DIRECTOR’S REPORT

National Advisory Council for Human Genome Research

February 2018

Eric Green, M.D., Ph.D.
Director, NHGRI
### Director's Report-Related Documents: February 2018

<table>
<thead>
<tr>
<th>No.</th>
<th>Relevant Documents</th>
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| 1   | 2017 Prince Mahidol Award  
Prince Mahidol Award  
Prince Mahidol Award Conference  
NIH News Release  
Award Ceremony Video  
*Bangkok Post Article*  
*The Nation Article* |
| 2   | New Director, Division of Genome Sciences |
Open Session Presentations

- En Route to a “2020 Vision for Genomics”: The Next Round of NHGRI Strategic Planning
  Eric Green

- Updates from Building 1: Next Generation Researchers Initiative and Clinical Trial Reforms
  Michael Lauer

- Concept Clearance: Novel Nucleic Acid Sequencing Technology Development
  Michael Smith
Open Session Presentations

- Report: The Human Microbiome Project
  Lita Proctor

- Report: Recommendations from the 2017 eMERGE and Beyond Workshop
  Sharon Plon

- NCBI in a Data-Enabled World
  Jim Ostell
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
Director’s Report Outline

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2017 Prince Mahidol Award

Field of Medicine: Human Genome Project
New Director, Division of Genome Sciences

Carolyn Hutter, Ph.D.
Departure of NHGRI Program Director

Lu Wang, Ph.D.
NHGRI Perspective: Prioritizing Diversity

- Published in *Nature Reviews Genetics*
- Highlights importance of diversity at all levels of research
- Focuses on lessons learned and near-term recommendations
- Reddit AMA in December
American Indian and Alaska Native Communities and Genomics Research

- New guide to genetics and genomics research for tribal communities

- Discusses key aspects of genetics and genomics research, with examples
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New Secretary, Department of Health and Human Services

Alex Azar, J.D.
New Director,
National Cancer Institute

Ned Sharpless, M.D.
New Director, National Center for Biotechnology Information

Jim Ostell, Ph.D.
New Scientific Director, National Institute on Minority Health and Health Disparities

Anna María Nápoles, Ph.D., M.P.H.
Roderic Pettigrew Departs as Director, National Institute of Biomedical Imaging and Bioengineering

Roderic Pettigrew, Ph.D., M.D.

Jill Heemskerk, Ph.D.
Lasker-DeBakey Clinical Medical Research Award

John Schiller, Ph.D. & Doug Lowy, M.D.
Updating Access to Genomic Summary Results

- Update the access procedures for Genomic Summary Results (GSR) under NIH Genomic Data Sharing Policy

- Proposed update:
  
  GSR from *most* genomic studies to be available through a new ‘rapid access’ tier
  
  GSR from ‘sensitive studies’ to remain accessible through controlled access
Delay in Common Rule Implementation

- Interim final rule delays effective date to July 19, 2018
- Institutions can begin implementing some provisions now
- A notice of proposed rulemaking will likely propose a further delay
New Policy on Certificates of Confidentiality (CoCs)

- New CoC policy to provide additional privacy protections to research participants
- Policy covers all applicable ongoing and new research funded by NIH on or after December 13, 2016
- Investigators issued CoCs are prohibited from disclosing identifying information about participants
Budget Update

FUNDING FEDERAL GOVERNMENT THROUGH MARCH 23

H R 1,892
YEA 228
NAY 8
PRES 2
NV 2

REPUBLICAN
DEMOCRATIC
INDEPENDENT

TOTALS 245
182

TIME REMAINING 0:00
## NIH Appropriations

<table>
<thead>
<tr>
<th></th>
<th>Fiscal Year 2017 Budget</th>
<th>Fiscal Year 2018 Senate Appropriations Labor-HHS Spending Bill</th>
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<tbody>
<tr>
<td><strong>NIH</strong></td>
<td>$34.1 B</td>
<td>$36.1 B</td>
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<tr>
<td><strong>NHGRI</strong></td>
<td>$528 M</td>
<td>TBD</td>
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Mourning the Loss of Arno Motulsky
George Cunningham Visionary Award in Newborn Screening

Jeff Botkin, M.D., M.P.H.

