



genome.gov

National Human Genome Research Institute

National Institutes of Health

# DIRECTOR'S REPORT

National Advisory Council  
for Human Genome Research

May 2012

Eric Green, M.D., Ph.D.  
Director, NHGRI



**National Advisory Council for Human Genome Research**  
Rockville, Maryland  
February 13, 2012




genome.gov  
 National Human Genome Research Institute  
 National Institutes of Health


Google™ Search


Research Funding | Research at NHGRI | Health | Education | Issues in Genetics | Newsroom | Careers & Training | About

Home > About > Institute Advisors > National Advisory Council for Human Genome Research > May 2012 NACHGR Meeting Agenda and Documents > Director's Report 2012

Director's Report Related Documents: May 2012

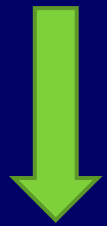
[Director's Report](#) 

[Director's Report](#) 

No.	Documents
1	<a href="#">Proposed NHGRI Reorganization</a>
2	<a href="#">NHGRI Staff Member Honored</a> [gazette.jhu.edu]
3	<a href="#">New Director of the National Heart, Lung and Blood Institute</a> [nih.gov]
4	<p><b>NIH Launches Genetic Testing Registry</b></p> <ul style="list-style-type: none"> <li>• <a href="#">NIH Genetic Testing Registry</a> [ncbi.nlm.nih.gov]</li> <li>• <a href="#">NIH Press Release</a> [nih.gov]</li> </ul>
5	<p><b>Big Data Research and Development Initiative</b></p> <ul style="list-style-type: none"> <li>• <a href="#">White House Press Release</a>  [whitehouse.gov]</li> <li>• <a href="#">NSF Press Release</a> [nsf.gov]</li> <li>• <a href="#">1000 Genomes Project data - exemplar of new White House big data initiative</a></li> </ul>

genome.gov/DirectorsReport

Document #



# Open Session Presentations

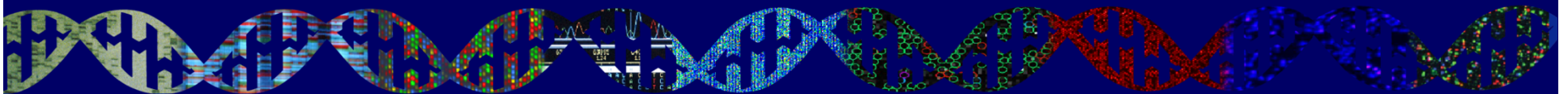
- **NHGRI Training Portfolio**
  - **Bettie Graham**
- **NIH Policy on Applicants with More than \$1.5M in Grant Support**
  - **Bettie Graham**
- **Update on the X Chromosome Program Notice**
  - **Anastasia Wise**



# Open Session Presentations

## Concept Clearances:

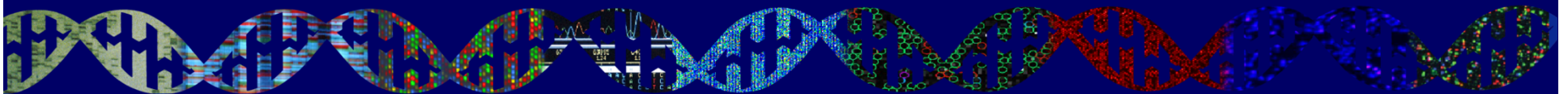
- **Genomic Sequencing and Newborn Screening Disorders**
  - **Anastasia Wise**
- **Clinically Relevant Variants Resource**
  - **Erin Ramos**



# Open Session Presentations

## Program Updates:

- **1000 Genomes Project**
  - **Lisa Brooks**



- I. General NHGRI Updates**
- II. General NIH Updates**
- III. Genomics Updates**
- IV. NHGRI Extramural Program**
- V. NIH Common Fund Programs**
- VI. NHGRI Office of the Director**
- VII. NHGRI Intramural Program**



# I. General NHGRI Updates

II. General NIH Updates

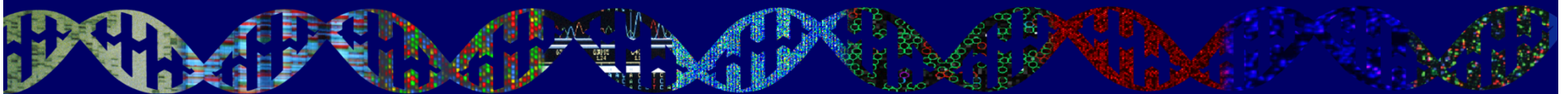
III. Genomics Updates

IV. NHGRI Extramural Program

V. NIH Common Fund Programs

VI. NHGRI Office of the Director

VII. NHGRI Intramural Program






# Proposed NHGRI Reorganization

## Proposed NHGRI Reorganization



**Times change and so, too, should institutions.** For the National Human Genome Research Institute (NHGRI) at the National Institutes of Health (NIH), a natural time for change has arrived, and the Institute is proposing an internal reorganization to reflect our current and future genomics research portfolio and associated activities more appropriately.

In 1988, NIH created an office that eventually became NHGRI; at the time, the single charge to that office was to oversee NIH's contributions to the [Human Genome Project](#). As such, the office started with a simple organization — a director's office and a team managing grants. Today, NHGRI manages dozens of named scientific projects and a research portfolio that is multifaceted and highly diverse. In aggregate, NHGRI's current suite of responsibilities requires a more sophisticated management structure.

Moreover, with the completion of the Human Genome Project in 2003, NHGRI has worked with the international community of genomics researchers to develop strategic plans to guide the field as a whole. NHGRI published its most recent plan in the journal *Nature* in February 2011 ([Charting a course for genomic medicine from base pairs to bedside](#)  ). This new strategic vision is organized around five domains of research activities that together chart a progression from basic research elucidating the structure and biology of genomes to understanding the biology of disease and advancing the science of medicine. The ultimate goal, of course, is to improve the effectiveness of healthcare and advance human health.

# Departure of Greg Feero



Genomic Healthcare  
Branch



GENETICS/GENOMICS COMPETENCY CENTER  
FOR EDUCATION



INTERACTIVE UNFOLDING CASE STUDIES

**My Family Health Portrait**  
A tool from the Surgeon General

Using My Family Health Portrait you can:

- Enter your family health history.
- Print your family health history to share with family or your health care worker.
- Save your family health history so you can update it over time.

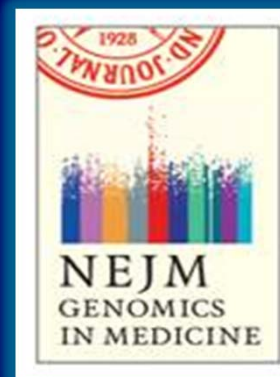
Talking with your health care worker about your family health history can help you stay healthy!

[Learn more about My Family Health Portrait](#)

Create a Family Health History    En Español

Use a Saved History    Em Português

In Italiano

A photograph of a family consisting of a woman, a man, and a young boy, all smiling and sitting together. The woman is on the left, the man is in the middle, and the boy is on the right.

NIH STATE-OF-THE-SCIENCE CONFERENCE

FAMILY HISTORY

and Improving Health

A graphic of a family tree structure, consisting of a central vertical line with horizontal branches extending to the left and right, ending in small circles representing family members.

# NHGRI Staff Member Honored (x2)



**Teri Manolio, M.D., Ph.D.**

I. General NHGRI Updates

**II. General NIH Updates**

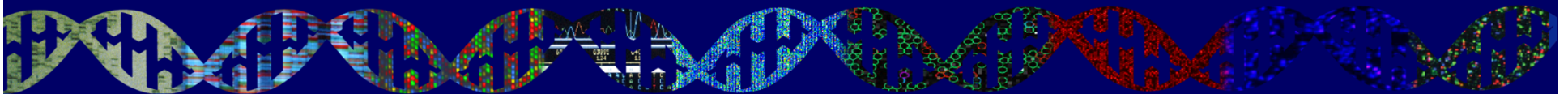
III. Genomics Updates

IV. NHGRI Extramural Program

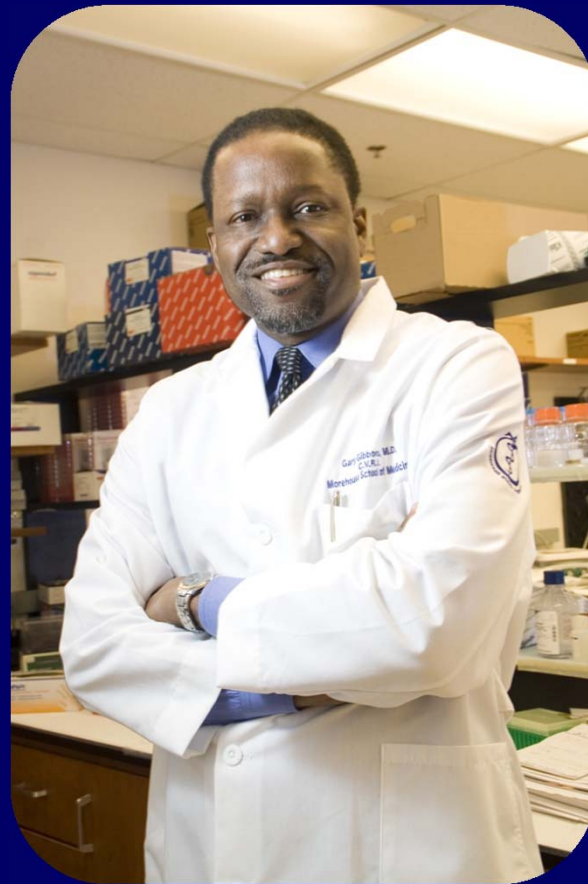
V. NIH Common Fund Programs

VI. NHGRI Office of the Director

VII. NHGRI Intramural Program



# New Director: National Heart, Lung, and Blood Institute



**Gary Gibbons, M.D.**

# NIGMS Leadership Changes



National Institutes of Health

National Institute of  
General Medical Sciences

BASIC DISCOVERIES FOR BETTER HEALTH

NIGMS Home

Research Funding

Research Training

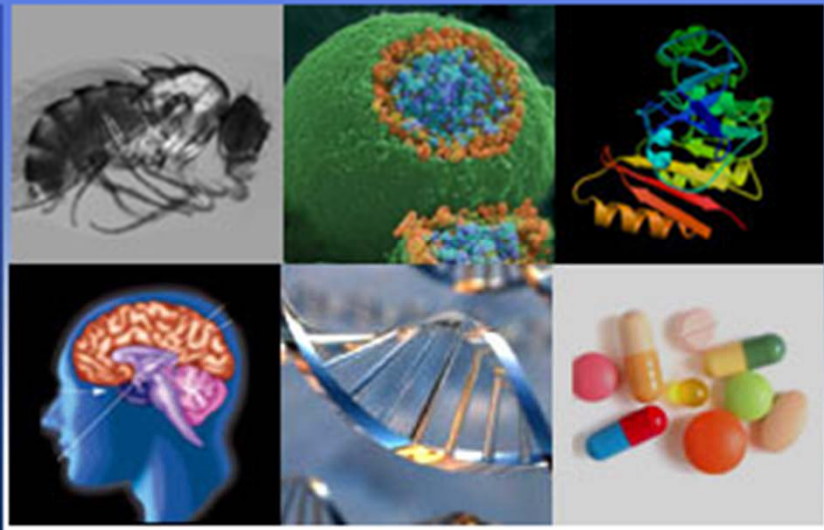
News & Meetings

## NIGMS Fact Sheets

*Basic biomedical research areas and  
their impact on biology and health*

[More Info ▶](#)

1 2 3 4 5




# NIH Launches Genetic Testing Registry

The screenshot shows the NIH Genetic Testing Registry (GTR) website. At the top, there is a navigation bar with the NCBI logo, "Resources" with a dropdown arrow, "How To" with a dropdown arrow, and "My NCBI Sign In". Below the navigation bar is a header section titled "GTR: GENETIC TESTING REGISTRY" with a background image of a DNA microarray. Underneath the header is a search interface with tabs for "All GTR", "Tests", "Conditions/Phenotypes", "Genes", "Labs", and "GeneReviews". The "Conditions/Phenotypes" tab is selected. There is a search input field and a "Search Conditions/Phenotypes" button. Below the search field, there is a text box that says "Find conditions and phenotypes by searching for disease names, traits, drugs, proteins and analytes." and a link to a YouTube video titled "GTR overview and search tips".

