DIRECTOR’S REPORT

National Advisory Council for Human Genome Research

May 2017

Eric Green, M.D., Ph.D.
Director, NHGRI
# Director's Report-Related Documents: May 2017

<table>
<thead>
<tr>
<th>No.</th>
<th>Relevant Documents</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>New Secretary, Department of Health and Human Services</td>
</tr>
<tr>
<td>2</td>
<td>Nominated Commissioner, Food and Drug Administration</td>
</tr>
<tr>
<td>3</td>
<td>H.R. 1313: Preserving Employee Wellness Programs Act</td>
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<tr>
<td>4</td>
<td>NIH Appropriations: Fiscal Year 2017</td>
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<td>5</td>
<td>NIH Appropriations: Fiscal Year 2018</td>
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<tr>
<td>6</td>
<td>American Society for Microbiology William A. Hinton Research Training Award</td>
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</tbody>
</table>
Open Session Presentations

- Update from the National Institute of Mental Health
  Josh Gordon

- DataScience@NIH: Current State, Future Directions
  Patti Brennan

- Report: IGNITE and Beyond Workshop
  Chanita Hughes-Halbert

- Concept Clearance: IGNITE II
  Ebony Madden
Open Session Presentations

- Concept Clearance: Centers of Excellence in ELSI Research (CEER)
  Joy Boyer

- Report: Computational Genomics and Data Science Workshop
  Ajay Pillai

- NHGRI History of Genomics Program
  Chris Donohue
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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(Some of) NHGRI will be Moving

“Rock Spring Park Cluster”

NIH Components:

<table>
<thead>
<tr>
<th>Component</th>
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<tbody>
<tr>
<td>NHGRI</td>
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<tr>
<td>NEI</td>
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VI. NHGRI Division of Policy, Communications, and Education

VII. NHGRI Intramural Research Program
New Secretary, Department of Health and Human Services

Tom Price, M.D.
Nominated Commissioner, Food and Drug Administration

Scott Gottlieb, M.D.
David Lipman Departing as Director, National Center for Biotechnology Information

David Lipman, M.D.  Jim Ostell, Ph.D.
H.R. 1313: Preserving Employee Wellness Programs Act

- House sponsor: Virginia Foxx (R-NC)
- Would exempt workplace wellness programs from provisions of Americans with Disabilities Act and Genetic Information Nondiscrimination Act
## NIH Appropriations: Fiscal Year 2017

<table>
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<tr>
<th>Entity</th>
<th>FY 16 Budget</th>
<th>FY 17 Budget</th>
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<td>NHGRI</td>
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<td>FY17 Budget</td>
<td>FY18 President’s Budget</td>
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<tr>
<td>NIH</td>
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American Society for Microbiology
William A. Hinton Research Training Award

Steven Finkel, Ph.D.
Acting President, Canadian Institute for Health Research

Rod McInnes, M.D., Ph.D.
Elected to National Academy of Sciences

Stephen Baylin
Karen Nelson
Sarah Tishkoff
BioGenomics2017: Global Biodiversity Genomics Conference

- Diversity of species
- Diversity of biological questions
- Multiple data types
- Synergy with work in human genomics
MIT Technology Review

Breakthrough Technologies for 2017

10 Breakthrough Technologies
2017

These technologies all have staying power. They will affect the economy and our politics, improve medicine, or influence our culture. Some are unfolding now; others will take a decade or more to develop. But you should know about all of them right now.

The Cell Atlas
Biology’s next mega-project will find out what we’re really made of.

Gene Therapy 2.0
Scientists have solved fundamental problems that were holding back cures for rare hereditary disorders. Next we’ll see if the same approach can take on cancer, heart disease, and other common illnesses.
Genomics In The News…

I took a public health disaster for the Zimbabwean government to recognize the power of precision medicine. In 2015, the country switched from a standard three-drug cocktail for HIV to a single-drug combination therapy. The change was made in order to save people in Harare from an outbreak of tuberculosis. However, the government’s recommendation to incorporate the antiretroviral drug efavirenz as a first-line therapy for public health programs, which is sold in demand in Zimbabwe, was put on hold. The reports were followed by many people getting sick in their homes.

