National Human Genome Research Institute

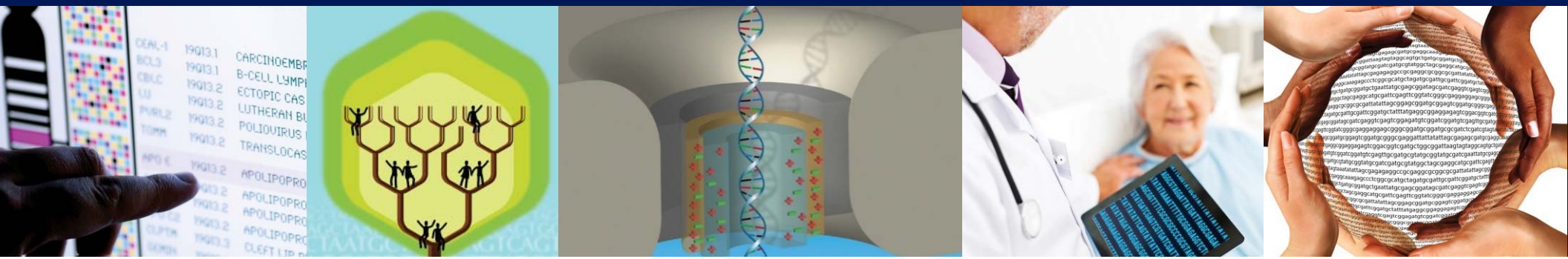
The Forefront of Genomics®

DIRECTOR'S REPORT

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

Director, NHGRI

September 2018



Director's Report-Related Documents: September 2018

Director's Report (MB)

Director's Report (MB)

No.	Relevant Documents
1	**New ASHG-NHGRI Fellows** Genetics and Public Policy Fellowship Genetics and Education Fellowship
2	NIH-ACMG Fellowship in Genomic Medicine Program Management
3	**'Genomics2020' Strategic Planning Process** 'Genomics2020' Website 'Genomics2020' News and Events Calendar
4	Genomics and Health Disparities Lecture Series

genome.gov/DirectorsReport

Document #

Open Session Presentations

- **Report: Genomics and Society Working Group Annual Report**

  Jeff Botkin

- **Report: National Academy of Science, Engineering, and Medicine**

  "Returning Individual Research Results to Participants: Guidance for a New Research Paradigm"

  Jeff Botkin

- **Concept Clearance: Human Genome Reference Program**

  Adam Felsenfeld

- **Report: Genomic Medicine Working Group Activities in 2018**

  Teri Manolio

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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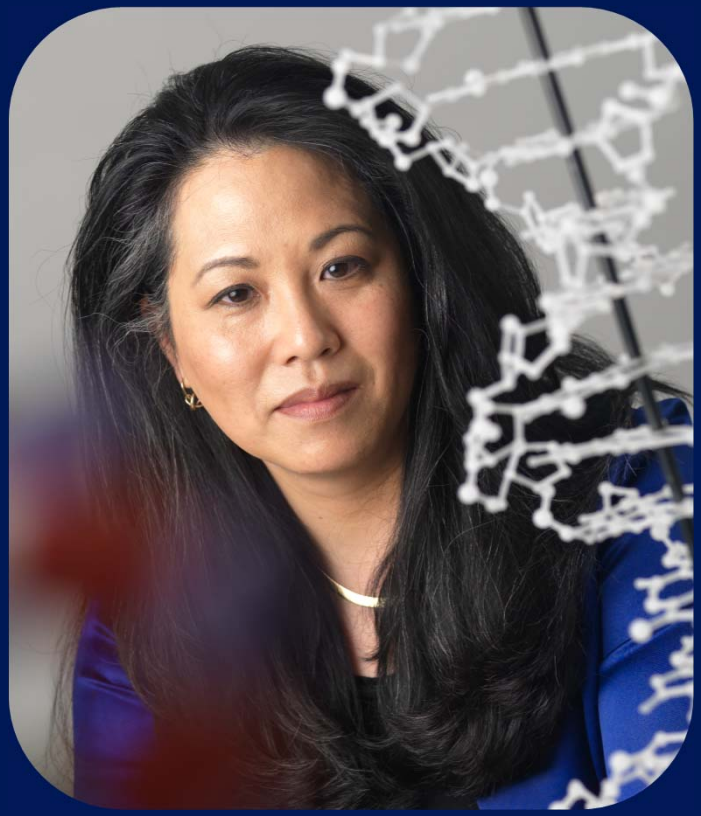
Retirement of NHGRI Program Director

Lita Proctor, Ph.D.