**IMPORTANT NOTE:** NIH does not independently verify information submitted to the GTR; it relies on submitters to provide information that is accurate and not misleading. NIH makes no endorsements of tests or laboratories listed in the GTR. GTR is not a substitute for medical advice. *Patients and consumers* with specific questions about a genetic test should contact a health care provider or a genetics professional.

**About GTR**

The Genetic Testing Registry (GTR) provides a central location for voluntary submission of genetic test information by providers. The scope includes the test's purpose, methodology, validity, evidence of the test's usefulness, and laboratory contacts and credentials. The overarching goal of the GTR is to advance the public health and research into the genetic basis of health and disease.

- [How to Use GTR](#)
- [GTR Information at NIH Office of the Director](#)
- [Contact GTR](#)
- [GTR News](#) 

**Clinical Resources**

[GeneReviews](#) Expert-authored, peer-reviewed disease descriptions that apply genetic testing to the diagnosis, management, and genetic counseling of patients and families with specific inherited conditions, University of Washington.

[OMIM](#) Online Mendelian Inheritance in Man: An Online Catalog of Human Genes and Genetic Disorders, Johns Hopkins University.

[Orphanet](#) A reference portal for information on rare diseases and orphan drugs, led by a European consortium.

# 'Big Data' Research and Development Initiative





# **'Big Data' Planning at NIH**

- **Data and Informatics Working Group**  
**Co-Chairs: Larry Tabak and David DeMets**  
**Report to NIH Director in June 2012**
- **Trans-NIH Subgroup on Molecular Data**  
**Co-Leads: NHGRI and NIGMS**
- **Potential Common Fund initiative in FY2014**



# Advisory Committee to the Director NCBI Working Group

- David Ginsburg (Chair)
- Robert Gentlemen
- Richard Gibbs
- Howard Jacob
- Jill Mesirov
- Deborah Nickerson
- Christine Seidman
- Paul Sternberg
- Marc Vidal



# Basic Behavioral and Social Science Opportunity Network (OppNet)

- **Mission: Pursue opportunities for strengthening basic behavioral and social science research at NIH**
- **Collectively funded and managed**  
**[NHGRI FY2012 contribution: \$349K]**
- **OppNet grants may come to September Council meeting**

National Institutes of Health | Department of Health and Human Services

[Contact Us](#) | [Site Map](#)

**OPPNET** Basic Behavioral & Social Science  
Opportunity Network

[SEARCH](#)

[Home](#) | [About OppNet](#) | [Funding Opportunities](#) | [News & Events](#) | [Resources](#)

**Document 6**

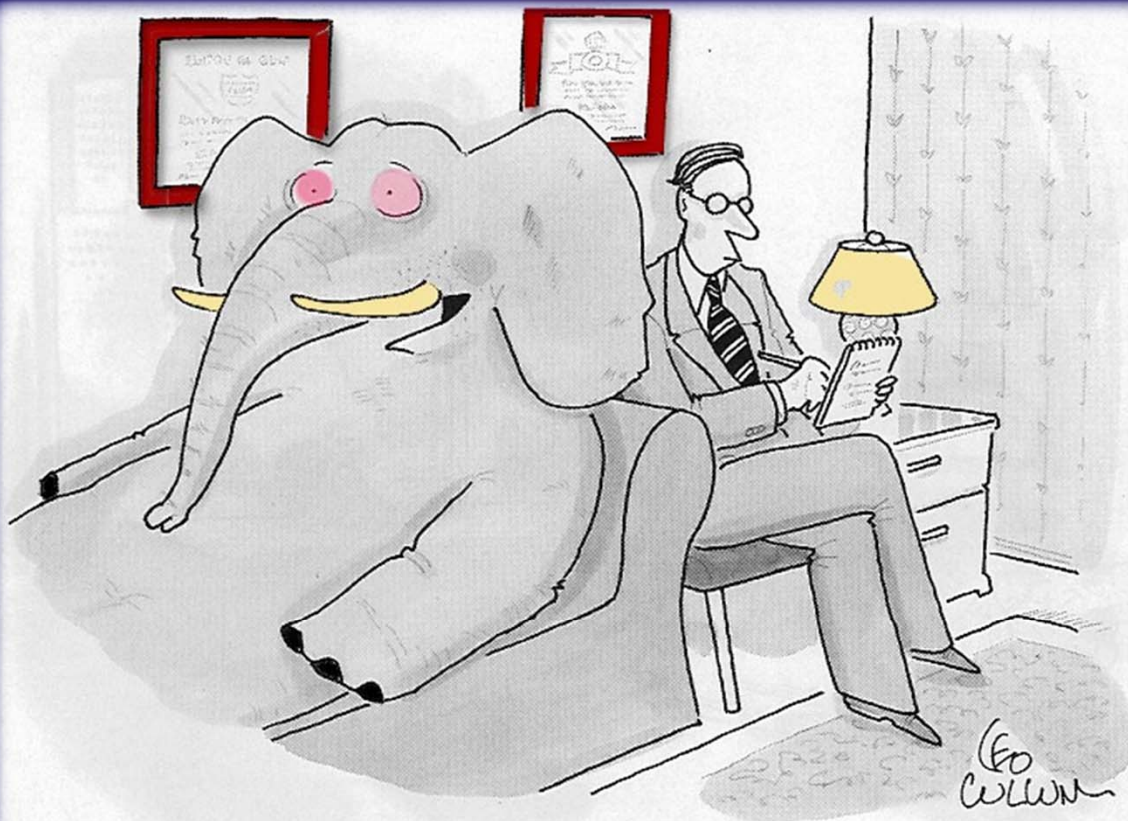
# **FY2013 NIH Appropriation: Overview**



**March 20: House NIH Hearing**

**March 28: Senate NIH Hearing**

# FY2013 NIH Appropriation: Sequestration?



*"I'm right there in the room, and no one even acknowledges me."*



# Warnings: Sequestration Impact on NIH

United for Medical Research

**“33,000 fewer jobs across the United States”**



**“11.1% (\$2.8 billion) reduction of the extramural budget”**

# FY2013 NIH Appropriation: Survival Tips



# Just Released: *Leadership in Decline*



**A CLEAR PICTURE EMERGES FROM THESE INDICATORS: THE COMPETITIVE POSITION OF THE U.S. LIFE SCIENCES INDUSTRY HAS BEEN ERODING OVER THE PAST DECADE.**

**GROWTH IN U.S. GOVERNMENT FUNDING FOR BIOMEDICAL RESEARCH HAS BEEN SLIGHTLY POSITIVE SINCE 1995, WHILE OTHER COUNTRIES ARE INCREASING.**

**Figure 4 | Government-funded R&D for Medical Research (SP)**

Year	U.S.	Other Countries
1995	0.05%	0.05%
1996	0.05%	0.05%
1997	0.05%	0.05%
1998	0.05%	0.05%
1999	0.05%	0.05%
2000	0.05%	0.05%

14 | INFORMATION TECHNOLOGY AND INNOVATION

**“KOREA’S GOVERNMENT PROMOTES PHARMACEUTICAL INDUSTRY-FIVE AND THREE THAN DOES THE UNITED STATES.”**

**“THE UNITED STATES ACCUMULATES A TRADE DEFICIT IN PHARMACEUTICALS LAST DECADE, AT A TIME WHEN TRADE BALANCES OF MANY COMPETITIVE INDUSTRIES ARE IN SURPLUS.”**

**“CHINA HAS THE CAPACITY, WITH MASSIVE INVESTMENT, TO OVERTAKE THE UNITED STATES AND TAKE LEADERSHIP IN LIFE SCIENCES.”**

4 | INFORMATION TECHNOLOGY AND INNOVATION

**FOR AT LEAST THE PAST HALF CENTURY, THE UNITED STATES HAS STOOD AT THE FOREFRONT OF THE GLOBAL LIFE SCIENCES REVOLUTION. BUT AMIDST INTENSIFYING GLOBAL COMPETITION, CONTINUED U.S. LIFE SCIENCES LEADERSHIP IS NOT ASSURED, AND IS UNDER CLEAR THREAT FROM SEVERAL FORCES.**

that America cannot afford to increase its investment in biomedical research is false; the reality is that America cannot afford not to increase its investment in life sciences research. We have seen this play before. The United States has lost leadership in numerous technologies and industries it created and in which it felt it once had unassailable leads—televisions and advanced displays, consumer electronics, and clean-energy technologies such as solar panels and rechargeable batteries for example—which it then let slip away for lack of strategic investment. If we repeat those short-sighted mistakes in the life sciences, the United States can expect similar results.

The United States must therefore re-establish as a national priority and strategic urgency the strong and continuing support for the National Institutes of Health and similar agencies. Specifically: Congress should maintain

the stability of funding levels with minimal fluctuations from year to year; and Congress should maintain NIH funding at a level commensurate with at least one quarter of one percent (0.25%) of national GDP or higher. Our nation’s baseline policy going forward should be to grow NIH funding at a rate that accounts for inflation, embraces emerging avenues of research that can propel U.S. innovative leadership, and reflects the catalytic effect biomedical research has on our nation’s economy.

Implementing these recommendations—committing to this level of sustained investment—will continue the long tradition of policies that have delivered such a robust record of economic growth and made the United States the preeminent global leader in life sciences for the past three-quarters of a century.

