DIRECTOR’S REPORT

National Advisory Council for Human Genome Research

September 2013

Eric Green, M.D., Ph.D.
Director, NHGRI
### Director's Report Related Documents: September 2013

#### NHGRI-Smithsonian Exhibition

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| 1   | - [Genome: Unlocking Life's Code Exhibition Website](unlockinglifesciencenwhr.org)  
  - [YouTube VOA Video](youtube.com)  
  - [GenomeWeb](genomeweb.com)  
  - [Wall Street Journal](online.wsj.com)  
  - [Washington Post](washingtonpost.com)  
  - [New York Times](nytimes.com) |
| 2   | [APA's Society for the Psychological Study of Ethnic Minority Issues Charles and Shirley Thomas Award](apa.org) |
| 3   | [Arrival of New Director, National Institute of General Medical Sciences](nigms.nih.gov) |
Open Session Presentations

Major Presentations:

- Assoc. for Molecular Pathology et al. v Myriad Genetics Inc. et al.
  Arti Rai

- Data Sharing and the HeLa Genome Sequence
  Kathy Hudson

Recent NHGRI Meetings:

- Report of the Genomic Medicine Working Group
  Teri Manolio
Open Session Presentations

Project Updates:

- The NHGRI-Smithsonian Genome Exhibition
  Vence Bonham

- The NHGRI Bioinformatics Research Portfolio
  Vivien Bonazzi

- NHGRI Training & Career Development Program
  Heather Junkins
I. General NHGRI Updates
II. General NIH Updates
III. General Genomics Updates
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Exhibition Opening: June 14, 2013
Genome Exhibition Visits
New ASHG/NHGRI Policy Fellow

Kate Donigan, Ph.D.
Extramural Staff Departure

Brad Ozenberger, Ph.D.
Ongoing NHGRI Recruitments

Director, Division of Genomics and Society

ELSI Program Director

Bioinformatics Program Directors

Chief, Genomics Healthcare Branch
APA’s Society for the Psychological Study of Ethnic Minority Issues
Charles and Shirley Thomas Award

Vivian Ota Wang, Ph.D.
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Arrival of New Director, National Institute of General Medical Sciences

Jon Lorsch, Ph.D.
Visits of Congressional Members to NIH

“I toured the clinic where the best medical researchers in the country are trying to solve the world’s most elusive medical mysteries – diseases that have yet to be identified let alone cured.”

– Sen. Harry Reid (Senate Floor, June 20 2013)
Surgeon General Steps Down

Regina Benjamin, M.D., M.B.A.
NIH Fiscal Year 2014 Appropriations

- Regular appropriations process will **not** be completed
- Continuing Resolution (CR) anticipated

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<tr>
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<th>FY 2013 Actual (after sequester)</th>
<th>President FY 2014</th>
<th>House FY 2014</th>
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<tr>
<td>NIH</td>
<td>$29.1B</td>
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<td>NHGRI</td>
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NHGRI Consequences of the Sequester

Bioinformatics Resources and Analysis Research Portfolio
REDUCED BY $5M

ENCODE RFA
REDUCED BY 16%

Genomics of Gene Regulation RFA
DELAYED FROM FISCAL YEAR 2012 TO 2014

Genomic Sequencing & Newborn Screening Disorders RFA
REDUCED BY 50%

Genomic Medicine Pilot Demonstration Projects RFA
REDUCED BY 20%

Intramural Research Program
NUMEROUS EXAMPLES OF DETRIMENTAL CUTS
Other Consequences of the Sequester

BD2K Data Catalog
REDUCED IN FISCAL YEAR 2014

BD2K Framework for Community-based Development of Data and Metadata Standards
REDUCED IN FISCAL YEAR 2014

BD2K Training
DEFERRED UNTIL FISCAL YEAR 2015

BD2K Software RFA
DEFERRED UNTIL FISCAL YEAR 2015

BD2K NIH-Initiated Centers RFA
DEFERRED UNTIL FISCAL YEAR 2015
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NIH announced new policy for access to HeLa cell whole-genome data in August

Presentation by Kathy Hudson later in the Open Session
White House Open Science 'Champions' Highlight Genomic Data Pioneers

Atul Butte, M.D., Ph.D.
Atul Butte is a pediatrician, geneticist, computer scientist, and entrepreneur at Stanford University and the Lucile Packard Children's Hospital. Atul's lab at Stanford builds and uses.

