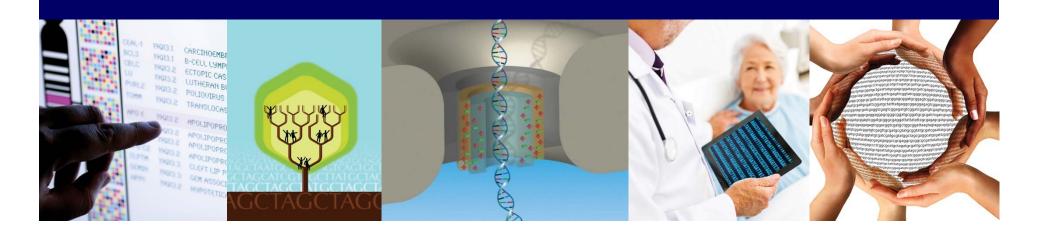
DIRECTOR'S REPORT

National Advisory Council for Human Genome Research

September 2016

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



Director's Report-Related Documents: September 2016

Director's Report

1

Director's Report



No.	Relevant Documents	
1	Genomics and Health Disparities Lecture Series	
2	New Director, National Institute of Mental Health	
3	New Director, National Institute of Child Health and Human Development	
4	New Director, Office of AIDS Research	
5	New Editor, Science	
6	Final NIH Policy on Use of Single IRB	

genome.gov/DirectorsReport

Open Session Presentations

 Seizing Unprecedented Opportunities: NHLBI Trans-Omics in Precision Medicine (TOPMed)

Gary Gibbons

 Opportunities for Synergy between the NHGRI Genome Sequencing Program and TOPMed

Adam Felsenfeld

Open Session Presentations

Genomic Medicine Working Group

Teri Manolio

Genomic Medicine IX Meeting

Carol Bult

Open Session Presentations

U.S. Precision Medicine Initiative

Eric Dishman

23 (Pairs) plus 1 Lessons Learned

Jeff Schloss

Director's Report Outline

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- II. General NIH Updates
- III. General Genomics Updates
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- VII. NHGRI Intramural Research Program

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Genomics and Health Disparities Lecture Series



Sarah Tishkoff, Ph.D.

November 15, 2016

David and Lyn Silfen University Professor
Departments of Genetics and Biology
University of Pennsylvania



Herman Taylor, Jr., M.D., M.P.H. March 9, 2017 Director, Cardiovascular Research Institute Professor of Medicine Morehouse School of Medicine



Mark Cullen, M.D.
June 8, 2017
Director, Stanford Center for Population Health Sciences
Professor of Medicine
Stanford School of Medicine

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New Director, National Institute of Mental Health

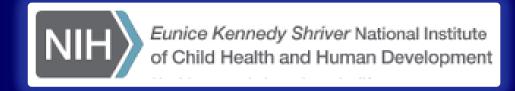




Joshua Gordon, M.D., Ph.D.

New Director, National Institute of Child Health and Human Development





Diana Bianchi, M.D.

New Director, Office of AIDS Research





Maureen Goodenow, Ph.D.

New Editor, Science







Final NIH Policy on Use of a Single IRB

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

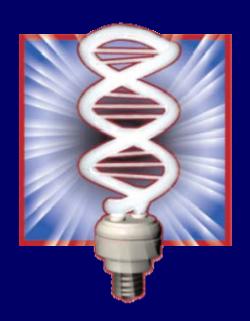
Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research

AGENCY: National Institutes of Health.

ACTION: Notice.

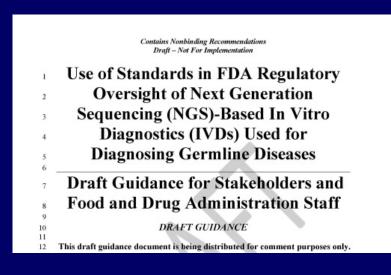
- Released on June 21, 2016
- All multi-site research funded by NIH must use a single IRB for ethical review
- Intended to promote efficiency while maintaining human subjects protections