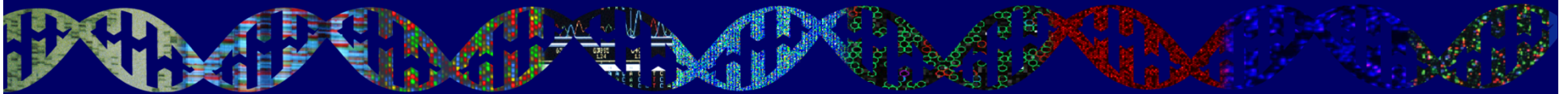
**ABOUT UNITED FOR MEDICAL RESEARCH**  
 United for Medical Research represents leading research institutions, patient and health advocates and private industry, joined together to seek steady increases in federal funding for the National Institutes of Health. The coalition groups consist of the American Cancer Society Cancer Action Network, American Diabetes Association, American Heart Association, Association of American Universities, Association of Public and Land Grant Universities, BID, Biotechnology Industry Organization, Harvard University, Johns Hopkins University, Life Technologies, Massachusetts Institute of Technology, Medicon Research Alliance, PhRMA, ResearchAmerica, Roche Diagnostics, Stanford University, The Endocrine Society, Thermo Fisher Scientific, University of Pennsylvania, University of Southern California, Vanderbilt University, and Washington University in St. Louis.

**ABOUT THE INFORMATION TECHNOLOGY AND INNOVATION FOUNDATION**  
 The Information Technology and Innovation Foundation (ITIF) is a Washington, D.C.-based think tank at the cutting edge of designing innovation strategies and technology policies to create economic opportunities and improve quality of life in the United States and around the world. Founded in 2006, ITIF is a 501(c)(3) nonprofit, non-partisan organization that documents the beneficial role technology plays in our lives and provides fact-based analysis and pragmatic ideas for improving technology-driven productivity, boosting competitiveness, and meeting today’s global challenges through innovation.

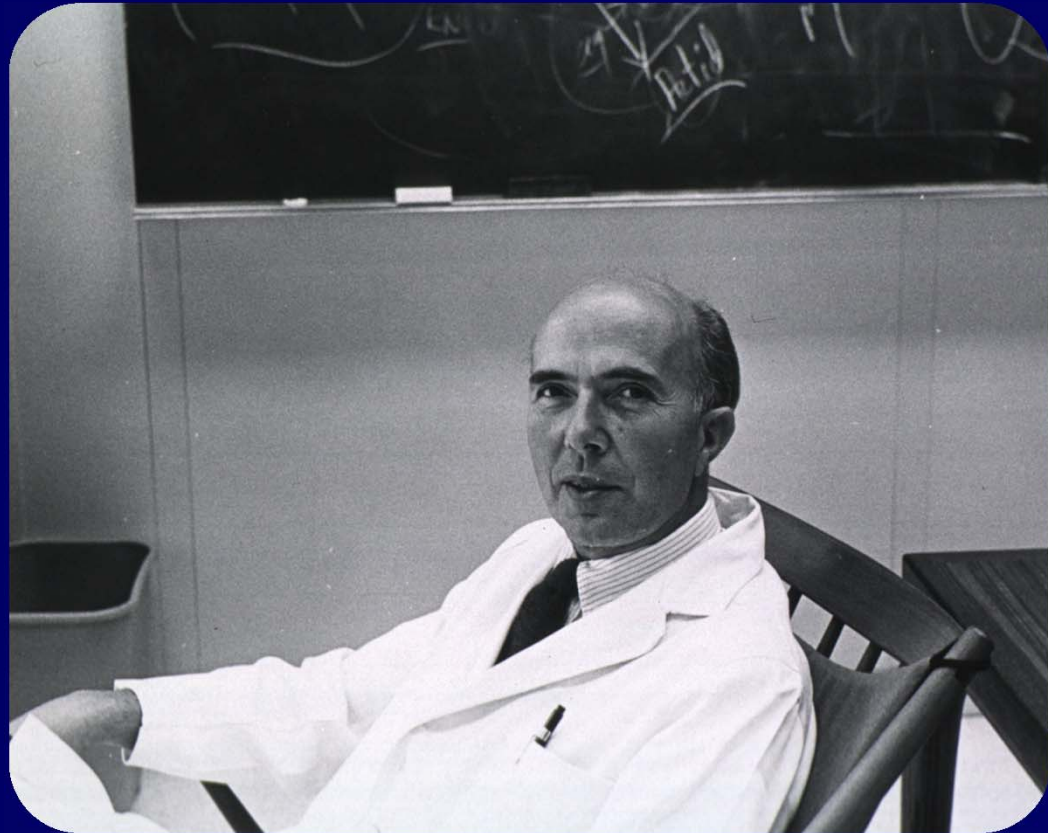
UNITED FOR MEDICAL RESEARCH | 19



- I. General NHGRI Updates
- II. General NIH Updates
- III. Genomics Updates**
- IV. NHGRI Extramural Program
- V. NIH Common Fund Programs
- VI. NHGRI Office of the Director
- VII. NHGRI Intramural Program



# Mourning the Loss of Renato Dulbecco

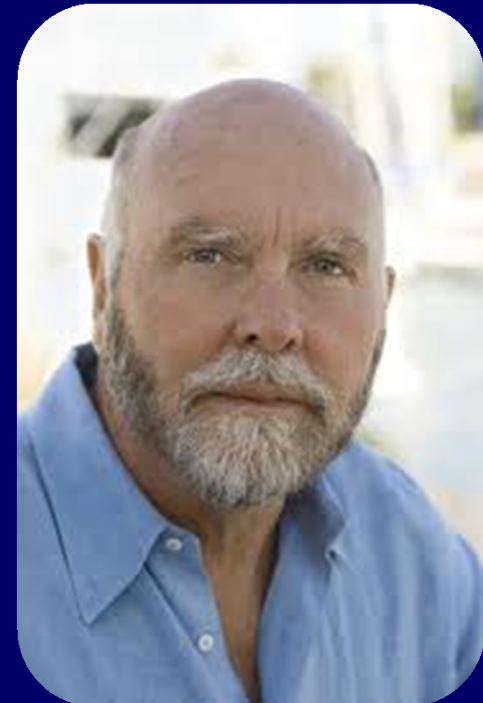


# 2012 Japan Prize



**Janet Rowley, M.D.**

# 2012 Dan David Prize



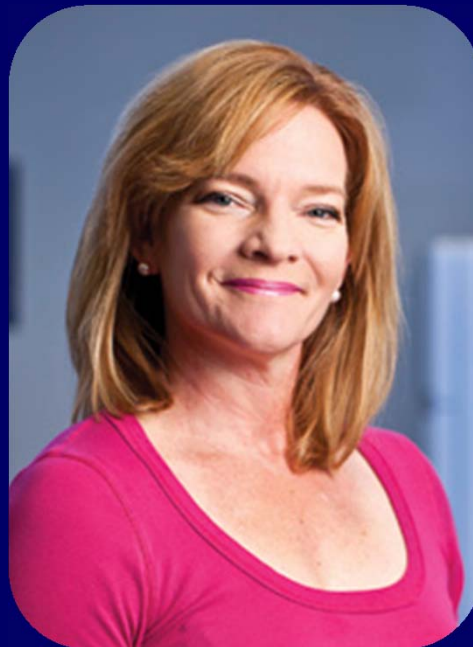
**David Botstein, Ph.D.**  
**Eric Lander, Ph.D.**  
**Craig Venter, Ph.D.**



# Outstanding St. Louis Scientists Award



**Tim Ley**  
**M.D.**



**Elaine Mardis**  
**Ph.D.**



**Rick Wilson**  
**Ph.D.**

# Newly Elected: National Academy of Sciences

- **Andy Clark**
- **Ron DePinho**
- **Evan Eichler**
- **Greg Hannon**
- **Harris Lewin**
- **Rick Young**
  
- **Subra Suresh**



# Bruce Korf: President of the ACMG Foundation for Genetic and Genomic Medicine



American College of  
Medical Genetics Foundation  
*Better Health Through Genetics™*

# Presidential Commission for the Study of Bioethical Issues

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Request for Comments on Issues of Privacy and Access With Regard to Human Genome Sequence Data

**AGENCY:** The Presidential Commission for the Study of Bioethical Issues, Office of the Secretary, Department of Health and Human Services.

**ACTION:** Notice.

**SUMMARY:** The Presidential Commission for the Study of Bioethical Issues is requesting public comment on the ethical issues raised by the ready availability of large-scale human genome sequence data, with regard to privacy and data access and the balancing of individual and societal interests.

**DATES:** To assure consideration, comments must be received by May 25, 2012. Comments received after this date will be considered only as time permits.



[info@bioethics.gov](mailto:info@bioethics.gov)

Document 15

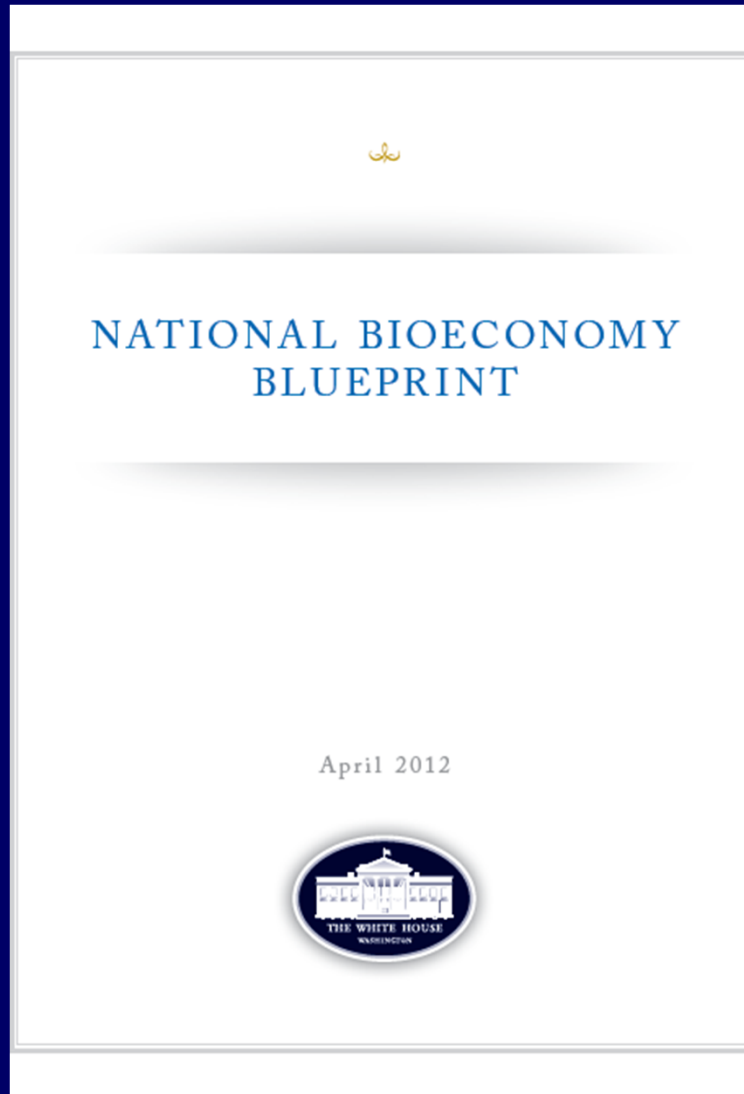


# DeciBio Report on Research Tools



- **Genomics sector:**  
From \$6.8B in 2011 to \$8.9B in 2016
- **‘Next-Gen’ DNA sequencing market:**  
From \$1.05B in 2011 to \$2.25B in 2016

# National Bioeconomy Blueprint



## I. BACKGROUND AND IMPACTS OF THE U.S. BIOECONOMY

### Foundational Technologies: Today and for the Bioeconomy of the Future

Decades of biological research have revealed detailed information about the components of complex systems that characterize life—genes, cells, organisms, ecosystems—and how they interact. As mentioned earlier, genetic engineering, DNA sequencing, and high-throughput technologies have transformed the practice and potential of biological research. Yet, there is substantial room for advancement and discovery; additional scientific and technological revolutions are needed to fundamentally improve the approaches needed to confront the complex societal challenges of the future.

