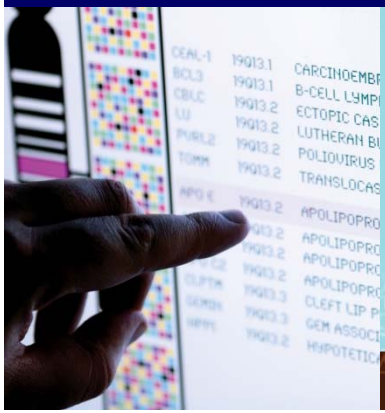
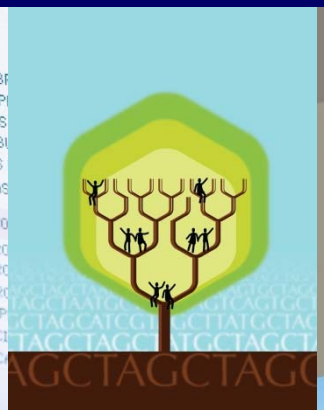
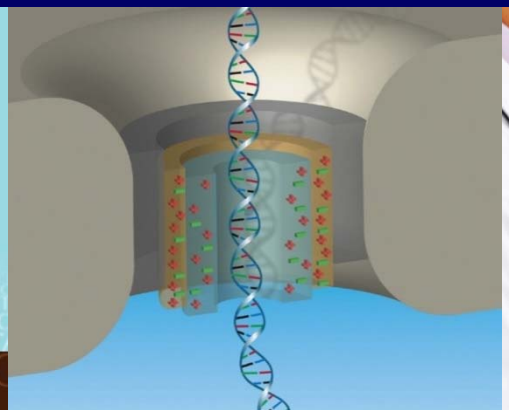
DIRECTOR'S REPORT

National Advisory Council for Human Genome Research

February 2016

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

Director's Report-Related Documents: February 2016

Director's Report

Director's Report

No.	Relevant Documents
1	25th Anniversary of the Launch of the Human Genome Project
2	New Chief Grants Management Officer
3	New Chief, Policy & Program Analysis Branch
4	ASHG/NHGRI Fellowships: 2016-2017 Application Process Open!
5	DHHS Career Achievement Award
6	Congressional Briefing: Precision Medicine and Cystic Fibrosis
7	**Challenges of Sustaining Data Resources** Sustaining the Big-Data Ecosystem Funding for Key Data Resources in Jeopardy

genome.gov/DirectorsReport

Document #

Open Session Presentations

- Report on the NHGRI Intramural Research Program

  Dan Kastner

- Update on the Human Heredity and Health in Africa (H3Africa) Initiative

  Jennifer Troyer

Open Session Presentations

Meeting Reports:

- **Roundtable on Inclusion and Engagement of Underrepresented Populations in Genomic Research**

  Vence Bonham

- **Integrating Genomic Sequencing into Clinical Care: CSER and Beyond**

  Dan Roden

Open Session Presentations

Concept Clearances:

- **Clinical Sequencing Evidence-generating Research (CSER2)**
- **Investigator-initiated Clinical Sequencing Research (iCSR)**

Lucia Hindorff

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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25th Anniversary of the Launch of the Human Genome Project

Document 1

Retirement of Center for Inherited Disease Research (CIDR) Scientific Review Officer

Camilla Day, Ph.D.

New Chief Grants Management Officer

Deanna Ingersoll

Document 2

New Chief, Policy & Program Analysis Branch

Cristina Kapustij, M.S.

ASHG/NHGRI Fellowships: 2016-2017 Application Process Open!

- Genetics and Public Policy Fellowship
- Genetics and Education Fellowship
- Application Deadline: April 25, 2016

Document 4

DHHS Career Achievement Award

Jeff Schloss, Ph.D. and
Sylvia Matthews Burwell, DHHS Secretary

Document 5

Congressional Briefing:
Precision Medicine and Cystic Fibrosis

Document 6

Visit by Israeli Minister of Health

Challenges of Sustaining Data Resources

OUTLOOK | BIG DATA IN BIOMEDICINE

PERSPECTIVE

Sustaining the big-data ecosystem

Organizing and accessing biomedical big data will require quite different business models, say Philip E. Bourne, Jon R. Lorsch *and* Eric D. Green.

Biomedical big data offer tremendous potential for making discoveries, but the cost of sustaining these digital assets and the resources needed to make them useful have received relatively little attention. Research budgets are flat or declining in inflation-adjusted terms in many countries (including the United States), and data are being generated at unprecedented rates, so the research community must find more efficient models for storing, organizing and accessing biomedical data. Simply putting more and more money into the current systems is unlikely to work in the long term.

To better understand this situation, we are examining the current and projected costs of managing biomedical data at the US National Institutes of Health (NIH). Our initial analyses indicate that even if we leave out the National Center for Biotechnology Information, which is a special case, the 50 largest NIH-funded data resources have a collective annual budget of US$110 million. And this figure represents just the tip of the iceberg for future needs.

UNDERSTANDING USAGE

Today's biomedical data resources typically treat all items in their collections equally. This does not always make sense, given that the usage patterns of the data vary. But how do we decide which data get more attention? As larger and larger data sets are generated more easily, and the cost of maintaining and annotating these data continues to rise, this question is becoming increasingly important.

Answering it requires a better understanding of how research data are used. This has rarely been thoroughly explored. Historically, funders have been interested primarily in knowing how the data resources that they support are used and by whom. They tended not to look closely at the details of how and why individual items and types of data within a collection are used.

Analyses of these details can be revealing. Preliminary studies suggest that typically a small subset of the data is used frequently, whereas most of the data are rarely accessed. However, the exact subset of data that is used heavily may change over time, and most of the data access may be performed after the data are downloaded, so this is not recorded. All of this means that absolute numbers are hard to interpret.

These caveats notwithstanding, more details of data usage are needed to inform funding decisions. Over time, such usage patterns could tell us how best to target annotation and curation efforts, establish which data should receive the most attention and therefore incur the largest cost, and determine which data should be kept in the longer term. The cost of data regeneration can also influence decisions about keeping data.

Funders should encourage the development of new metrics to ascertain the usage and value of data, and persuade data resources to provide such statistics for all of the data they maintain. We can learn here from the private sector: understanding detailed data usage patterns through data analytics forms the basis of highly successful companies such as Amazon and Netflix.

FAIR AND EFFICIENT

When we have a better understanding of data usage, we can develop business models that consider supply and demand, and develop sustainable practices. In addition, finding economies of scale and harnessing market forces will be essential.

For a typical biomedical data resource, the cost of simply keeping the data is only a small fraction of the total cost of data management. The remainder is largely the cost needed to support the finding, accessing, interoperating and reusing (the FAIR principles; see go.nature.com/axkjiv) of the data — a cost that is widely underappreciated.

THE RESEARCH COMMUNITY MUST FIND MORE **EFFICIENT** MODELS FOR **STORING, ORGANIZING AND ACCESSING** BIOMEDICAL DATA.

Is the FAIR fraction of the cost justified? Are services from different data resources redundant? Are resources subject to 'feature creep' — the addition of costly 'bells and whistles' that are of limited value? Do our funding mechanisms contribute to these problems? And most importantly, is the way we currently maintain biomedical data optimal for the science that needs to be done both today and in the future?

Current practices typically use many disparate sources of data to conduct a study. These data are located in a variety of repositories, often with different modes of access. This lack of centralization and commonality may hinder their ease of use and reduce productivity. We need a better understanding of usage patterns across multiple data resources to use as a basis for redesigning such resources to preserve valuable expertise and curation, and for improving how the data are found, accessed, integrated and reused.

The nature of curation and the quality assurance for biomedical data must also change. Complete and accurate automated or semi-automated extraction of literature is needed to provide metadata and annotation. We should consider crowdsourcing curation, with appropriate validation and incentives. Additionally, the role of professional curators must be better appreciated by data users, by the institutions where the curators work, and by the funders.

BIOMEDICAL RESOURCES

Funding for key data resources in jeopardy

NIH genome institute wants to scale back support of human and model organism databases

By Jocelyn Kaiser

As the world's most authoritative catalog of human disease-related genes approaches its 50th birthday, it faces unsettling change. Over the next few years, the National Human Genome Research Institute (NHGRI) expects to bow out as sole funder for the granddaddy of genomic databases, known as Online Mendelian Inheritance in Man (OMIM). Who will pick up the tab is not yet clear. Other, newer databases supported by NHGRI are facing a similar threat as the National Institutes of Health (NIH) takes stock of all its data resources.

Users are concerned. These free-to-use resources, which cover everything from yeast genomics to proteins, are "critical for our daily life as geneticists and biomedical researchers," says University of California, Berkeley, geneticist Jasper Rine, president of the Genetics Society of America. Ada Hamosh of Johns Hopkins University in Baltimore, Maryland, who oversees OMIM, adds: "If NIH is going to develop new funding models, they need to make sure they don't compromise the integrity of existing, heavily used resources."

NHGRI Director Eric Green says that nothing has been decided and that rumors that his institute plans to phase out all of its funding are incorrect. But he and other NIH leaders are searching for ways to make the databases more efficient, and are urging databases to consider charging for use.

Biology databases have long had funding woes. Science agencies often complain that database support diverts resources from their mission of funding research. Philip Bourne, NIH's first associate director for data science, estimates that the 50 largest NIH-supported resources—not counting GenBank and other databases at the National Library of Medicine (NLM)—require $110 million of the agency's $30 billion annual budget. An explosion in data is making them ever more costly to run. "There is a sustainability issue. We need to do something," Bourne says.

In addition to OMIM, NHGRI supports five databases for model organisms and others such as UniProt, which holds data on protein function. All are troves of molecular data annotated with information that curators have gleaned from the literature. OMIM, which began 50 years ago as a paper resource and moved to the Web in 1995, draws more than 23 million page views a year. Clinicians use it to diagnose patients with rare diseases, while basic researchers rely on OMIM and model organism databases as go-to references for genes and their protein products.

Last May, Green called together leaders of these databases to tell them that by 2020 they need to find new options for funding. Grantees across many NIH institutes use the NHGRI databases, he said, and the nearly $30 million a year NHGRI now provides isn't enough as the databases expand beyond genomes to biological data. "We're not a good long-term home," Green says. "We need to think about new ways to do business."

Bourne's office plans to compile data on database usage across NIH, although he notes this can't be the only measure of value: "You can have a relatively small number of users, but it's absolutely critical for those users," he says. He and Green wonder whether some databases could be combined to lower costs. Further automating curation might also help. But humans still need to read papers and pull out data, in part because formats and nomenclatures vary.

Shifting some databases to other institutes could cut NHGRI's costs, as could adopting a subscription model. The Arabidopsis Information Resource (TAIR), the central database for a model organism in plant science, started charging fees in 2013 after the National Science Foundation phased out funding. "We resisted very strongly," says TAIR Director Eva Huala in San Francisco, California, but in the end, "we were converted."

TAIR tailors its prices to how much individuals, institutions, and companies use the database. "It's a great way to ensure that those who benefit the most from a resource also contribute the most," Huala says. As a bonus, she adds, because TAIR doesn't rely on federal grants, it no longer has to please peer reviewers and can focus instead on what users want, mainly up-to-date data.

The shift required some major changes, however. Huala and her staff left the Carnegie Institution for Science, which had hosted TAIR, to start a nonprofit, Phoenix Bioinformatics, to run it. They also had to set up accounting and business systems.

Several of the NHGRI-funded databases are wary of this model. "It isn't practical for many reasons," says Janan Eppig of the Jackson Laboratory in Bar Harbor, Maine, principal investigator for the Mouse Genome Database. One problem is that paywalls may prevent researchers from linking to genetic data in other databases. And researchers would need to use their grant money to subscribe. "NIH ultimately pays the bill anyway," says Monte Westerfield of the University of Oregon in Eugene, who heads the Zebrafish Model Organism Database.

Bourne says an NIH-wide committee hopes to begin considering new funding schemes later this year. The fate of these data troves may not be clear, however, until the agency has hired a new director for NLM—a possible new home for the beleaguered databases. ■

Data troves in transition

These databases supported by the National Human Genome Research Institute have 4 years to develop new funding models.

