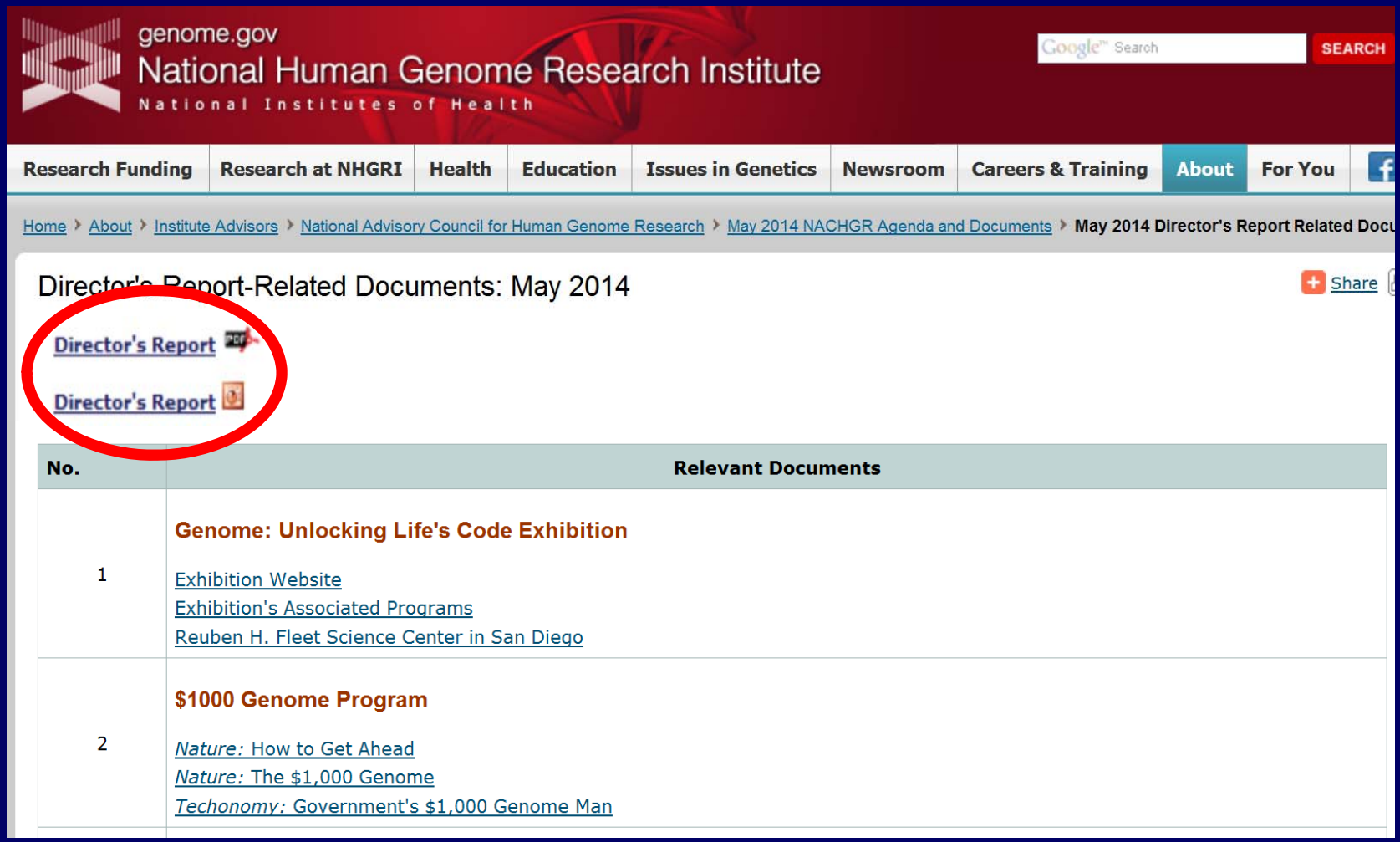
DIRECTOR'S REPORT

National Advisory Council for Human Genome Research

May 2014

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

NIH National Human Genome Research Institute



genome.gov/DirectorsReport

Document #

Open Session Presentations

Presentation from NIGMS Director

Jon Lorsch

Concept Clearance: eMERGE III

Teri Manolio

Genome Sequencing Program Presentations:

- **Clinical Sequencing Exploratory Research Program**

  Jim Evans

- **Centers for Mendelian Genomics**

  Rick Lifton

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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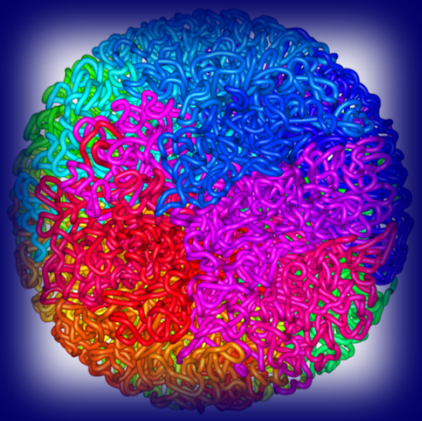
Genome: Unlocking Life's Code Exhibition

GENOME
UNLOCKING
LIFE'S
CODE



- >2.3 million visitors since June 2013 opening
- 15% of museum visitors specifically came to see genome exhibition
- Exhibition programming: Neanderthal genomics, drama and genomics, & Saturday lectures
- 1St stop on 4-5 year traveling tour: San Diego

Document 1

Featured Presentation at Advances in Genome Biology and Technology Meeting

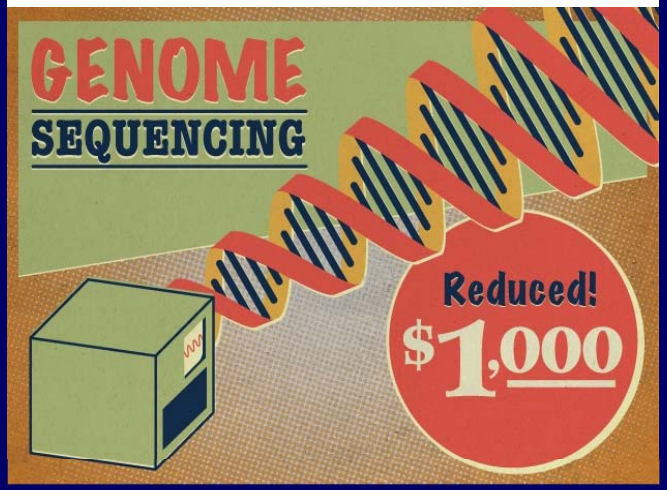
Jeff Schloss, Ph.D.

$1000 Genome Program

nature International weekly journal of science

How to get ahead

The success of the $1,000 genome programme offers lessons for fostering innovation.



The $1,000 genome

With a unique programme, the US government has managed to drive the cost of genome sequencing down towards a much-anticipated target.

BY ERIKA CHECK HAYDEN

In Silicon Valley, Moore's law seems to stand on equal footing with the natural laws codified by Isaac Newton. Intel co-founder Gordon Moore's iconic observation that computing power tends to double — and that its price therefore halves — every 2 years has held true for nearly 50 years with only minor revision. But as an exemplar of rapid change, it is the target of playful abuse from genome researchers.

In dozens of presentations over the past few years, scientists have compared the slope of Moore's law with the swiftly dropping costs of DNA sequencing. For a while they kept pace, but since about 2007, it has not even been close. The price of sequencing an average human genome has plummeted from about US$10 million to a few thousand dollars in just six years. That does not just outpace Moore's law — it makes the once-powerful predictor of unbridled progress look downright sedate. And just as the easy availability of personal computers changed the world, the breakneck pace of genome-technology development has revolutionized bioscience research. It is also set to cause seismic shifts in medicine.

In the eyes of many, a fair share of the credit for this success goes to a grant scheme run by the US National Human Genome Research Institute (NHGRI). Officially called the Advanced Sequencing Technology awards, it is known more widely as the $1,000 and $100,000 genome programmes. Started in 2004, the scheme has awarded grants to 97 groups of academic and industrial scientists, including some at every major sequencing company.

It has encouraged mobility and cooperation among technologists, and helped to launch dozens of competing companies, staving off the stagnation that many feared would take hold after the Human Genome Project wrapped up in 2003. "The major companies in the space have really changed the way people do sequencing, and it all started with the NHGRI funding," says Gina Costa, who has worked for five influential companies and is now a vice-president at Cypher Genomics, a genome-interpretation firm in San Diego, California.