Emerging technologies such as synthetic biology, proteomics, and information technologies, including bioinformatics and computational biology, have the potential to create a vibrant bioeconomy.

**Synthetic Biology:** The ability to quickly and cheaply read and synthesize DNA sequences has transformed biological research. As shown in Figure 2, the costs of sequencing a genome decreased dramatically from 2004 to 2011. Expansive genetic libraries, with billions of genome variants created daily, are now available due to huge strides in “reading and writing” DNA. While the sequencing of the first human genome took 13 years and cost \$2.7 billion, researchers can now sequence a human genome for a fraction of that cost (~\$7,700) and within two weeks’ time. Synthetic biology, the design and wholesale construction of new biological parts and systems, and the re-design of existing, natural biological systems for tailored purposes, integrates engineering and computer-assisted design approaches with biological research. Since natural biological systems are so complicated, a primary focus of synthetic biologists is developing technologies that make the engineering of biology easier, faster, and more predictable. This ability to quickly engineer organisms in laboratories holds vast potential for the bioeconomy, as engineered organisms could dramatically transform modern practices in high-impact fields such as agriculture, manufacturing, energy generation, and medicine. Much work lies ahead, including identifying and standardizing biological and molecular components, but this powerful new area of

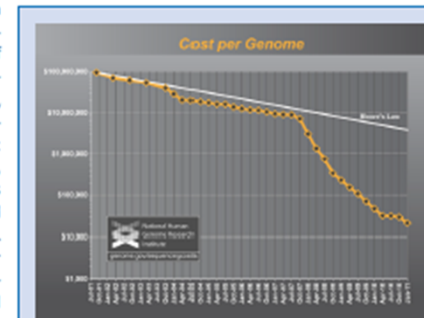
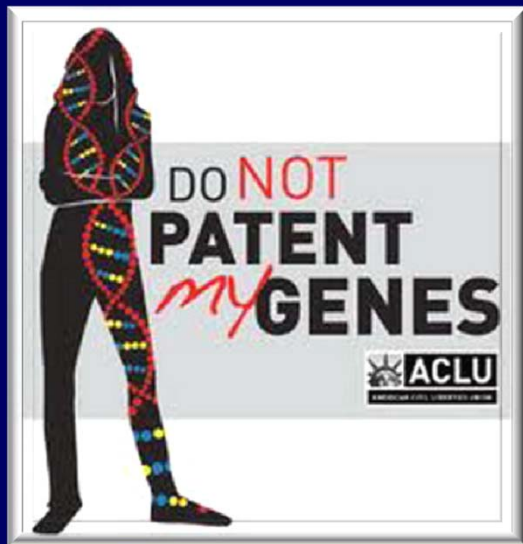


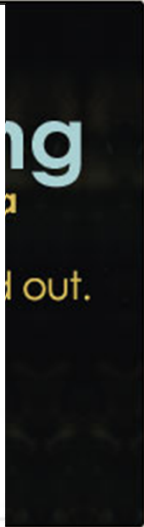
Figure 2. “Cost per Genome” – the cost of sequencing a human-sized genome. Data from 2001 through October 2007 represent the costs of generating DNA sequence using first generation sequencing technology. Beginning in January 2008, the data represent the costs of generating DNA sequence using ‘second-generation’ (or ‘next-generation’) sequencing platforms. The change in instruments represents the rapid evolution of DNA sequencing technologies that has occurred in recent years.<sup>38</sup>

38. Wetterstrand KA. DNA Sequencing Costs: Data from the NHGRI Large-Scale Genome Sequencing Program Available at: [www.genome.gov/sequencingcosts](http://www.genome.gov/sequencingcosts).

# Biotech Patents and the Courts



# 2012 Advances in Genome Biology and Technology Meeting



2012 Sponsors

Gold



PACIFIC  
BIOSCIENCES™

Bronze



Caliper  
a PerkinElmer company



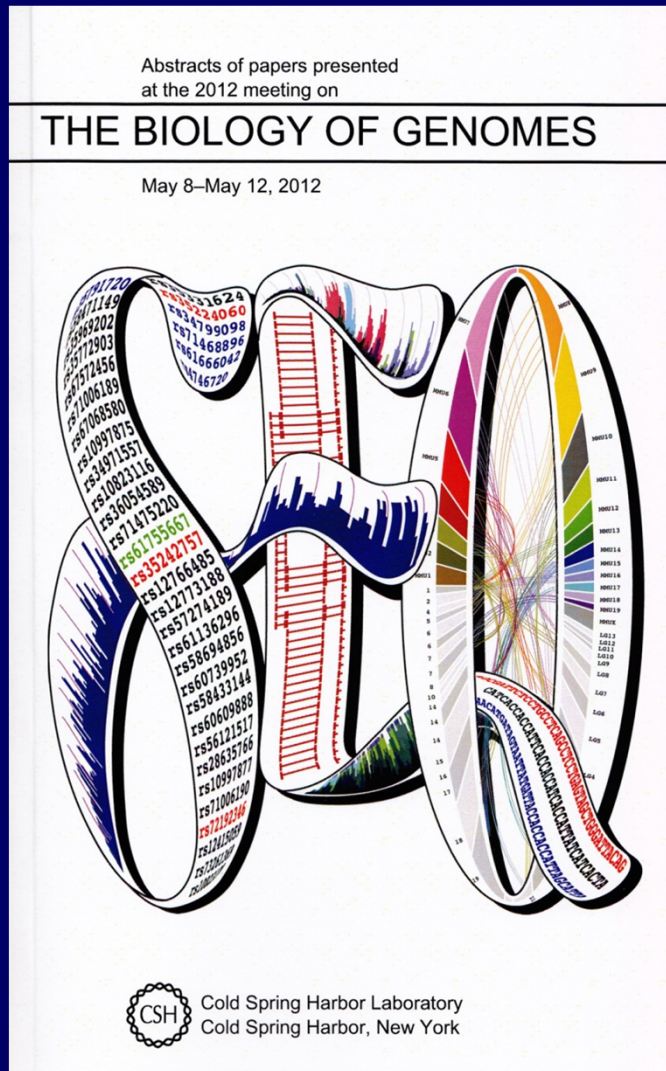
organized by:



PMB 221,738 MAIN STREET, WALTHAM, MA 0

Site by the [ranDimension](#).

# 2012 Biology of Genomes Meeting Cold Spring Harbor Laboratory



# NOVA: "Cracking Your Genetic Code"

The screenshot shows the NOVA website interface. At the top, there is a navigation bar with the NOVA logo and 'beta' tag, followed by menu items: ANCIENT WORLDS, BODY + BRAIN (highlighted), EVOLUTION, MILITARY + ESPIONAGE, NATURE, PHYSICS + MATH, PLANET EARTH, SPACE + FLIGHT, and TECH + ENGINEERING. Below the navigation bar is a search bar labeled 'Search NOVA Beta' with a 'GO' button, and buttons for 'TV SCHEDULE', 'NOVA EDUCATION', and 'SHOP NOVA'. On the right side of the navigation bar are 'PRINT', 'SHARE', and 'A A' icons.

The main content area features a 'COMING SOON' badge next to the article title 'Cracking Your Genetic Code'. The article text reads: 'We are on the brink of a new era of personalized, gene-based medicine. Are we ready for it? Airing 3/28/12 on PBS'. Below the text is the date 'Posted 01.24.12'.

The article includes a large image of a DNA microarray with the text 'CRACKING YOUR GENETIC CODE' overlaid. To the right of the image is a video player with a play button icon and the text 'Watch the Preview | 00:44'. Below the video player are social media sharing options: 'Like' (439), 'Tweet' (85), and 'EMAIL A FRIEND'.

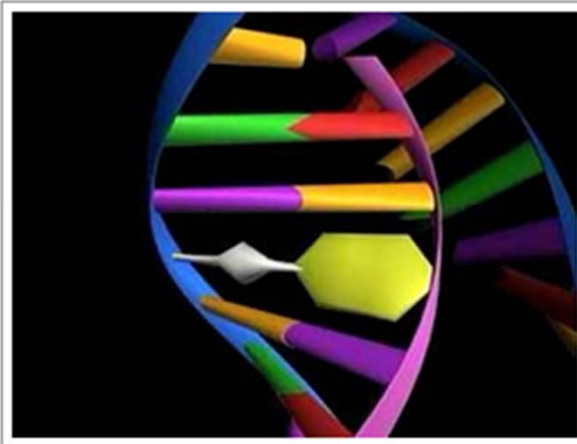
# NHGRI Genome Advance of the Month

Harnessing the full 'omics potential of personalized medicine

By Danielle Daee, Ph.D.  
Postdoctoral Fellow

## Discovering the Mutants Among Us

By Joy Yang  
Post-baccalaureate Fellow



Last year, the Sanger Institute boldly announced "[We are all mutants](#)" when a study was published showing that healthy individuals carry around 60 new mutations from their parents. However, not all of these mutations are meaningful, as some may fall in regions of the genome without any currently known function. The next Genome Advance of the Month focuses on a particular class of mutations, "loss-of-function (LoF) variants."

LoF is defined as a genetic variant that is predicted to cause a loss of function in protein-coding genes; in other words, some change in the genome sequence that prevents the production of a normal protein. Because LoF variants can result in debilitating diseases such as cystic fibrosis and Duchenne muscular dystrophy, they are usually thought to be rare;

however, many scientists suspect that LoF variants may actually be quite common, even among healthy people. In fact, the first few whole genome sequences produced following the Human Genome Project each contained several hundred LoF variants in apparently normal individuals.



# ***Genomics In The News...***



**New insights on  
evolution from  
the study of  
sticklebacks**



**Insights about  
human evolution  
from the gorilla  
genome sequence**





# Genomics In The News...



The New York Times

## Research

WORLD U.S. N.Y. / REGION BUSINESS TECHNOLOGY SCIENCE HEALTH SPORTS OPINION

### Scientists Link Gene Mutation to Autism Risk

A photograph of three men in a laboratory or office setting. The man in the foreground is wearing a red jacket and looking towards the camera. Behind him are two other men, one in a blue shirt and one in a white shirt, standing in front of a whiteboard with some diagrams on it.