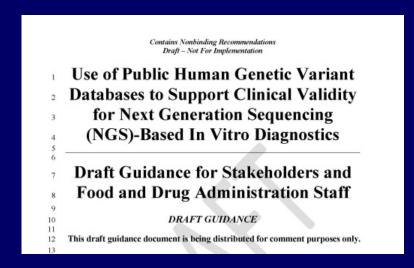
SBIR/STTR Reauthorization





New FDA Draft Guidances on Next-Generation Sequencing (NGS) Tests





- Analytical validity standards for NGS tests used to detect germline diseases
- Use of public genomic variant databases to support clinical validity of NGS tests
- Public comment period closes October 6, 2016

New EEOC Rules: GINA and Workplace Wellness Programs



- GINA: Incentives for employees' spouses' health information
- ADA: Incentives for employees' health information

'Cures' Legislation Update



- Proposes funding increases for NIH
- Congressional movement hoped for in September

NIH Appropriations and Budget

	FY2016 Enacted	FY2017 President Obama Request
NIH	\$32.3 B	\$33.1 B
NHGRI	\$513.2 M	\$513.2 M

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Mardis & Wilson Heading to Nationwide Children's Hospital



Elaine Mardis, Ph.D. Rick Wilson, Ph.D.



Global Alliance for Genomics and Health Perspective in *Science*

GENOMICS

A federated ecosystem for sharing genomic, clinical data

Silos of genome data collection are being transformed into seamlessly connected, independent systems

The Global Alliance for Genomics and Health*

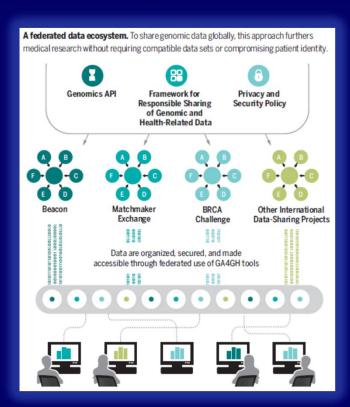
arly data-sharing efforts have led to improved variant interpretation and development of treatments for rare diseases and some cancer types (1-3). However, such benefits will only be available to the general population if

repositories, a federated system will allow legal data control to remain within the originating jurisdiction (see the figure). International consortia such as the International Cancer Genome Consortium (ICGC) have already adopted federated databases because the model allows local databases to maintain autonomy (5).



Global Alliance for Genomics & Health

Collaborate. Innovate. Accelerate.



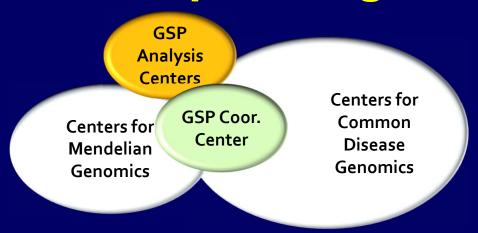


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Genome Sequencing Program



New Addition: Analysis Centers

Harvard School of Public Health Broad Institute Brigham and Women's Hospital







Stanford University University of California San Francisco Mount Sinai







Carlos Bustamante Esteban Burchard Eimear Kenny

Vanderbilt University



Bingshan Li Nancy Cox

~\$11M total over 4 years

Document 15

Genome Sequencing Program

High-Quality Genome Sequences

University of California Santa Cruz



Richard (Ed) Green

Washington University University of Washington



Richard Wilson Evan Eichler

~\$8M total over 4 years

THE CANCER GENOME ATLAS

Cell; 2015;164:550-63. doi: 10.1016/j.cell.2015.12.028

Resource

Cancer Cell; 2016;29:723-36. doi: 10.1016/j.ccell.2016.04.002

Nat Genet; 2016;48:607-16. doi: 10.1038/ng.3564. Epub 2016.05.9

Article

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npj Breast Cancer 2; 2016; pii: 16007 doi:10.1038/npjbcancer.2016.7

no Breast Cancer

www.nature.com/npjbcancer All rights reserved 2374-4677/16

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ARTICLE OPEN

DNA defects, epigenetics, and gene expression in cancer-adjacent breast: a study from The Cancer Genome Atlas