Departure of NHGRI Program Director

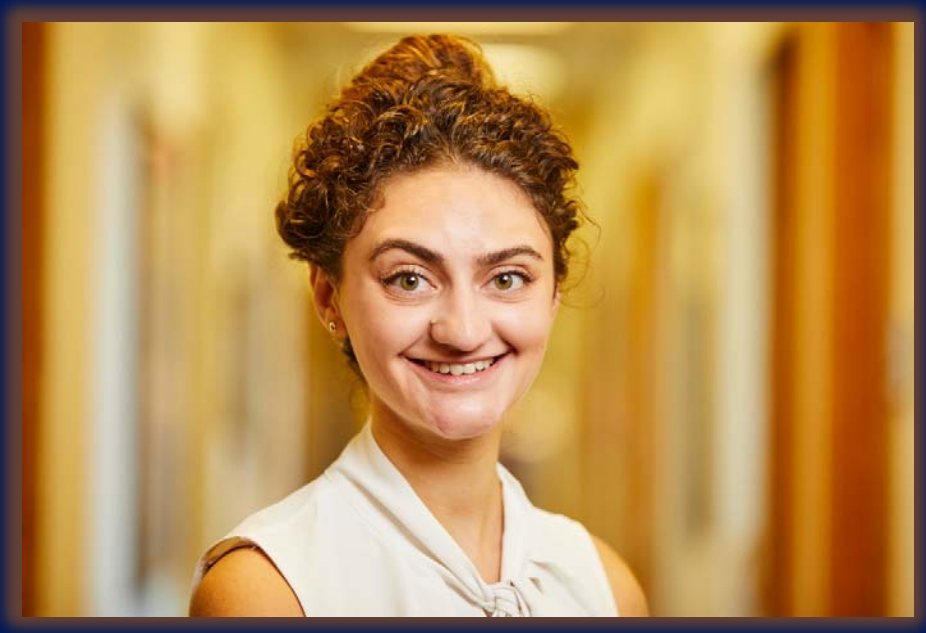


Vivian Ota Wang, Ph.D.

New Extramural Program Director

Lisa Chadwick, Ph.D.

New ASHG-NHGRI Fellows



Eve Granatosky, Ph.D.
Genetics and Public Policy Fellow

Dyanna Christopher, M.P.H.
Genetics and Education Fellow

NIH-ACMG Fellowship in Genomic Medicine Program Management

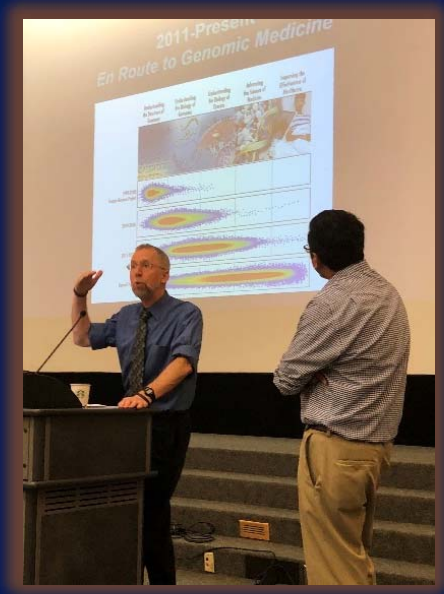
National Institutes of Health

ACMG
American College of Medical Genetics and Genomics

- Increase the pool of physicians trained in managing research and implementation programs in genomic medicine
- Up to two qualified physicians selected annually to acquire credentials and experience at NIH and other organizations
- Applications for two-year fellowship due annually on December 1

Document 2

‘Genomics2020’ Strategic Planning Process



- **Traveling Town Halls:**
  - Seattle, WA
  - Bay Area, CA
- **Upcoming Events:**
  - Town Hall in Atlanta, GA
  - Ancillary Session at ASHG Meeting

Document 3

Genomics and Health Disparities Lecture Series

John Carpten, Ph.D.

University of Southern California

"Towards Understanding the Role of Population Diversity in Cancer Genome Science"

Esteban Burchard, M.D., M.P.H.

University of California, San Francisco

"Making Precision Medicine Socially Precise"

Document 4

Alaska Native Genomics Research Workshop

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Patricia Grady Departs as Director, National Institute of Nursing Research

Patricia Grady, Ph.D., R.N., FAAN

Ann Cashion, Ph.D., R.N., FAAN

Document 5

New Director, National Center for Complementary and Integrative Health

Helene Langevin, M.D., Ph.D.