David Altshuler, M.D., Ph.D.
Endocrinologist and human geneticist David Altshuler is one of four founding members of the Broad Institute of Harvard and MIT and serves as the Institute's Deputy Director and Chief Academic.

David J. Lipman, M.D.
In his 24 years as the founding director of the National Center for Biotechnology Information (NCBI) at the National Institutes of Health's National Library of Medicine (NLM), Dr. Lipman has had a.

Stephen Friend, M.D., Ph.D.
Dr. Stephen Friend is a world leader in efforts to make large scale, data-intensive biology more openly accessible to citizens and the entire research community in order to accelerate scientific.

John Quackenbush, Ph.D.
John Quackenbush is Professor of Biostatistics and Computational Biology at the Dana-Farber Cancer Institute and the Harvard School of Public Health. Since the Human Genome Project began in the...
2013 Abbott Award in Clinical and Diagnostic Immunology

Jennifer Puck, M.D.
Founding Director, Jackson Laboratory for Genomic Medicine

Charles Lee, Ph.D.
International partners describe global alliance to enable secure sharing of genomic and clinical data

By Broad Communications, June 4th, 2013

Over 70 leading health care, research, and disease advocacy colleagues in over 40 countries have taken the first step to enabling secure sharing of genomic and clinical data one-million fold, and more and more people are choosing to make available for research, clinical, and personal use. How to build an evidence base for biomedicine that is larger than any one group, to the highest standards of ethics and privacy. These will be best served if we work together to develop and share (both effective and responsible).

5 June 2013
Alliance will build data-sharing future

World’s health researchers join together to share and use ‘big data’

More than 60 leading health care, research and disease advocacy organisations from across the world are joining together to form an international alliance dedicated to enabling secure sharing of genomic and clinical data.

Each of these organisations has signed a ‘Letter of Intent’, pledging to work together to create a not-for-profit, inclusive, public-private, international, non-governmental organisation (modelled on the World Wide Web Consortium, W3C) that will develop a common framework.

The cost of genome sequencing has fallen one-million fold, and ever increasing numbers of people are making their genetic and clinical data available for research and clinical use. However, interpreting people’s genetic data requires a standardised biomedicial evidence base that is larger than any one party alone can develop, and that adheres to the highest ethical and privacy standards.

“In recent years, many groups around the world have recognized the need for improved approaches to bring together genomic and clinical data, and some have made progress addressing this,” said Professor Mike Stratton, Director of the Wellcome Trust Sanger Institute. “But if coming together, and studying the challenges, we recognised that something was missing: an international body that spans diseases and institutions, committed to furthering progress in an innovative and responsible fashion.”
Jeremy Hunt launches genomics body to oversee healthcare revolution

Genomics England will aim to attract private investment in life sciences, but campaigners raise patient privacy concerns

Randeeep Ramesh, social affairs editor
The Guardian, Thursday 4 July 2013

Jeremy Hunt, the health secretary. Photograph: Jonathan Brady/PA
Genomics and the Economy

The Impact of Genomics on the U.S. Economy

Federal research investment has contributed to medical science, improved public health, created American jobs and helped generate nearly $1 trillion in economic impacts to date.