DATABASE	ORGANISM	UNIQUE USERS PER MONTH	2015 NHGRI FUNDING
FlyBase	*Drosophila*	51,300	$4.2 million
Gene Ontology Consortium	Multiple	36,000	$3.7 million
Mouse Genome Database	Mouse	53,100	$4.7 million
Online Mendelian Inheritance in Man	Human	300,000	$2.1 million (2014)
Reactome (biological pathways)	Human	19,400	$1.2 million
Saccharomyces Genome Database	Yeast	65,000	$2.7 million
UniProt (protein function)	Multiple	433,100	$4.9 million
WormBase	*Caenorhabditis elegans*	15,500	$2.9 million
Zebrafish Model Organism Database	Zebrafish	23,300	$3.1 million

DATA: FLYBASE/GO CONSORTIUM/MGD/OMIM/REACTOME/SGD/UNIPROT/WORMBASE/ZFIN

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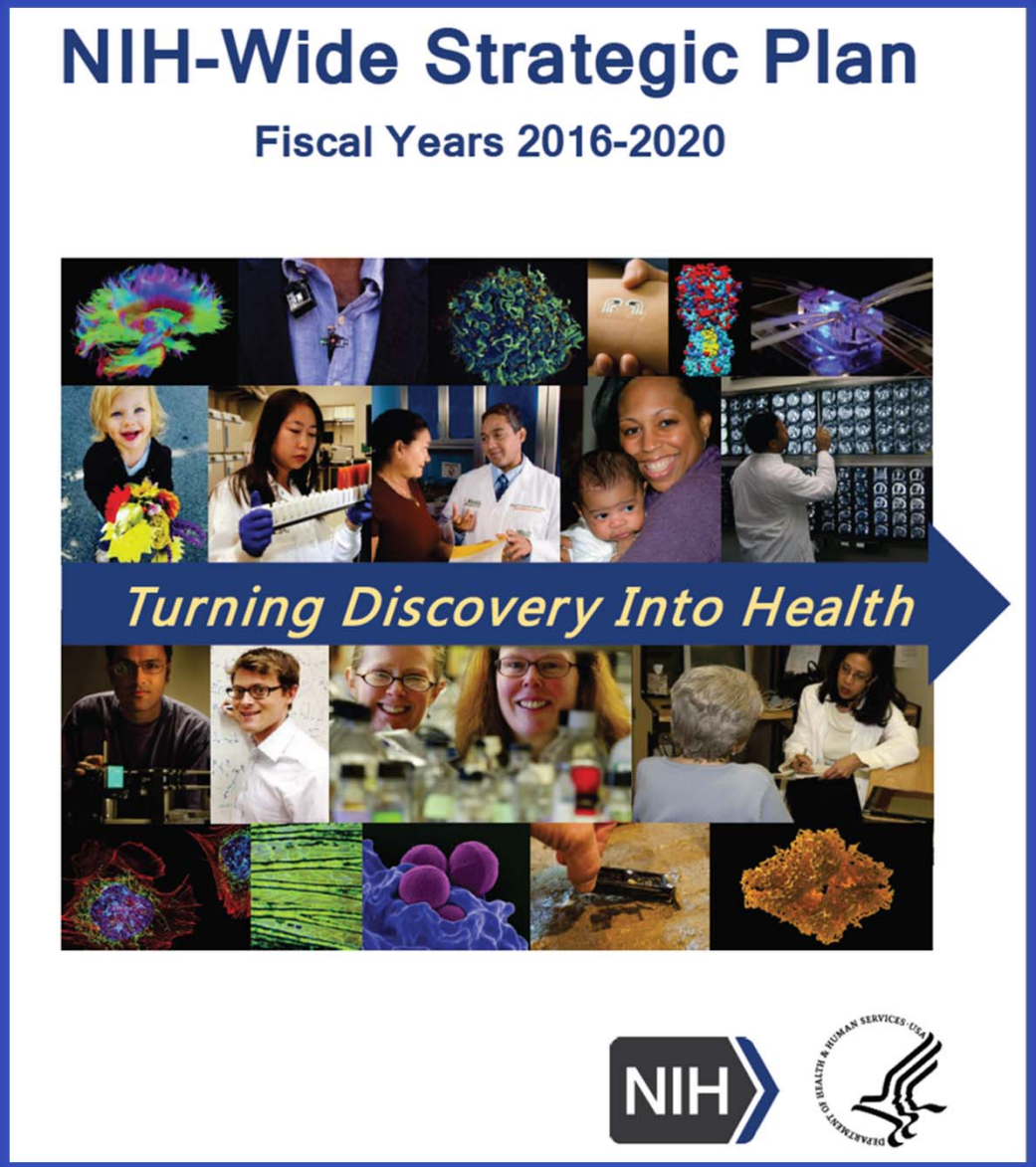
New Deputy Director for Extramural Research

NIH National Institutes of Health
Office of Extramural Research

Michael Lauer, M.D.

New NIH-Wide Strategic Plan



Document 9

NIH Appropriations and Budget

Fiscal Year 2016 Appropriations

	FY15	FY16	% Change	Difference
NIH	$30.3B	$32.3B	6.6% Increase	+$2.0B
NHGRI	$499M	$519M	3.9% Increase	+$20M

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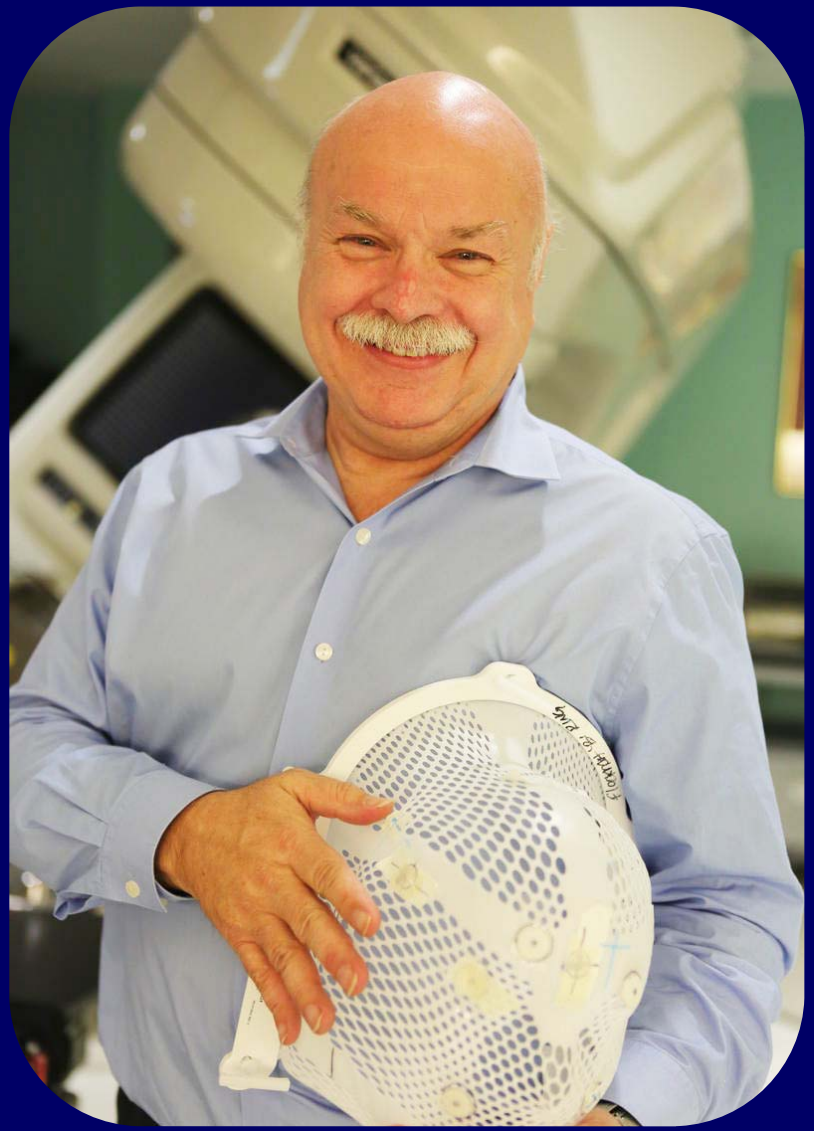
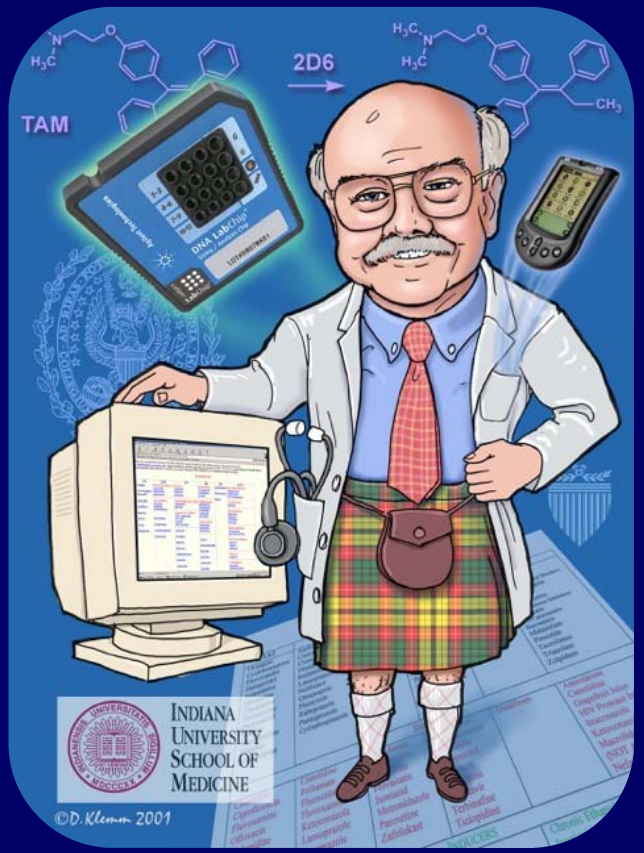
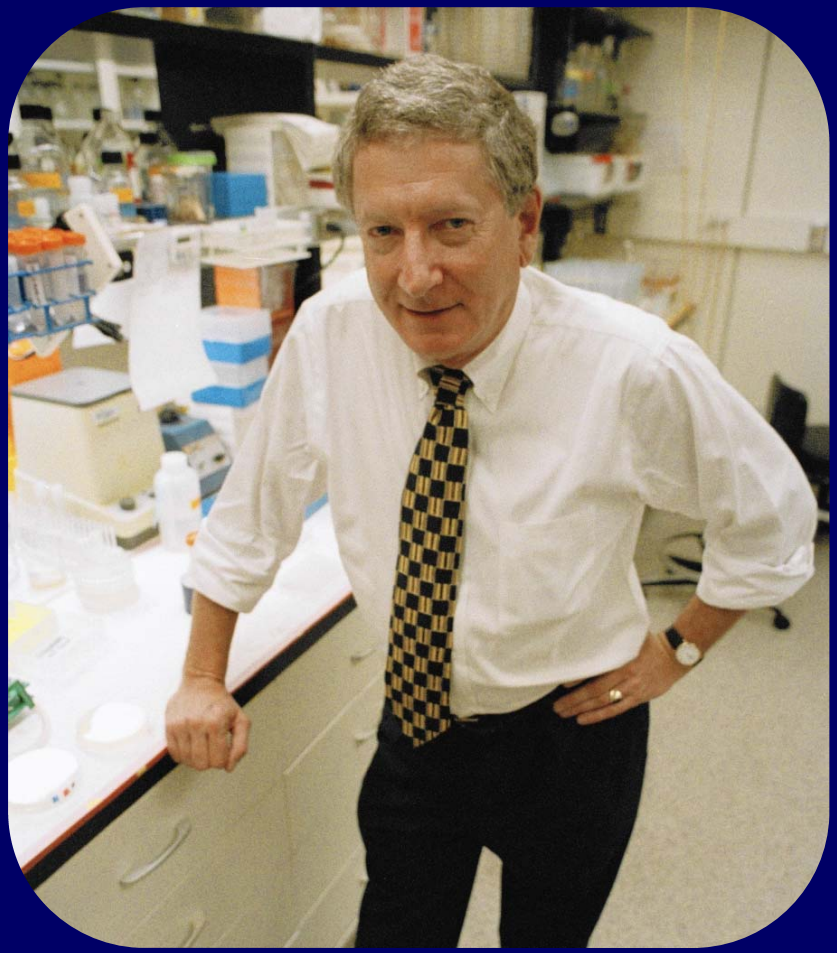
Mourning the Loss of Dave Flockhart





Document 11

Mourning the Loss of Alfred Gilman



Document 12

National Medal of Science & National Medal of Technology and Innovation

Mary Claire-King, Ph.D.

Johnathan Rothberg, Ph.D.

Document 13

2015 Breakthrough Prize in Life Sciences

John Hardy, Ph.D.

Helen Hobbs, M.D.

Svante Pääbo, Ph.D.

2015 ASHG Awards

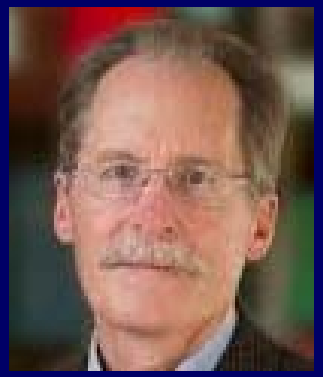
Kay Davies, D. Phil.

R. Rodney Howell, M.D.

Leonid Kruglyak, Ph.D.

Robert Nussbaum, M.D.

Roderick McInnes, M.D., Ph.D.



Huntington Willard, Ph.D.

Document 15

Memorial Sloan Kettering
2015 Paul Marks Prize for Cancer Research

Bradley Bernstein, M.D., Ph.D.

Howard Chang, M.D., Ph.D.