NIH
NCCIH

Document 6

NIH Strategic Plan for Data Science

- A roadmap for modernizing the NIH-funded biomedical data science ecosystem
- Five overarching goals focus on:
  1. Research data infrastructure
  2. Data resources ecosystem
  3. Data management, analytics, and visualization tools
  4. Data science workforce development
  5. Stewardship and sustainability of data resources

Science and Technology Research Infrastructure for Discovery, Experimentation, and Sustainability (STRIDES)

Budget Update

Document 9

Fiscal Year 2019 Appropriations

	Actual Fiscal Year 2018 Labor-HHS Appropriations	Proposed Fiscal Year 2019 Labor-HHS Appropriations	$ Increase	% Increase
NIH	$37.1B	$39.1B	~$2.0B	~5.1%
NHGRI	$556M	$575M	~$19M	~3.3%

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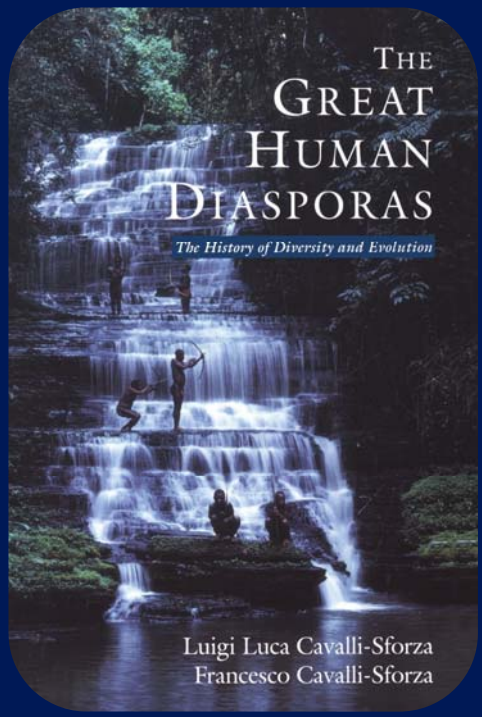
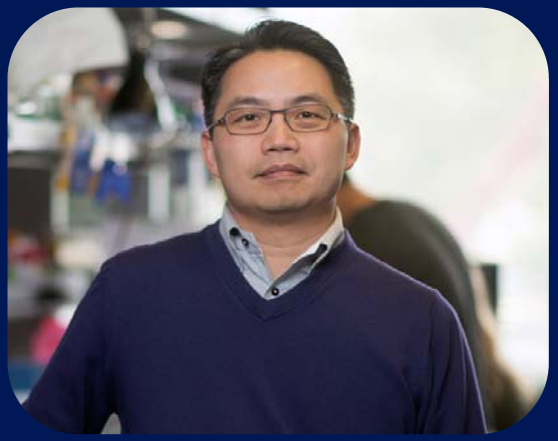
Mourning the Loss of Luca Cavalli-Sforza