Melissa A Troester^{1,2,3}, Katherine A Hoadley^{1,4}, Monica D'Arcy^{1,2}, Andrew D Chemiack⁵, Chip Stewart⁵, Daniel C Koboldt⁶, A Gordon Robertson⁷, Swapna Mahurkar⁸, Hui Shen⁹, Matthew D Wilkerson^{1,4}, Rupninder Sandhu¹, Nicole B Johnson¹⁰, Kimberly H Allison¹¹, Andrew H Beck¹², Christina Yau¹³, Jay Bowen¹⁴, Margi Sheth¹⁵, E Shelley Hwang¹⁶, Charles M Perou^{1,3,4}, Peter W Laird9, Li Ding6,17 and Christopher C Benz13

Dist ader

> Joshua I Chandra Marcin Aruna F Roel G Cancer Matthey

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Recurrence rates after breast-conserving therapy may depend on genomic characteristics of cancer-adjacent, benign-appearing tissue. Studies have not evaluated recurrence in association with multiple genomic characteristics of cancer-adjacent breast tissue. To estimate the prevalence of DNA defects and RNA expression subtypes in cancer-adjacent, benign-appearing breast tissue at least 2 cm from the tumor margin, cancer-adjacent, pathologically well-characterized, benign-appearing breast tissue specimens from The Cancer Genome Atlas project were analyzed for DNA sequence, copy-number variation, DNA methylation, messenger RNA (mRNA) sequence, and mRNA/microRNA expression. Additional samples were also analyzed by at least one of these genomic data types and associations between genomic characteristics of normal tissue and overall survival were assessed. Approximately 40% of cancer-adjacent, benign-appearing tissues harbored genomic defects in DNA copy number, sequence, methylation, or in RNA sequence, although these defects did not significantly predict 10-year overall survival. Two mRNA/microRNA expression phenotypes were observed, including an active mRNA subtype that was identified in 40% of samples. Controlling for tumor characteristics and the presence of genomic defects, this active subtype was associated with significantly worse 10-year survival among estrogen receptor (ER)-positive cases. This multi-platform analysis of breast cancer-adjacent samples produced genomic findings consistent with current surgical margin guidelines, and provides evidence that extratumoral RNA expression patterns in cancer-adjacent tissue predict overall survival among patients with ER-positive disease.

npj Breast Cancer (2016) 2, 16007; doi:10.1038/npjbcancer.2016.7; published online 4 May 2016

THE CANCER GENOME ATLAS



CCG Web Site | Contact Us | Launch Data Portal | ##GDC Apps

Search this website

About the GDC

About the Data

Access Data

Submit Data

For Developers

Support

News

The Next Generation Cancer Knowledge Network

Case Distribution by Disease Type

The NCI's Genomic Data Commons (GDC) provides the cancer research community with a unified data repository that enables data sharing across cancer genomic studies in

Access Data



The GDC Data Portal

provides a platform for efficiently querying and downloading high quality and complete data. The GDC also provides a GDC Data Transfer Tool and a GDC API for programmatic access.

ssing Data



sion including the on Portal, a bmitting clinical, all volumes of II as the GDC Data

Document 16

Technology Development Program



 Novel Nucleic Acid Sequencing Technology Development

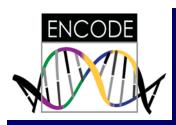
RFA-HG-15-031 (to 33; R01, R21, and R43/44)

Upcoming due date: June 15, 2017

Novel Genome Technology Development

PAR-16-14 (to 17; R01, R21, R43/44, and R44)

Upcoming due dates: October 31, 2016 and 2017



Encyclopedia of DNA Elements (ENCODE)