# Genomics In The News...





# Genomics In The News...



## N.Y. Preschool Starts DNA Testing For Admission

by NPR STAFF



**Listen to the Story**

*All Things Considered*

[3 min 41 sec]

- + Add to Playlist
- ↓ Download
- 📄 Transcript

# April Fools



iStockphoto.com

At the Porsafillo Preschool Academy, there are 32 spots but more than 12,000 applications.

showed off "Porsafillo Pre," as it's called.

"Over here, we have computer labs, C++ learning, which of course, as I'm sure you know, is a language of computers," she says. Wait, computer language? These preschoolers are learning C++?

their children.

The preschool is housed in a modern glass and steel building designed by IM Pei. It's situated in a leafy corner of the Upper West Side. On a recent afternoon, Headmaster Rebecca Unsinn

I. General NHGRI Updates

II. General NIH Updates

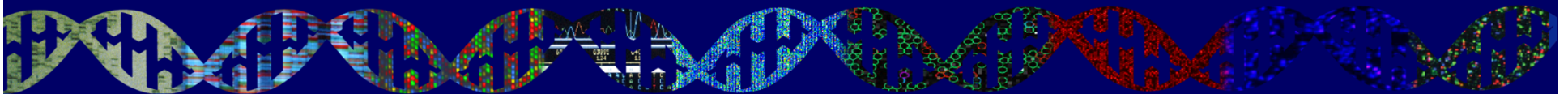
III. Genomics Updates

**IV. NHGRI Extramural Program**

V. NIH Common Fund Programs

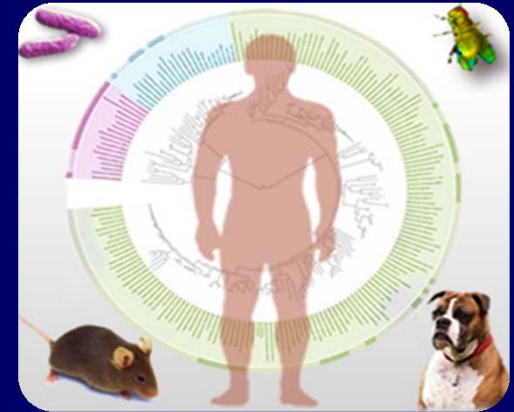
VI. NHGRI Office of the Director

VII. NHGRI Intramural Program



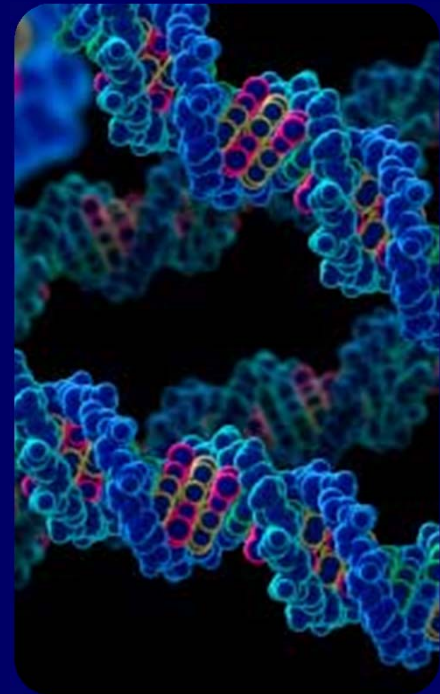
# NHGRI Genome Sequencing Program

- Large-Scale Genome Sequencing Centers
- Mendelian Disorders Genome Centers
- Clinical Sequencing Exploratory Research Projects
- Informatics Tools for High-Throughput Sequence Data Analysis
- Meeting involving all components: October 2012



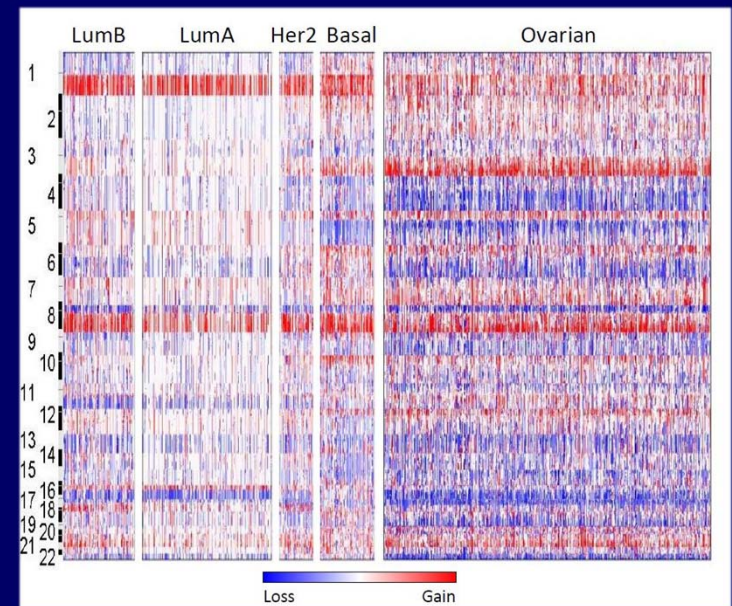
# Large-Scale Genome Sequencing Centers

- **New: Alzheimer's disease sequencing project**
- **Recent Publications:**
  - **Autism Sequencing Consortium**
  - **Schizophrenia allele spectrum**
  - **Six Cancer genomics papers**
  - **Gorilla genome**
  - **Macaque Y chromosome**
  - **Stickleback adaptive evolution**
  - **Drosophila population genomics**





- **TGCA papers on three cancers (in press or under review):**
  - Colorectal Carcinoma**
  - Breast Carcinoma**
  - Lung Squamous Cell Carcinoma**
- **Each paper reports the comprehensive integrative analyses of genome sequences for 100's of tumors**
- **Several additional manuscripts are anticipated in 2012**



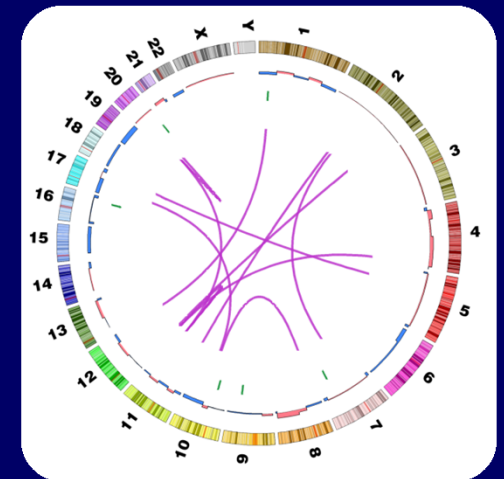


- **CGHub (TCGA sequence data repository) opens at UCSC**

New innovations (e.g., BAM slicing) to be implemented soon

First 'NIH Trusted Partner' for redistribution of genome sequence data

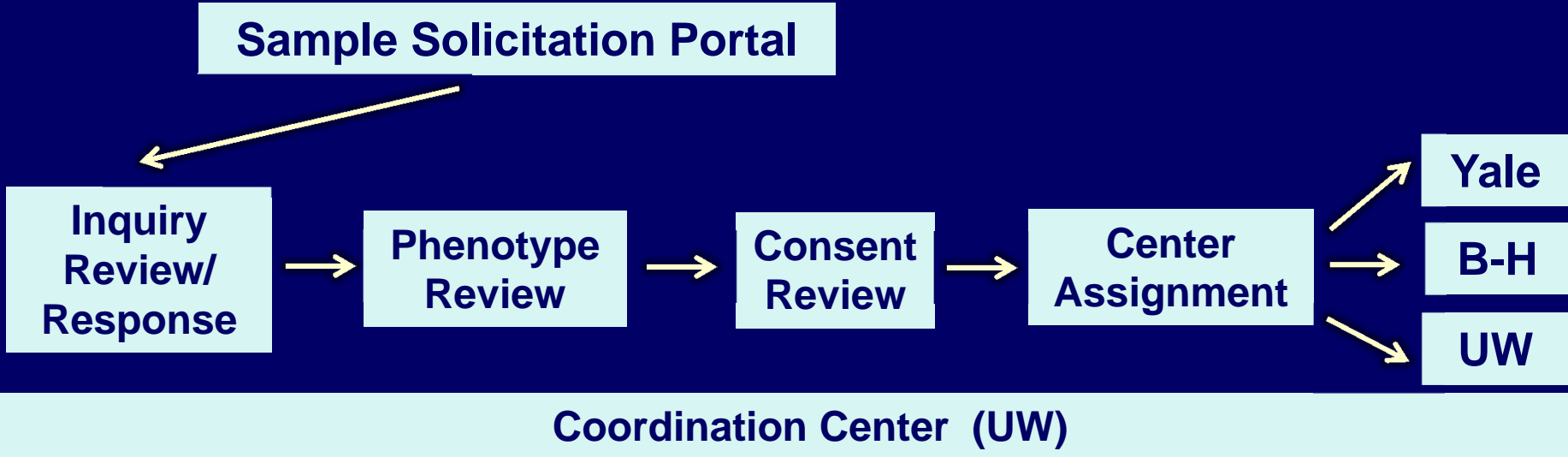
- **>6,000 tumors analyzed from 20 cancer types; on track to achieve program goals by 2014 target**







- Implemented pipeline from the Program's sample solicitation portal through sample assignment to the Centers



- Educational program on Mendelian Genomics at the 2012 Annual ASHG Meeting
- Disease gene discovery is ongoing at various stages from sequencing to the identification of disease genes

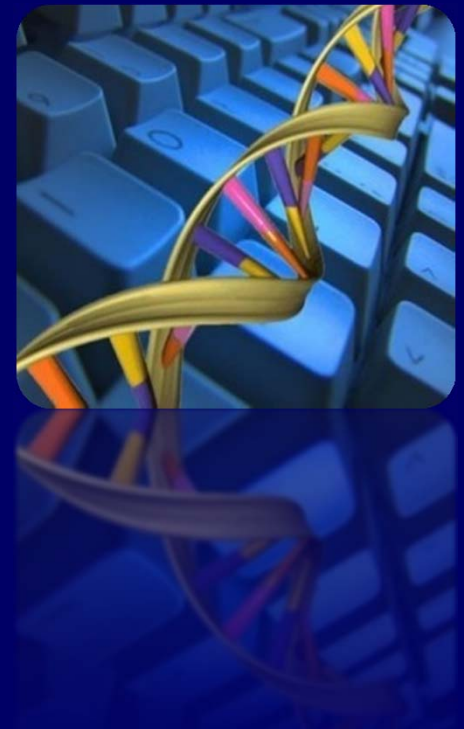
# Clinical Sequencing Exploratory Research (CSER) Projects

- **First meeting of the CSER Steering Committee and the Return of Results Consortium**
- **New RFAs released:**
  - **Reissue of original CSER solicitation**
  - **CSER Coordinating Center**



# Informatics Tools for High-Throughput Sequence Data Analysis

- “iSeqTools” Network aims to develop robust and reliable analysis tools for researchers without specialized computational skills
- Leveraging NHGRI’s investment in sequencing centers and initiatives (e.g., 1000 Genomes, Galaxy, and others)
- Building iSeqTools wiki as a knowledgebase



# DNA Sequencing Technology Development



**Grantee Meeting (April 2012)**

# DNA Sequencing Technology Development

## LETTERS

nature  
biotechnology

### Automated forward and reverse ratcheting of DNA in a nanopore at 5-Å precision

Gerald M Chefert, Kate R Lieberman, Hytham Rashid, Christopher E Lam, Kevin Karplus & Mark Akeson

An emerging DNA sequencing technique uses protein or solid-state pores to analyze individual strands as they are driven in single-file order past a nanoscale sensor<sup>1-3</sup>. However, uncontrolled electrophoresis of DNA through these nanopores is too fast for accurate base reads<sup>4</sup>. Here, we describe forward and reverse ratcheting of DNA templates through the  $\alpha$ -hemolysin nanopore controlled by phi29 DNA polymerase without the need for active voltage control. DNA strands were ratcheted through the pore at median rates of 2.5-40 nucleotides per second and were examined at one nucleotide spatial precision in real time. Up to 500 molecules were processed at ~130 molecules per hour through one pore. The probability of a misassignment (an insertion or deletion)

through the nanopore. This event results in a brief current blockade that is influenced by DNA strand length<sup>5</sup> and base composition<sup>6</sup>.