American Public Health Laboratory Association
Brotman Baty Institute for Precision Medicine Launched

Jay Shendure, M.D., Ph.D.
2017 ASHG Awards

Kári Stefánsson, M.D.
Arthur Beaudet, M.D.
John Mulvihill, M.D.
Daniel MacArthur, Ph.D.
National Academy of Sciences Award in Molecular Biology

2018 NAS Award in Molecular Biology

Howard Y. Chang
Stanford University School of Medicine
Elected to National Academy of Medicine

Cori Bargmann
Howard Chang
Mark Daly
Josh Denny
Karen DeSalvo
Evan Eichler
Christine Grady
Chanita Hughes-Halbert
George Koob
Elected to AAAS

Susan Dutcher
Joshua Gordon
Gail Jarvik
Hongzhe Li
Mona Miller

Bhramar Mukherjee
Griffin Rodgers
Michelle Southard-Smith
Monte Westerfield
New Vice President for Genomic Research at AbbVie

Howard Jacob, Ph.D.
2017 Science Breakthrough of the Year Runners Up

Pinpoint Gene Editing
Cancer Drug’s Broad Swipe
Gene Therapy Triumph
2017 *Nature* Science Events that Shaped the Year

**Genetics Bonanza**
The Scientist’s Top Ten Innovations 2017

Dharmacon | Edit-R crRNA Library—Human Genome
10x Genomics | Chromium
Thermo Fisher Scientific | Invitrogen TrueCut Cas9 Protein v2
Genomes In The News...
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- 51,000 whole genomes and 38,000 whole exomes
- Freeze 1 data (20,000 WGS) delivered to the consortium
- Collaboration with NHLBI’s TOPMed Program on joint data calls and analyses
- GSP-TOPMed joint analysis workshop at Vanderbilt
>2,600 conservative or suggestive genes implicated

Public list of phenotypes and genes

65 presentations at 2017 ASHG Meeting

>400 publications co-authored with researchers and patient families

Data are included in driver projects for GA4GH
Advanced Genomic Technology Development Meeting

- Grantee Meeting: May 30-31, 2018
- Public Meeting: June 1, 2018
An Erythroid Enhancer of BCL11A Subject to Genetic Variation Determines Fetal Hemoglobin Level

Functional footprinting of regulatory DNA

Sangamo And Bioverativ Announce FDA Acceptance Of IND Application For ST-400 -- A Gene-Edited Cell Therapy Candidate -- To Treat Beta-Thalassemia
Centers of Excellence in Genomic Science (CEGS) Program

Challenges and recommendations for epigenomics in precision health

To the Editor: In March 2017, US life...
Bias toward European participants remains (78%)

Non-European populations contribute disproportionately more associations
1. What race or races do you consider yourself to be? Please select one or more.

**MEASURE:** Race #010600

**Definition:**

Question asking the respondent his or her race. U.S. Office of Management and Budget (OMB) standards for the classification of federal data on race and ethnicity state that "race and ethnicity may be thought of in terms of social and cultural characteristics as well as ancestry."

**Purpose:**

Race is used to stratify study populations and to associate those populations with physical, geographic, biological, social, and cultural characteristics (e.g., African Americans). Race is a social and epidemiological factor, and individuals of some races are at greater risk for certain diseases.

- 0 [ ] OTHER
- 99 [ ] DON’T KNOW
- 77 [ ] REFUSED
eMERGE and Beyond: The Future of EHR and Genomics Workshop

- Develop better phenotyping methods and technologies
- Build pipelines to automatically interpret/reinterpret genomic variants and to integrate data into EMRs
- Promote shareable electronic clinical decision support
- Generate evidence for genomic medicine
Examined the Institutional Review Board (IRB) process at 9 academic institutions

Information can help investigators more effectively engage with IRBs
Clinical Genome Resource

Phase 2

- Multi-PI Teams
  J. Berg, K. Goddard, M. Watson, & M. Williams
  C. Bustamante & S. Plon
  H. Rehm, D. Ledbetter, & C. Martin

- Goals
  Accelerate curation and expand to new disease areas
  Develop quantitative approaches to enhance the ACMG sequence variant interpretation guidelines
  Define consent and disclosure recommendations
Collaborations

Hematology Curation
- Myeloid Malignancies
- Genetic Platelet Disorders

Child Health Curation
- Brain Malformations
- Mitochondrial Disorders
- Maturity Onset Diabetes of the Young
Clinical Sequencing Evidence-Generating Research Program

CSER Working Groups

- Clinical Utility, Health Economics, & Policy
- ELSI & Diversity
- Education & Return of Results
- Survey Measures & Outcomes
- Patient, Community, & Clinical Stakeholder Engagement
- Sequence Analysis & Diagnostic Yield
Newborn Sequencing In Genomic medicine and public Health (NSIGHT)