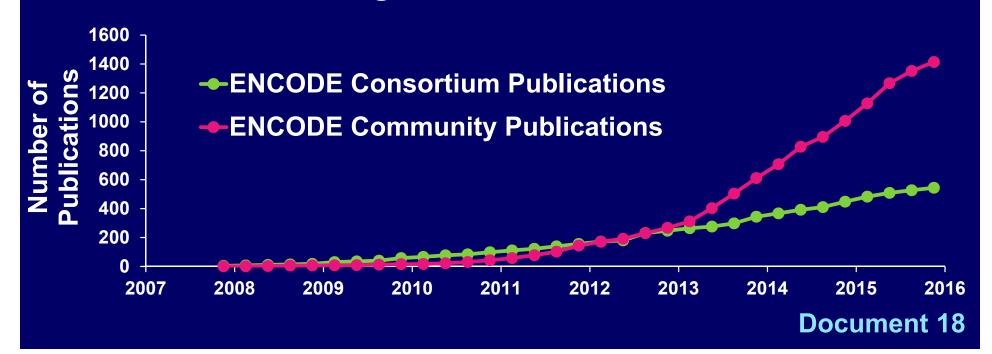
ENCODE Outreach

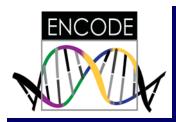
ENCODE 2016: Research Applications and Users Meeting

June 8-10: Palo Alto, CA

Tutorials at 2016 ASHG Meeting October 18, 21: Vancouver, BC

Publications Using ENCODE Data





Encyclopedia of DNA Elements (ENCODE)

Applications received and reviewed for these FOAs:

Expanding the Encyclopedia of DNA Elements (ENCODE) in the Human and Mouse (RFA-HG-16-002)

Characterizing the Functional Elements in the Encyclopedia of DNA Elements (ENCODE) Catalog (RFA-HG-16-003)

Computational Analysis of the Encyclopedia of DNA Elements (ENCODE) Data (RFA-HG-16-004)

ENCODE Data Coordination Center (RFA-HG-16-005)

ENCODE Data Analysis Center (RFA-HG-16-006)

Key Dates:

Scientific Merit Review Summer 2016

Advisory Council Review September 2016

Anticipated Start Date February 2017

Document 18

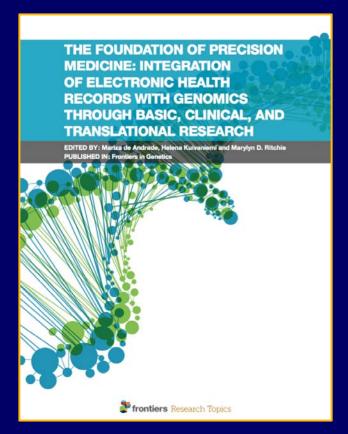
Non-Coding Variants (NoVa) Program

- Develop computational approaches to implicate noncoding genomic variants with phenotypes and test predictions using experimental data
- 5 new awards (1 by NCI), joining 6 existing ones
- Autoimmune disorders, cancer, schizophrenia, arthritis, heart disease, and chemotherapy response



emerge network

ELECTRONIC MEDICAL RECORDS AND GENOMICS





eMERGE eBook: Description of the Network's contribution to genomics

- 70,599 total views
- 12,379 articles downloaded

ClinGen: Sharing Data. Building Knowledge. Improving Care.

Official journal of the American College of Medical Genetics and Genomics ORIGINAL RESEARCH ARTICLE

Genetics inMedicine

Open

A standardized, evidence-based protocol to assess clinical actionability of genetic disorders associated with genomic variation

Jessica Ezzell Hunter, MS, PhD1, Stephanie A. Irving, MHS1, Leslie G. Biesecker, MD2, Adam Buchanan, MS, MPH3, Brian Jensen, MD4, Kristy Lee, MS5, Christa Lese Martin, PhD6, Laura Milko, PhD5, Kristin Muessig, MS1, Annie D. Niehaus, BA7, Julianne O'Daniel, MS5, Margaret A. Piper, PhD, MPH¹, Erin M. Ramos, MPH, PhD⁷, Sheri D. Schully, PhD⁸, Alan F. Scott, PhD⁹, Anne Slavotinek, MBBS, PhD10, Nara Sobreira, MD, PhD9, Natasha Strande, PhD5, Meredith Weaver, ScM, PhD11, Elizabeth M. Webber, MS¹, Marc S. Williams, MD³, Jonathan S. Berg, MD, PhD⁵, James P. Evans, MD, PhD⁵, Katrina A.B. Goddard, PhD¹; on behalf of the ClinGen Resource









Clinical Sequencing Exploratory Research Program

- Enrolled 4,954 adults and 1,261 children
- 289 publications, 18 working group publications