A GIANT'S LEGACY

The $1,000 genome programme, now close to achieving its goal, will award its final grants this year. As technology enthusiasts look to future challenges, the coming milestone raises questions about how the roughly $230-million government programme managed to achieve such success, and whether its winning formula can be applied elsewhere. It benefited from fortuitous timing and the lack of an entrenched industry. But Jeffery Schloss, director of the division of genome sciences at the NHGRI in Bethesda, Maryland, who has run the programme from its inception, says that its achievements also suggest that there are ways to navigate public–private partnerships successfully. "One of our challenges is to figure out what is the right role for the government; to not get in the way, but feed the pipeline of private-sector technology development," he says.

The quest to sequence the first human genome was a massive

"In the eyes of many, a fair share of the credit for this success goes to a grant scheme run by the US National Human Genome Research Institute (NHGRI)."

Document 2

$1000 Genome Program

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Talking with the Government's $1,000 Genome Man

By Meredith Salisbury | March 21, 2014, 11:57 AM | *Techonomy Exclusive*

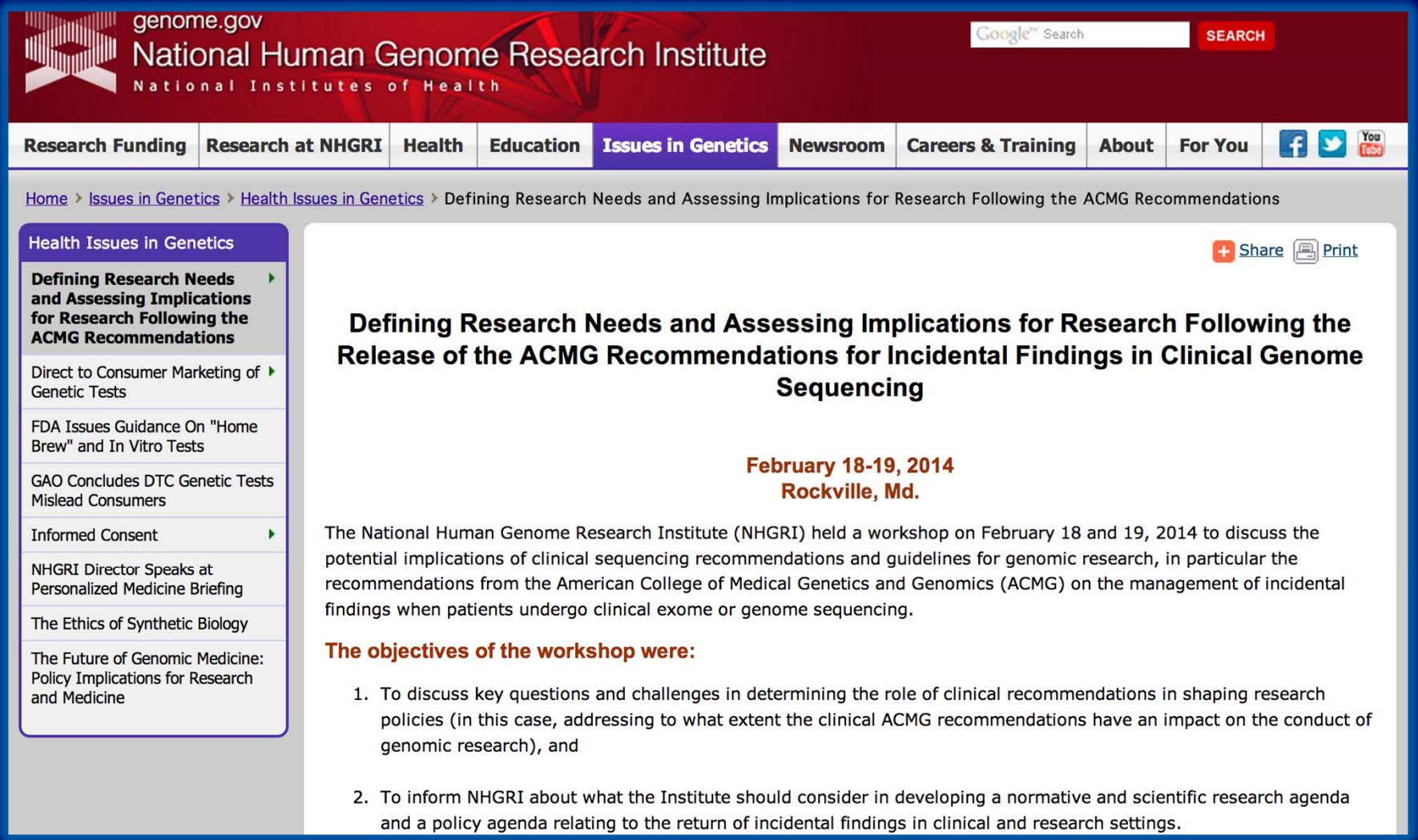
(Photo courtesy NHGRI)

There's been a lot of attention paid to the tremendous progress in making DNA sequencing so cheap that scanning a person's genome could cost just $1,000. This pricing free-fall—in contrast to the massive Human Genome Project, which allocated hundreds of millions of dollars to sequencing a single genome in the late '90s—has occurred markedly faster than with comparable drops for other technologies, such as computers.

Most people would assume that credit is due mostly to the progress made by companies,

Document 2

NHGRI Incidental Findings Workshop



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National Human Genome Research Institute
National Institutes of Health

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Home › Issues in Genetics › Health Issues in Genetics › Defining Research Needs and Assessing Implications for Research Following the ACMG Recommendations

Health Issues in Genetics

- **Defining Research Needs and Assessing Implications for Research Following the ACMG Recommendations**
- Direct to Consumer Marketing of Genetic Tests
- FDA Issues Guidance On "Home Brew" and In Vitro Tests
- GAO Concludes DTC Genetic Tests Mislead Consumers
- Informed Consent
- NHGRI Director Speaks at Personalized Medicine Briefing
- The Ethics of Synthetic Biology
- The Future of Genomic Medicine: Policy Implications for Research and Medicine

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Defining Research Needs and Assessing Implications for Research Following the Release of the ACMG Recommendations for Incidental Findings in Clinical Genome Sequencing

February 18-19, 2014
Rockville, Md.

The National Human Genome Research Institute (NHGRI) held a workshop on February 18 and 19, 2014 to discuss the potential implications of clinical sequencing recommendations and guidelines for genomic research, in particular the recommendations from the American College of Medical Genetics and Genomics (ACMG) on the management of incidental findings when patients undergo clinical exome or genome sequencing.

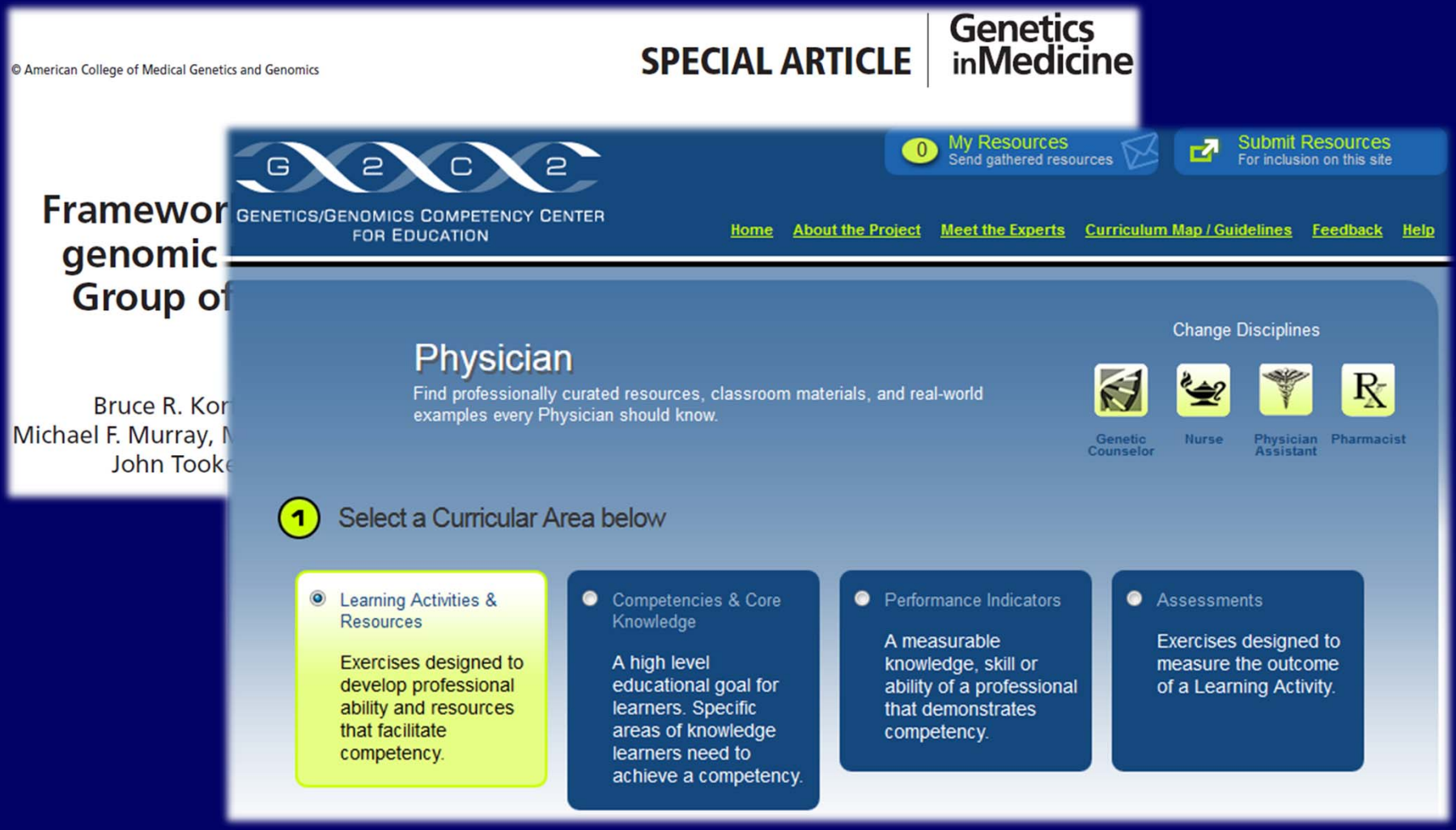
The objectives of the workshop were:

1. To discuss key questions and challenges in determining the role of clinical recommendations in shaping research policies (in this case, addressing to what extent the clinical ACMG recommendations have an impact on the conduct of genomic research), and

2. To inform NHGRI about what the Institute should consider in developing a normative and scientific research agenda and a policy agenda relating to the return of incidental findings in clinical and research settings.

Document 3

Inter-Society Coordinating Committee for Practitioner Education in Genomics



Document 4

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DHHS Secretary: Nomination of Sylvia Mathews Burwell

Retirement of Stephen Groft, Rare Disease Research Champion

Stephen Groft, Pharm.D.

Pamela McInnes, D.D.S.

NIH National Center for Advancing Translational Sciences

OFFICE OF RARE DISEASES RESEARCH

Document 5

National Institute on Minority Health and Health Disparities

John Ruffin, Ph.D.

Yvonne Maddox, Ph.D.

NIH National Institute on Minority Health and Health Disparities

Document 6

NIH Office of Behavioral and Social Sciences Research

Robert Kaplan, Ph.D.

William Riley, Ph.D.

OBSSR
OFFICE OF BEHAVIORAL AND SOCIAL SCIENCES RESEARCH

Document 7

C-SPAN's Washington Journal: NIH Feature Round 2

FEBRUARY 2014

NIAMS Director Dr. Stephen Katz talked about musculoskeletal and skin diseases and the importance of developing new ways to prevent and treat these diseases.

NHLBI Director Dr. Gary Gibbons talked about leading chronic diseases such as heart disease and lung disease, and how healthy habits can help in preventing some of these diseases.

NICHD Director Dr. Alan Guttmacher talks about advances in treating child development and health issues such as preterm birth and child leukemia.

NINDS Director Dr. Story Landis talked about the most common neurological disorders such as stroke, Parkinson's disease, multiple sclerosis, and epilepsy.

C-SPAN

Document 8

NIH Fiscal Year 2015 Appropriations

	Fiscal Year 2012	Fiscal Year 2013	Fiscal Year 2014	Fiscal Year 2015 President's Budget
NIH	$30.9 B	$29.2 B	$30.2 B	$30.4 B
NHGRI	$513 M	$483 M	$497 M	$498 M

Document 9

Congressional Appropriations Hearings

Document 9

Congressional Hearings:
"A Path to 21st Century Cures"

April 30

May 6

A PATH TO DISCOVERY DEVELOPMENT DELIVERY 21st CENTURY CURES

Document 9

Accelerating Medicines Partnership (AMP)

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ILCHUN Molecular Medicine Award

Geoffrey Ginsburg, M.D., Ph.D.

Harrington Prize for Innovation in Medicine

Hal Dietz, M.D.

Document 11

Passano Foundation Award

Jeff Gordon, M.D., Ph.D.

National Academy of Sciences: Newly Elected

Cynthia Burrows
Bob Darnell
Julian Davies
Michael Green
Vamsi Mootha
Monty Slatkin
Henry Yang

Document 13

U.K. Royal Society: Newly Elected

Ewan Birney

Julian Parkhill

Document 14

Global Alliance for Genomics & Health

Meeting Agenda: March 4, 2014
Location: Wellcome Trust Offices, 6th Floor

The Wellcome Trust
215 Euston Road, London, England

Welcome	**David Altshuler** **Kay Davies**	**Time:** **8:30 – 8:45 a.m.**

- **Four Working Groups have been established:**
  - **Regulatory and Ethics Working Group**
  - **Genomic Data Working Group**
  - **Security Working Group**
  - **Clinical Working Group**

Document 15

Special Issue:
American Journal of Medicine Genetics

American Journal of Medical Genetics Part C (Seminars in Medical Genetics) 166C:1–7 (2014)

INVITED COMMENT

Leading the Way to Genomic Medicine

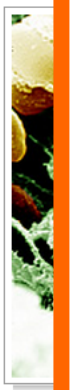
TERI A. MANOLIO* AND ERIC D. GREEN

Document 16

NHGRI Genome Advance of the Month

The evolutionary mark of *Y. pestis* and the Black Death

By Roseanne Zhao
NIH M.D./Ph.D. Partnership Training Program Scholar



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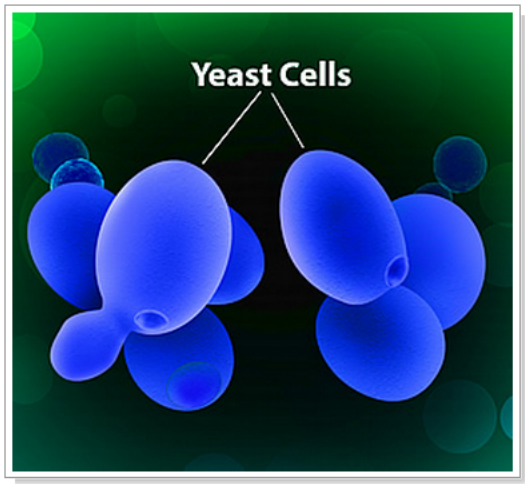
Circulating tumor DNA: A new generation of cancer biomarkers

By Elizabeth Burke, Ph.D.
Intramural Postdoctoral Fellow, NHGRI

Scientis
into th

Constructing the first designer yeast chromosome opens door to reengineering cells

By Jacqueline Odgis
Scientific Program Analyst, NHGRI



Demystifying the intricate underpinnings of genetic processes has been, for many years, a "look, don't touch" endeavor for biologists. Genetic material and the complex machinery within cells that direct these processes are delicate and complicated. Tampering with these elements has proven difficult, both to alter and track the cells as they pass on their genes to their daughter cells.

In the March Genome Advance of the Month, we learn how scientists have dared to redesign a species of yeast - *Saccharomyces cerevisiae* - that has been instrumental to winemaking, baking and brewing since ancient times. Researchers chose to redesign some of the *S. cerevisiae* genome, the yeast's complete set of genetic material. After cutting and shuffling the genes on a segment of the yeast genome using a computer simulation, they created a blueprint for a sleeker sequence that can be rearranged on command. The scientists stitched together many nucleotides, the basic building blocks of DNA, following the map of the simulated reference sequence. The end result was a synthetic chromosome called synIII, which functions correctly when inserted into a host yeast cell.

Scientists have constructed synthetic bacterium and virus genomes, but have never before succeeded in creating a chromosome from more complex cells like yeast from scratch. Unlike much simpler bacteria, known to scientists as prokaryotes, the genomes of eukaryotic cells are larger and more complex; their DNA is twisted tightly into multiple tiny packages called chromosomes. Bacteria, on the other hand, usually contain just one compact loop of DNA, which are often easier to work with and replicate, due to their simpler structure and smaller size.

The synIII chromosome is the first entirely man-made designer chromosome in a complex cell. This marks a major milestone for the international team behind this study, who will use these methods to construct an entire synthetic eukaryotic genome, Sc2.0 (www.syntheticyeast.org), creating a complete artificial yeast genome from scratch to implant into a host cell.