*Time* (October 2, 2017)
Computational Genomics and Data Science Program

NHGRI Meeting of the AGR and MODs Spring 2018

- Assess the progress of the AGR
- Discuss future directions of the AGR and MODs

External Scientific Panel

Mark Johnston (U. Colorado)  Hugo Bellen (BCM)
Owen White (U. Maryland)  Jim Ostell (NLM)
Valerie Reinke (Yale U.)  Bill Pavan (NHGRI)
4th iDASH Genomic Privacy Challenge

- Challenge tasks: (1) de-duplicating patient identifiers, (2) secure GWAS, (3) machine learning with genotype & phenotype data

- Industry partners: Microsoft Research & Intel

- Wang et al. paper in *Genomic Medicine* (2017): “A community effort to protect genomic data sharing, collaboration and outsourcing"
<table>
<thead>
<tr>
<th>Small Business</th>
<th>Phase I Proof of Principle</th>
<th>Phase II Pre-Commercialization</th>
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<tr>
<td>Innovation Research (SBIR)</td>
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<tr>
<td>Technology Transfer (STTR)</td>
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Human Microbiome Project

2007-2017, $215M

Community Resource Effort

Open Session Presentation
Knockout Mouse Phenotyping Project (KOMP2)

- KOMP-CMG Joint Meeting at ASHG 2017

- Articles in *Nature Communications*
  
  “A large scale hearing loss screen reveals an extensive unexplored genetic landscape for auditory dysfunction”

  “Identification of genetic elements in metabolism by high-throughput mouse phenotyping”
Knockout Mouse Phenotyping Project (KOMP2)

- >1,400 publications using KOMP2 resources from 2004-2017
- KOMP SELENBP1-knockout mouse used to confirm genetic variation that causes extra-oral halitosis

Scientist Find Genetic Basis For Bad Breath

By studying a range of individuals with persistent cabbage-scented breath, scientists have isolated a gene called SELENBP1 that generates sulphur-containing molecules and results in bad breath. What do you think?

- "Ugh.—Fine, I’ll cut down on the amount of SELENBP1 I’ve been eating."
  STEPHEN WEST - URINAL CAKE REPLACER
- "This is a huge win for supporters of eugenics."
  NICOLE BIANCH - FOOT STYLIST
- "It’s good to know it’s my unchangeable genetics, and not some personal failing, that’s made me repellent to people."
  TIM BANKS - WIND CHIME JINGLER
A more personal gene expression catalogue

We meet a new frontier in biomedical research with publications from the Genotype-Tissue Expression (GTEx) Consortium, that of cataloguing genetic variation and its influence on gene expression within and between all major tissues in the human body. The GTEx project was proposed in 2008 with the lofty goals of establishing a resource database and associated tissue biobank to study the relationship between genetic variation and gene expression in all major human tissues across 1000 individuals. This nearly decade long
Genotype-Tissue Expression (GTEx)

The impact of rare variation on gene expression across tissues
The authors show that rare genetic variants contribute to large gene expression changes across diverse human tissues and provide an integrative method for interpretation of rare... show more
Xin Li, Yu Hui Kim, [..] & Stephen B. Montgomery

The impact of structural variation on human gene expression
Ira Hall, Donald Conrad, the GTEx consortium and colleagues identify 23,602 high-confidence structural variants (SVs) and 24,884 cis expression quantitative trait loci (eQTLs) across 13... show more
Colby Chiang, Alexandra J Scott, [..] & Ira M Hall

Landscape of X chromosome inactivation across human tissues
Multiple transcriptome approaches, including single-cell sequencing, demonstrate that escape from X chromosome inactivation is widespread and occasionally variable between cells... show more
Taru Tukiainen, Alexandra-Chloé Villani, [..] & Daniel G. MacArthur
Human Heredity and Health in Africa (H3Africa)

- 10th Annual Meeting of the African Society of Human Genetics in November 2017 (Egypt)
- 11th Consortium Meeting in March 2018 (Uganda)

Total H3A Publications

Document 42
# Human Heredity and Health in Africa (H3Africa)