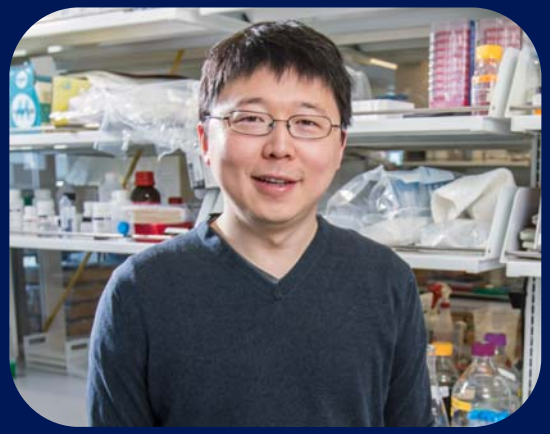
Document 10

New Investigators, Howard Hughes Medical Institute



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

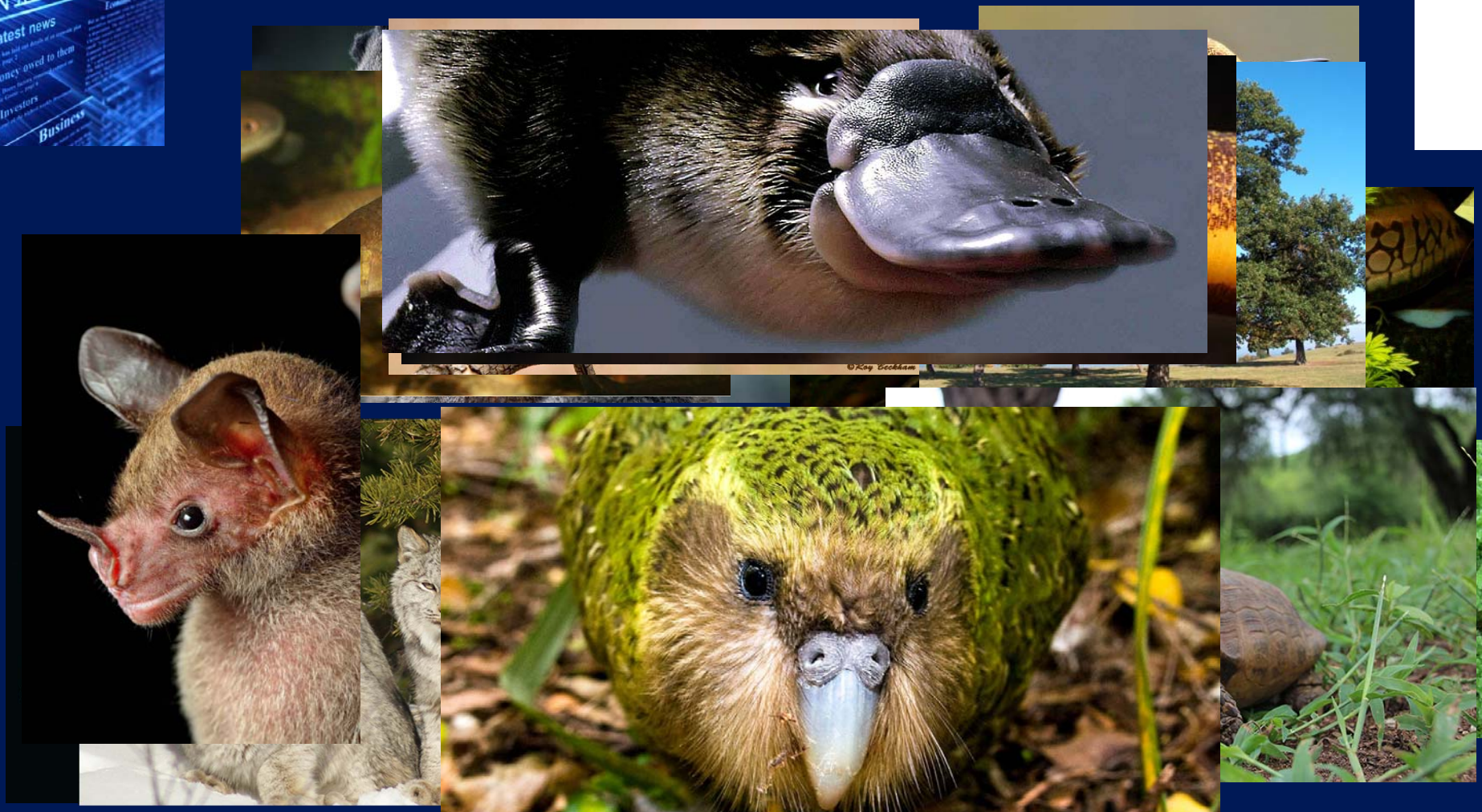
Beth Shapiro,
D.Phil.



Feng Zhang,
Ph.D.