Implementing Genomics In Practice (IGNITE) Network

Unifying the Evaluation and Implementation of Genomic Medicine

- Create a process for providing information on clinical utility of genomic results
- Consider coverage for time spent communicating genomic results
- Consider coverage for periodic re-analysis of genome sequence data
- Ensure genome sequence data follow the patient between insurers







Implementing Genomics In Practice (IGNITE) Network

IGNITE & Beyond: The Future of Genomic Medicine Implementation



- Follow-up single-site studies with larger-scale studies
- Collaborate with community centers to increase access in underrepresented and lower socioeconomic populations
- Partner with stakeholders throughout study design, conduct, and interpretation phases

Ethical, Legal, and Social Implications (ELSI) Research Program



- Sample applications and summary statements available on the ELSI website
- 4th ELSI Congress June 5-7, 2017



Genomics and Society Working Group



In-person meeting in June

ELSI research issues related to precision medicine Effectiveness of embedded ELSI research Boundary between ELSI research and health services research

Update at February Council meeting

New Centers of Excellence in ELSI Research (CEERs) Awards

- ELSI for Precision Medicine and Infectious Disease (Johns Hopkins)
- Genetic Privacy and Identity in Community Settings (Vanderbilt University)
- Utah Center of Excellence in ELSI Research (University of Utah)
- Center on American Indian and Alaska Native Genomic Research (University of Oklahoma)

Computational Genomics and Data Science Program

Reorganization of the Model Organism Databases

New organizational model:

GO Consortium, MGD, SGD, ZFIN, WormBase, FlyBase

- Meetings in May 2015 and May 2016
- Supplement request submitted in July 2016 to establish the Alliance of Genome Resources



Training and Career Development

New T32s – Genomic Medicine
 University of Utah – Lynn Jorde
 Vanderbilt University – Josh Denny
 University of Alabama/HudsonAlpha –

Bruce Korf and Greg Barsh

New T32 – ELSI
 Stanford University – Mildred Cho

Training and Career Development

 2017 NHGRI Research Training and Career Development Meeting April 12-14, 2017 in St. Louis

Re-issued Diversity Action Plan announcement

PAR-16-345 published in June 2016

No longer limited competition

Expand into genomic medicine and ELSI research



International Genomics Education Meeting



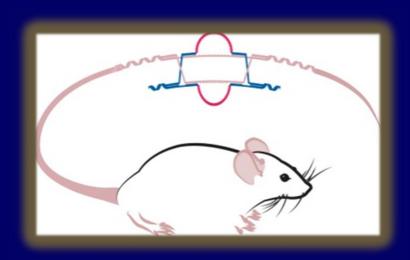
- Genomics training for healthcare providers
- USA, Australia, Canada, England, and Wales
- Certificate and master's programs
- Coordinated resources including point-of-care

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Knockout Mouse Phenotyping Project (KOMP2)





- Entering second 5-year phase of NIH Common Fund support
- Awards issued in August
- Annual Meeting Oct. 12-14, 2016
- Characterization of embryo lethal strains (*Nature*, in press)

Document 29



Human Heredity and Health in Africa (H3Africa)

9th Consortium Meeting in October (Mauritius)
 Opening by Mauritius President Ameenah Gurib
 Ethics workshop – provision of research findings
 Science workshop – HIV co-morbidities





Human Heredity and Health in Africa (H3Africa)

Seven RFAs for second phase (2016-2021)



Applications due November 15, 2016

Undiagnosed Diseases Network (UDN)

Publications from the UDN

A recurrent p.Arg92Trp variant in steroidogenic factor-1 (NR5A1) can act as a molecular switch in human sex development

7/4/2016

Human Molecular Genetics

The NIH Undiagnosed Diseases Program and Network: Applications to modern medicine

4/2016

Molecular Genetics and Metabolism

The Undiagnosed Diseases Network of the National Institutes of Health: A National Extension

11/3/2015

JAMA

Participant Pages

- > Participant Page 001
- > Participant Page 002
- > Participant Page 003
- > Participant Page 004

Genes of Interest

- > ARHGFF17 Gene
- > CACNA1A Gene
- > DUOX2 Gene
- > NACC1 Gene
- TBX2 Gene
- > ZBTB24 Gene