A consensus has emerged that the average rate of ssDNA electrophoresis through nanopores (~3  $\mu\text{s nt}^{-1}$  at 120 mV for  $\alpha$ -HL) is too fast to allow bases to be accurately identified<sup>4</sup>. Therefore, a functional nanopore sequencing device will require a means to systematically slow DNA template movement. One proposed strategy involves coupling an enzyme motor to the nanopore<sup>7</sup>. This strategy is attractive because many processive enzymes, including polymerases, ratchet along DNA strands one nucleotide at a time, up to tens of thousands of times in succession in bulk phase<sup>8</sup>. Systematic, enzyme-driven displacement of a captured DNA strand relative to the nanopore would be anticipated at millisecond

© 2012 Nature America, Inc. All rights reserved.

Single-molecule sequencing

nature  
biotechnology

## LETTERS

### Reading DNA at single-nucleotide resolution with a mutant MspA nanopore and phi29 DNA polymerase

Elizabeth A Manrao<sup>1</sup>, Ian M Derrington<sup>1</sup>, Andrew H Laszlo<sup>1</sup>, Kyle W Langford<sup>1</sup>, Matthew K Hopper<sup>1</sup>, Nathaniel Gillgren<sup>1</sup>, Mikhail Pavlenok<sup>2</sup>, Michael Niederweis<sup>2</sup> & Jens H Gundlach<sup>1</sup>

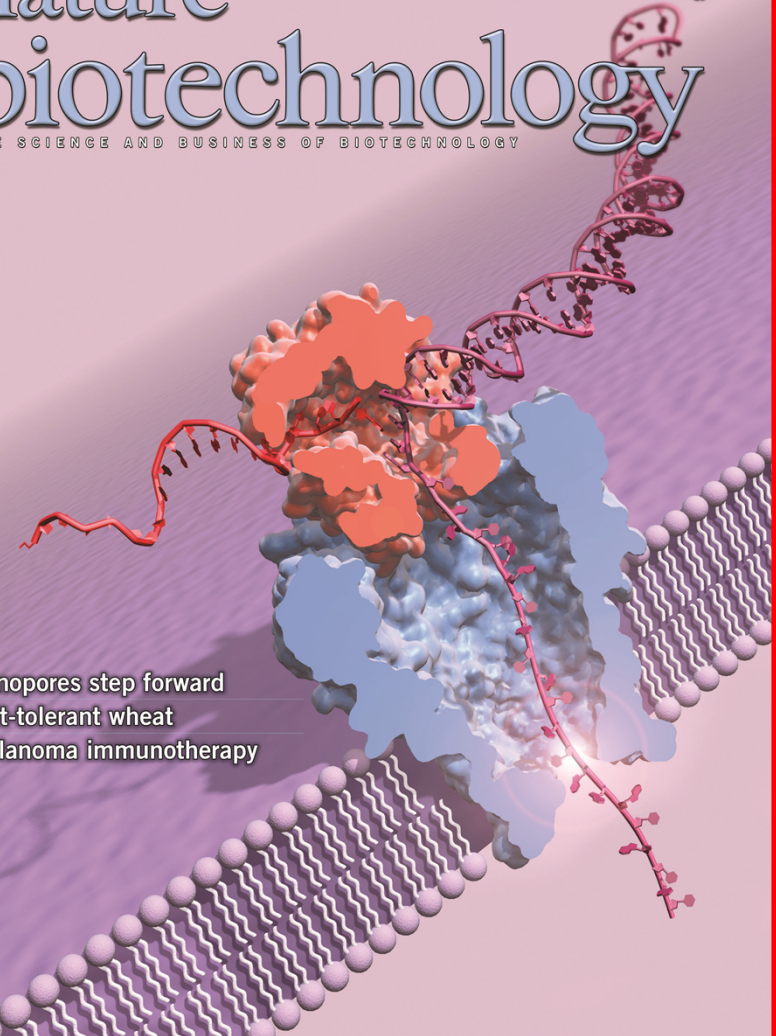
Nanopore technologies are being developed for fast and direct sequencing of single DNA molecules through detection of ionic current modulations as DNA passes through a pore's constriction<sup>1,2</sup>. Here we demonstrate the ability to resolve changes in current that correspond to a known DNA sequence by combining the high sensitivity of a mutated form of the protein pore *Mycobacterium smegmatis* porin A (MspA)<sup>3</sup> with phi29 DNA polymerase (DNAP)<sup>4</sup>, which controls the rate of DNA translocation through the pore. As phi29 DNAP synthesizes DNA and functions like a motor to pull a single-stranded template through MspA, we observe well-resolved and reproducible ionic current levels with median durations of ~28 ms and ionic current differences of up to 40 pA. Using six different DNA sequences with readable regions 42-53 nucleotides long, we record current traces that map to the known DNA sequences. With single-nucleotide resolution and DNA translocation control, this system integrates solutions to two long-standing hurdles to nanopore sequencing<sup>2</sup>.

nanopore sequencing because it has a short and narrow constriction ~1.2 nm wide and ~0.6 nm long<sup>12</sup> (Fig. 1a). Thus, the ionic current through MspA is affected by a smaller number of nucleotides compared with other pores<sup>3,7,8</sup>. Previously, we engineered mutants of MspA by replacing negative charges in the constriction with neutral residues, which enabled DNA to electrophoretically pass through the pore<sup>13</sup>. We also added 24 positively charged residues in the vestibule and entrance, which enhanced the rate of entry of DNA into the pore<sup>13</sup>. This mutant, previously called M2-NNN MspA, is used in the present study and is here designated MspA. When DNA was held statically in the constriction of a mutant MspA by a conjugated NeutrAvidin molecule<sup>3</sup>, different homopolymer strands resulted in conductance differences of as much as ~0.23 nS, nearly ten times more separation than that observed with the widely used  $\alpha$ -hemolysin nanopore (~0.028 nS)<sup>7,8</sup>. However, this was not sufficient for nanopore sequencing because freely translocating DNA acting under the force of an electric field moves through nanopores at an average rate greater than one nucleotide/ $\mu\text{s}$  ~1,000 times too fast to distinguish nucleotide-specific current changes from noise<sup>12,13,14</sup>. Simple techniques for reducing the velocity of translocating DNA, such

© 2012 Nature America, Inc. All rights reserved.

nature  
biotechnology  
THE SCIENCE AND BUSINESS OF BIOTECHNOLOGY

VOLUME 30 NUMBER 4 APRIL 2012  
www.nature.com/naturebiotechnology



Nanopores step forward  
Salt-tolerant wheat  
Melanoma immunotherapy

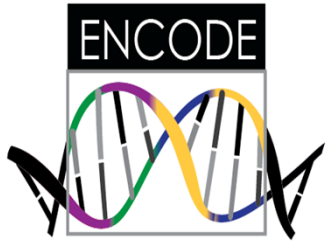
# DNA Sequencing Technology Development

**Gundlach**                      **Branton, Deamer, Church**  
**Akeson**



**Manrao**                      **Cherf Derrington Lazlo**

**Nanopore sequencing demonstrated**



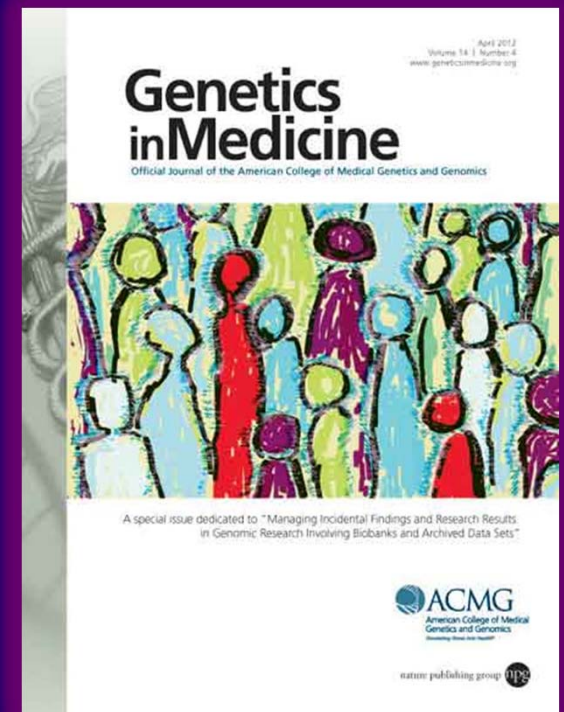
# ENCODE & modENCODE



- **ENCODE Technology Development awards funded this spring**
- **modENCODE Symposium: June 20-21, 2012**
- **Integrative analysis papers planned:**
  - ENCODE – integrative manuscript submitted along with many companion papers**
  - modENCODE/ENCODE – comparison of fly, worm, and human**
  - Mouse – comparison of mouse and human**

# ELSI Program

- New RFAs for Centers of Excellence in ELSI Research (CEER) Program: P20 and P50
- Return of Results Consortium launched
- April 2012 issue of *Genetics in Medicine* focused on return of results and incidental findings, featuring multiple papers by ELSI-funded investigators





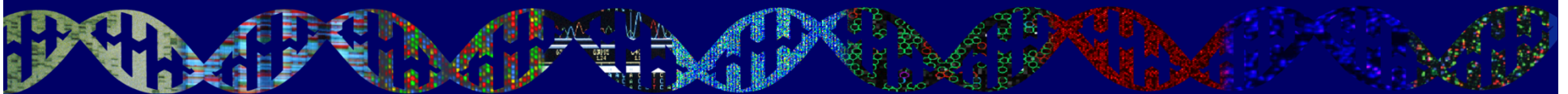
# Upcoming Planning Meeting

- July 2012 Workshop:

## Integrating Functional Data for Connecting Genotype to Phenotype



- I. General NHGRI Updates
- II. General NIH Updates
- III. Genomics Updates
- IV. NHGRI Extramural Program
- V. NIH Common Fund Programs**
- VI. NHGRI Office of the Director
- VII. NHGRI Intramural Program



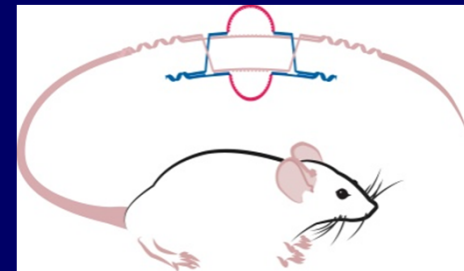
# Human Microbiome Project (HMP)

- HMP funding ends in FY2012
- Two major HMP Consortium papers to be published in *Nature*; coordinated release of >20 companion papers in *PLoS* ('HMP Collection')
- HMP2 proposal submitted to Common Fund
- Report at September Council meeting



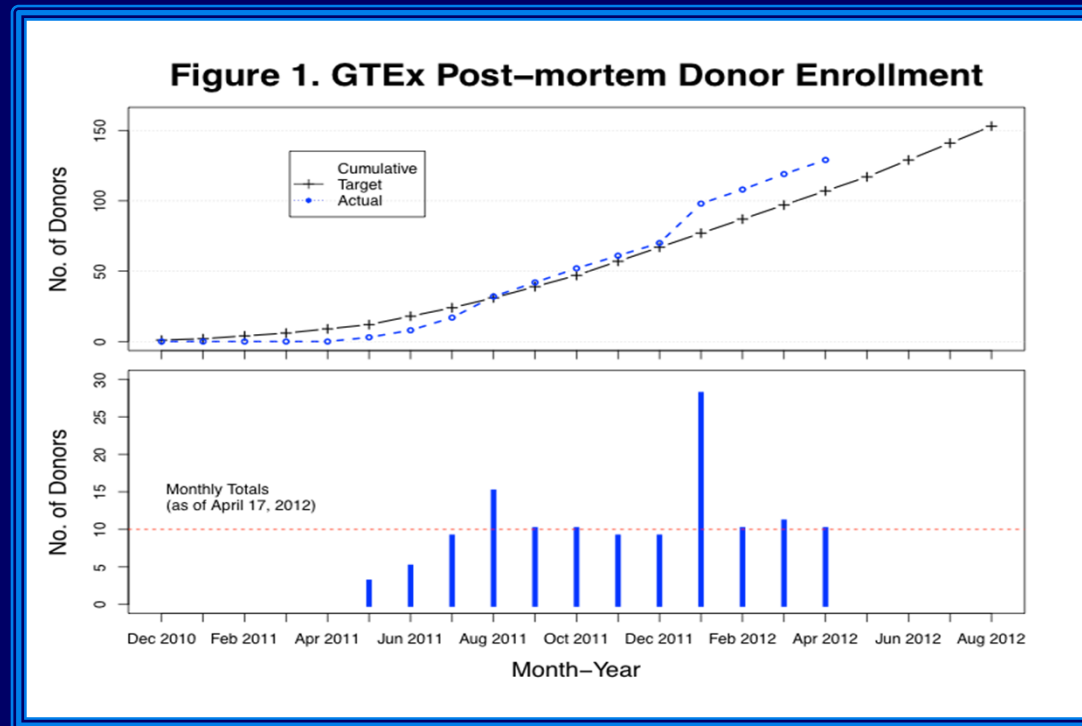
# Knockout Mouse Phenotyping Project (KOMP<sup>2</sup>)

- In 5 years, make 2,500 live mouse strains from knockout ES cells
- Comprehensively phenotype the mouse strains
- Make data and mice available to researchers
- Collaborate with other international projects to achieve a total of 5,000 phenotyped strains through the IMPC

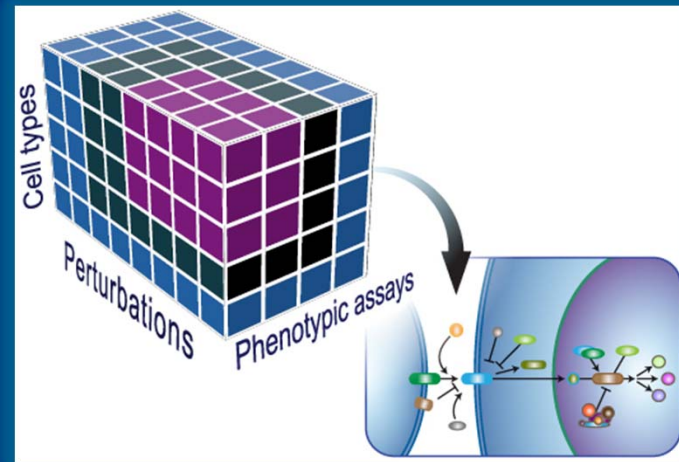


# Genotype-Tissue Expression (GTEx)

- Pilot goals have been met
- Scale-up is under consideration
- First dbGaP data release later this month



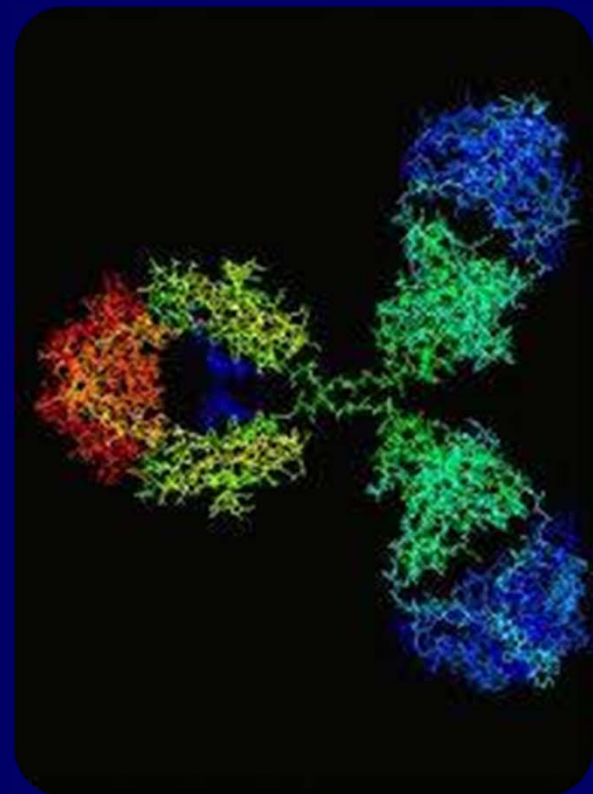
# Library of Integrated Network-based Cellular Signatures (LINCS)



- Consortium meeting in November 2012
- Request to the Common Fund for a 1-year extension of pilot (FY2013 bridge funds)
- Quarterly public release of LINCS data and metadata (started March 2012)

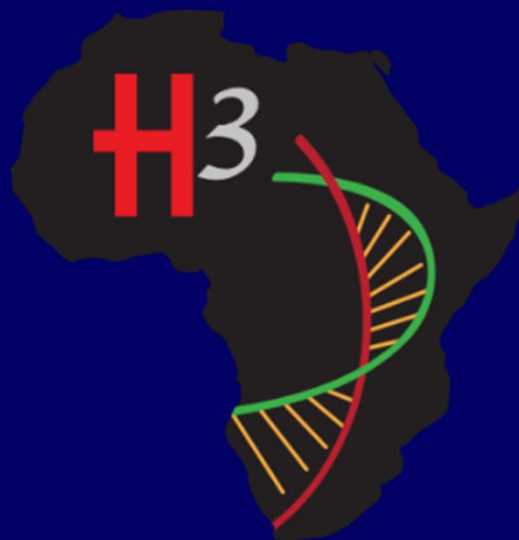
# Protein Capture Reagents Program

- **New working groups:**
  - **Data dissemination**
  - **Validation**
  - **Target list prioritization**
- **Soliciting community input about production of human transcription factor reagents**



# Human Heredity and Health in Africa (H3Africa)

- Applications reviewed in March and April
- A funding plan will be discussed in Closed Session of this Council meeting
- Inaugural H3Africa Research Network meeting will be held in Ethiopia in October 2012





# Single Cell Analysis

- **Three RFAs:**

- Evaluate cellular heterogeneity using transcriptional profiling

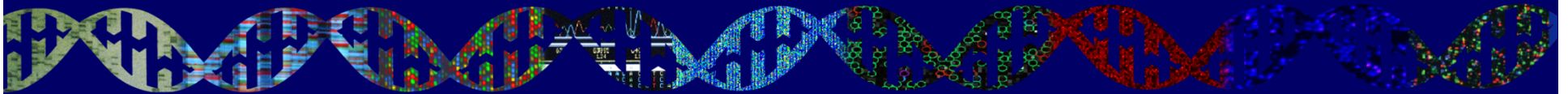
- Innovative tools and technologies

- Single cell technology validation in clinical setting

- **Single Cell Analysis workshop recently held**



- I. General NHGRI Updates
- II. General NIH Updates
- III. Genomics Updates
- IV. NHGRI Extramural Program
- V. NIH Common Fund Programs
- VI. NHGRI Office of the Director**
- VII. NHGRI Intramural Program



# The eMERGE Network

electronic Medical Records & Genomics

*A consortium of biorepositories linked to electronic medical records data for conducting genomic studies*

## PheKB

a knowledgebase for discovering phenotypes from electronic medical records

Home Phenotypes Implementations Groups Institutions

### What is the Phenotype KnowledgeBase?



The reuse of data from electronic medical records (EMRs) and other clinical data systems holds tremendous promise for improving the efficiency and effectiveness of health research. Clinical data in the EMR is a potential source of rich longitudinal data for research, and the recent government efforts to promote the use of EMRs in the clinical setting may further promote the use of such systems in the US healthcare system. As the use of EMRs expands, the demand for usable data from these systems for research has also expanded.

One such effort by the Electronic Medical Records and Genomics Network (eMERGE) has investigated whether data captured through routine clinical care using EMRs can identify disease phenotypes with sufficient positive and negative predictive values for use in genome-wide association studies (GWAS). Most EMRs captured key information (diagnoses, medications, laboratory tests) used to define phenotypes in a structured format; in addition, natural language

processing has also been shown to improve case identification rates.\*

- **Purpose: To provide a collaborative environment for building and validating electronic phenotype algorithms**

# eMERGE Testimony to the National Committee on Vital and Health Statistics

- **Data collection: community engagement models, community advisory boards, and promotion of research to the community**
- **Data utilization: data use agreement for sharing data in the consortium**
- **Data dissemination: de-identified data submitted to dbGaP for sharing data beyond the eMERGE sites**



# GENEVA Initiative Complete

- 20 datasets posted to dbGaP, all imputed

Addiction

Glaucoma

Oral Clefts

Blood Clotting

Heart Disease

Prematurity

Blood Pressure

Lung Cancer

Prostate Cancer

COPD

Maternal

Stroke

Dental Carries

Metabolism

Venous

Diabetes

Melanoma

Thombosis

- 50+ publications
- GWASTools website developed

GENE.ENVIRONMENT  
ASSOCIATION.STUDIES **GENEVA**



Home

**NIDA provided funds to expand the Toolkit to include additional substance use measures**

- 43 new measures included in the Toolkit
- Measures selected and vetted by content experts in NIDA extramural community

**Measures address:**

- substance use and intermediate phenotypes
- cognitive and psychosocial risk factors
- co-morbidities and health-related outcomes

- NIDA is encouraging all grant applicants proposing human-subjects research to use the PhenX Toolkit

**NEW!**



Substance Abuse and Addiction

Measures from the PhenX Toolkit version March 23 2012, Ver 5.1 (www.phenxtoolkit.org) were included in this study. PhenX (consensus measures of Phenotypes and eXposures) is supported by NHGRI award No. U01 HG004597.