In 2016, the government of Zimbabwe was criticized by the United Nations for not doing enough to control the epidemic. The country’s health ministry acknowledged its mistakes and decided to reverse course. However, critics say the government’s efforts to address the crisis have been hindered by a lack of funds and the need for more effective treatment options.

The current approach to treating TB in Zimbabwe is to give patients a combination of drugs. This is expensive and can be difficult to monitor. A recent study found that 40% of patients who started on the standard therapy did not complete the full course of treatment. The government is considering introducing a new treatment option, which would include a shorter course of medication.

Population Scale Precision

There’s a big problem, however: Precision medicine is expensive. It’s a commitment that, for the most part, requires pharmaceutical companies to invest in large-scale clinical trials and expensive research facilities. For many developing countries, this is simply too much to bear.

In an effort to improve access to precision medicine, some countries are turning to alternative models. These include using artificial intelligence to predict which patients are most likely to benefit from certain treatments, and leveraging existing medical records to inform decisions about care.

Putting Genomes To Work In Africa

Investment promises to bring new medicine to Africans. But will it help?

BY LINDA HARDING

In order to improve access to new treatments, governments and organizations around the world are investing in genomic research. The idea is to use this knowledge to develop treatments that are tailored to the specific needs of individual patients.

This is already happening in some places. Botswana — a middle-income country — is using the data to treat a rare form of HIV, and the success rates have been impressive.

However, the challenges are significant. In many African countries, there are significant gaps in the availability of data. Without this information, it’s difficult to develop effective treatments.

The race is on to find solutions. If we can develop better ways to use genomic data, we may be able to provide better care for people around the world.
Genomes In The News…
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<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Sample Type</th>
<th>Sequenced Samples</th>
<th>Approved Samples</th>
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<td>Cardiovascular Genomes</td>
<td>Genomes</td>
<td>16,096</td>
<td>46,300</td>
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<td></td>
<td>Exomes</td>
<td>10,861</td>
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<td>Immune-Mediated Genomes</td>
<td>Genomes</td>
<td>4,718</td>
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<td></td>
<td>Exomes</td>
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<td>2,000</td>
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<tr>
<td>Neuropsychiatric Genomes</td>
<td>Genomes</td>
<td>8,670</td>
<td>15,300</td>
</tr>
<tr>
<td></td>
<td>Exomes</td>
<td>11,374</td>
<td>32,000</td>
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<tr>
<td>TOTAL</td>
<td></td>
<td>51,719</td>
<td>141,600</td>
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</table>
Genome Sequencing Program
Centers for Mendelian Genomics

Exome Sequence Production

- **Phase I**: 20,612 samples
- **Phase II**: 11,285 samples

Disease Gene Discovery

- **Conservative**
  - Novel: 928 genes
  - Known: 728 genes
- **Suggestive**
  - Novel: 532 genes
  - Known: 239 genes

Publications

- **Total**: ~350 publications
- **Y1**: 18 publications
- **Y2**: 36 publications
- **Y3**: 73 publications
- **Y4**: 99 publications
- **Y5**: 115 publications

Centers for Mendelian Genomics

Document 13
Genome Sequencing Program

2017 Consortium Meeting

- Progress updates
- Collaborative analysis plans
- Data sharing and distribution
- New research directions
Technology Development Program

- Advanced Genomic Technology Development Meeting – May 22-25
- Novel Nucleic Acid Sequencing Technology Development
  RFA-HG-15-031 (R01, also linked R21 and R43/44)
  Next due date: June 15, 2017
- Novel Genomic Technology Development
  PAR-16-14 (R01, also linked R21 and R43/44)
  Next due date: October 31, 2017
## Program Announcements

<table>
<thead>
<tr>
<th>Announcement Number</th>
<th>Primary IC</th>
<th>Title</th>
<th>Release Date</th>
<th>Expiration Date</th>
</tr>
</thead>
</table>
Centers of Excellence in Genomic Science (CEGS)