795 applications 281 acceptances



Document 31

Precision Medicine Initiative (PMI)







Precision Medicine Initiative (PMI) PMI Cohort Program Awards Announced

NEWS RELEASES

Wednesday, July 6, 2016

NIH awards \$55 million to build million-person precision medicine study

Launch expected later this year

Francis S. Collins @NIHDirector · Jul 6
Great Op Ed by @POTUS in
@BostonGlobe on giant steps forward on
#PrecisionMedicine Initiative at #NIH &
beyond:

The more we understand about individual differences, the better able we will be to effectively prevent and treat illness.

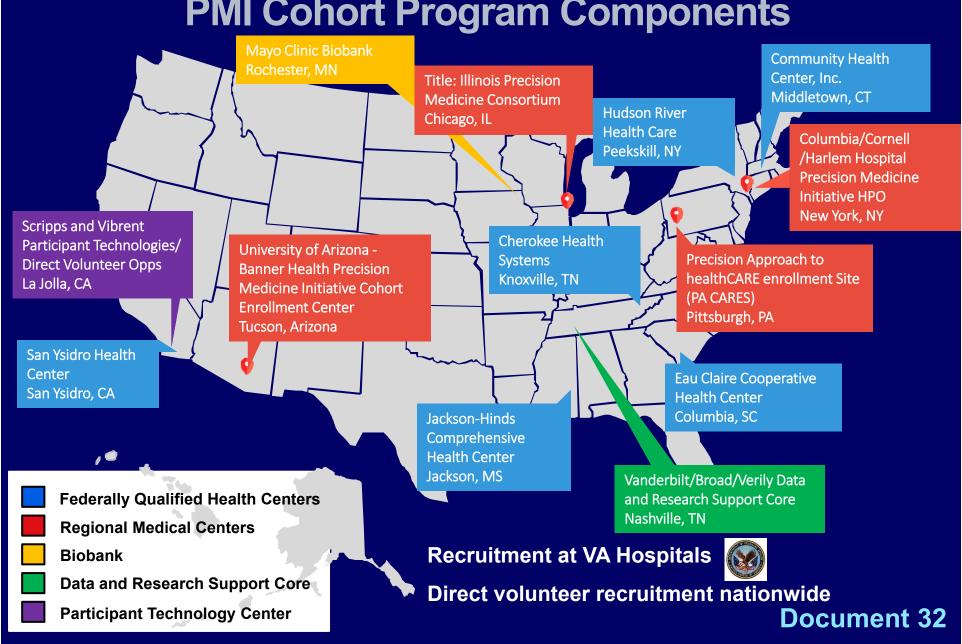
--- Francis S. Collins, M.D. Ph.D., NIH Director

[Precision medicine is..] one of the greatest opportunities we've ever seen for new medical breakthroughs, but it only works if we collect enough information first."

--- Barak Obama, President of the United States



Precision Medicine Initiative (PMI) PMI Cohort Program Components



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New ASHG-NHGRI Fellows



Christa Wagner, Ph.D.

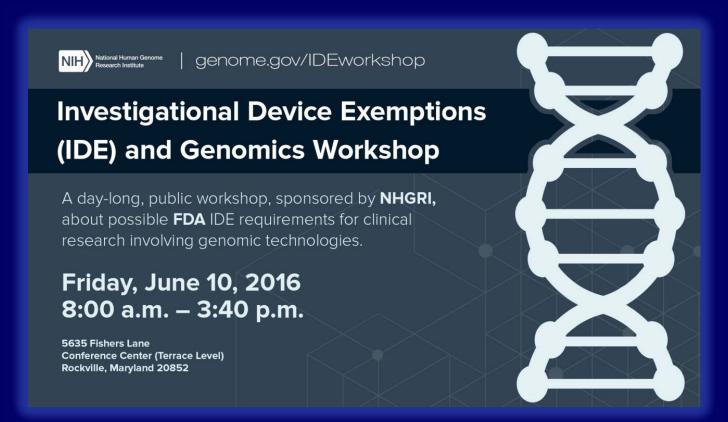
Genetics and Public
Policy Fellow



Teresa Ramirez, Ph.D.