hhmi | Howard Hughes Medical Institute

Genomes In The News…



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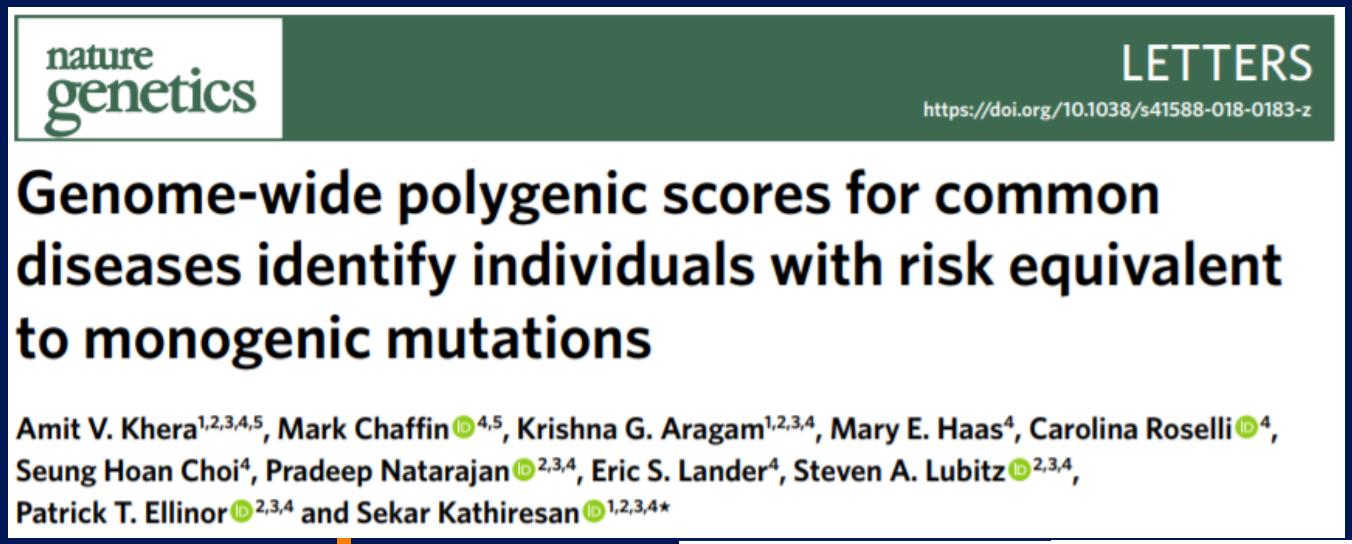
Genome Sequencing Program



nature genetics

LETTERS

https://doi.org/10.1038/s41588-018-0183-z

Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations

Amit V. Khera[1,2,3,4,5], Mark Chaffin[4,5], Krishna G. Aragam[1,2,3,4], Mary E. Haas[4], Carolina Roselli[4], Seung Hoan Choi[4], Pradeep Natarajan[2,3,4], Eric S. Lander[4], Steven A. Lubitz[2,3,4], Patrick T. Ellinor[2,3,4] and Sekar Kathiresan[1,2,3,4*]

Centers for Common Disease Genomics

Centers for Mendelian Genomics

CSH PRESS

GENOME RESEARCH

Predicting human genes susceptible to genomic instability associated with *Alu*/*Alu*-mediated rearrangements

Xiaofei Song, Christine R. Beck, Renqian Du, et al.

Genome Res. published online June 15, 2018
Access the most recent version at doi:10.1101/gr.229401.117

Document 13

Genome Sequencing Program

Science

Phenotype risk scores identify patients with unrecognized Mendelian disease patterns

Lisa Bastarache,[1] Jacob J. Hughey,[1] Scott Hebbring,[2] Joy Marlo,[1] Wanke Zhao,[3] Wanting T. Ho,[3] Sara L. Van Driest,[4,5] Tracy L. McGregor,[5] Jonathan D. Mosley,[4] Quinn S. Wells,[4,6] Michael Temple,[1] Andrea H. Ramirez,[4] Robert Carroll,[1] Travis Osterman,[1,4] Todd Edwards,[4] Douglas Ruderfer,[4] Digna R. Velez Edwards,[7] Rizwan Hamid,[5] Joy Cogan,[5] Andrew Glazer,[4] Wei-Qi Wei,[1] QiPing Feng,[6] Murray Brilliant,[2] Zhizhuang J. Zhao,[3] Nancy J. Cox,[4] Dan M. Roden,[1,4,6] Joshua C. Denny[1,4]*