1884

Memorial Sloan Kettering Cancer Center

Document 16

Elected to the National Academy of Medicine

Chris Austin
Atul Butte
Mario Capecchi
Michael Green
Murat Gunel
Kenneth Kinzler
Walter Koroshetz
Kevin Struhl

Document 17

Elected to the AAAS

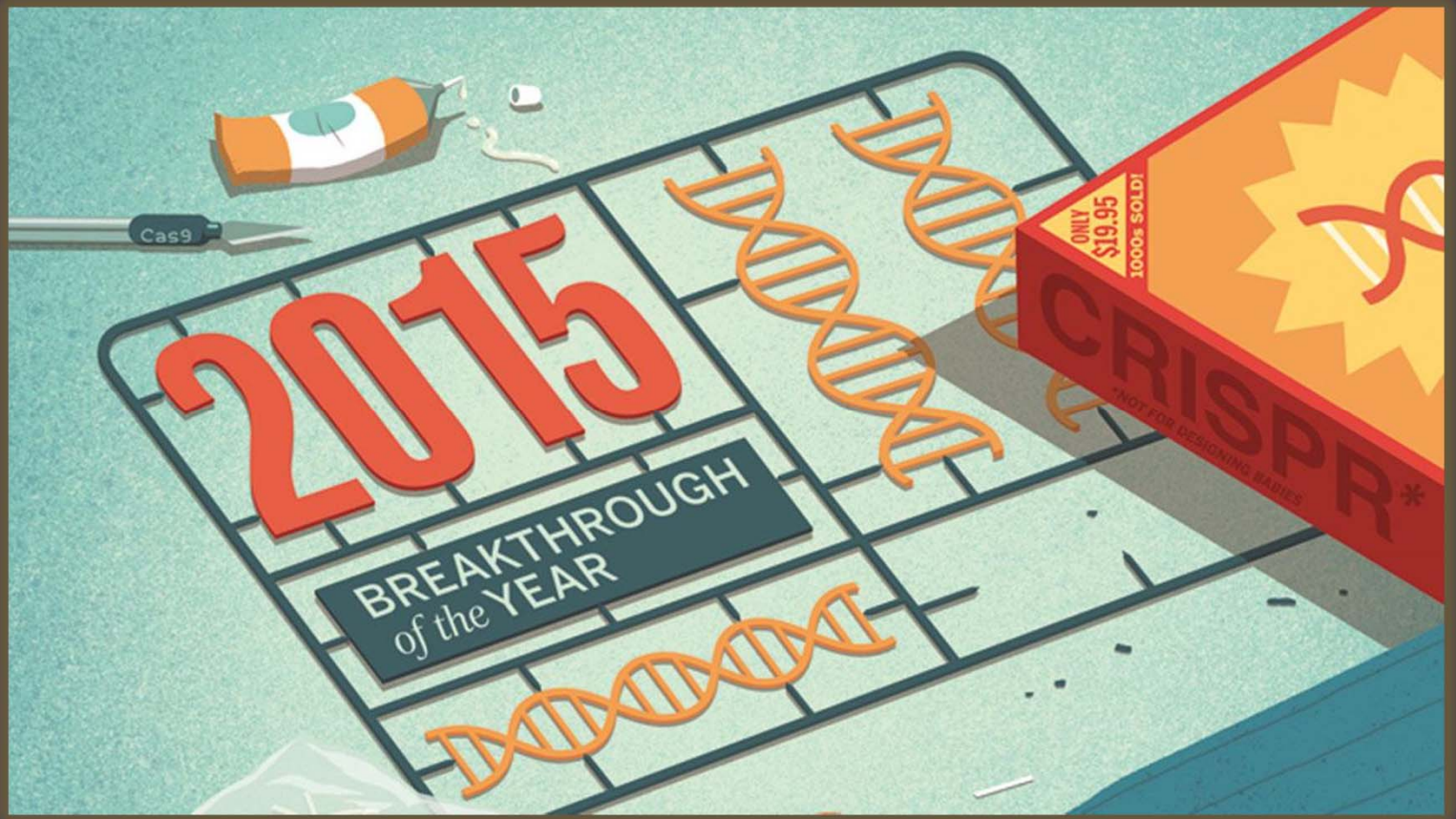
Robert David Burk
Andrea Califano
Nancy Cox
Gerald Crabtree
Gerald Fink
Helen Hobbs
Cynthia Morton
Robert Moyzis
Alan Scott
Temple Smith
Beth Sullivan

Document 18

2015 Breakthrough of the Year

Science

AAAS



Document 19

The Scientist's Top Ten Innovations 2015

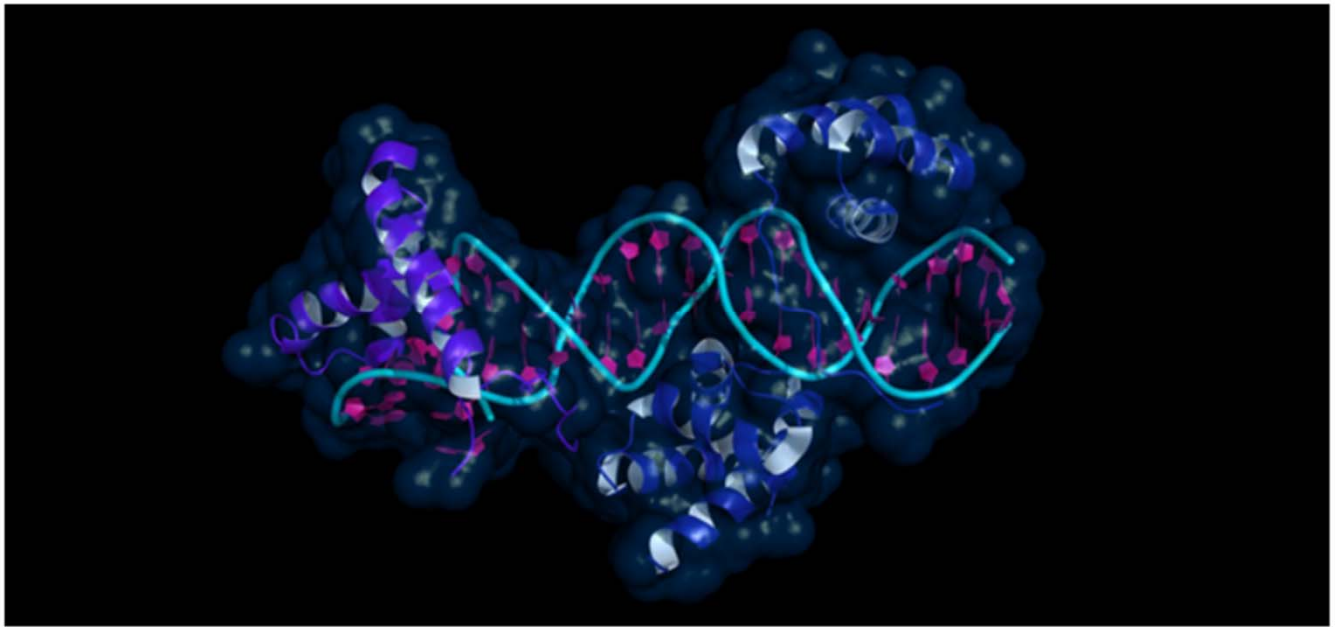
1. GemCode Platform | 10X Genomics
2. MiSeq FGx Forensic Genomics System | Illumina
3. Ion S5 & Ion S5 XL | Thermo Fisher Scientific
4. On Demand Deletions in Human Hap1 Cells | Horizon Discovery
6. CRISPR Epigenetic Activator | Sigma Aldrich

Document 20

ThinkProgress's Scientific Breakthrough:

"Prove We're Already Living In The Future"

Mapping The Epigenome



*Computer-generated representation of DNA binding domains of the transcription factors Oct1 and Sox2*CREDIT: SHUTTERSTOCK/

LAUREL RAYMOND

THINKPROGRESS

Document 21

NHGRI Genome Advance of the Month

Gene-editing technology uncovers genetic link to infertility

By Kyle Davis
ScM Candidate, Genetic Counseling, JHU/NHGRI

of hormon
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cells how

Women with inherited breast cancer risk face numerous challenges

By Bianca Patel
Scientific Program Analyst, NHGRI

carried the
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of all inheri

Gene-editing technology harnessed to protect plants from viruses

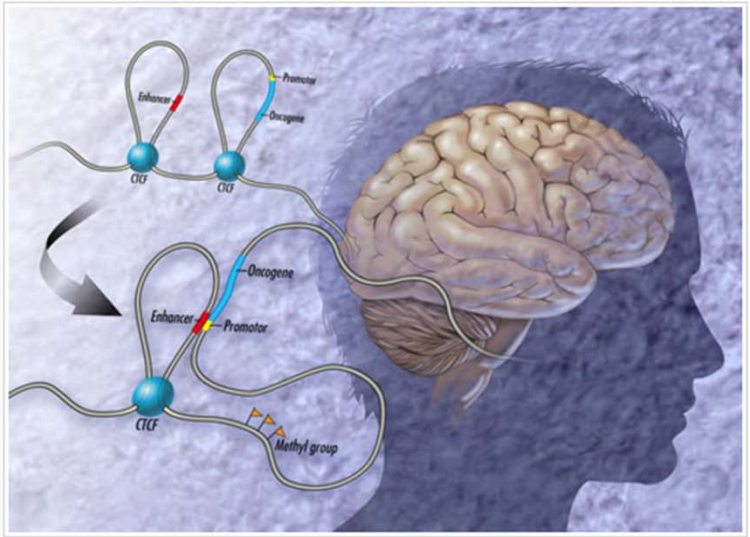
By Julie Coursen
Scientific Program Analyst, NHGRI

palindromic

While using
technologie
the editing

The "Bunny Ear" hypothesis: How defective DNA looping may contribute to cancer

By Hannah Naughton
Scientific Program Analyst, NHGRI



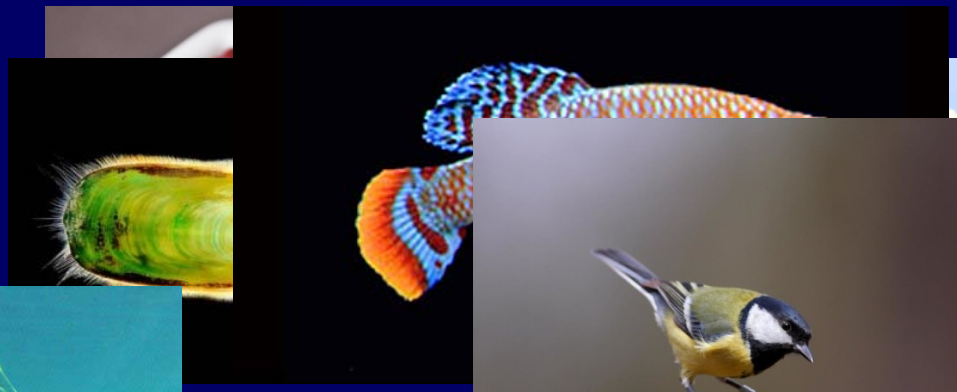
Your DNA forms thousands of loops, like those of a shoe lace. Just as you learned to tie your shoes by forming separate "bunny ear" loops of string, your DNA forms many of these loops to create "genetic neighborhoods" within each bunny ear loop. These neighborhoods bring distant genes and specific gene control switches into close proximity. Genetic neighborhoods can be autonomous and remain separate from other neighborhoods.

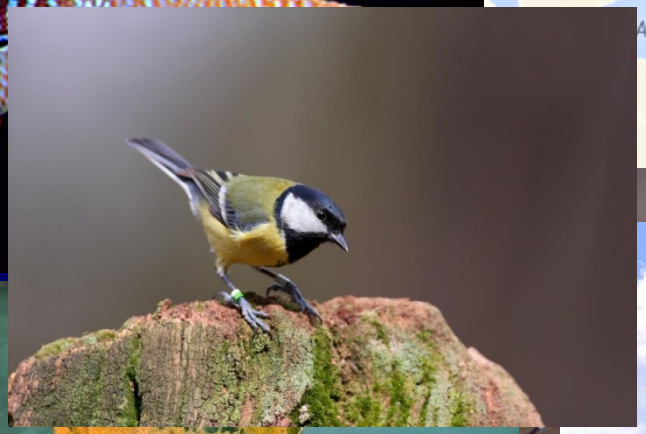
This *Genome Advance of the Month* highlights a landmark study in *Nature* that describes what happens when two genetic neighborhoods merge in brain tumor cells. Researchers found that one gene came under the control of a gene control switch from a different genetic neighborhood, turning on a cancer-growth gene. The research team was led by Dr. Bradley E. Bernstein of the Broad Institute who is also a member of the Encyclopedia of DNA Elements (ENCODE) Consortium, funded by the National Human Genome Research Institute (NHGRI).