Genetics and Education
Fellow

NHGRI IDE and Genomics Workshop

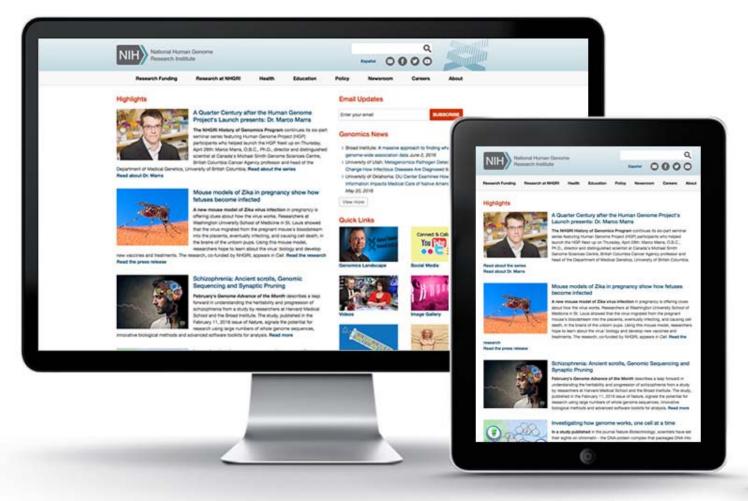


- Meeting report and video available on genome.gov
- White paper offering points for investigators to consider now being drafted

Workshop on Sharing Aggregate Genomic Data

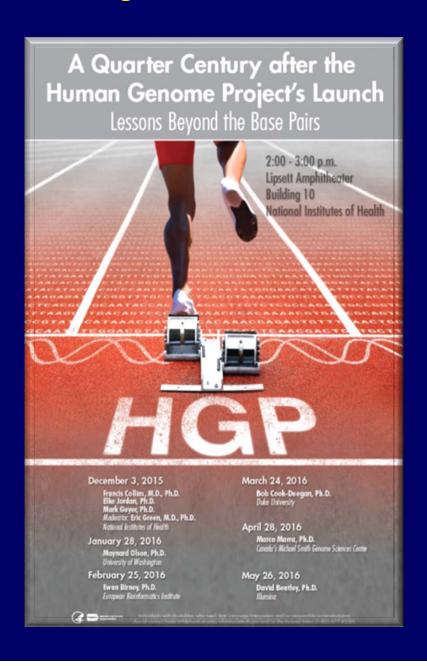


Mobile Friendly Genome.gov





History of Genomics Program Lecture Series





David Bentley, D.Phil.

Genome: Unlocking Life's Code Exhibition Travel Schedule

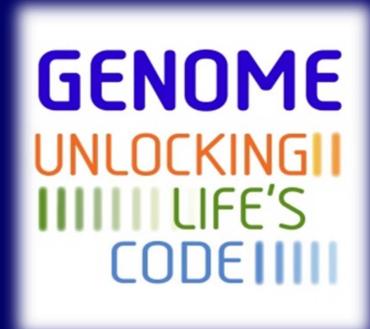
2016

May 21-September 5
Natural History Museum of Utah
Salt Lake City, UT

September 30-January 1
Exploration Place
Wichita, KS

2017

January 28-May 29
Peoria Riverfront Museum
Peoria, IL



Smithsonian's Pulse on Modern Medicine

The Pulse on Modern Medicine

Insights from NIH Experts

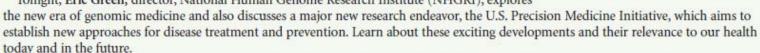
Our new series, presented in collaboration with the National Institutes of Health, reveals what is currently "hot" in biomedical research—and what it all means for our health and medicine.