Document 17

Genomics In The News…

MIT Technology Review

50 SMARTEST COMPANIES

Introduction
The 50 Companies
FAQ

Illumina on Top
Tesla's Tech Advantage
Google's Next Act
Third Rock is Biotech's Top VC
Cree: Reinventing the Lightbulb

1366: Solar Survivor
Xiaomi's Smartphone Success
Cheap Gas from Siluria
Upworthy: Going Viral
Ripple Labs: New Money

1 Illumina	2 Tesla Motors	3 Google	4 Samsung	5 Salesforce.com	6 Dropbox	7 BMW	8 Third Rock Ventures	9 Square	10 Amazon
11 Tencent									20 Second Sight
21 SpaceX									30 Xiaomi
31 Oculus VR									40 D-Wave Systems
41 Siluria Technologies	Kaiima Bio-Agritech	Datawind	Freescale Semiconductor	Upworthy	LG	Expect Labs	AngelList	Arcadia Biosciences	50 Ripple Labs

1

Illumina

39

Genomics England

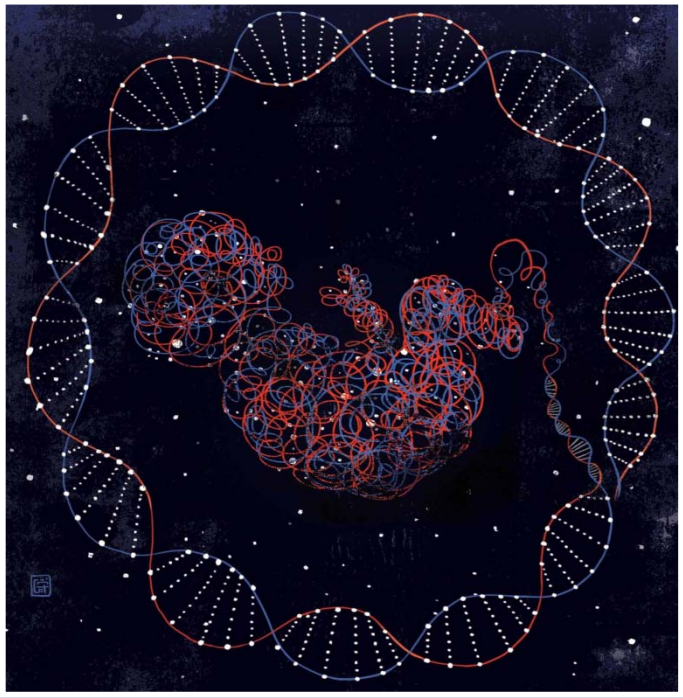
Document 18

Genomics In The News…

The New York Times

The Path to Reading a Newborn's DNA Map

By ANNE EISENBERG FEB. 8, 2014



The Washington Post

The triumph of genomic medicine is just beginning

BY VIVEK WADHWA March 13 at 7:16 am

Document 18

Genomes In The News…

Document 19

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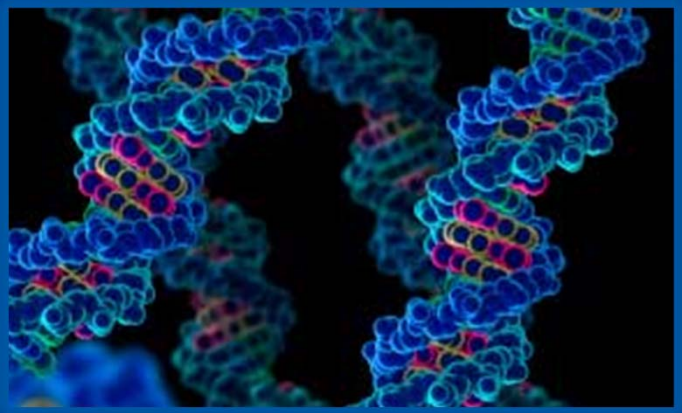
Large-Scale Genome Sequencing and Analysis Centers



Major Projects Include:

- **Alzheimer's Disease Sequencing Project (with NIA)**
- **T2D-Genes (with NIDDK)**
- **TCGA (with NCI)**

Alzheimer's Disease Sequencing Project

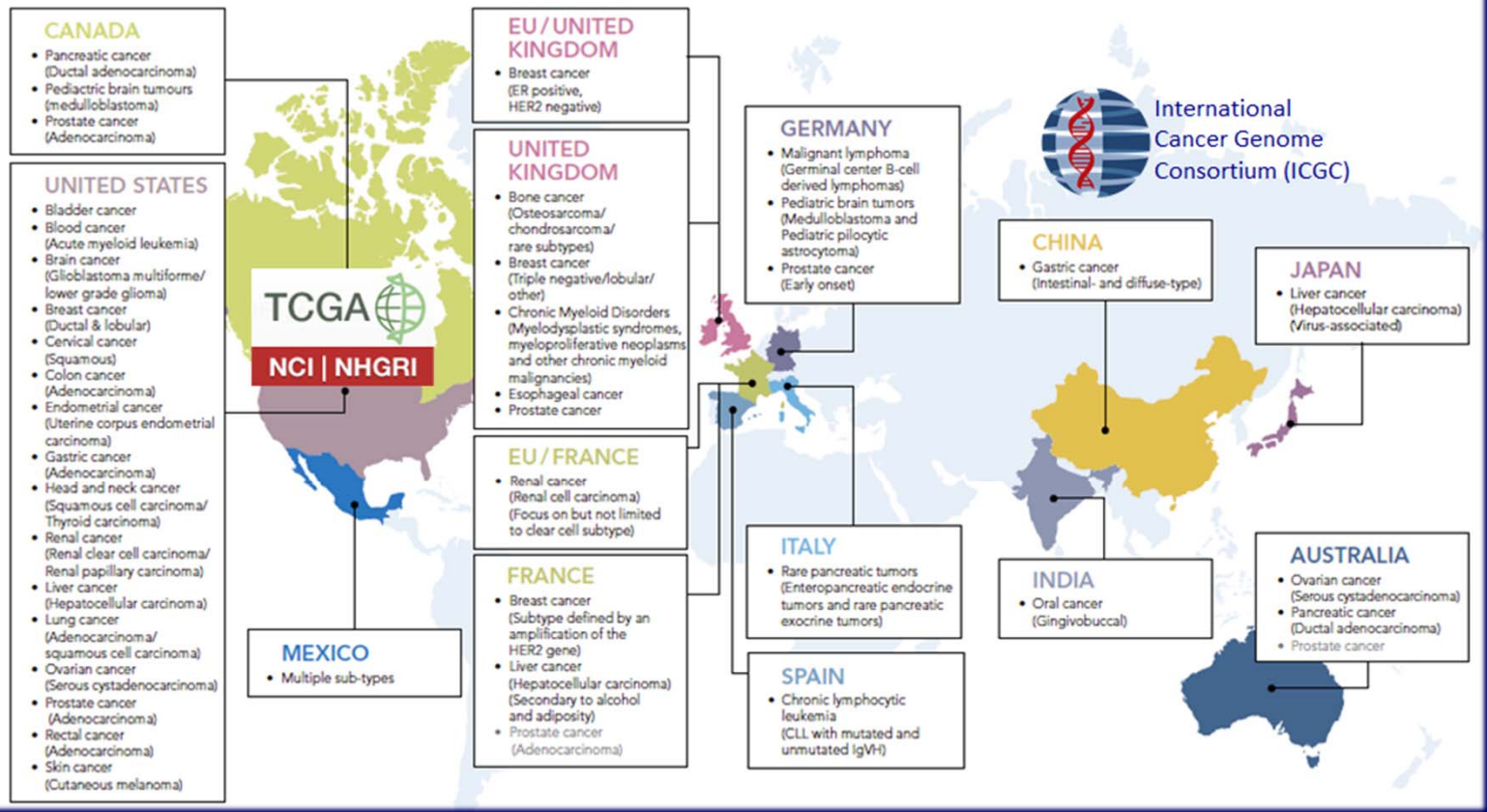
- 584 whole-genome sequences from affected families (sequencing complete, analysis ongoing)
- 10,000 case/control whole-exome sequences (~4,500 completed to date)
- Replication study of up to 40,000 individuals (samples identified)
- NIA data-analysis RFA to be funded in May

Type 2 Diabetes Multiethnic Genetic Consortium (T2D-Genes)

- NIDDK initiated, with NHGRI providing genome sequencing capacity
- Whole-exome sequences from 5000 cases/ controls from five ancestry groups
- Whole-genome sequences from over 600 members of 20 Mexican-American pedigrees
- Multiethnic GWAS analysis published
- Follow up (GWAS and targeted DNA sequencing) in up to 50,000 cases/controls

The WGS Pan-Cancer Analysis Project

Analysis of >2,000 cancer genomes from >20 cancer types.