Prepared by Battelle Technology Partnership Practice for United for Medical Research (UMR)

June 2013
Disruptive technologies: Advances that will transform life, business, and the global economy
An End to Gene Patents?
First GINA Cases Filed

1. Settled v. Fabricut

2. Pending v. Founders Pavilion

Document 19
U.S. Supreme Court Upholds ‘DNA Swabbing’ of People Under Arrest

SUPREME COURT OF THE UNITED STATES

Syllabus

MARYLAND v. KING

CERTIORARI TO THE COURT OF APPEALS OF MARYLAND


After his 2009 arrest on first- and second-degree assault charges, respondent King was processed through a Wicomico County, Maryland, facility, where booking personnel used a cheek swab to take a DNA sample pursuant to the Maryland DNA Collection Act (Act). The swab was matched to an unsolved 2003 rape, and King was charged with that crime. He moved to suppress the DNA match, arguing that the Act violated the Fourth Amendment, but the Circuit Court Judge found the law constitutional. King was convicted of rape. The Maryland Court of Appeals set aside the conviction, finding unconstitutional the portions of the Act authorizing DNA collection from felony arrestees.

Held: When officers make an arrest supported by probable cause to hold for a serious offense and bring the suspect to the station to be detained in custody, taking and analyzing a cheek swab of the arrestee’s DNA is, like fingerprinting and photographing, a legitimate police booking procedure that is reasonable under the Fourth Amendment. Pp. 3–94.
NCHPEG Ceases Operations

- Promoted health professional education for two decades
- NCHPEG founded in 1996 through partnership of the American Medical Association, American Nurses Association, and NHGRI
- Ceased operations on August 31
- Resources will be maintained at the American Society of Human Genetics website
NHGRI Genome Advance of the Month

Digging into the past to uncover the cause of our cavities

Child abuse leaves epigenetic marks
By Roseanne Zhao, Ph.D.
NIH Medical Scientist Training Program Track 3 Scholar

Close encounters of the microbial kind
By Katie Y. Sun
NHGRI Scientific Program Analyst

Alzheimer’s disease: Putting the pieces together with integrative genomics
By Elizabeth Burke, Ph.D.
Intramural Postdoctoral Fellow, NHGRI

Alzheimer’s disease - a neurological disorder causing progressive dementia, disorientation and behavioral changes - will affect more than 5 million Americans this year. While five percent of those with Alzheimer’s disease develop it between the ages of 30-65 as a result of any one of several rare, inherited, single-gene mutations, the large majority of affected individuals develop a non-familial form after the age of 65, called late-onset Alzheimer’s disease (LOAD).

In comparison to the early-onset form, the underlying cause of LOAD is much more complex; it is thought to be caused by a combination of several genetic and non-genetic risk factors. Genetic risk factors refer to common human genetic variations, or alleles, that increase a person’s chance of developing a disease without directly causing it. While each risk factor is not sufficient to cause the disease on its own, multiple risk factors can combine their modest individual effects to develop LOAD.

Though advancing age is currently the strongest known risk factor for LOAD, the most influential genetic factor to be identified is one of three common alleles for the gene apolipoprotein E (APOE) that is referred to as APOE4. A person who inherits the APOE4 allele from only one parent has a three-fold increase in LOAD risk, whereas a person that inherits APOE4 from both parents is ten times more likely to develop LOAD. Despite this strong association, it has remained unclear how APOE4 contributes to the disease. July’s Genome Advance of the Month describes a study, published in the August 1, 2013, issue of Nature, which combined several genomic methods to identify important regulatory processes that link the common genetic variation APOE4 to the development of LOAD.
“In the past we tended to think that the absence of microbes made people healthy, but as we're learning, bacteria are not just a source of disease—they're a source of health.” Lita Proctor, PhD
Genomics In The News…
Genomes In The News…

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Large-Scale Genome Sequencing and Analysis Centers

- 15 publications this quarter
- Current major projects:
  - TCGA
  - Alzheimer’s disease
  - Other complex genetic disorders
Changes in TCGA leadership:

TCGA Program Directors Brad Ozenberger and Kenna Shaw left NIH

Lou Staudt named Director of the NCI Center for Cancer Genomics

- On target to meet goals
- Data available for 8,500 tumor specimens (from 26 tumor types)
- On course to reach ~11,000 specimens by project’s end
‘Pan-cancer’ analyses reveal additional features of disease