Two recent CEGS awards:

Center for Cell Circuits
Broad Institute – Aviv Regev

Center for Dynamic RNA Epitranscriptomes
University of Chicago – Chuan He
AGR Community Meeting

- Share AGR plans with the community and review progress

- Participants:
  - Model organism researchers
  - AGR investigators and key personnel
  - Scientific Advisory Board members
  - NIH staff
NHGRI ‘Sandbox’ Update

- Resource to democratize genomic data access, sharing, and computing
- Cooperative agreement funding mechanism
- $5M per year for 5 years
35 abstracts accepted for 2017 ACMG

16 abstracts accepted for 2017 AMIA
Evaluating the clinical validity of gene-disease associations: an evidence-based framework developed by the Clinical Genome Resource


doi: https://doi.org/10.1101/biorxiv.015614

Clinical laboratories collaborate to resolve differences in variant interpretations submitted to ClinVar

Steven M. Harrison PhD, Jill S. Dolinsky MS, Amy E. Knight Johnson MS, Tina Pesaran MA, MS, Daniele R. Azzariti MS, Sherri Bale PhD, Elizabeth C. Chao MD, Somas Das PhD, Lisa Vincent PhD & Heidi L. Rehm PhD

Curating the Clinical Genome Meeting 2017

June 28-30, Washington DC

Document 20
Enrolled 5,241 adults and 1,357 children

312 publications, 20 working group publications
Clinical Sequencing Exploratory Research Program


A guide to genomic test results for non-genetics providers

Created by the Practitioner Education Working Group of the Clinical Sequencing Exploratory Research (CSER) Consortium

Glossary

Autosomal recessive: genetic conditions that occur only when mutations are present in both copies of a given gene (i.e., the person is homozygous for a mutation, or carries two different mutations of the same gene, a state referred to as compound heterozygosity).

(Source – NCI Dictionary of Genetics Terms)

Benign (variant): an alteration in a gene distinct from the normal, wild-type allele that does.

(Source – Illustrated Glossary)

Carrier frequency: the proportion of individuals in a population who have a single copy of a specific recessive gene mutation; also sometimes applied to the prevalence of mutations in dominantly acting genes such as BRCA1 and BRCA2. Also called carrier rate.

(Source – NCI Dictionary of Genetics Terms)
Implementing Genomics In Practice (IGNITE) Network

- 92 publications
- 259 presentations
4th ELSI Congress: Expanding the ELSI Universe
June 5-7, 2017 (Farmington, Connecticut)

- Keynote and Plenary Speakers: Eric Dishman, Alondra Nelson, Wylie Burke, James Evans, and Pearl O’Rourke
- Topics: Precision medicine; genome sequencing in the clinic; and genes, ancestry, and identity
- Program and registration available online
Outgoing Members:
- Arti Rai
- Lisa Parker

Current Members:
- Gail Henderson
- Chanita Hughes-Halbert
- Dave Veenstra

New Members:
- Jeff Botkin
- Steve Joffe
- Max Mehlman
- Melanie Myers
- Sandra Soo-Jin Lee
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- Midcourse review in January
- Recommendations for enhancing utility of data:
  - Generate transcriptomics data at each center
  - Hire joint postdocs focused on integrative analysis
- Satellite session at April AACR meeting
Human Heredity and Health in Africa (H3Africa)

- 10th Consortium Meeting, May 12-15 (Botswana)
Undiagnosed Diseases Network (UDN)

UDN Site Locations

1,387 Applications
545 Acceptances
The Undiagnosed Diseases Network: Accelerating Discovery about Health and Disease

Rachel B. Ramoni,1,2,* John J. Mulvihill,3 David R. Adams,3 Patrick Allard,4,5 Euan A. Ashley,6 Jonathan A. Bernstein,7 William A. Gahl,3 Rizwan Hamid,8 Joseph Loscalzo,9 Alexa T. McCray,1 Vandana Shashi,10 Cynthia J. Tifft,3 Undiagnosed Diseases Network, and Anastasia L. Wise3