Centers for Mendelian Genomics

Finding the genes underlying human Mendelian conditions

- **CMG Network: >410 investigators, 33 countries**
- **~80 publications**

CLP1 Founder Mutation Links tRNA Splicing and Maturation to Cerebellar Development and Neurodegeneration

Ashleigh E. Schaffer,[1] Veerle R.C. Eggens,[2] Ahmet Okay Caglayan,[3] Miriam S. Reuter,[4] Eric Scott,[1] Nicole G. Coufal,[1] Jennifer L. Silhavy,[1] Yuanchao Xue,[5] Hulya Kayserili,[6] Katsuhito Yasuno,[2] Rasim Ozgur Rosti,[1] Mostafa Abdellateef,[1] Caner Caglar,[3] Paul R. Kasher,[2] J. Leonie Cazemier,[2] Marian A. Weterman,[2] Vincent Cantagrel,[1,7] Na Cai,[1] Christiane Zweier,[4] Umut Altunoglu,[6] N. Bilge Satkin,[6] Fesih Aktar,[8] Beyhan Tuysuz,[9] Cengiz Yalcinkaya,[10] Huseyin Caksen,[11] Kaya Bilguvar,[5] Xiang-Dong Fu,[5] Christopher R. Trotta,[12] Stacey Gabriel,[13] André Reis,[4] Murat Gunel,[3,14] Frank Baas,[2,14] and Joseph G. Gleeson[1,14,*]

Human CLP1 Mutations Alter tRNA Biogenesis, Affecting Both Peripheral and Central Nervous System Function

Ender Karaca,[1,21] Stefan Weitzer,[2,21] Davut Pehlivan,[1,21] Hiroshi Shiraishi,[2,21] Tasos Gogakos,[3] Toshikatsu Hanada,[2,20] Shalini N. Jhangiani,[4] Wojciech Wiszniewski,[1] Marjorie Withers,[1] Ian M. Campbell,[1] Serkan Erdin,[5] Sedat Isikay,[6] Luis M. Franco,[1,7] Claudia Gonzaga-Jauregui,[1] Tomasz Gambin,[1] Violet Gelowani,[1] Jill V. Hunter,[8] Gozde Yesil,[9] Erkan Koparir,[10] Sarenur Yilmaz,[11] Miguel Brown,[3] Daniel Briskin,[3] Markus Hafner,[3] Pavel Morozov,[3] Thalia A. Farazi,[3] Christian Bernreuther,[12] Markus Glatzel,[12] Siegfried Trattnig,[13] Joachim Friske,[13] Claudia Kronnerwetter,[13] Matthew N. Bainbridge,[4] Alper Gezdirici,[10] Mehmet Seven,[10] Donna M. Muzny,[4] Eric Boerwinkle,[4,14] Mustafa Ozen,[10] Baylor Hopkins Center for Mendelian Genomics, Tim Clausen,[15] Thomas Tuschl,[3] Adnan Yuksel,[10] Andreas Hess,[16,17] Richard A. Gibbs,[1,4] Javier Martinez,[2,*] Josef M. Penninger,[2,*] and James R. Lupski[1,4,18,19,*]

Cell *157*, 636–650, April 24, 2014

Mutations in Alström protein impair terminal differentiation of cardiomyocytes

Lincoln T. Shenje[1,*], Peter Andersen[1,*], Marc K. Halushka[2], Cecillia Lui[1], Laviel Fernandez[1], Gayle B. Collin[3], Nuria Amat-Alarcon[1], Wendy Meschino[4], Ernest Cutz[5], Kenneth Chang[5,6], Raluca Yonescu[2,7], Denise A.S. Batista[2,7], Yan Chen[1], Stephen Chelko[1], Jane E. Crosson[8], Janet Scheel[8], Luca Vricella[9], Brian D. Craig[7], Beth A. Marosy[7], David W. Mohr[7,10], Kurt N. Hetrick[7], Jane M. Romm[7], Alan F. Scott[7,10], David Valle[7], Jürgen K. Naggert[3], Chulan Kwon[1], Kimberly F. Doheny[7] & Daniel P. Judge[1]

NATURE COMMUNICATIONS | 5:3416 | DOI: 10.1038/ncomms4416 |

Mutations in *TJP2* cause progressive cholestatic liver disease

Melissa Sambrotta[1], Sandra Strautnieks[2], Efterpi Papouli[3], Peter Rushton[4], Barnaby E Clark[4], David A Parry[5], Clare V Logan[5], Lucy J Newbury[6], Binita M Kamath[7,8], Simon Ling[7,8], Tassos Grammatikopoulos[1,9], Bart E Wagner[10], John C Magee[11], Ronald J Sokol[12], Giorgina Mieli-Vergani[1,9], University of Washington Center for Mendelian Genomics[13], Joshua D Smith[14], Colin A Johnson[5], Patricia McClean[15], Michael A Simpson[16], A S Knisely[2], Laura N Bull[17,18] & Richard J Thompson[1,9]

VOLUME 46 | NUMBER 4 | APRIL 2014 NATURE GENETICS

Mutations in *PIEZO2* Cause Gordon Syndrome, Marden-Walker Syndrome, and Distal Arthrogryposis Type 5

Margaret J. McMillin,[1,40] Anita E. Beck,[1,2,40] Jessica X. Chong,[1] Kathryn M. Shively,[1] Kati J. Buckingham,[1] Heidi I.S. Gildersleeve,[1] Mariana I. Aracena,[3,4] Arthur S. Aylsworth,[5] Pierre Bitoun,[6] John C. Carey,[7] Carol L. Clericuzio,[8] Yanick J. Crow,[9] Cynthia J. Curry,[10] Koenraad Devriendt,[11] David B. Everman,[12] Alan Fryer,[13] Kate Gibson,[14] Maria Luisa Giovannucci Uzielli,[15] John M. Graham, Jr.,[16] Judith G. Hall,[17] Jacqueline T. Hecht,[18] Randall A. Heidenreich,[8] Jane A. Hurst,[19] Sarosh Irani,[20] Ingrid P.C. Krapels,[21] Jules G. Leroy,[22] David Mowat,[23,24] Gordon T. Plant,[25] Stephen P. Robertson,[26] Elizabeth K. Schorry,[27] Richard H. Scott,[19] Laurie H. Seaver,[28] Elliott Sherr,[29] Miranda Splitt,[30] Helen Stewart,[31] Constance Stumpel,[21] Sehime G. Temel,[32,33,34] David D. Weaver,[35] Margo Whiteford,[36] Marc S. Williams,[37] Holly K. Tabor,[2,38] Joshua D. Smith,[39] Jay Shendure,[39] Deborah A. Nickerson,[39] University of Washington Center for Mendelian Genomics, and Michael J. Bamshad[1,2,39,*]

The American Journal of Human Genetics *94*, 1–11, May 1, 2014 11

A general framework for estimating the relative pathogenicity of human genetic variants

Martin Kircher[1,5], Daniela M Witten[2,5], Preti Jain[3,4], Brian J O'Roak[1,4], Gregory M Cooper[3] & Jay Shendure[1]

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Document 21

Centers for Mendelian Genomics

Finding the genes underlying human Mendelian conditions

Document 21

Clinical Sequencing Exploratory Research

Moving the Genome Into the Clinic

377 Researchers
20 Institutions
1 Consortium

Genet Med. 2014 Mar 13. doi: 10.1038/gim.2014.26. [Epub ahead of print]

Social and behavioral research in genomic sequencing: approaches from the Clinical Sequencing Exploratory Research Consortium Outcomes and Measures Working Group.

Gray SW[1], Martins Y[2], Feuerman LZ[3], Bernhardt BA[4], Biesecker BB[5], Christensen KD[6], Joffe S[7], Rini C[8], Veenstra D[9], McGuire AL[3].

Am J Bioeth. 2014 Mar;14(3):3-9. doi: 10.1080/15265161.2013.879945.

Addressing the ethical challenges in genetic testing and sequencing of children.

Clayton EW[1], McCullough LB, Biesecker LG, Joffe S, Ross LF, Wolf SM, For The Clinical Sequencing Exploratory Research Cser Consortium Pediatrics Working Group.

In press, AJHG

Return of Genomic Results to Research Participants: The floor, the ceiling, and choices in-between

Gail P. Jarvik, MD, PhD[1,2]; Laura M. Amendola, MS[1]; Jonathan S. Berg, MD, PhD[3]; Kyle Brothers, MD[4,5]; Ellen W. Clayton, MD, JD[6]; Wendy Chung, MD, PhD[7]; Barbara J. Evans, JD[8]; James P. Evans, MD, PhD[9]; Stephanie M. Fullerton, PhD[9]; Carlos J. Gallego, MD[1]; Nanibaa' A. Garrison, PhD[6]; Stacy W. Gray, MD[10,11]; Ingrid A. Holm, MD, PhD[12]; Iftikhar J. Kullo, MD[13]; Lisa Soleymani Lehmann, MD, PhD[10]; Cathy McCarty, PhD, MPH, RD[14]; Cynthia A. Prows, MSN, RN[15]; Heidi L. Rehm, PhD[16]; Richard R. Sharp, PhD[17]; Joseph Salama, BS[1]; Saskia Sanderson, PhD[7]; Sara L. Van Driest, MD, PhD[5]; Marc S. Williams, MD[18]; Susan M. Wolf, JD[19]; Wendy A. Wolf, PhD[20]; eMERGE ROR Committee & CERC Committee; CSER Act-ROR Working Group; Wylie Burke, MD, PhD[9]

Public Health Genomics. 2014 Mar 13. [Epub ahead of print]

Parents' Preferences for Return of Results in Pediatric Genomic Research.