## Stage II Awards (Fall 2017)

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<th>Funded Initiative</th>
<th>Funding ICs</th>
<th>Participating African Countries</th>
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<td>Coordinating Center</td>
<td>Common Fund, FIC, NCI, NEI,</td>
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<td>NHGRI, NICHD, NIDCD, NIDDK,</td>
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<td>NIEHS, NHLBI, NIMH, NINDS,</td>
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<td>OAR, ORWH</td>
<td>South Africa, Morocco, Zimbabwe, Botswana, Egypt, Nigeria, Sudan, Senegal, Tunisia, Ghana, Malawi, United Republic of Tanzania, Uganda, Mauritius, Mali, Kenya, Cameroon, Swaziland, Gambia, Sierra Leone, Rwanda, Democratic Republic of the Congo</td>
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<td>Bioinformatics Network</td>
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<td>ELSI Collaborative Center</td>
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<td>ELSI Projects</td>
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Undiagnosed Diseases Network (UDN)

UDN Applications and Acceptances

- Applications Received: 1918
- Applications Under Review: 588
- Applications Accepted: 824
- Participants Evaluated: 329
- Participants Diagnosed: 167

Follow us on social media for real-time research updates. udnconnect and @UDNconnect

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Human BioMolecular Atlas Program (HuBMAP)

- New Common Fund Program
- RFA-RM-17-025: Transformative Technology Development
- RFA-RM-17-027: Tissue Mapping Centers
- COMING SOON – HuBMAP Integration, Visualization and Engagement (or HIVE)
Somatic Cell Genome Editing

- Develop quality tools to perform effective and safe genome editing in human patients
- Program elements: delivery systems, novel editors, improved assays for safety and efficacy, and a dissemination center
- Funding announcements published in January 2018
### NIH Data Commons Pilot Phase

#### Data Commons Pilot Phase OT Awardees

<table>
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<tr>
<th>Name &amp; Institution</th>
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<tbody>
<tr>
<td>Stanley Ahalt, RENCI</td>
<td>Isaac Kohane, Harvard</td>
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<tr>
<td>Titus Brown, UC Davis</td>
<td>Avi Ma’ayan, Mt. Sinai</td>
</tr>
<tr>
<td>Merce Crosas, Harvard</td>
<td>Lucila Ohno-Machado, UCSD</td>
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<td>Brandi Davis-Dusenbery, SevenBridges</td>
<td>Benedict Paten, UCSC; Robert Grossman, UChicago; Anthony Philippakis, Broad Institute</td>
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<tr>
<td>Ian Foster, UChicago</td>
<td>Owen White, UMD</td>
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- **Datasets:**
  - GTEx
  - TOPMed
  - ALLIANCE of GENOME RESOURCES

- **Pilot Phase Kickoff Meeting:** December 2017
- **Establishment of an NIH cloud ‘marketplace’**
Feedback Due February 23!
- Genomics Working Group Report
- Considerations:
  - Genome-wide genotyping
  - Exome sequencing
  - Whole-genome sequencing
- Potential pilot of 50,000 participants
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2017 ASHG Meeting Policy Luncheon: FDA Oversight of Genomics Research

- Discussed FDA’s Investigational Device Exemption (IDE) regulation for genomics studies
Genomic Literacy, Education, and Engagement (GLEE) Initiative

Engaging Stakeholders to Promote Genomic Literacy

NIH SCI ED 2017

ASHG 2017
ORLANDO • OCTOBER 17-21, 2017
SHARING DISCOVERIES. SHAPING OUR FUTURE.

NABT
National Association of Biology Teachers
National DNA Day

‘15 for 15’ Celebration

- 15 topics shared each day via social/digital media
- Partner engagement
- NHGRI-hosted events
Genome: Unlocking Life’s Code Exhibition

Travel Schedule

2018

January 28-April 24
Rochester Museum and Science Centre
Rochester, NY

June 23-September 15
Mayo Clinic
Rochester, MN
Global Genetics and Genomics Community Case Study

- New case study: Familial Hypercholesterolemia
- ‘Expert Commentary’ provided by Robert Shamburek (NHLBI)
National Family Health History Day
Inter-Society Coordinating Committee for Practitioner Education (ISCC)

7th In-Person Meeting
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Society for the Indian Academy of Medical Genetics S. S. Agarwal Oration Honor

Les Biesecker, M.D.
New Editor in Chief, *American Journal of Medical Genetics*

Max Muenke, M.D.
Multimodal mapping of the brain’s functional connectivity and the adult outcome of attention deficit hyperactivity disorder.

Loci associated with skin pigmentation identified in African populations.

Noonan syndrome in diverse populations.
To receive *The Genomics Landscape*, go to list.nih.gov

Search for **NHGRILANDSCAPE**

Past issues can be accessed at: [genome.gov/27541196](http://genome.gov/27541196)
Thanks!

Special Thanks!
Advancing human health through genomics research