Genome Sequencing Program Analysis Centers

High-Quality Reference Genome Sequences

Science

gh-resolution comparative analysis of great ape genomes

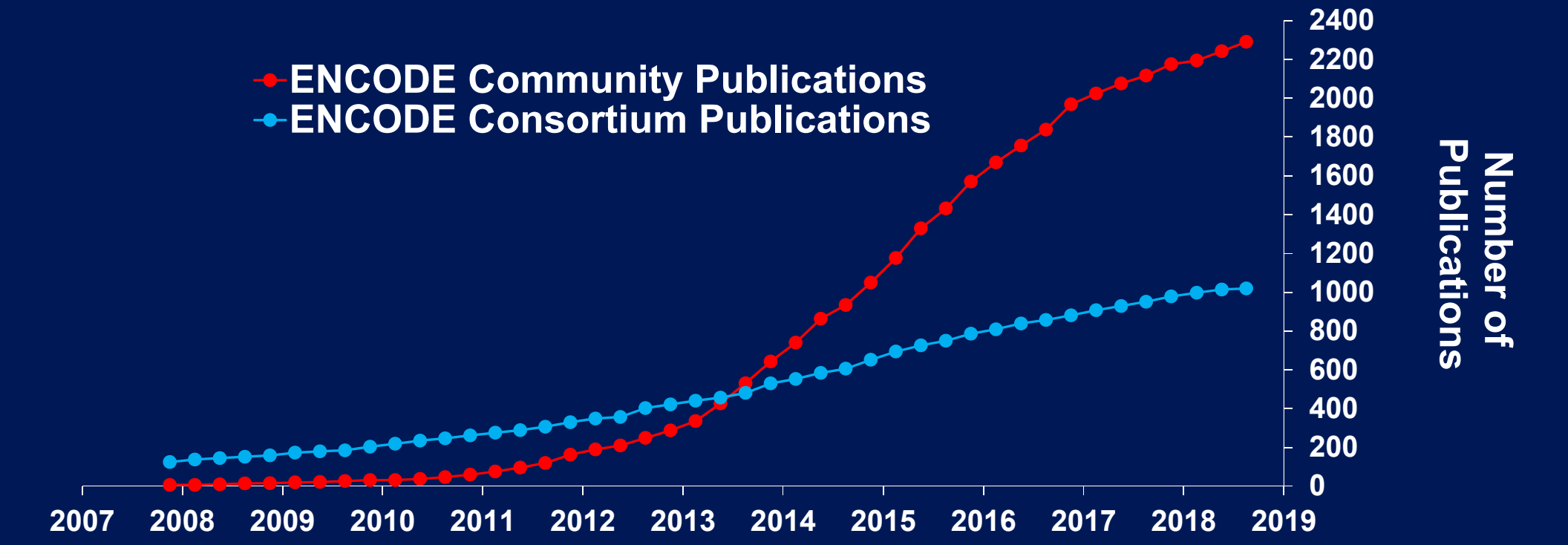
Zev N. Kronenberg, Ian T. Fiddes*, David Gordon*, Shwetha Murali*, Stuart Cantsilieris*, Olivia S. Meyerson*, Jason G. Underwood*, Bradley J. Nelson*, Mark J. P. Chaisson, Max L. Dougherty, Katherine M. Munson, Alex R. Hastie, Mark Diekhans, Fereydoun Hormozdiari, Nicola Lorusso, Kendra Hoekzema, Ruolan Qiu, Karen Clark, Archana Raja, AnneMarie E. Welch, Melanie Sorensen, Carl Baker, Robert S. Fulton, Joel Armstrong, Tina A. Graves-Lindsay, Ahmet M. Denli, Emma R. Hoppe, PingHsun Hsieh, Christopher M. Hill, Andy Wing Chun Pang, Joyce Lee, Ernest T. Lam, Susan K. Dutcher, Fred H. Gage, Wesley C. Warren, Jay Shendure, David Haussler, Valerie A. Schneider, Han Cao, Mario Ventura, Richard K. Wilson, Benedict Paten, Alex Pollen, Evan E. Eichler†

Document 13

Technology Development Program

- **Advanced Genomic Technology Development Meetings**
  May 2018 at Northeastern University Next: May 29-31, 2019
- **Novel Genomic Technology Development Program Announcements** – Next due date: October 2, 2018
- **Novel Nucleic Acid Sequencing Technology Development Program Announcements** – Next due date: June 27, 2019

ENCyclopedia Of DNA Elements (ENCODE)



Document 15

ENCyclopedia Of DNA Elements (ENCODE)

nature neuroscience

A common haplotype lowers PU.1 expression in myeloid cells and delays onset of Alzheimer's disease

Kuan-lin Huang[1,30], Edoardo Marcora[2,3,30], Anna A Pimenova[3], Antonio F Di Narzo[2], Manav Kapoor[2,3], Sheng Chih Jin[4], Oscar Harari[5], Sarah Bertelsen[3], Benjamin P Fairfax[6], Jake Czajkowski[7], Vincent Chouraki[8], Benjamin Grenier-Boley[9–11], Céline Bellenguez[9–11], Yuetiva Deming[5], Andrew McKenzie[2], Towfique Raj[2,3], Alan E Renton[3], John Budde[5], Albert Smith[12], Annette Fitzpatrick[13], Joshua C Bis[14], Anita DeStefano[15], Hieab H H Adams[16], M Arfan Ikram[16], Sven van der Lee[16], Jorge L Del-Aguila[5], Maria Victoria Fernandez[5], Laura Ibañez[5], The International Genomics of Alzheimer's Project[17], The Alzheimer's Disease Neuroimaging Initiative[18], Rebecca Sims[19], Valentina Escott-Price[19], Richard Mayeux[20], Jonathan L Haines[21], Lindsay A Farrer[15,22–24], Margaret A Pericak-Vance[24,25], Jean Charles Lambert[9–11], Cornelia van Duijn[16], Lenore Launer[26], Sudha Seshadri[8], Julie Williams[19], Philippe Amouyel[9–11,27], Gerard D Schellenberg[28], Bin Zhang[2], Ingrid Borecki[7], John S K Kauwe[29], Carlos Cruchaga[5], Ke Hao[2] & Alison M Goate[2,3]