Ziniel SI[1], Savage SK, Huntington N, Amatruda J, Green RC, Weitzman ER, Taylor P, Holm IA.

Am J Med Genet C Semin Med Genet. 2014 Mar;166(1):85-92. doi: 10.1002/ajmg.c.31395. Epub 2014 Mar 10.

Refining the structure and content of clinical genomic reports.

Dorschner MO, Amendola LM, Shirts BH, Kiedrowski L, Salama J, Gordon AS, Fullerton SM, Tarczy-Hornoch P, Byers PH, Jarvik GP.

J Genet Couns. 2014 Mar 1. [Epub ahead of print]

Traditional Roles in a Non-Traditional Setting: Genetic Counseling in Precision Oncology.

Everett JN[1], Gustafson SL, Raymond VM.

CSER Steering Committee meeting | May 13-14, 2014

- Streamlining variant pathogenicity annotation
- Best practices for clinical genomics implementation

Document 22

Clinical Sequencing Exploratory Research

*Moving the **Genome** Into the **Clinic***

377 Researchers
20 Institutions
1 Consortium

Genome Sequencing Informatics Tools

TVAP

Turnkey Variant Analysis Project

iSeqTools

BreakDancer
SV caller using paired-end sequencing data

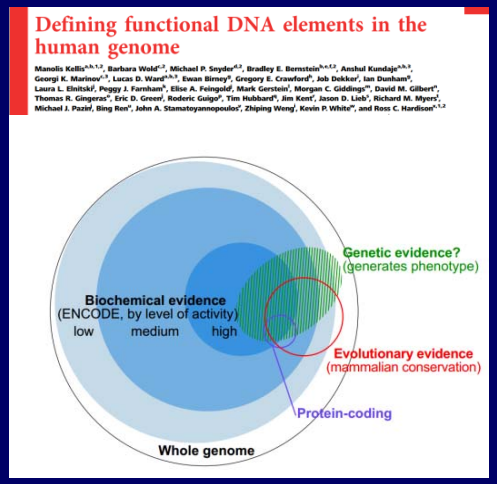
Pindel
Indel caller using pattern growth

VarScan
Germline & somatic SNV & CNV caller

- **GS-IT projects are putting iSeqTools in the cloud**
- **Genomics tools in cloud are more readily accessible by wider range of users**
- **iSeqTools Network workshop on 'De-Mystify the Cloud' at 2014 ASHG meeting**

Document 23

ENCODE

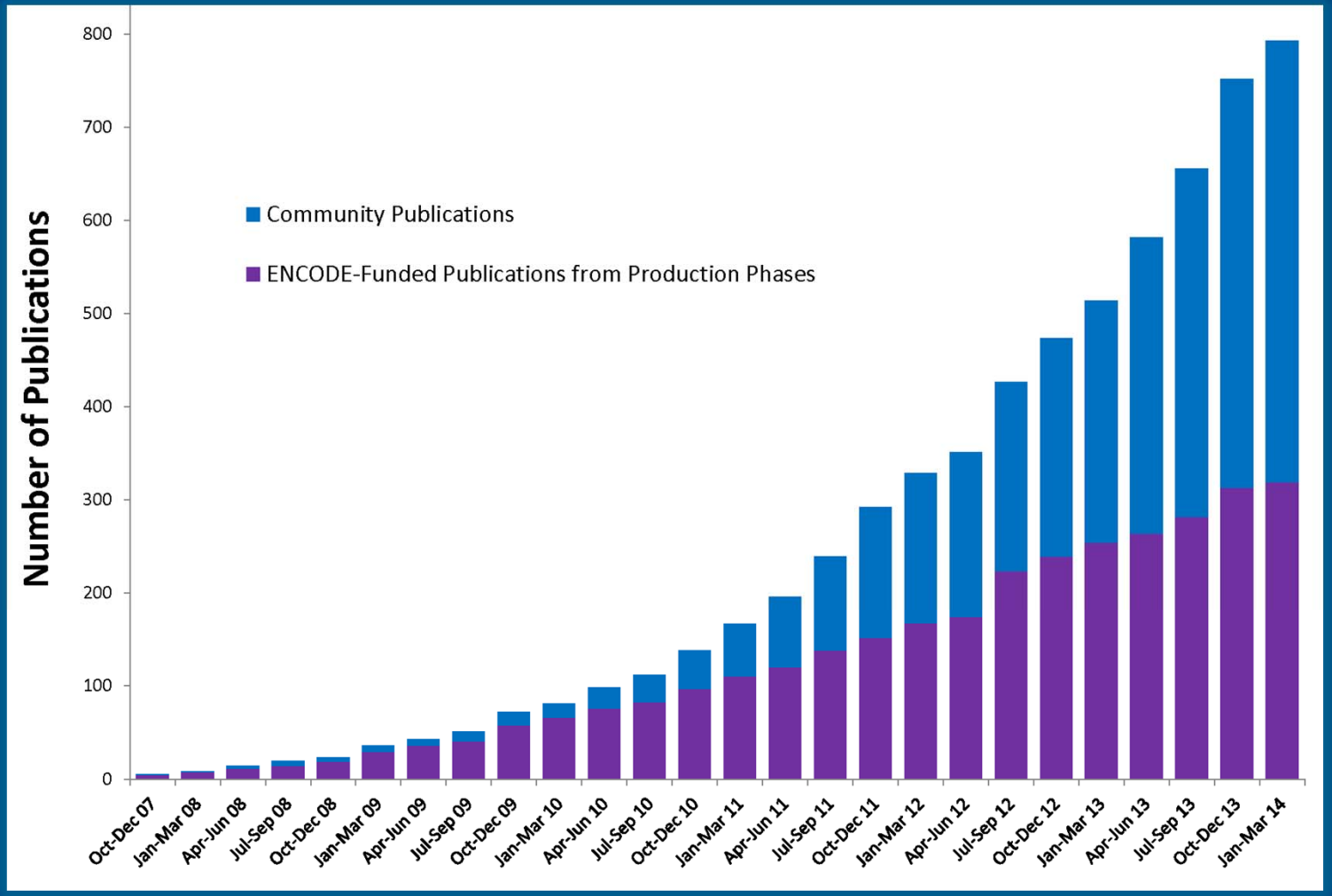


- **ENCODE Outreach Activities:**
  - **ENCODE Workshop at HUGO Meeting (April 2014)**
  - **ENCODE Workshop at ESHG Conference (June 2014)**
- **ENCODE Consortium Meeting (July 2014)**
- ***PNAS* Perspective:**

  “Defining functional DNA elements in the human genome”

Document 24

ENCODE Publications



Centers of Excellence in Genomic Science (CEGS) Program

- CEGS program announcement published in the NIH Guide: PAR-14-195
- Application receipt dates:
  July 2, 2014 | May 20, 2015 | May 20, 2016