User ID:

Password:

Log In

# NEJM Genomic Medicine Series

## Genomics, Intellectual Disability, and Autism

Heather C. Mefford, M.D., Ph.D., Mark L. Batshaw, M.D.,  
and Eric P. Hoffman, Ph.D.



**I**NTELLECTUAL DISABILITY, WHICH IS CHARACTERIZED BY SIGNIFICANT LIMITATIONS in both intellectual functioning and adaptive behavior, is often diagnosed by the age of 18 years. A diagnosis of intellectual disability is made when the individual is less than 70, which is often in early adulthood. Intellectual disability has long been recognized as detectable by chromosomal analysis. Important chromosomal abnormalities have been identified for autosomal and X-linked forms of inherited syndromes in male patients.

### Realizing Genomic Medicine

Elizabeth G. Phimister, Ph.D., W. Gregory Feero, M.D., Ph.D., and Alan E. Guttmacher, M.D.

The current series of Genomic Medicine review articles concludes in this issue of the *Journal* with the publication of an article on cognitive impairment and autism by Mefford and colleagues.<sup>1</sup> The topic of this article is an appropriate capstone for the Genomic Medicine series: it highlights the clinical advances in genomics regarding the care of patients with neurologic conditions, and it shows the potential of genomic science to further accelerate the pace of discovery in the neurosciences.

solved. Their resolution will be critical to realizing the full benefit of genomic advances. Central to some of these issues is the boundary between research and clinical care, as defined in the Belmont Report produced by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and the "Common Rule" that governs much of federally funded biomedical research in the United States.<sup>2,3</sup>

Making clinical use of the vast complexity of

# 2012 DNA Day Chat Room

- April 20, 8:00 am to 5:00 pm EST
- More than 70 experts answered questions
- Received more than 900 questions and experts answered 764 of the questions
- Questions from 37 states and internationally





# USA Science and Engineering Festival



## Celebrate Science at the 2<sup>nd</sup> USA Science & Engineering Festival

Expo and Book Fair: April 28 & April 29, 2012  
Walter E. Washington Convention Center, DC  
A Free Event



search...



FESTIVAL HOST  
LOCKHEED MARTIN

[Home](#) ★ [About](#) ★ [2012 Festival](#) ★ [Sponsors](#) ★ [Book Fair](#) ★ [Satellite Events](#) ★ [Newsroom](#) ★ [Contact Us](#) ★

**Pre-Register  
for the Expo**

**GET YOUR GIRLS MOTIVATED WITH  
SPACE TOURIST ANOUSHEH ANSARI**



**Browse Exhibits**

**Browse Stage Shows**

**Browse Book Fair**

**What:**

Science Festival Expo and Book Fair

**When:**

Sat, April 28, 2012, 10am-6pm  
Sun, April 29, 2012, 10am-4pm

**Where:**

Washington, D.C.  
Walter E. Washington Convention Center  
[801 Mount Vernon Place, NW](#)  
[Washington, DC 20001](#)



# USA Science and Engineering Festival



# **GENOMICS** in Medicine Lecture Series

**First Friday of each month, 8-9 AM**

**Suburban Hospital Auditorium**

**June 1, Barbara Biesecker, NHGRI**  
*Genomics in Maternal Child Health*

**Invited Speakers: July 2012 through January 2013**

**Paul Sieving, NEI**

**Dan Kastner, NHGRI**

**Kenneth Fishbeck, NINDS**

**Ellen Sidransky, NHGRI**

**Max Muenke, NHGRI**



**JOHNS HOPKINS**  
M E D I C I N E

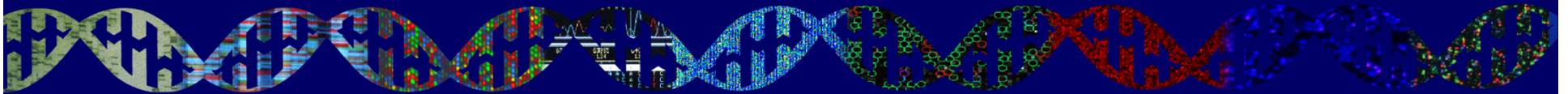


National  
Human Genome  
Research Institute



**SUBURBAN HOSPITAL**  
JOHNS HOPKINS MEDICINE

- I. General NHGRI Updates
- II. General NIH Updates
- III. Genomics Updates
- IV. NHGRI Extramural Program
- V. NIH Common Fund Programs
- VI. NHGRI Office of the Director
- VII. NHGRI Intramural Program**



# NHGRI Intramural Research Highlights



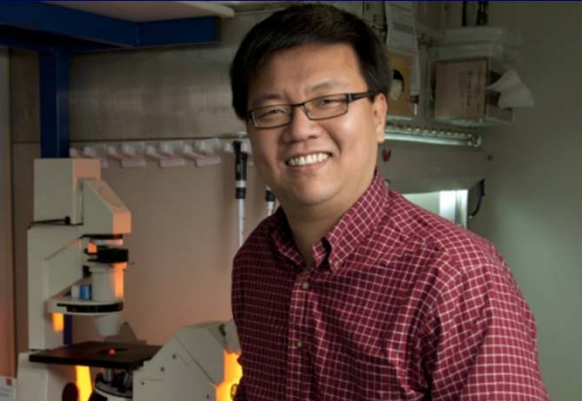
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## HLA Class II Locus and Susceptibility to Podoconiosis

Fasil Tekola Ayele, Ph.D., M.P.H., Adebowale Adeyemo, M.D., Chris Finan, Ph.D., Elena Hailu, M.Sc., Paul Sinnott, Ph.D., Natalia Diaz Burlinson, M.Sc., Abraham Aseffa, M.D., Ph.D., Charles N. Rotimi, Ph.D., M.P.H., Melanie J. Newport, M.D., Ph.D., and Gail Davey, M.D.

N Engl J Med 2012; 366:1200-1208 | March 29, 2012



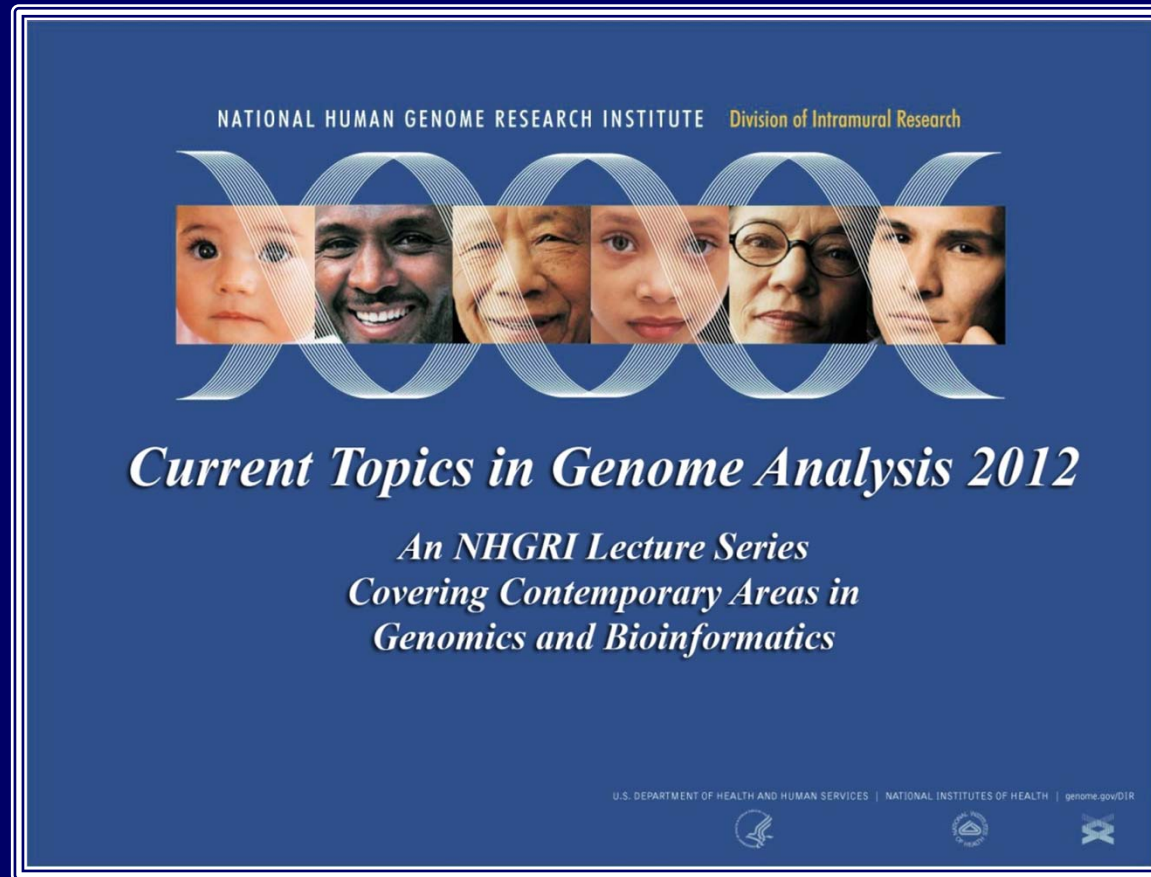
PNAS

Proceedings of the National Academy of Sciences of the United States of America

## High-throughput genotoxicity assay identifies antioxidants as inducers of DNA damage response and cell death

Jennifer T. Fox<sup>a</sup>, Srilatha Sakamuru<sup>b</sup>, Ruili Huang<sup>b</sup>, Nedelina Teneva<sup>a</sup>, Steven O. Simmons<sup>c</sup>, Menghang Xia<sup>b</sup>, Raymond R. Tice<sup>d</sup>, Christopher P. Austin<sup>b</sup>, and Kyungjae Myung<sup>a,1</sup>

# Current Topics in Genome Analysis



- Views to date for 2012 Series: **22,852**
- Views for 2010 Series: **202,812**

# Blue Ribbon Panel Review of NHGRI Intramural Research Program

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





genome.gov

National Human Genome Research Institute

National Institutes of Health



**Special Thanks!**





genome.gov



THE  
BRIGHT  
OF  
FUTURE  
HUMAN  
GENOMICS