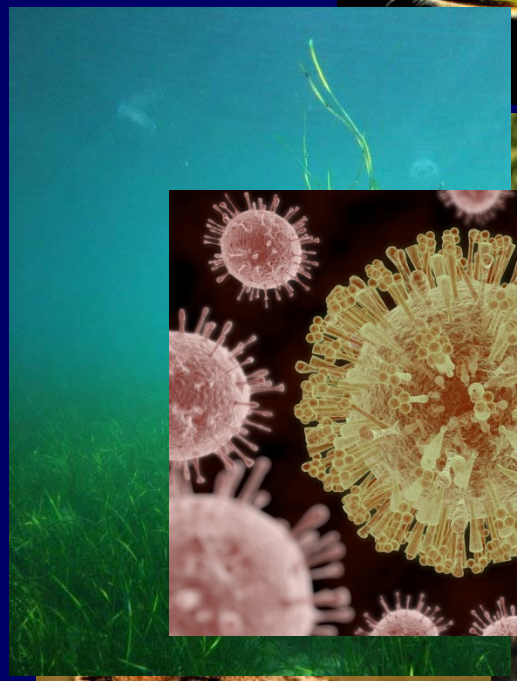
Gliomas are the most common type of brain tumor in adults, but these tumors are difficult to treat. The research team noticed that up to 80 percent of low- and moderate-grade gliomas had a mutation in a common gene called isocitrate dehydrogenase, or *IDH*. This puzzled the scientists, as *IDH*, a housekeeping gene involved in energy production, seemed to have no relevance to cancer. Dr. Bernstein and his colleagues found that when the IDH gene was mutated, particular portions of the cancer cells' DNA became studded with chemical tags called methyl groups. Just as if your shoe lace was covered in thorns, these tags were disrupting the way the DNA was folded, causing genetic neighborhoods to merge.

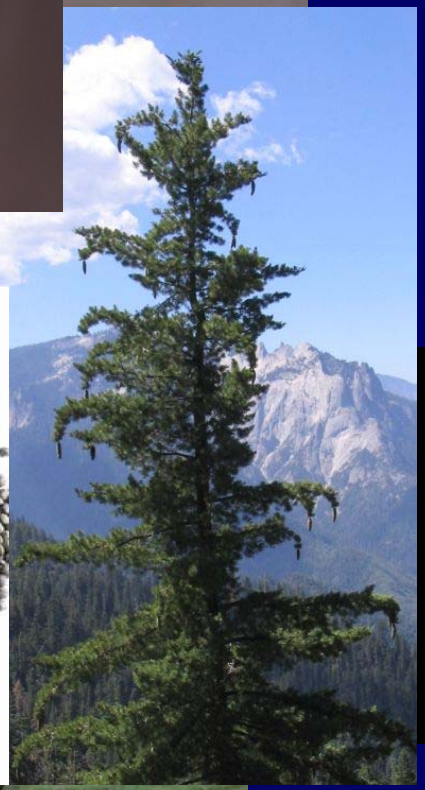
Document 22

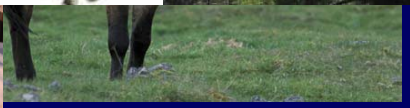
Genomes In The News…











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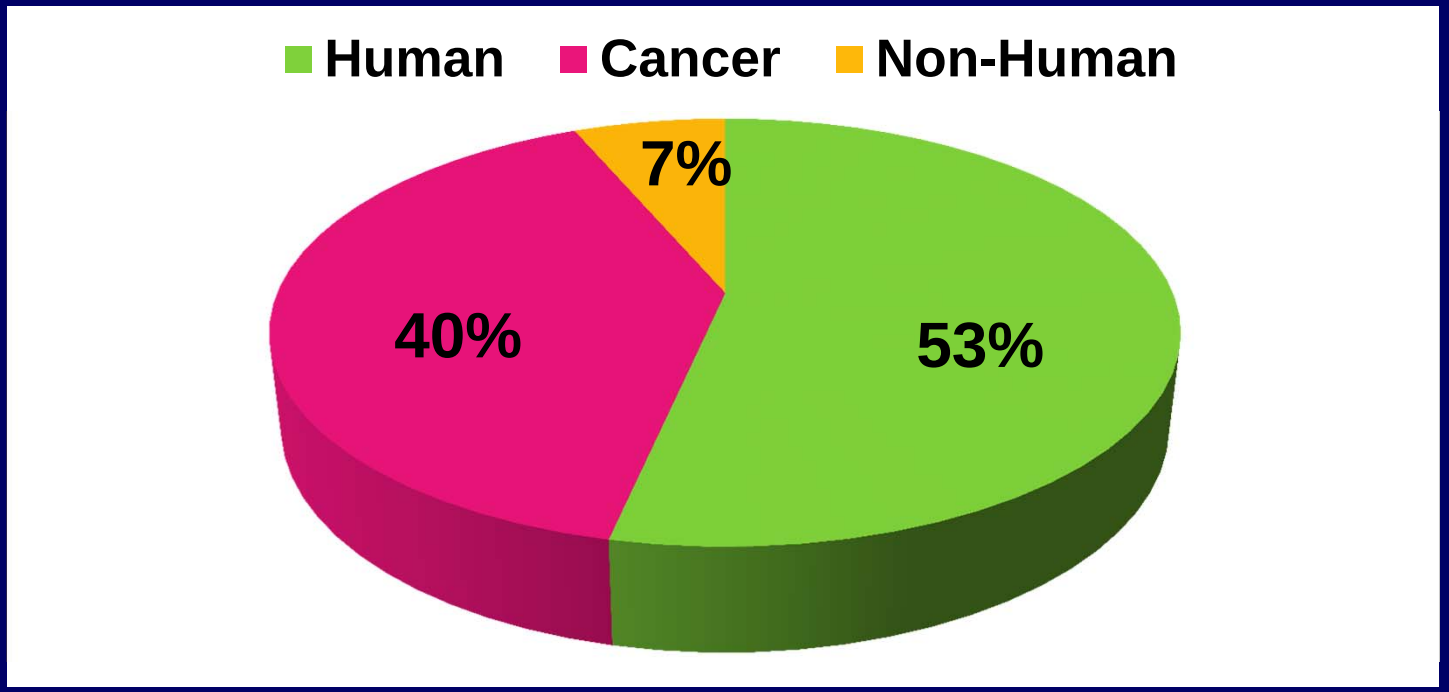
Large-Scale Genome Sequencing and Analysis Centers



Baylor College of Medicine HGSC HUMAN GENOME SEQUENCING CENTER

BROAD INSTITUTE

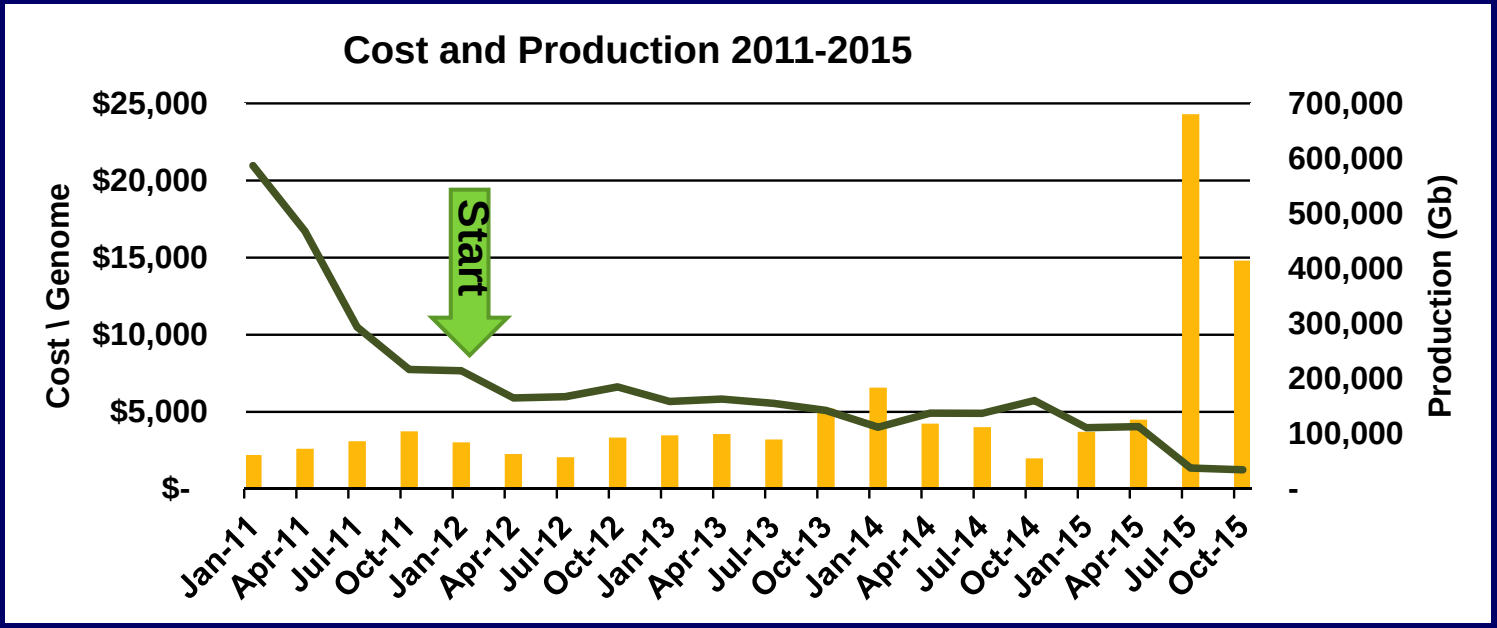
McDONNELL GENOME INSTITUTE

Since 2012: >600 publications and >200 projects

Document 24

Large-Scale Genome Sequencing and Analysis Centers

- >2.8B gigabases produced from 2012-2015
- ~$1,500 per whole human genome sequence



Baylor College of Medicine HGSC HUMAN GENOME SEQUENCING CENTER

BROAD INSTITUTE

McDONNELL GENOME INSTITUTE

1000 Genomes

A Deep Catalog of Human Genetic Variation

ARTICLE

OPEN

doi:10.1038/nature15393

A global reference for human genetic variation

The 1000 Genomes Project Consortium*

Nature **(Oct. 1, 2015)**

ARTICLE

OPEN

doi:10.1038/nature15394

An integrated map of structural variation in 2,504 human genomes

A list of authors and their affiliations appears at the end of the paper.

Nature **(Oct. 1, 2015)**

Variety of life

An effort to sequence thousands of people's genomes reaches the end of the beginning.

Nature Editorial **(Oct. 1, 2015)**

HUMAN GENOMICS

The end of the start for population sequencing

In the final phase of a seven-year project, the genomes of 2,504 people across five continental regions have been sequenced. The result is a compendium of in-depth data on variation in human populations. SEE ARTICLES P.68 & P.75

Nature News & Views **(Oct. 1, 2015)**

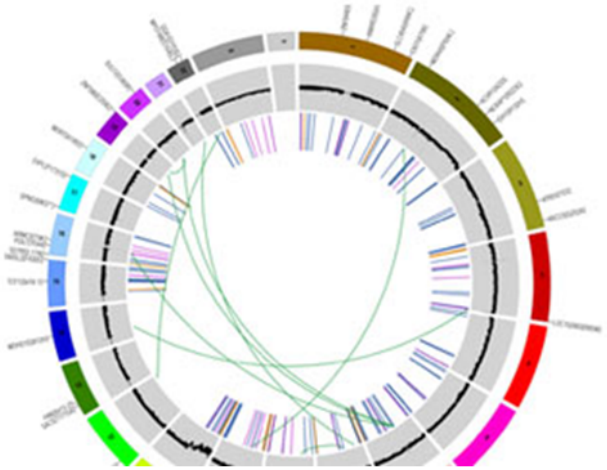
Document 25

NIH **THE CANCER GENOME ATLAS**
National Cancer Institute
National Human Genome Research Institute

Launch Data Portal | Contact Us | For the Media

Search | Search

Home | About Cancer Genomics | Cancers Selected for Study | Research Highlights | Publications | News and Events | About TCGA



Program Overview

Explore how The Cancer Genome Atlas works, the components of the TCGA Research Network and TCGA's place in the cancer genomics field in the Program Overview.

Learn More


Profile of Researcher Dr. Hui Shen


TCGA's Study of Prostate Cancer


Cancers Selected for Study


About TCGA

Launch Data Portal

The Cancer Genome Atlas (TCGA) Data Portal provides a platform for researchers to search, download, and analyze data sets generated by TCGA.

Questions About Cancer

Visit www.cancer.gov

Call 1-800-4-CANCER

Use LiveHelp Online Chat

Multimedia Library

Document 26

TCGA Project 2015 Service to America Medal People's Choice Award

JEAN C. ZENKLUSEN, CAROLYN HUTTER and the Cancer Genome Atlas Team

2015 WINNER
PEOPLE'S CHOICE AWARD

Mapped thousands of gene sequences for more than thirty types of cancer, advancing precision medicine in the diagnosis, treatment and prevention of these deadly diseases.