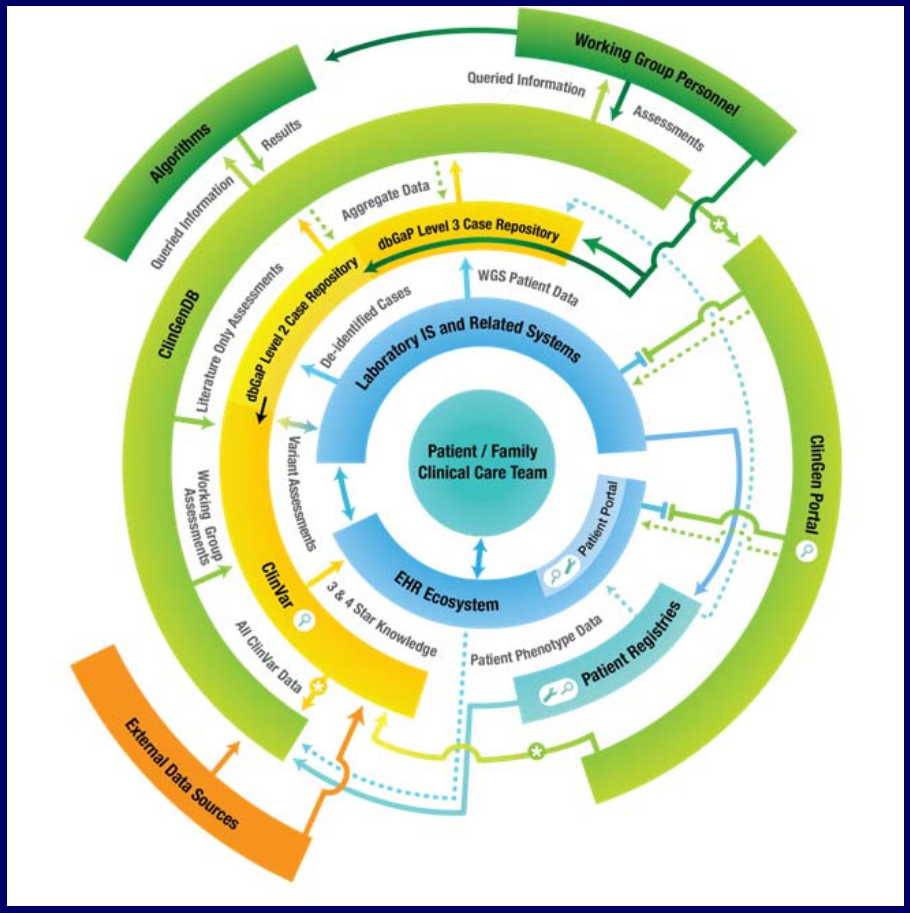
Document 25

ClinGen
Clinical Genome Resource

2014 | ACMG Annual Clinical Genetics Meeting
MARCH 25–29 | EXHIBIT DATES: MARCH 26–28
NASHVILLE, TENNESSEE

cser
Clinical Sequencing Exploratory Research

ClinGen



CSER

Expected rate of returnable mutations:

6503 Exome Variant Server (EVS) Results by Ancestry Group

Participants with classification	European ancestry* N=4300	African ancestry N=2203
Pathogenic variants from HGMD	37 (0.9%)	9 (0.4%)
Likely pathogenic variants from HGMD	55 (1.3%)	15 (0.7%)
Novel disruptive variants	6 (0.1%)	8 (0.4%)
Total	**98 (2.3%)**	**32 (1.5%)**

Courtesy of Gail Jarvik

cser
Clinical Sequencing Exploratory Research

Genomics and Society Working Group

- Third in-person meeting held April 2014
- Key topics discussed included:
  - Training
  - GSWG progress and future directions
- Annual report planned for September Council
- Council member Arti Rai joining the Working Group

Document 27

ELSI Research Program

- **CEER Annual Meeting (March 2014)**
  - Mock grant review for trainees
  - ELSI ‘horizon scanning’
- **Upcoming Re-Issuance of ELSI Program Announcements**
  - Shorter, more streamlined format
  - Input from Genomics and Society Working group and NIH partners
  - Scheduled release: August 2014

Document 28

Director's Report Outline

I. General NHGRI Updates

II. General NIH Updates

III. General Genomics Updates

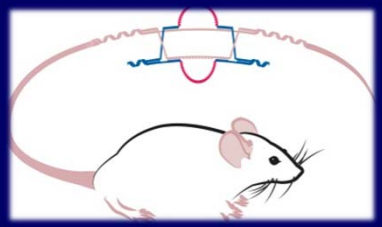
IV. NHGRI Extramural Research Program

V. NIH Common Fund/Trans-NIH

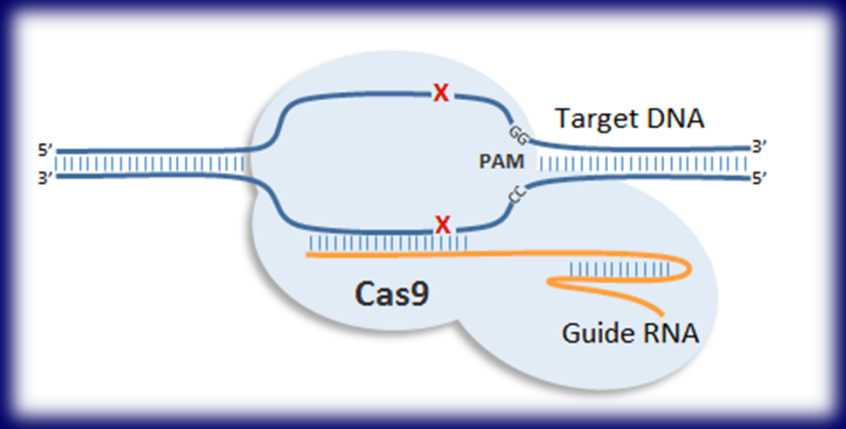
VI. NHGRI Division of Policy, Communications, and Education

VII. NHGRI Intramural Research Program

Knockout Mouse Phenotyping Project (KOMP2)



- IMPC evaluating CRISPR technology



- KOMP centers to make and phenotype ~100 knockout strains testing the CRISPR method
- Plan to award $3M in supplemental funds provided by Common Fund

GTEx
Genotype-Tissue Expression Project

- **Scale-up phase underway**
  - **>650 donors enrolled**
  - **~11,500 RNA-Seq studies**
- **Biospecimen Access Policy implemented**
- **2nd GTEx Community Scientific Meeting in June**

- **LINCS Pilot Phase wrapping up**
- **LINCS Phase 2 begins this summer**

  Phase 2 Data and Signature Generation Centers will be discussed in Closed Session

  BD2K-LINCS Data Integration and Coordination Center (RFA HG-14-001) applications will be reviewed in July and go to NHLBI Council

H3Africa

- **Biorepositories scale-up: Administrative review to be discussed in Closed Session**
- **Marker paper ("*Enabling African Scientists for the Genomic Revolution*") in press at *Science***
- **>5,000 samples accrued as of March 31**
- **H3ABioNet accrediting nodes**
- **4th Consortium Meeting moved from Uganda to Cape Town (to be held in late May)**

Companion Workshops: Cardiovascular Diseases, Ethics, and Genome Analysis and Data Management

Document 32

Big Data to Knowledge (BD2K)

- **Phil Bourne started as NIH Associate Director for Data Science in March**
- **Status of BD2K Components:**

  Centers of Excellence (Closed Session)

  LINCS-BD2K Perturbation Data Coordination and Integration Center (NHLBI Council in September)

Big Data to Knowledge (BD2K)

- **Status of BD2K Components (con't):**

  Training:

  K01s & R25s (NHGRI Council in September)

  T32s: new and supplements (FOAs issued)

  Data Discovery Index (NHLBI Council in September)

  Targeted Software Development (June receipt date)

BD2K Multi-Council Working Group

- BD2K and the envisioned NIH Office of Data Science cannot issue FOAs
- Because BD2K is a trans-NIH initiative, a trans-NIH approach to obtaining input has been devised
- Multi-Council Working Group: representative from each council that wishes to participate and has relevant expertise
- First meeting in July

Document 33

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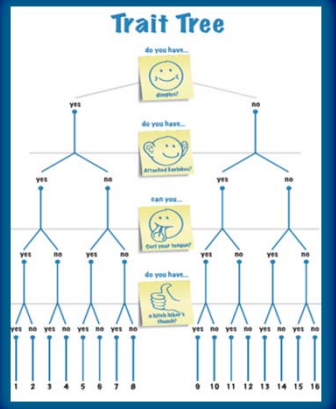
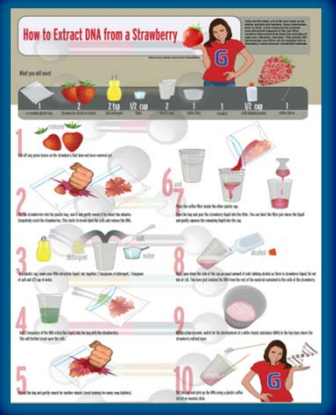
Effective Strategies for Engaging Communities Around Genomic Medicine

2014 USA Science and Engineering Festival (USASEF) and DNA Day 2014





Document 34

Communications Staff Departure

Larry Thompson

Jeannine Mjoseth

Director's Report Outline

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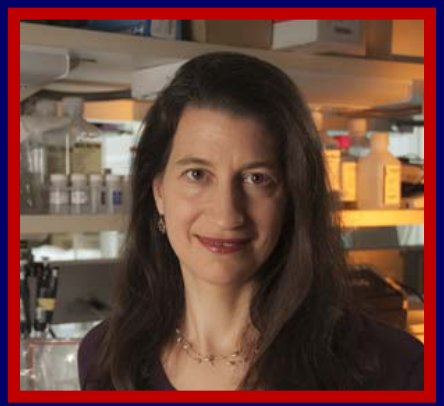
NHGRI Intramural Research Program: Reorganization Update