~30 papers to be published in the next several weeks
Disease Gene Discovery:

• >9600 whole-exome sequences for >617 diseases
• Discovery of 199 disease genes underlying 114 diseases
• Publications (31)
  
  Discoveries of diseases genes (22)
  Methods and resources (6)
  Practices for data sharing (3)

Network and Outreach:

• Collaborative Network: 384 investigators, 189 institutions, and 30 countries
• IRDiRC committees and working groups
Clinical Sequencing Exploratory Research (CSER) Program

- Three new CSER sites:
  - HudsonAlpha Institute
  - Kaiser Foundation Research Inst.
  - University of Michigan

- Coordinating Center:
  - University of Washington

- Enhanced integration with ELSI studies
Genome Sequencing Informatics Tools

- iSeqTools Portal provides a ‘subway map’ for genome analysis

- User can drill down to details and individual tools with a ‘semantic zoom’ web feature
DNA Sequencing Technology Development

- 8 awards made this year
- RFAs posted in June with application receipt date of October 17, 2013
ENCODE Outreach Activities:
- ENCODE Tutorial at ASHG Meeting
- ENCODE Tutorial at CHARGE Consortium Meeting

Cross-Species Comparison Papers Under Review:
- modENCODE (fly/worm/human)
- mouse ENCODE (mouse/human)
Publications Using ENCODE Data

Number of Publications

- Papers from Non-ENCODE Authors
- Papers from ENCODE 2 Production Groups

Document 31
Genomics of Gene Regulation RFA

- Concept Clearance approved in May 2011
- RFA-HG-13-012: Genomics of Gene Regulation (U01)
- Exploring genomic approaches to understand the role of DNA sequence in gene regulatory networks
- Applications due November 15, 2013

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<td>Catalog of Federal Domestic Assistance (CFDA) Number(s)</td>
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Centers of Excellence in Genomic Science (CEGS) Program

- Annual meeting at the U. of Wisconsin in October

- New CEGS applications to be reviewed this fall for discussion at February 2014 Council meeting
Genomic Medicine Working Group

- 5th Genomic Medicine Meeting
  (May 2013): Federal-wide strategies

- 6th Genomic Medicine Meeting
  (January 2014): International approaches

- Progress of the Genomic Medicine Working Group will be discussed later in the Open Session
Inter-Society Coordinating Committee

- Inter-Society Coordinating Committee for Practitioner Education in Genomics to meet in September
- 20 professional societies currently participating

AACC, AACME, AAFP, AAP, ABMG, ABMS, ACC, ACGME, ACMG, ACOG, ACP, AHA, AMP, APHMG, ASCO, ATS, CAP, CMSS, ISPG, SGIM
Population Architecture using Genomics and Epidemiology (PAGE) II

- Study Cohorts in PAGE II:
  - Women’s Health Initiative
    Fred Hutchinson Cancer Research Center
  - Mount Sinai Biobank
    Mount Sinai School of Medicine
  - CALiCo Consortium
    University of North Carolina
  - Multiethnic Cohort Study
    University of Hawaii

- Coordinating Center: Rutgers University

- Genotyping: Center for Inherited Disease Research
Genomic Sequencing and Newborn Screening Disorders

- Brigham and Women’s Hospital
- Children’s Mercy Hospital
- University of California, San Francisco
- University of North Carolina at Chapel Hill
Genome-Wide Association Studies (GWAS) Catalog

Webinar: “Current uses of and future directions for the Genome-Wide Association Studies Catalog”
eMERGE Tools

- My Results web page
- Clinical Decision Support (CDS) tools: CLIPMERGE
- SMART Genomics Advisor will be evaluated and piloted to standardize CDS approaches across eMERGE sites
Centers of Excellence in ELSI Research (CEER) Program

CEERs Grants Funded this Summer:

- University of North Carolina (P50)
- Columbia University (P50)
- University of Utah (P20)
- Johns Hopkins University (P20)
- Kaiser/UCSF (P20)
Genomics & Society Working Group