Document 26

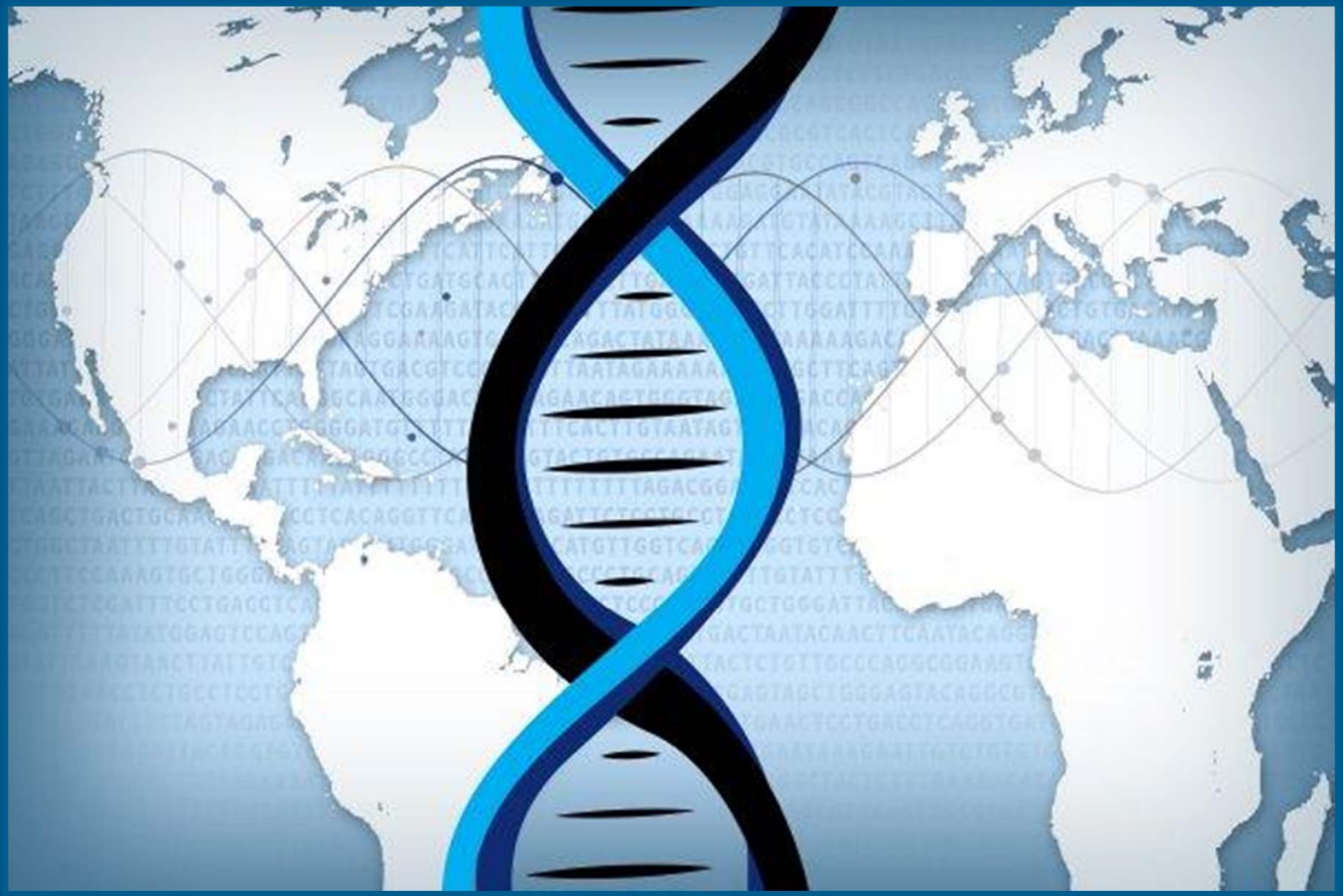
Centers for Mendelian Genomics

Finding the genes underlying human Mendelian conditions

Long-Term Goal: Find All 'Causal' Genes

- **>20,000 exome sequences**
- **>1,600 causal genes**
- **>200 publications**
- **Tools disseminated:**
  - **PhenoDB, GeneMatcher, and data-analysis methods**
- **Data sharing:**
  - **Sequence, variants, and phenotypes to dbGaP**
  - **Candidate causal gene names pre-publication**

Genome Sequencing Program



Document 28

Genome Sequencing Program

Centers for Common Disease Genomics

The Broad Institute	Eric Lander, Mark Daly, Stacey Gabriel, Sekar Kathiresan
Washington University in St. Louis	Richard Wilson
Baylor College of Medicine	Richard Gibbs
New York Genome Center	Robert Darnell

~$240M + ~$20M (NHLBI) total over 4 years

Genome Sequencing Program

Centers for Mendelian Genomics

The Broad Institute	Daniel MacArthur, Heidi Rehm
University of Washington Baylor College of Medicine	Deborah Nickerson, Michael Bamshad, Suzanne Leal
Yale University	Rick Lifton, Mark Gerstein, Murat Gunel, Shirkant Mane
Johns Hopkins University Baylor College of Medicine	David Valle, James Lupski

~$40M + ~$8M (NHLBI) + ~$1M (NEI) total over 4 years

Genome Sequencing Program Coordinating Center

Rutgers University	Tara Matise, Steven Buyske

~$4M total over 4 years

Document 28

Clinical Sequencing Exploratory Research Program

- **Enrolled 4,205 adults and 1,072 children**
- **244 publications (13 working group publications)**

THE JOURNAL OF

LAW, MEDICINE & ETHICS

CONTENTS

VOLUME 43:3 • FALL 2015

OXFORD

JNCI J Natl Cancer Inst (2016) 108(4): djv351

doi:10.1093/jnci/djv351
First published online November 21, 2015
Commentary

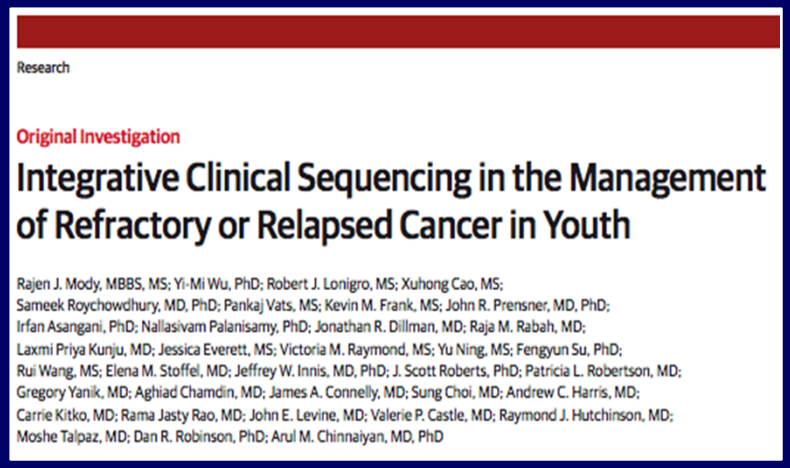
COMMENTARY

Germline Findings in Tumor-Only Sequencing: Points to Consider for Clinicians and Laboratories

Victoria M. Raymond, Stacy W. Gray, Sameek Roychowdhury, Steve Joffe, Arul M. Chinnaiyan, D. Williams Parsons, Sharon E. Plon; on behalf of the Clinical Sequencing Exploratory Research Consortium Tumor Working Group

Affiliations of authors: Departments of Internal Medicine (VMR) and Pathology (AMC), University of Michigan, Ann Arbor, MI; Dana-Farber Cancer Institute, Boston, MA (SWG); Harvard Medical School, Boston, MA (SWG); The Ohio State University, Columbus, OH (SR); University of Pennsylvania Perelman School of Medicine, Philadelphia, PA (SJ); Texas Children's Cancer Center, Houston, TX (DWP, SEP); Baylor College of Medicine, Houston, TX (DWP, SEP).

Correspondence to: Victoria M. Raymond, MS, University of Michigan, 5309 CCC 5940, 400 E. Medical Center Drive, Ann Arbor, MI 48109-0940 (e-mail: vraymond@umich.edu).



Research

Original Investigation

Integrative Clinical Sequencing in the Management of Refractory or Relapsed Cancer in Youth

Rajen J. Mody, MBBS, MS; Yi-Mi Wu, PhD; Robert J. Lonigro, MS; Xuhong Cao, MS; Sameek Roychowdhury, MD, PhD; Pankaj Vats, MS; Kevin M. Frank, MS; John R. Prensner, MD, PhD; Irfan Asangani, PhD; Nallasivam Palanisamy, PhD; Jonathan R. Dillman, MD; Raja M. Rabah, MD; Laxmi Priya Kunju, MD; Jessica Everett, MS; Victoria M. Raymond, MS; Yu Ning, MS; Fengyun Su, PhD; Rui Wang, MS; Elena M. Stoffel, MD; Jeffrey W. Innis, MD, PhD; J. Scott Roberts, PhD; Patricia L. Robertson, MD; Gregory Yanik, MD; Aghiad Chamdin, MD; James A. Connelly, MD; Sung Choi, MD; Andrew C. Harris, MD; Carrie Kitko, MD; Rama Jasty Rao, MD; John E. Levine, MD; Valerie P. Castle, MD; Raymond J. Hutchinson, MD; Moshe Talpaz, MD; Dan R. Robinson, PhD; Arul M. Chinnaiyan, MD, PhD

Document 29

Clinical Sequencing Exploratory Research Program

Integrating Genomic Sequencing into Clinical Care: CSER and Beyond

September 28, 2015

DoubleTree by Hilton Hotel Bethesda - Washington D.C.
8120 Wisconsin Ave.
Bethesda, Md. 20814

On September 28, 2015, the National Human Genome Research Institute (NHGRI) sponsored the ***Integrating Genomic Sequencing into Clinical Care: CSER and Beyond*** meeting at the DoubleTree by Hilton Hotel in Bethesda, Md.

The objectives for the meeting were:

- To summarize and evaluate key scientific contributions of the Clinical Sequencing Exploratory Research (CSER) Program.
- To identify and prioritize scientific opportunities and questions for the next 5-10 years that would address informed integration of genomic sequencing into clinical care.
- To identify optimal organizational features of a potential follow-up program.

YouTube Video Playlist

Workshop Report PDF

Tweets from the Meeting: #CSERandBeyond PDF

Printable Agenda PDF

CSER Background Document PDF

- **Workshop report available on genome.gov**

Document 29

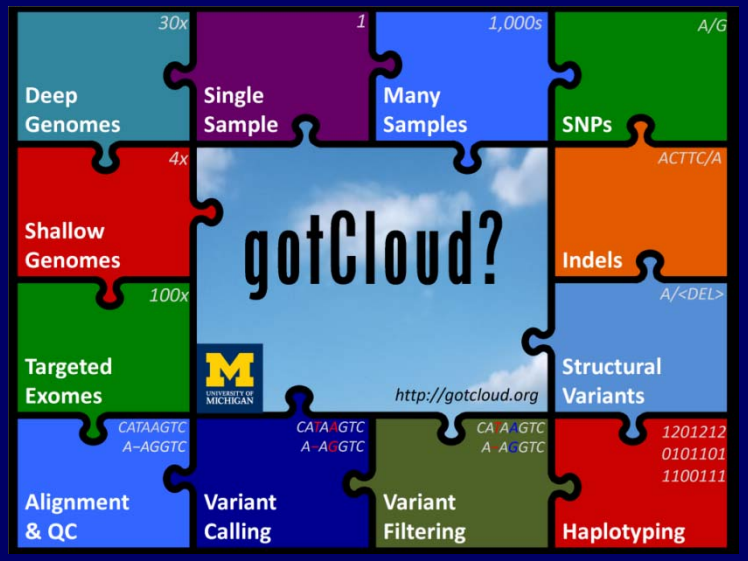
Genome Sequencing Informatics Tools

- Robust software
- Social engineering
- Innovative use of cloud and ‘app’ frameworks

iSeqTools

gatk

genome strip
Structure in Populations



Pindel-C

Document 30

Technology Development Program

- **Novel Nucleic Acid Sequencing**
  - RFA-HG-15-031 (to 33; R01, R21, and R43/44)
  - RFA-HG-15-039 (Direct to Phase II R44) released
  - Upcoming due dates: July 14, 2016 & June 15, 2017
- **Novel Genome Technology Development**
  - PAR-16-14 (to 17; R01, R21, R43/44, and R44) released
  - Upcoming due dates: October 31, 2016 & 2017

Encyclopedia of DNA Elements (ENCODE)