- **Appointment of New Branch Chiefs:**

  Charles Rotimi: Metabolic, Cardiovascular, and Inflammatory Diseases Branch

  Pam Schwartzberg: Genetic Disease Research Branch

  Julie Segre: Translational and Functional Genomics Branch



National Human Genome Research Institute

Office of the Director

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

Division of Intramural Research

Office of the Scientific Director

Board of Scientific Counselors

Daniel Kastner, M.D., Ph.D.
Scientific Director

Paul Liu, M.D., Ph.D.
Deputy Scientific Director

Cancer Genetics and Comparative Genomics Branch

Elaine Ostrander, Ph.D.
Chief

Computational and Statistical Genomics Branch

Joan Bailey-Wilson, Ph.D.
Alexander Wilson, Ph.D.
Co-Chiefs

Genetic Disease Research Branch

Pamela Schwartzberg, M.D., Ph.D.
Chief

Genetics and Molecular Biology Branch

David Bodine, Ph.D.
Chief

Medical Genetics Branch

Maximilian Muenke, M.D.
Chief

Medical Genomics and Metabolic Genetics Branch

Leslie Biesecker, M.D.
Chief

Metabolic, Cardiovascular, and Inflammatory Disease Genomics Branch

Charles Rotimi, Ph.D.
Chief

Translational and Functional Genomics Branch

Julie Segre, Ph.D.
Chief

Social and Behavioral Research Branch

Laura Koehly, Ph.D.
Chief (Acting)

Office of the Clinical Director

William Gahl, M.D., Ph.D.
Clinical Director

Office of Laboratory Animal Medicine

Intramural Training Office

Intramural Publication Support Office

Technology Transfer Office

Center for Inherited Disease Research

Center for Research on Genomics and Global Health

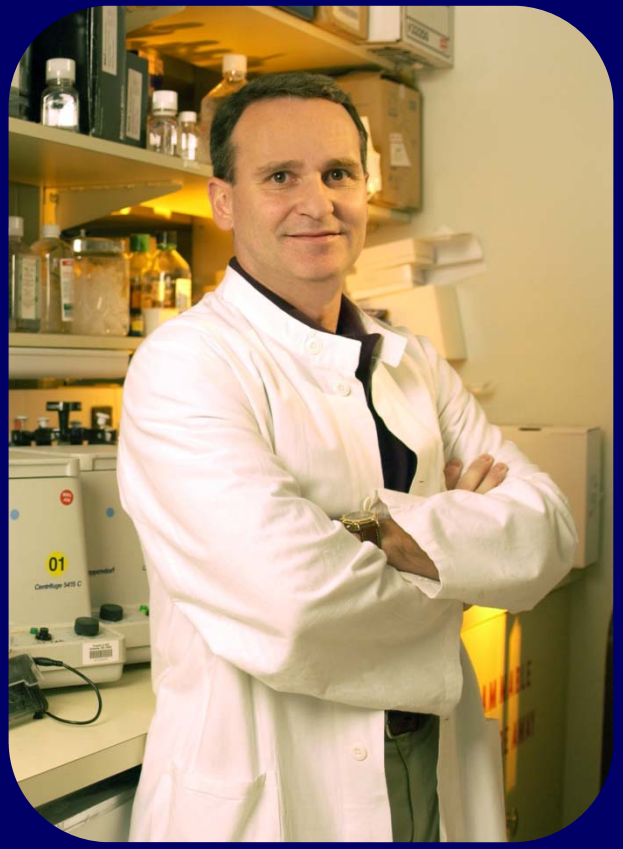
NIH Intramural Sequencing Center

Undiagnosed Diseases Program

Document 35

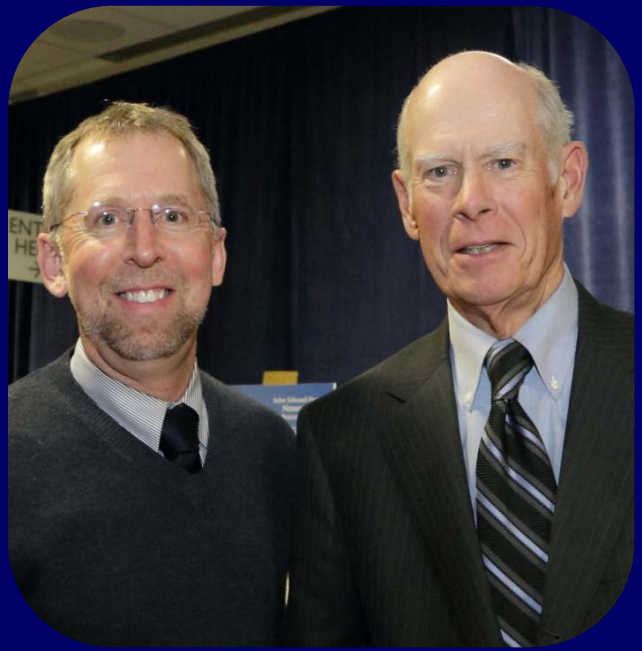
Intramural Investigator Departures

Colleen McBride, Ph.D.



Fabio Candotti, M.D.

Dedication of John Edward Porter Neuroscience Research Center



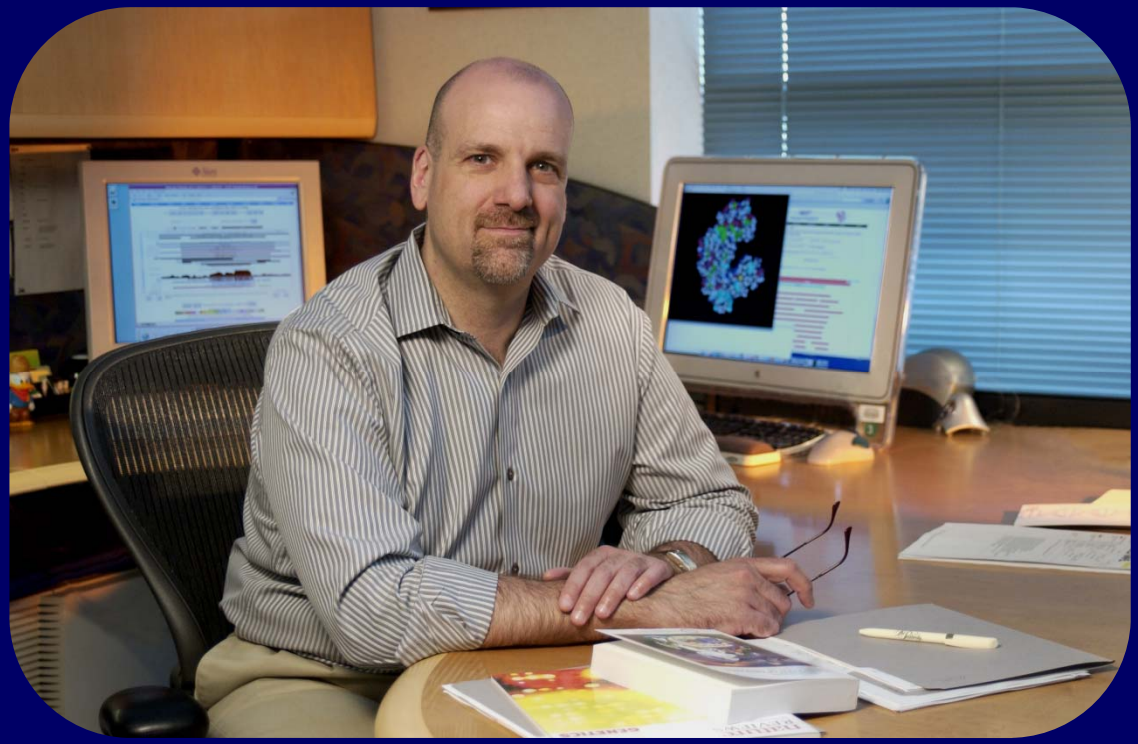
Document 36

NIH Clinical Center Genomics Opportunity

- **Sponsors: NIH Office of Intramural Research, NHGRI, and NIH Clinical Center**
- **Goals:**
  - **Infrastructure for clinical genomics at the NIH Clinical Center**
  - **Develop capabilities within institutes for using genomic data in clinical research and care**
- **1,000 whole-exome sequences**

Document 37

Johns Hopkins Society of Scholars



JOHNS HOPKINS
UNIVERSITY

Andy Baxevanis, Ph.D.

NHGRI Intramural Research Highlights

The NEW ENGLAND JOURNAL of MEDICINE

Early-Onset Stroke and Vasculopathy Associated with Mutations in ADA2

Cell

Cell PRESS

Global Analyses of Human Immune Variation Reveal Baseline Predictors of Postvaccination Responses

The NEW ENGLAND JOURNAL of MEDICINE

Glycosylation, Hypogammaglobulinemia, and Resistance to Viral Infections

NIH Undiagnosed Diseases Program

The Genomics Landscape

A monthly update from the NHGRI Director

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

Search for NHGRILANDSCAPE

Past issues can be accessed at: genome.gov/27527308

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Thanks!

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Advancing human health
through genomics research