- Next Meeting: November 2013
- Areas to be discussed:
  - Priority Setting
  - Funding Mechanisms
  - Boundaries of ELSI Research
Training and Career Development

- To align research training and career development programs with NHGRI strategic plan
- To prepare future leaders in genomic science and genomic medicine
- To harmonize our training and career investment with the rest of NIH
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Molecular Libraries Program (MLP)

- Final year of production phase
- Screening Centers’ Goals:
  - Completing projects
  - Placing all data in PubChem
  - Filing probe reports
Human Microbiome Project (HMP)
HMP Data to be Hosted in Amazon Cloud

- September 2013: HMP data publically available on Amazon cloud

- December 2013: Collection of HMP analysis tools, tutorials, and documentation will be made available on Amazon cloud
Knockout Mouse Phenotyping Project (KOMP2)

- ‘Perfect Host’ technology
- KOMP2 production on track
- GTEx pilot data available in dbGaP

- Scale-up phase started
  - 900 genotyped donors
  - >25,000 RNA-Seq studies

- June 2013 GTEx Community Meeting

- Funding plan for RFA “Enhancing GTEx with molecular analyses of stored biospecimens (U01)” will be presented in Closed Session
Library of Integrated Network-based Cellular Signatures (LINCS)

- New LINCS RFA (RM13-013) published
- LINCS-BD2K Coordinating Center RFA being drafted
- LINCS 2013 Community Meeting and Workshop at Broad Institute in November
H3Africa

- H3Africa Consortium has funded 21 projects
  - Bioinformatics network
  - Pilot biorepositories
  - Projects working on:
    - Obesity
    - Sickle Cell Disease
    - HIV
    - Kidney disease
    - Stroke
    - Microbiome
    - Trypanosomes
    - Fevers of unknown origin
    - Heart disease
    - Diabetes
    - Neurological disorders
    - Schizophrenia

- Next Consortium meeting in October
Undiagnosed Diseases Network (UDN)

- UDN aims to increase the capacity for and use of genomic data in the diagnosis and management of rare and new diseases

- RFA-RM-13-018: DNA Sequencing Core for an Undiagnosed Diseases Network (U01)

Application Due Date: November 19, 2013
NIH Data Science Components

- Associate Director for Data Science (ADDS)
- Scientific Data Council (SDC)
- Big Data to Knowledge (BD2K)
Scientific Data Council: Membership

Acting Chair: Eric Green (Acting ADDS & NHGRI)

Members: James Anderson (DPCPSI)
Sally Rockey (OER)
Michael Gottesman (OIR)
Kathy Hudson (OD)
Amy Patterson (OSP)
Andrea Norris (CIT)
Judith Greenberg (NIGMS)
Betsy Humphreys (NLM)
Douglas Lowy (NCI)
John J. McGowan (NIAID)
Alan Koretsky (NINDS)
Michael Lauer (NHLBI)
Belinda Seto (NIBIB)

Acting Executive Secretary: Allison Mandich (NHGRI)
Big Data to Knowledge (BD2K): Update

- Sequester is delaying launch of training, software development, and second round of centers components
- Three RFIs published, all with excellent responses
- Two workshops have been held, with two more coming later this month
Big Data to Knowledge (BD2K): Update

- FOA published for Investigator-Initiated Centers of Excellence (U54)

  Applicant Information Webinar: September 12

  Questions to BD2KCenterRFA@mail.nih.gov
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G2C2 Pharmacist Resources

- Pharmacist G2C2 Resource Review meeting was held in June

- Planned availability this Fall
Honorary Professor
University of Cape Town

Charles Rotimi, Ph.D.
Topographic diversity of fungal and bacterial communities in human skin

Targeting proximal tubule mitochondrial dysfunction attenuates the renal disease of methylmalonic acidemia

A Congenital Neutrophil Defect Syndrome Associated with Mutations in VPS45
Special Thanks!
Advancing human health through genomics research