From the Human Genome Project to Precision Medicine

A Journey to Advance Human Health

Since the launch of the Human Genome Project in 1990, spectacular achievements in genomics have fueled the study of human biology and disease. Revolutionary new technologies have been used to explain the complex workings of our genomes and to unravel the genomic bases of disease. There have also been advances in electronic health records, data science, and technologies for capturing a person's environmental, physiological, and lifestyle information—providing more

powerful ways to decipher the underpinnings of health and disease. Tonight, Eric Green, director, National Human Genome Research Institute (NHGRI), explores





William Gahl



Anthony Fauci



Gary Gibbons



Iulie Segre

An introductory talk by Larry Brody, director of the Division of Genomics and Society and senior investigator in the Medical Genomics and Metabolic Genetics Branch, NHGRI, from 6:45-7:30 p.m., provides appropriate background information on genetics and genomics. Refreshments will be offered during a 15-minute break between the presentations.

Opening session: Eric Green, director, National Human Genome Research Institute; Tues., Sept. 6, 6:45-8:45 p.m.; location indicated on ticket; CODE 1B0-171; Members \$30; Nonmembers \$45

Upcoming sessions: William Gahl, clinical director, National Human Genome Research Institute and director, NIH Undiagnosed Diseases Program; Thurs., Oct. 13, CODE 180-172; Anthony Fauci, director, National Institute of Allergy and Infectious Diseases; Thurs., Nov. 17, CODE 1B0-173; Julie Segre, head, Microbial Genomics Section and chief, Translational and Functional Genomics Branch, NHGRI; Thurs., Dec. 8, CODE 1B0-174; Gary Gibbons, director, National Heart, Lung, and Blood Institute; Jan. 24, CODE 1B0-175; Members \$30; Nonmembers \$45

Full Series: 5 sessions; Tues., Sept. 6; Thurs., Oct. 13; Thurs., Nov. 17; Thurs., Dec. 8; Tues., Jan. 24, 6:45-8:45 p.m.; Ripley Center; CODE 1B0-176; Members \$130; Nonmembers \$200



Eric Green

Partnership for Community Outreach and Engagement in Genomics



Local Community Outreach Programs







NHGRI 2016 Short Course in Genomics



Short Course in Genomics: Nurse, Physician Assistant, and Faculty Track

- Enhance genomics education of health professionals to aid integration of genomics into practice
- Nurse and physician assistant educator participants
- Genomics primer, competencies, resources, curriculum strategies, and integration into clinical practice
- Website and 'Community of Practice' listserv





Webinars for Health Insurers and Payers: Understanding Genetic Testing



- Webinar series for medical staff in insurance industry
- Goal: Prepare insurers to understand genetic testing strategies, interpretation, outcomes, and patient care
- Live monthly audiences consisted of ~70 participants
- Recorded webinars available for continuing education

Family Health History Tool Meeting



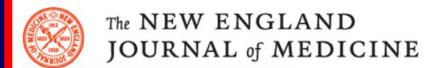
- 14 tool developers/vendors (4 NHGRI-funded)
- Data standards, EHR integration, and clinical decision support

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NHGRI Intramural Research Highlights



Will Precision Medicine Move Us Beyond Race?





nature

The Genetic Architecture of Type 2 Diabetes



A New Glucocerebrosidase Chaperone Reduces α -Synuclein and Glycolipid Levels in iPSC-Derived Dopaminergic Neurons from Patients with Gaucher Disease and Parkinsonism



Changes at the NIH Clinical Center



REDUCING RISK AND PROMOTING PATIENT SAFETY FOR NIH INTRAMURAL CLINICAL RESEARCH

ARCH Committee

ARCH to the

Director,

The Clinical Center

Working

Report to

Themes of 'Red Team' Recommendations:

- Culture of safety and quality
- Leadership for care, oversight, and compliance
- Sterile processing procedures and facilities

Enhancing Accountability & Consistency



- Clinical Center Research Hospital Board held first meeting in July
- Clinical Practice Committee to review standards for patient care and further enhance patient safety and quality
- Town meetings and focus groups to engage Institute and Clinical Center communities on next steps

NIH Clinical Center Leadership Updates



Recruiting a Clinical Center CEO



John Gallin, M.D.
Associate Director for Clinical
Research



Andy Griffith, M.D., Ph.D.
Acting Director, Office of Research
Support and Compliance



To receive *The Genomics Landscape*, go to list.nih.gov

Search for NHGRILANDSCAPE

Past issues can be accessed at: genome.gov/27527308



National Human Genome Research Institute

Advancing human health through genomics research



Special Thanks!