- **ENCODE Outreach Activities**

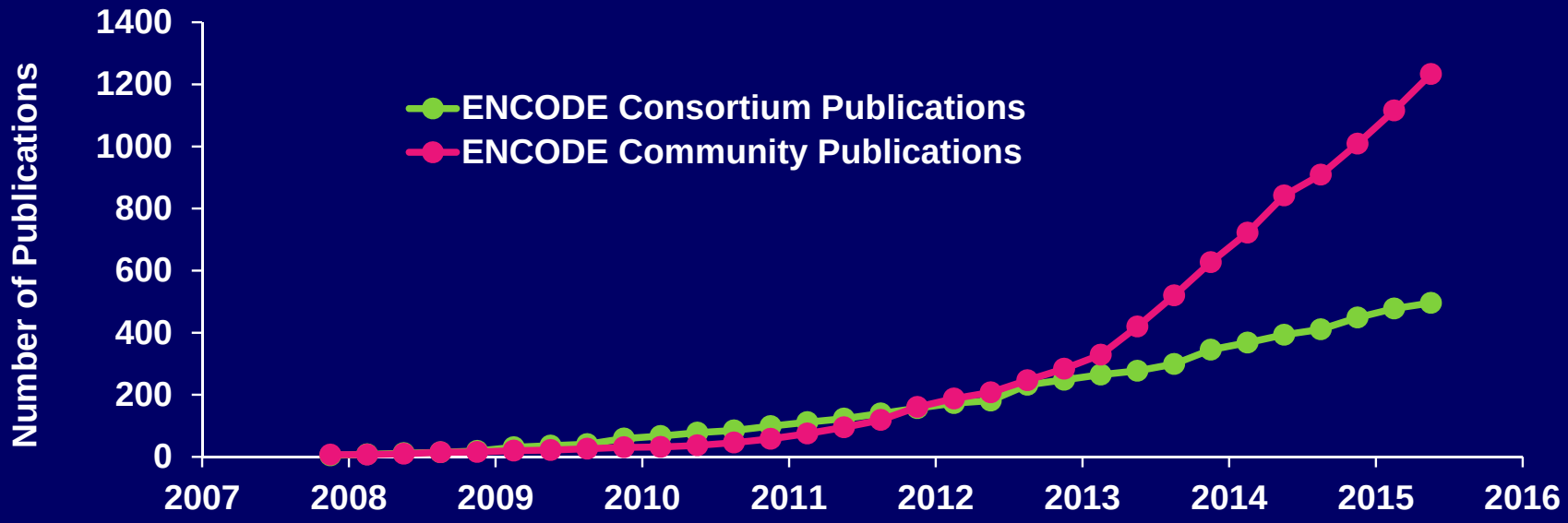
  ENCODE 2016: Research Applications and Users Meeting - June 8-10: Palo Alto, CA

  2016 Keystone Chromatin and Epigenetics Meeting - March 20-24: Whistler, BC

  2016 Society of Toxicology Meeting - March 13-17: New Orleans, LA

  2015 ASHG Workshop - Baltimore, MD (completed)

- **Publications Using ENCODE Data**



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Encyclopedia of DNA Elements (ENCODE)

- **New 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:**

Application Due Date	March 21, 2016
Scientific Merit Review	June 2016
Advisory Council Review	October 2016
Earliest Start Date	December 2016

emerge network

ELECTRONIC MEDICAL RECORDS AND GENOMICS

Association of Arrhythmia-Related Genetic Variants With Phenotypes Documented in Electronic Medical Records

Sara L. Van Driest, MD, PhD; Quinn S. Wells, MD, PharmD, MSCI; Sarah Stallings, PhD; William S. Bush, PhD, MS; Adam Gordon, PhD; Deborah A. Nickerson, PhD; Jerry H. Kim, MD; David R. Crosslin, PhD; Gail P. Jarvik, MD, PhD; David S. Carrell, PhD; James Ralston, MD, MPH; Eric B. Larson, MD, MPH; Suzette J. Bielinski, PhD; Janet E. Olson, PhD; Zi Ye, MD, PhD; Iftikhar J. Kullo, MD; Noura S. Abul-Husn, MD, PhD; Stuart A. Scott, PhD; Erwin Bottinger, MD; Berta Almoguera, PhD; John Connolly, PhD; Rosetta Chiavacci, BSN, CCRC; Hakon Hakonarson, MD, PhD; Laura J. Rasmussen-Torvik, PhD, MPH; Vivian Pan, MS, CGC; Stephen D. Persell, MD, MPH; Maureen Smith, MS, CGC; Rex L. Chisholm, PhD; Terrie E. Kitchner, CCRP; Max M. He, PhD; Murray H. Brilliant, PhD; John R. Wallace, MS; Kimberly F. Doheny, PhD; M. Benjamin Shoemaker, MD, MCSI; Rongling Li, MD, PhD, MPH; Teri A. Manolio, MD, PhD; Thomas E. Callis, PhD; Daniela Macaya, MQC; Marc S. Williams, MD; David Carey, PhD; Jamie D. Kapplinger, BA; Michael J. Ackerman, MD, PhD; Marylyn D. Ritchie, PhD; Joshua C. Denny, MD, MS; Dan M. Roden, MD

***JAMA* (2016)**

Official journal of the American College of Medical Genetics and Genomics

SYSTEMATIC REVIEW | Genetics inMedicine

Open

A systematic literature review of individuals' perspectives on broad consent and data sharing in the United States

Nanibaa' A. Garrison, PhD[1,2], Nila A. Sathe, MA, MLIS[3,4], Armand H. Matheny Antommaria, MD, PhD[5], Ingrid A. Holm, MD, MPH[6,7], Saskia C. Sanderson, PhD[8], Maureen E. Smith, MS, CGC[9], Melissa L. McPheeters, PhD, MPH[3,4] and Ellen W. Clayton, MD, JD[1,2,4,10]

***Genetics in Medicine* (2015)**

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emerge network

ELECTRONIC MEDICAL RECORDS AND GENOMICS

Paul Harris, Ph.D.

Donald A.B. Lindberg Award for Innovation in Informatics (AMIA 2015)

AMIA Honors Paul A. Harris, PhD, FACMI, with Donald A.B. Lindberg Award for Innovation in Informatics

Monday, November 16, 2015

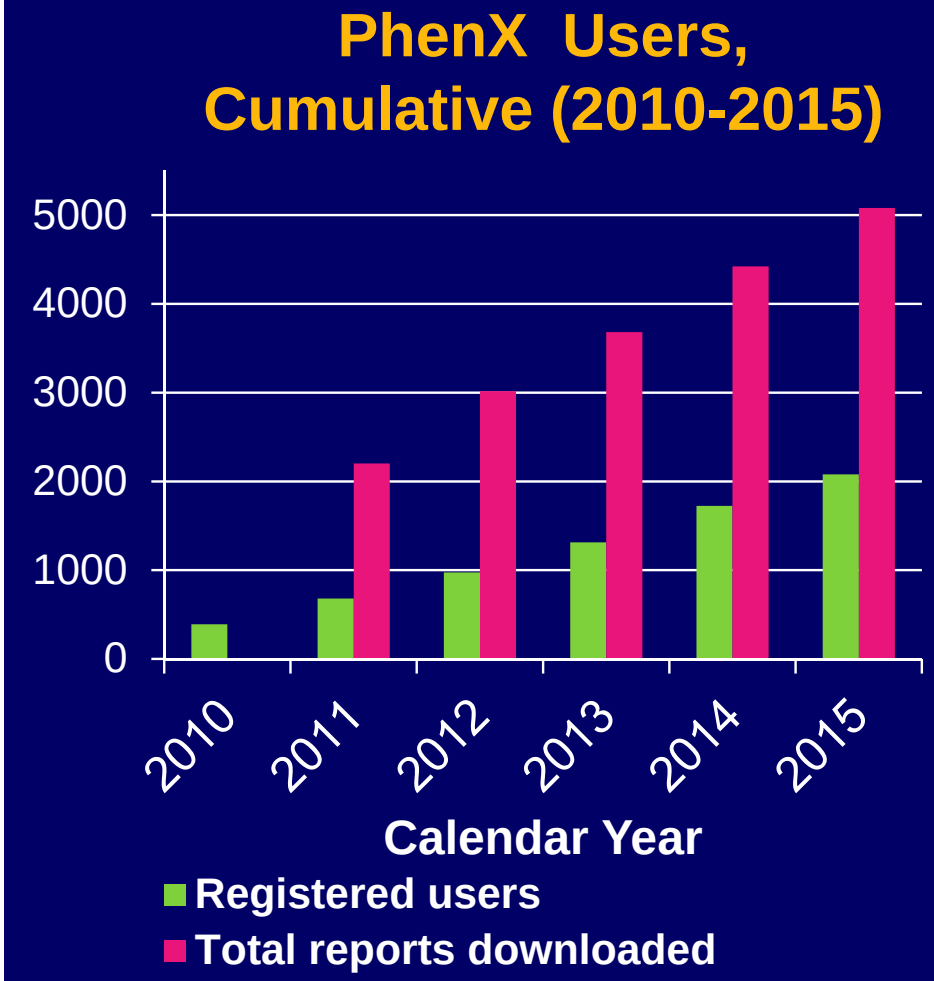
BETHESDA, MD – The American Medical Informatics Association (AMIA) presented Paul A. Harris, PhD, FACMI, with the Donald A.B. Lindberg Award for Innovation in Informatics during AMIA's Annual Symposium, Nov. 14 – 18 in San Francisco. Dr. Harris is professor of biomedical informatics and biomedical engineering, and director of the Office of Research Informatics for Vanderbilt University.

Dr. Harris devised and created REDCap, a research data collection and management software platform, and the ResearchMatch program.

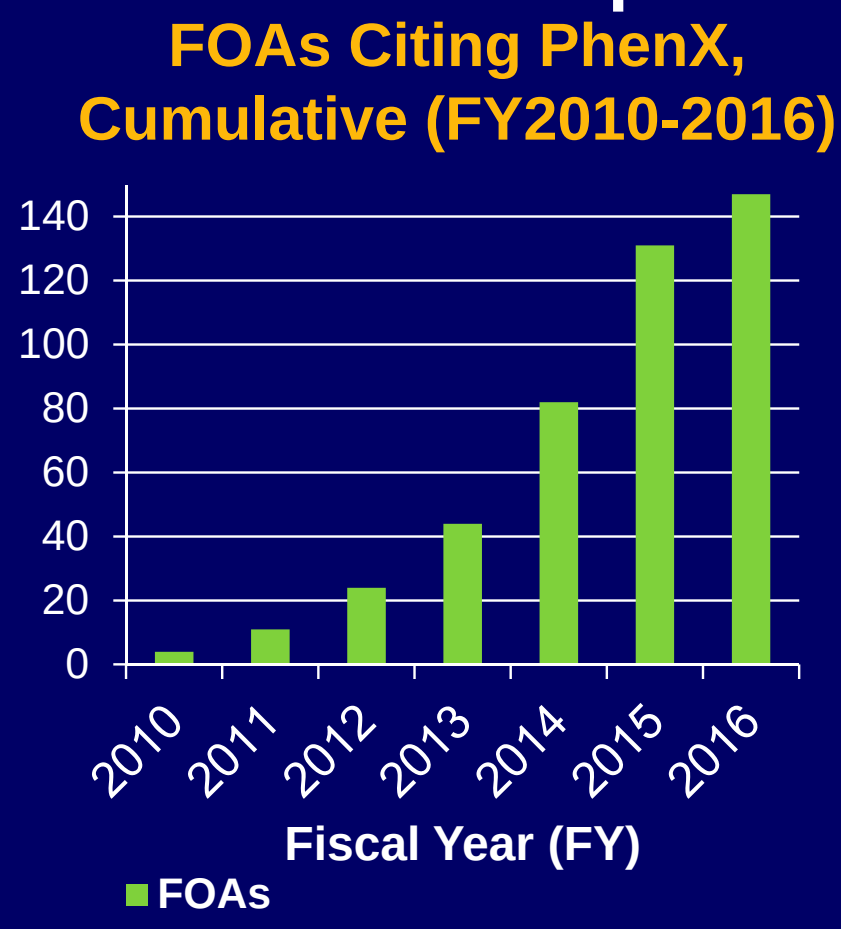
Document 33

The PhenX Toolkit

- Redesigned web page



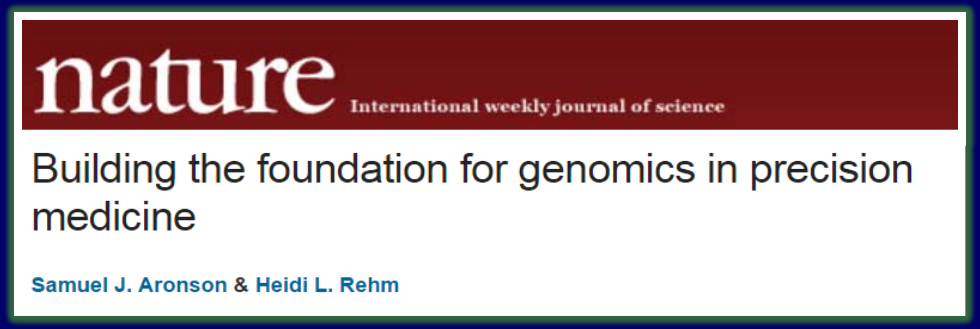
- Pregnancy measures under development



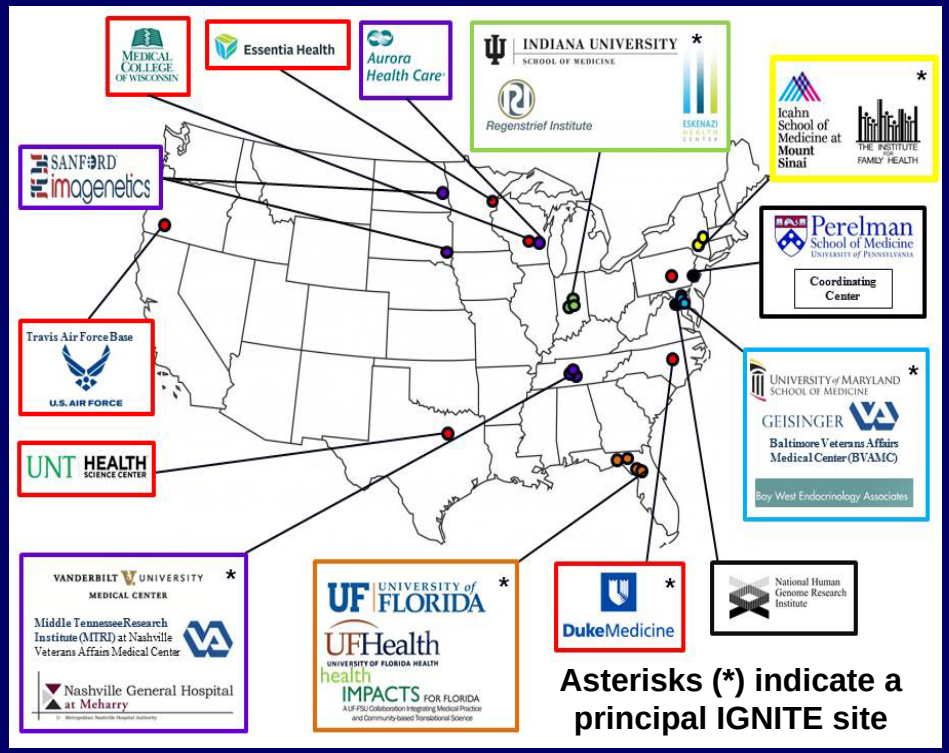
Document 34

ClinGen: Sharing Data. Building Knowledge. Improving Care.