Variation, Function, and Disease Program

Novel approaches for relating genomic variation to function and disease

R01s – first receipt date is October 5
R21s – first receipt date is October 16

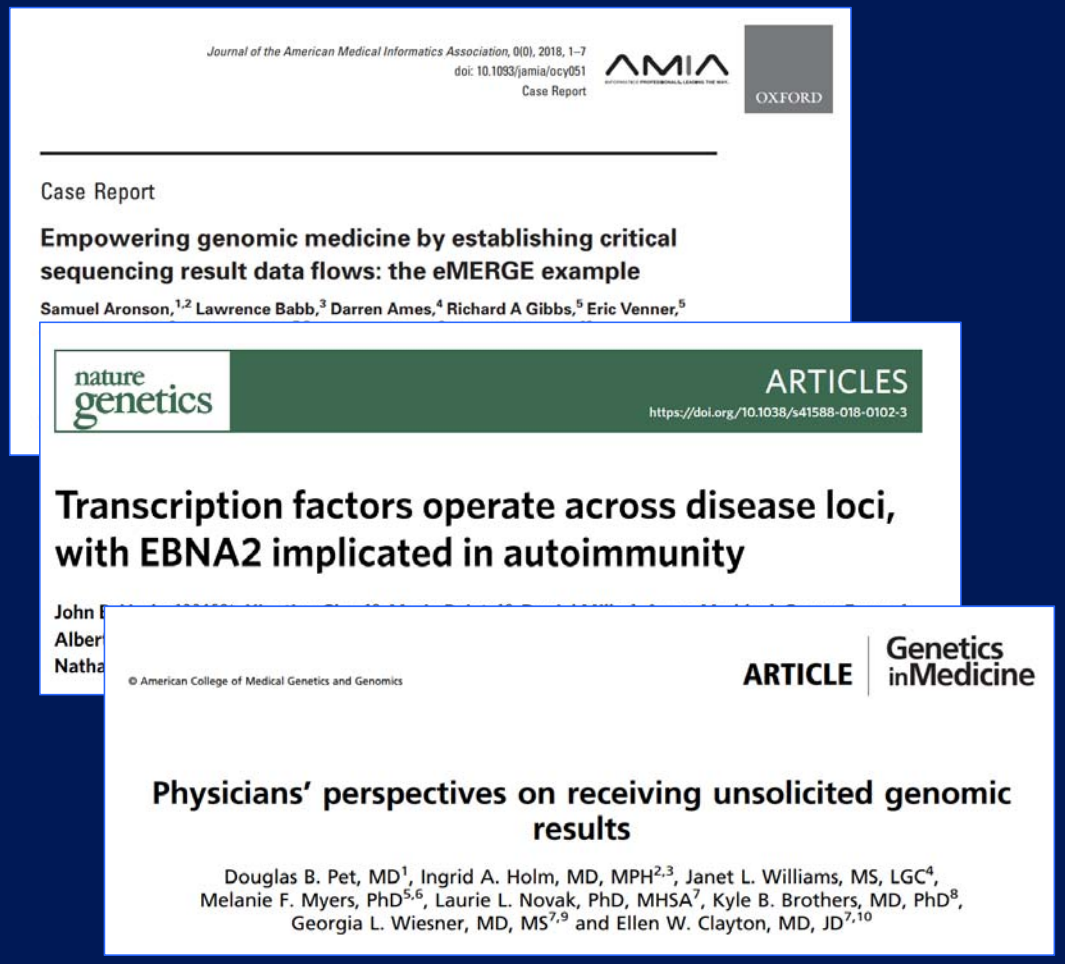
Centers of Excellence in Genomic Science (CEGS)

