2010 to gather recommendations about the direction of the Protein Capture Initiative. The general consensus of the workshop was that production efforts should be geared towards existing monoclonal and recombinant antibodies in the pilot phase of production and analysis. The proposed budgets drawn up by the NIH were determined to be grossly underestimated, so more funding may be required in future phases to provide adequate production and validation expenses.

The Initiative is currently funding an Immunogen Center to assemble a collection of optimized immunogens representing the complete set of human transcription factors. The program is also reviewing applications for production centers and for technology development. The production effort is planned to be scalable, with initial focus on high-quality affinity capture reagents for all human transcription factors. This component will be a five-year effort with one or two funded centers. In parallel, technology development will be undertaken to produce better approaches for producing high quality reagents in three to five years. Plans are to support three to five technology projects

- **NEWBORN SCREENING IN THE GENOMIC ERA.** Council member David Valle was a co-organizer of a joint NICHD-NHGRI workshop in December 2010 to discuss newborn screening in the genomic era and to develop a research agenda based on a partnership between the institutes. Newborn screening refers to a suite of efficient, cost-effective tests to identify individuals at risk for one of several targeted diseases. The workshop attendees represented several scientific and stakeholder communities, and the agenda focused on opportunities for introducing genomics-based approaches. Presentations were made on new technologies and ELSI issues, and the workshop involved several breakout sessions as well as general discussion.

It was clear that there are several issues to consider, including the expansion of carrier detection to a larger number of diseases; the potential for using whole genome or whole exome sequencing to understand the genetics of individuals with known disorders; and the possibility of interaction with the private sector to develop creative new technologies in order to run tests efficiently and accurately. Another issue is the potential for whole genome sequencing of blood spot DNA to synergize with traditional biochemical testing. Whole genome sequencing early in life might also provide an “on ramp” to individualized medicine that would affect healthcare for individuals throughout their lives.

In Council discussion, the issue was raised that the public will need a higher level of general genetics education before it will buy into large-scale genetic testing on a commercial basis. Council members also raised the problem of predictability of genetic tests, but Dr. Valle noted that this issue was not discussed much at the meeting. Rick Myers asked that Council hear more about the latest thinking on the problem of genetic predictability at a future meeting. Alan Guttmacher suggested leveraging newborn screening as a research platform to understand more about the predictability of disease, and suggested that other ICs would have an interest in participating in such a research initiative. Regarding the technological innovations needed, Rhonda Schoenberg pointed out that health insurance companies currently have very little support for molecular tests. She advocated for sequencing diagnosed patients as a way to understand how DNA sequence impacts disease.

**POPULATION TRACKING.** Ms. Anna Rossoshek gave a presentation on the inclusion of women and minorities in NHGRI clinical studies. A biennial report on this topic is required by the 1993 NIH Revitalization Act to ensure that Institutes are in compliance in NIH mandate to include women and minorities in clinical research. Ms. Rossoshek’s presentation compared target demographic data (data in grant applications) and actual enrollment data (from grant progress reports) for participants of phase III trials.

By comparing NIH enrollment data and the census data, Ms. Rossoshek’s analysis concluded that, overall, NHGRI’s enrollment rate for racial minorities followed similar trends as NIH, with overall lower inclusion levels in clinical studies compared to the population. However, in DER and OPG clinical studies, African-Americans and Hispanics were enrolled at a higher rate than their proportion in the US population. With respect to gender, the ratio of women in DER and OPG clinical studies is higher than for the general population, but lower in DIR clinical studies.

**MEMORANDUM OF UNDERSTANDING.** Dr. Guyer led the annual discussion of the Memorandum of Understanding Between the Staff of the NHGRI and the National Advisory Council for Human Genome Research. There were no proposed changes in the MOU this year, and Council unanimously approved the MOU.

#### **COUNCIL-INITIATED DISCUSSION**

Rex Chisholm advocated that Council should consider how to raise the issue of IRBs and liability for whole genome or whole exome data to effect a fundamental revision of policy on this subject. Eric Green responded that Laura Rodriguez will help determine how to move this discussion forward.

**ANNOUNCEMENTS AND ITEMS OF INTEREST**

Mark Guyer recommended the American College of Medical Genetics Report to Council.

**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 140 applications, requesting \$75,909,873 (total cost). The applications included 10 research center grants, 6 conference grants, 1 career transition award, 18 SBIR Phase I grants, 1 SBIR Phase II grant, 3 STTR Phase I grant, 1 individual training grant, 8 education project awards, and 2 mentored quantitative research center awards. A total of 92 applications totaling \$42,255,933 were recommended.

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

\_\_\_\_\_  
Date

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

\_\_\_\_\_  
Date

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