- **ClinGen clinical validity framework finalized**
- **Collaborating with the Global Alliance for Genomics and Health (GA4GH) and the Wellcome Trust's Translational Genomics Initiative**
- **ClinGen publications**



Implementing Genomics In Practice (IGNITE) Network



The IGNITE Network: A Model for Genomic Medicine Implementation and Research

Kristin Wiisanen Weitzel, PharmD[1], Madeline Alexander, PhD[2], Barbara A. Bernhardt, MS, CGC[3], Neil Calman, MD[4], David J. Carey, PhD[5], Larisa H. Cavallari, PharmD[1], Julie R. Field, PhD[6], Diane Hauser[4], Heather A. Junkins, MS[7], Phillip A. Levin, MD[8], Kenneth Levy, PhD, MBA[9], Ebony B. Madden, PhD[7], Teri A. Manolio, MD, PhD[7], Jacqueline Odgis[7], Lori A. Orlando, MD, MHS[10], Reed Pyeritz, MD, PhD[3], R. Ryanne Wu, MD[10], Alan R. Shuldiner, MD[11,12], Erwin P. Bottinger, MD[13], Joshua C. Denny, MD, MS[14], Paul R. Dexter, MD[9], David A. Flockhart, MD[9], Carol R. Horowitz, MD[15], Julie A. Johnson, PharmD[1], Stephen E. Kimmel, MD, MSCE[2,16], Mia A. Levy, MD, PhD[17], Toni I. Pollin, MS, PhD[11], Geoffrey S. Ginsburg, MD, PhD[18] on behalf of the IGNITE Network.

Document 36

Newborn Sequencing In Genomic medicine and public HealTh (NSIGHT)

NSIGHT Public Webinar

November 18, 2015

6001 Executive Blvd.
North Bethesda, Md. 20852

The Newborn Sequencing in Genomic Medicine and Public Health (NSIGHT) program was started in September 2013 with support from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) and the National Human Genomic Research Institute (NHGRI), two components of the National Institutes of Health.

The purpose of the program is to explore the implications, challenges and opportunities associated with the possible use of genomic sequence information during the newborn period.

The NSIGHT program consists of four sites: Brigham and Women's Hospital, Boston Children's Hospital, Children's Mercy Hospital, Kansas City, University of California San Francisco and University of North Carolina at Chapel Hill.

Each site presented an update on their research during the webinar.

YouTube Video Playlist

Tweets from the Webinar: #NIH_NSIGHT

- NIH Media Contacts
- Public Information Officers

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

Human Microbiome Project (HMP)

Integrative HMP (iHMP)

- 3rd Annual iHMP Consortium Meeting
  June 2016 (Bethesda)

- 2016 iHMP 'Landmark' Meetings
  Keystone Symposium "Genomics and Personalized Medicine" (February 2016)
  6th International Human Microbiome Consortium Congress (November 2016)

Fast Track Action Committee on Mapping the Microbiome (FTAC-MM)

- **Chartered by OSTP**
- **Microbiome research portfolio analysis:**

  Fiscal Years 2012-2014

  14 Federal agencies

  $922M total

  NIH: 59%

nature microbiology

CONSENSUS STATEMENT

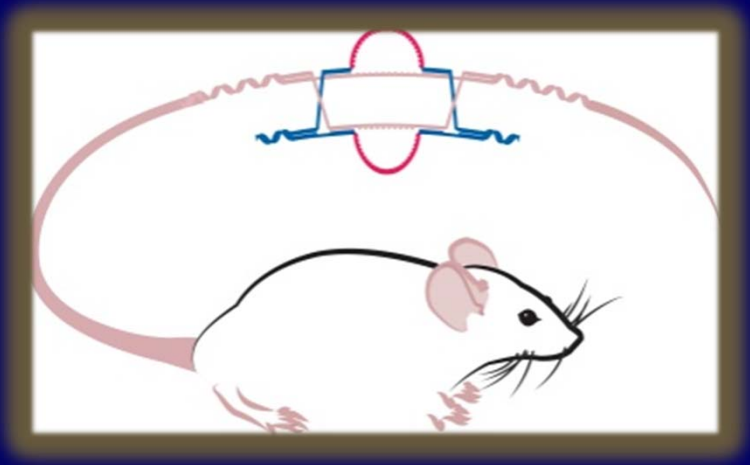
PUBLISHED: 11 JANUARY 2016 | ARTICLE NUMBER: 15015 | DOI: 10.1038/NMICROBIOL.2015.15

An assessment of US microbiome research

Elizabeth Stulberg[1*], Deborah Fravel[2], Lita M. Proctor[3], David M. Murray[4], Jonathan LoTempio[3], Linda Chrisey[5], Jay Garland[6], Kelly Goodwin[7,8], Joseph Graber[9], M. Camille Harris[10], Scott Jackson[11], Michael Mishkind[12], D. Marshall Porterfield[13] and Angela Records[14]

Document 38

Knockout Mouse Phenotyping Project (KOMP2)



IMPC
International Mouse Phenotyping Consortium

- Approved for continuation
- Total funds: ~$100M over five years
- FOAs published in November
- Review in March
- Discuss funding plan at May Council meeting

Document 39

Human Heredity and Health in Africa (H3Africa)

- Session at 2015 ASHG Annual Meeting
- 7th Consortium Meeting (Washington DC)
  - PI presentations at NIH
  - Trans-NIH/H3Africa Community Engagement Workshop

- Planning for renewal

Document 40

Undiagnosed Diseases Network (UDN)

Undiagnosed Diseases Network | **UDN Site Locations**

Click button on any UDN webpage to apply!

APPLY

Document 41

Gabriella Miller Kids First Pediatric Research Program

- NIH Common Fund Program ($12.6M/year for ten years)
- Clinical and genome-sequence data resource
- Projects identified, genome sequencing underway
- Genome Sequencing Center(s) funding opportunity

  RFA-16-011, Applications due April 1, 2016

Document 42

Precision Medicine Initiative (PMI)

U.S. Department of Health & Human Services

NIH National Institutes of Health
Turning Discovery Into Health

NIH Employee Intranet | Staff Directory | En Español

Health Information | Grants & Funding | News & Events | Research & Training | Institutes at NIH | About NIH

Home » Research & Training

PRECISION MEDICINE INITIATIVE COHORT PROGRAM

PMI Cohort Program

- Scale and Scope
- Participation
- Funding Opportunities
- FAQ
- Advisory Groups
- Events
- Announcements
- PMI in the News
- Multimedia

Frequently Asked Questions.

NIH issues new Request for Information.

About the Precision Medicine Initiative Cohort Program

Far too many diseases do not have a proven means of prevention or effective treatments. We must gain better insights into the biological, environmental, and behavioral influences on these diseases to make a difference for the millions of

Email Updates

Sign up to receive email updates about the Precision Medicine Initiative.

Sign up for updates

Related Links

- PMI Working Group Final Report pdf
- NEJM Perspective: A New Initiative on Precision Medicine
- White House Precision Medicine Web Page
- White House Fact Sheet: President Obama's Precision Medicine Initiative
- Precision Medicine Initiative and Cancer Research

Document 43

PMI Cohort Program Funding Opportunities

Type	Title	Year $M	# of awards	Project Period	Application	Award
OTA	Direct Volunteers Pilot Studies	TBD	1	1 yr	Dec. 2015	Feb. 2016
OTA	Communication Support for the Precision Medicine Initative Research Programs	TBD	1	2 yrs	Dec. 2015	Feb. 2016
U24	PMI Cohort Program Biobank	15	1	5 yrs	Feb 4, 2016	July 2016
U2C	PMI Cohort Program Coordinating Center	21	1	5 yrs	Feb 17, 2016	July 2016
UG3/ UH3	PMI Cohort Program Healthcare Provider Organization Enrollment Centers	28	≤7	5 yrs	Feb 17, 2016	July 2016
U24	PMI Cohort Program Participant Technologies Center	8	1	5 yrs	Feb 17, 2016	July 2016

PMI Cohort Program Advisory Panel

Lon Cardon, Ph.D.
GlaxoSmithKline

Alta Charo, J.D.
University of Wisconsin

Tony Coles, M.D., M.P.H.
Yumanity Therapeutics

Rory Collins, FRS
University of Oxford

Eric Dishman
Intel

Alejandra Gepp, M.A.
National Council of La Raza

Sachin Kheterpal, M.D., M.B.A.
University of Michigan

Marie Lynn Miranda, Ph.D.
Rice University

Bray Patrick-Lake, M.F.S.
Duke University

Dara Richardson-Heron, M.D.
YWCA

Gregory Simon, M.D., M.P.H.
Group Health Research Institute

Sharon Terry, M.A.
Genetic Alliance

David Williams, Ph.D., M.P.H.
Harvard University

NIH Announces ECHO Program

Funding Announcement	Number
Clinical Sites for the IDeA States Pediatric Clinical Trials Network (UG1)	RFA-OD-16-001
Data Coordinating and Operations Center for the IDeA States Pediatric Clinical Trials Network (U24)	RFA-OD-16-002
ECHO Patient Reported Outcomes Research Resource Center Core (U24)	RFA-OD-16-003
ECHO Pediatric Cohorts (UG3/UH3)	RFA-OD-16-004
ECHO Data Analysis Center (U24)	RFA-OD-16-005
ECHO Coordinating Center (U2C)	RFA-OD-16-006
Limited Competition: Exposure Analysis Services for the ECHO Program (Admin Supplement)	PA-16-046

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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

Inter-Society Coordinating Committee for Practitioner Education in Genomics (ISCC)

- In-person meeting (January)
- Theme: Implementation of practical education strategies
- Added ‘patient’s voice’ to discussion
- Discussion of international partnerships

Document 45

Nursing Scholarship Award

JOURNAL OF NURSING SCHOLARSHIP

J Nurs Schol 2013; 45:1, 96–104

A Blueprint for Genomic Nursing Science

Genomic Nursing State of the Science Advisory Panel: Kathleen A. Calzone, PhD, RN, APNG, FAAN[1], Jean Jenkins, PhD, RN, FAAN[2], Alexis D. Bakos, PhD, MPH, RN[3], Ann K. Cashion, PhD, RN, FAAN[4], Nancy Donaldson, PhD, RN, FAAN[5], W. Gregory Feero, MD, PhD[6], Suzanne Feetham, PhD, RN, FAAN[7], Patricia A. Grady, PhD, RN, FAAN[8], Ada Sue Hinshaw, PhD, RN, FAAN[9], Ann R. Knebel, PhD, RN, FAAN[10], Nellie Robinson, MS, RN, FAAN[11], Mary E. Ropka, PhD, RN, FAAN[12], Diane Seibert, PhD, CRNP, FAANP[13], Kathleen R. Stevens, EdD, RN, ANEF, FAAN[14], Lois A. Tully, PhD[15], & Jo Ann Webb, MHA, RN[16]

- International Award for Nursing Excellence
  "Best of Journal of Nursing Scholarship in World Health"
- Web platform in development to disseminate strategies and resources

