### Director's Report-Related Documents: September 2016

<table>
<thead>
<tr>
<th>No.</th>
<th>Relevant Documents</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Genomics and Health Disparities Lecture Series</td>
</tr>
<tr>
<td>2</td>
<td>New Director, National Institute of Mental Health</td>
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<tr>
<td>3</td>
<td>New Director, National Institute of Child Health and Human Development</td>
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<tr>
<td>4</td>
<td>New Director, Office of AIDS Research</td>
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<tr>
<td>5</td>
<td>New Editor, <em>Science</em></td>
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<tr>
<td>6</td>
<td>Final NIH Policy on Use of Single IRB</td>
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</tbody>
</table>

[genome.gov/DirectorsReport](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

I. General NHGRI Updates
II. General NIH Updates
III. General Genomics Updates
IV. NHGRI Extramural Research Program
V. NIH Common Fund/Trans-NIH
VI. NHGRI Division of Policy, Communications, and Education
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

Jeremy Berg, Ph.D.
Final NIH Policy on Use of a Single IRB

- 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

SBIR • STTR
America’s Seed Fund™
POWERED BY SBA
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

<table>
<thead>
<tr>
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<th>FY2016 Enacted</th>
<th>FY2017 President Obama Request</th>
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<tr>
<td>NIH</td>
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<td>$33.1 B</td>
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<tr>
<td>NHGRI</td>
<td>$513.2 M</td>
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Mardis & Wilson Heading to Nationwide Children’s Hospital

Elaine Mardis, Ph.D.
Rick Wilson, Ph.D.
A federated ecosystem for sharing genomic, clinical data

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

Early 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).
Genomes In The News...
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## Genome Sequencing Program

### New Addition: Analysis Centers

<table>
<thead>
<tr>
<th>Institution</th>
<th>Centers</th>
<th>Coordinators</th>
</tr>
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<tbody>
<tr>
<td>Harvard School of Public Health</td>
<td></td>
<td>Xihong Lin</td>
</tr>
<tr>
<td>Broad Institute</td>
<td></td>
<td>Benjamin Neale</td>
</tr>
<tr>
<td>Brigham and Women’s Hospital</td>
<td></td>
<td>Shamil Sunyaev</td>
</tr>
<tr>
<td>Stanford University</td>
<td></td>
<td>Carlos Bustamante</td>
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<tr>
<td>University of California San Francisco</td>
<td></td>
<td>Esteban Burchard</td>
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<tr>
<td>Mount Sinai</td>
<td></td>
<td>Eimear Kenny</td>
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<tr>
<td>Vanderbilt University</td>
<td></td>
<td>Bingshan Li</td>
</tr>
<tr>
<td></td>
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<td>Nancy Cox</td>
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~$11M total over 4 years
## Genome Sequencing Program

### High-Quality Genome Sequences

<table>
<thead>
<tr>
<th>University of California Santa Cruz</th>
<th>Richard (Ed) Green</th>
</tr>
</thead>
<tbody>
<tr>
<td>Washington University</td>
<td>Richard Wilson</td>
</tr>
<tr>
<td>University of Washington</td>
<td>Evan Eichler</td>
</tr>
</tbody>
</table>

~$8M total over 4 years
DNA defects, epigenetics, and gene expression in cancer-adjacent breast: a study from The Cancer Genome Atlas

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 survival margin guidelines, and provides evidence that extratumoral RNA expression patterns in cancer-adjacent tissue predict overall survival among patients with ER-positive disease.
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.
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
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
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
- Anticipated Start Date: February 2017
Develop computational approaches to implicate non-coding 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 eBook: Description of the Network’s contribution to genomics

- 70,599 total views
- 12,379 articles downloaded
A standardized, evidence-based protocol to assess clinical actionability of genetic disorders associated with genomic variation

Jessica Ezzell Hunter, MS, PhD, Stephanie A. Irving, MHS, Leslie G. Biesecker, MD, Adam Buchanan, MS, MPH, Brian Jensen, MD, Kristy Lee, MS, Christa Lese Martin, PhD, Laura Milko, PhD, Kristin Muessig, MS, Annie D. Niehaus, BA, Julianne O’Daniel, MS, Margaret A. Piper, PhD, MPH, Erin M. Ramos, MPH, PhD, Sheri D. Schully, PhD, Alan F. Scott, PhD, Anne Slavotinek, MBBS, PhD, Nara Sobreira, MD, PhD, Natasha Strande, PhD, Meredith Weaver, ScM, PhD, Elizabeth M. Webber, MS, Marc S. Williams, MD, Jonathan S. Berg, MD, PhD, James P. Evans, MD, PhD, Katrina A.B. Goddard, PhD, 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
- Characterization of embryo lethal strains (*Nature*, in press)
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
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*

795 applications 281 acceptances
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, M.D. Ph.D., NIH Director

**Great Op Ed by @POTUS in @BostonGlobe on giant steps forward on PrecisionMedicine Initiative at NIH & beyond:**

**The Boston Globe**

**Medicine’s next step**

--- Barak Obama, President of the United States

**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
Recruitment at VA Hospitals

Direct volunteer recruitment nationwide
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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

Investigational Device Exemptions (IDE) and Genomics Workshop

A day-long, public workshop, sponsored by NHGRI, about possible FDA IDE requirements for clinical research involving genomic technologies.

Friday, June 10, 2016
8:00 a.m. – 3:40 p.m.

5635 Fishers Lane
Conference Center (Terrace Level)
Rockville, Maryland 20852

- Meeting report and video available on genome.gov
- White paper offering points for investigators to consider now being drafted
History of Genomics Program Lecture Series

A Quarter Century after the Human Genome Project’s Launch
Lessons Beyond the Base Pairs

2:00 - 3:00 p.m.
Lipsett Amphitheater
Building 10
National Institutes of Health

December 3, 2015
Israe1 Litten, M.D., Ph.D.
Elise Jordan, Ph.D.
Mark Guyer, Ph.D.
National Institutes of Health

January 28, 2016
Maynard Olson, Ph.D.
University of Washington

February 25, 2016
Ewen Birney, Ph.D.
European Bioinformatics Institute

March 24, 2016
Bob Cook-Deegan, Ph.D.
Duke University

April 28, 2016
Marco Mann, Ph.D.
Canada’s Michael Smith Genome Sciences Center

May 26, 2016
David Bentley, Ph.D.
Ilumina

David Bentley, D.Phil.

Document 37
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 the new era of genomic medicine and also discusses a major new research endeavor, the U.S. Precision Medicine Initiative, which aims to establish new approaches for disease treatment and prevention. Learn about these exciting developments and their relevance to our health today and in the future.

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 Cahn, clinical director, National Human Genome Research Institute and director, NIH Undiagnosed Diseases Program; Thurs., Oct. 13, CODE 1B0-172; 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
Partnership for Community Outreach and Engagement in Genomics

NHGRI

Partnership for Community Outreach & Engagement in Genomics
Local Community Outreach Programs
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?

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

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](http://list.nih.gov)

Search for **NHGRILANDSCAPE**

Past issues can be accessed at:
[genome.gov/27527308](http://genome.gov/27527308)
Special Thanks!
Advancing human health through genomics research