Diagnosis at the edges of our knowledge calls upon clinicians to be data driven, cross-disciplinary, and collaborative in unprecedented ways. Exact disease recognition, an element of the concept of precision in medicine, requires new infrastructure that spans geography, institutional boundaries, and the divide between clinical care and research. The National Institutes of Health (NIH) Common Fund supports the Undiagnosed Diseases Network (UDN) as an exemplar of this model of precise diagnosis. Its goals are to forge a strategy to accelerate the diagnosis of rare or previously unrecognized diseases, to improve recommendations for clinical management, and to advance research, especially into disease mechanisms. The network will achieve these objectives by evaluating patients with undiagnosed diseases, fostering a breadth of expert collaborations, determining best practices for translating the strategy into medical centers nationwide, and sharing findings, data, specimens, and approaches with the scientific and medical communities. Building the UDN has already brought insights to human and medical geneticists. The initial focus has been on data sharing, establishing common protocols for institutional review boards and data sharing, creating protocols for referring and evaluating patients, and providing DNA sequencing, metabolomic analysis, and functional studies in model organisms. By extending this precision diagnostic model nationally, we strive to meld clinical and research objectives, improve patient outcomes, and contribute to medical science.
All of Us Research Program
Return of Genetic Results Workshop

Topics related to returning genomic results at scale
Attendees represented broad range of perspectives
Half the panelists were NHGRI grantees
Chief Engagement Officer, All of Us Research Program

Dara Richardson-Heron, M.D.
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23andMe Receives Approval to Return Risk Information for 10 Conditions

FDA News Release

FDA allows marketing of first direct-to-consumer tests that provide genetic risk information for certain conditions

For Immediate Release

April 6, 2017
National Academies Report on Evidence for Genetic Testing

- Commissioned by the Department of Defense
- Provides recommendations for evidence-based decisions on coverage for genetic testing
NHGRI Participates in Reddit’s “Ask Me Anything” Series

NIH & UCSF SCIENTISTS AMA
TOTAL REACH: 13.19m
8,149 USERS CLICKED THROUGH TO READ THEIR ANSWERS
6,623 TOTAL VOTES

UNDIAGNOSED DISEASES AMA
TOTAL REACH: 2.83m
3,369 USERS CLICKED THROUGH TO READ THEIR ANSWERS
3,007 TOTAL VOTES
Genome: Unlocking Life’s Code Exhibition
Travel Schedule

2017

April 1-May 29
Peoria Riverfront Museum
Peoria, IL

June 12-September 11
Health Museum
Houston, TX

September 30-January 1
Science North
Sudbury, Ontario, Canada
NHGRI & National DNA Day

National DNA Day
April 25

Twitter Chat
#DNADayChat @DNADay

Tuesday, April 25, 1:00-2:00 pm ET
Join us for a DNA Day chat! @NASA_Astronauts #AstroKate & @NIHDirector will answer your questions and we’ll highlight genomics & genetics resources for students, teachers, & the general public.
Genomic Literacy, Education, and Engagement (GLEE) Initiative
Community Health Studio at Gallaudet University
Inter-Society Coordinating Committee for Practitioner Education (ISCC)

6th In-Person Meeting

- Share members’ genomic education activities, needs, and interests
- Learn about opportunities and needs for funding provider education activities
- Included presentations about activities in other countries
- Establish a new “Building Bridges” working group
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Elected to the Association of American Physicians

Ellen Sidransky, M.D.
New Chief, Social and Behavioral Research Branch

Laura Koehly, Ph.D.
22q11.2 deletion syndrome in diverse populations

Single-molecule sequencing and chromatin conformation capture enable de novo reference assembly of the domestic goat genome

Hypoxia-induced HIF1α targets in melanocytes reveal a molecular profile associated with poor melanoma prognosis

Genetic structure of the purebred domestic dog
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/27541196](http://genome.gov/27541196)
Thanks!

Special Thanks!
Advancing human health through genomics research