Document 46

Summary of Proposed Changes to the Common Rule: New Resource

The Notice of Proposed Rulemaking (NPRM) for Revisions to the Common Rule

Summary of Proposed Changes Relevant to Genomics Research

Background

The Notice of Proposed Rulemaking (NPRM) for revisions to the Common Rule was published in the Federal Register on September 8, 2015. The proposed revisions aim to "modernize, simplify, and enhance" oversight for human subjects research in the United States to address changes in the nature of research since the original publication of the Common Rule in 1991. The NPRM follows the July 2011 Advance Notice of Proposed Rulemaking (ANPRM) and is the next step toward publication of the Final Rule. The following page aims to outline the proposed changes that will be most relevant for genomics research. . The information presented is not an official interpretation by the National Institutes of Health (NIH) or the Office of Human Research Protections (OHRP); instead, it is intended to highlight information in the NPRM that is relevant to the field and point members of the genomics community to resources that might inform their own considerations and comments to OHRP. Please see OHRP's NPRM page for more information: NPRM for Revisions to the Common Rule

The NPRM aims to achieve two primary goals: to enhance protections for research participants and to facilitate valuable research by reducing delay, burden, and ambiguity for researchers. The proposed changes to the Common Rule would:

1. Require consent for any use of biospecimens, regardless of whether personal identifiers are attached to the biospecimens
2. Improve informed consent practices with shorter and clearer consent forms
3. Facilitate research through protections that are proportional to risks and review of research that reduces burden, delay, and ambiguity for investigators
4. Increase uniformity in guidance and consistency in how protections are applied
5. Promote privacy with new data security standards

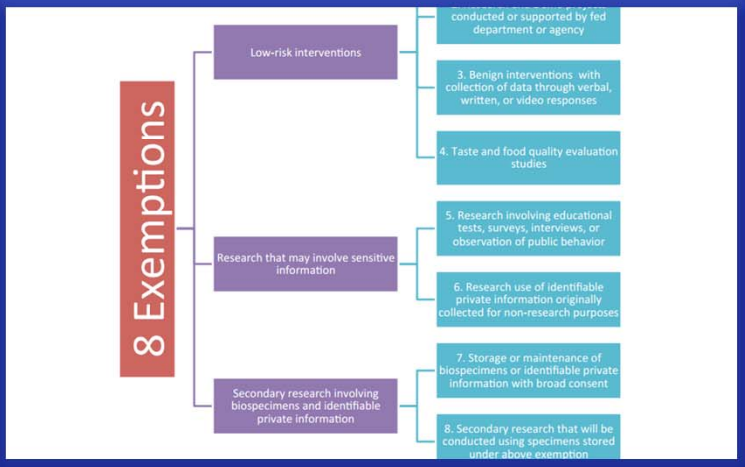
The NPRM is open for comments through January 6, 2016. The comments will be used to revise the regulations before publication of the Final Rule. Compliance with the Final Rule will begin one year after its publication with the exception of provisions .102(e) (revised definition for 'human subject') and .114(b) (requirement for a single reviewing IRB for cooperative research), which will be given three years. Provisions that give additional flexibility and reduce burdens to researchers can be voluntarily implemented 90 days after publication of the Final Rule.

Please provide all feedback and comments about the NPRM to OHRP by the January 6th deadline. Submit comments at: Federal Policy for the Protection of Human Subjects

Top of page

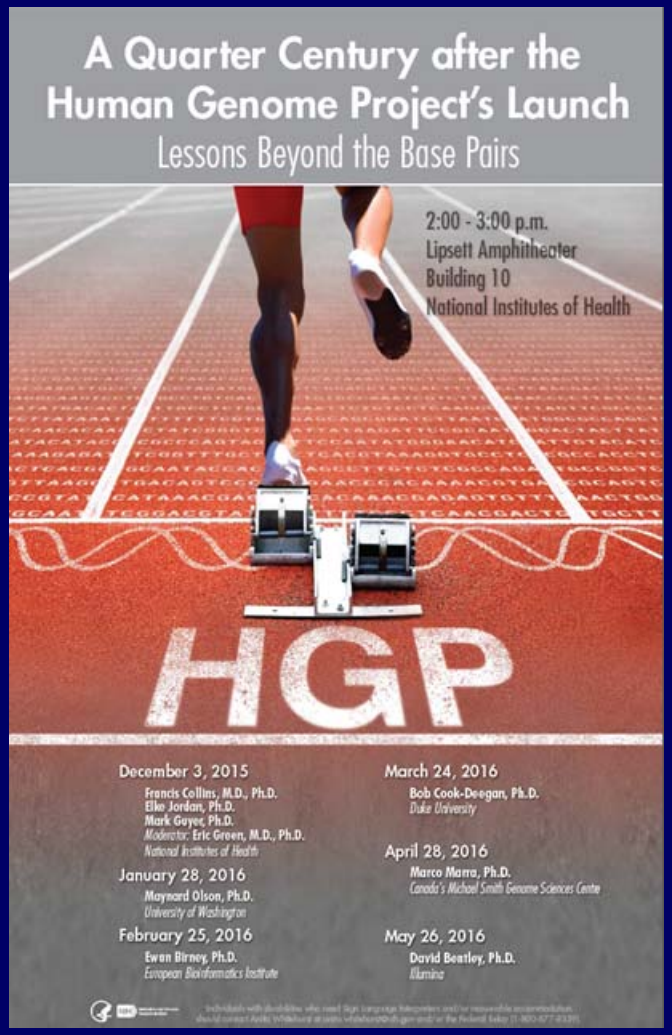
Proposals for changing the definition of human subject

	What type of research is considered human subjects research and requires consent?	Primary consideration behind proposal	Scope	Can non-identified information be used without consent?
Primary proposal	Storage, maintenance, and secondary research use of biospecimens and identifiable private information	Respect for persons	Most broad	Yes, but any use of biospecimens for research would require consent, regardless of identifiability. However, seq data collected for clinical use could be non-IDed and used without consent (if not originally anticipated for research use).
Alternative A	Whole genome sequence data	Potential identifiability	Most narrow	Yes, unless it is part of the data generated as a consequence of whole genome sequencing.
Alternative B	"Bio-unique" information; includes even small sections of genome	Potential identifiability	Narrower than primary, broader than Alternative A	Yes, unless it is information that would qualify as bio-unique.



Document 47

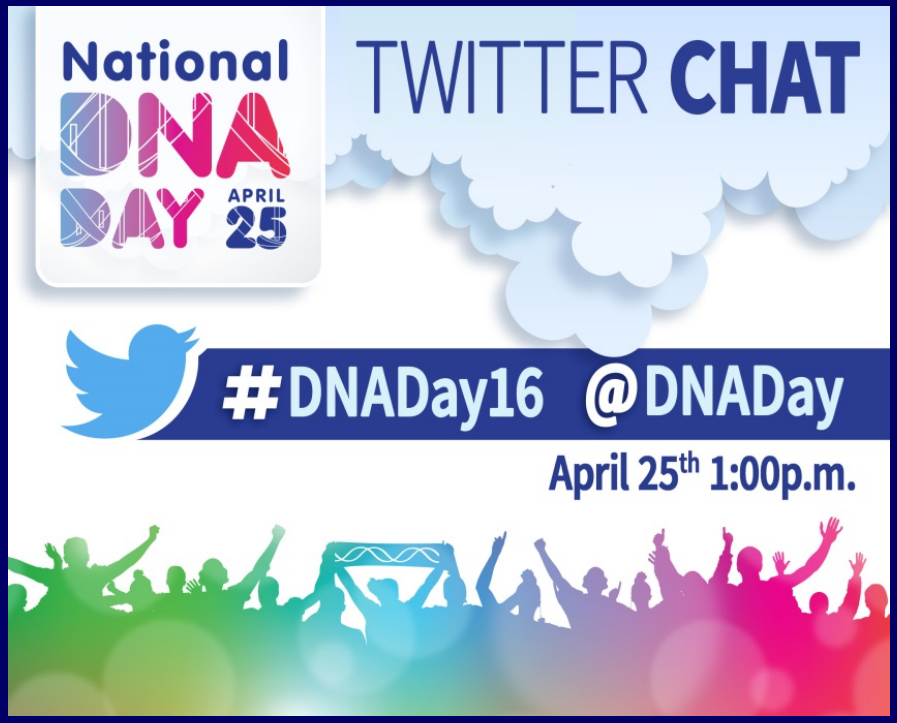
NHGRI History of Genomics Program



- **Seminar series commemorating launch of Human Genome Project 25 years ago**

Document 48

National DNA Day 2016



Document 49

Trans-NIH H3Africa Community Engagement Meeting

Effective Strategies and Practices for Engaging with Communities Around Biomedical Research

Document 50

Genome: Unlocking Life's Code

Exhibition Travel Schedule

2016

January 23-April 25
Discovery World
Milwaukee, WI

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

September 30-January 1
Exploration Place
Wichita, KS

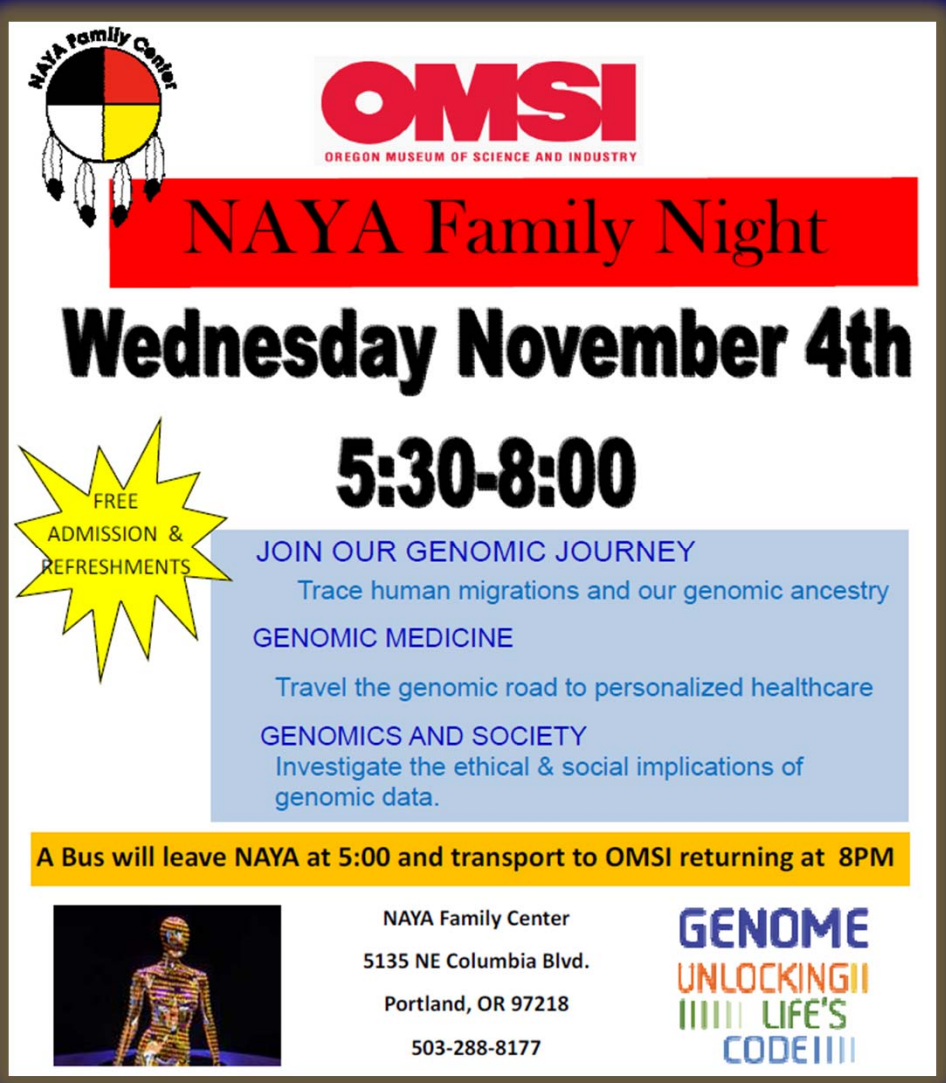
2017

January 28-May 29
Peoria Riverfront Museum
Peoria, IL

Document 51

Genome: Unlocking Life's Code Exhibition

Native American Youth and Family Center Family Night



Document 51

Genome: Unlocking Life's Code Exhibition

Website Interactive

Document 51

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

Thomas A. Waldmann Award for Excellence in Human Immunology

Dan Kastner, M.D., Ph.D.

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2015 Distinguished Alumnus of the University of Texas Graduate School of Biomedical Sciences in Houston

Paul Liu, M.D., Ph.D.

Document 53

NHGRI Intramural Research Highlights

Cell Reports

TCF1 Is Required for the T Follicular Helper Cell Response to Viral Infection

nature genetics

Loss-of-function mutations in *TNFAIP3* leading to A20 haploinsufficiency cause an early-onset autoinflammatory disease

PNAS

Proceedings of the National Academy of Sciences of the United States of America www.pnas.org

*HLA-DRB1*11* and variants of the MHC class II locus are strong risk factors for systemic juvenile idiopathic arthritis

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

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