Center for Sub-Cellular Genomics
Junhyong Kim
University of Pennsylvania

Center for Synthetic Regulatory Genomics
Jef Boeke
New York University

eMERGE network

ELECTRONIC MEDICAL RECORDS AND GENOMICS



Journal of the American Medical Informatics Association, 0(0), 2018, 1–7
doi: 10.1093/jamia/ocy051
Case Report

Case Report

Empowering genomic medicine by establishing critical sequencing result data flows: the eMERGE example

Samuel Aronson,[1,2] Lawrence Babb,[3] Darren Ames,[4] Richard A Gibbs,[5] Eric Venner,[5]

nature genetics

ARTICLES

https://doi.org/10.1038/s41588-018-0102-3

Transcription factors operate across disease loci, with EBNA2 implicated in autoimmunity

© American College of Medical Genetics and Genomics

ARTICLE | Genetics inMedicine

Physicians' perspectives on receiving unsolicited genomic results

Douglas B. Pet, MD[1], Ingrid A. Holm, MD, MPH[2,3], Janet L. Williams, MS, LGC[4], Melanie F. Myers, PhD[5,6], Laurie L. Novak, PhD, MHSA[7], Kyle B. Brothers, MD, PhD[8], Georgia L. Wiesner, MD, MS[7,9] and Ellen W. Clayton, MD, JD[7,10]

Domains	Physicians' Main Concerns
Actionability	• Genomic results must be actionable
Impact on patients	• Patient anxiety/regret • Unnecessary interventions and costs
Health care workflow	• Time burden on physicians • Enhanced clinical decision support
Responsibility of returning results	• Whoever orders the test, or • Genetic specialist/counselor

Clinical Genome Resource (ClinGen)

ClinGen
Clinical Genome Resource

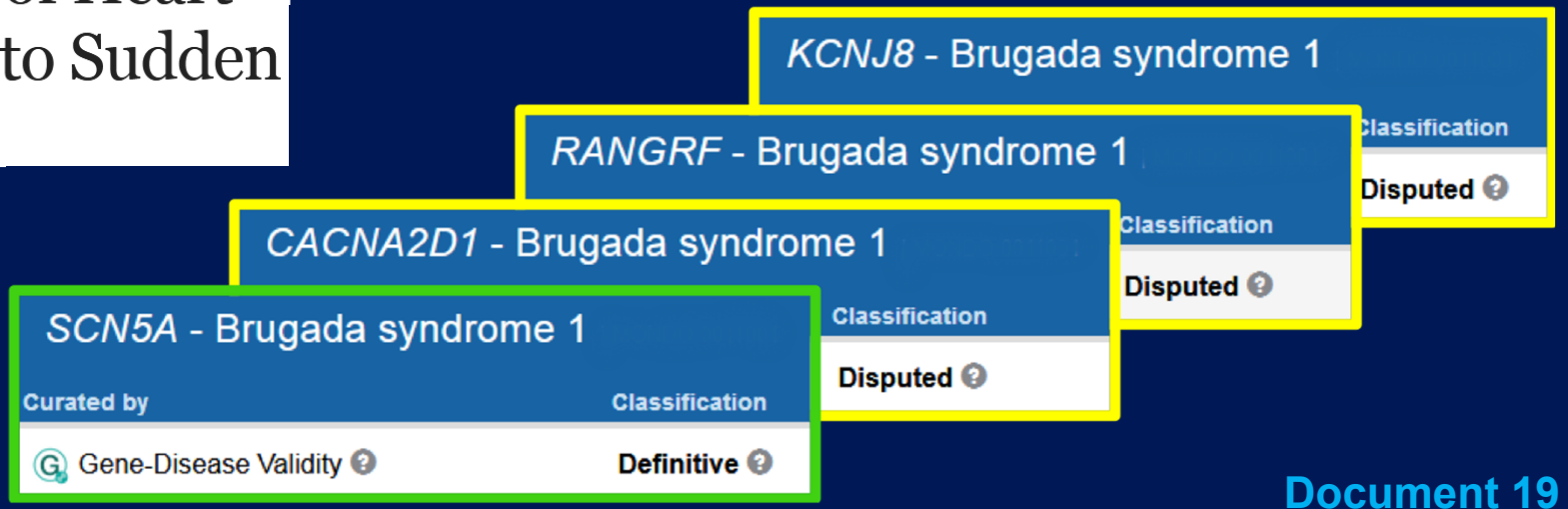
Sudden Cardiac Arrest Foundation

Key Discovery Made in Genetic Make-Up of Heart Condition Linked to Sudden Cardiac Death

Circulation

Reappraisal of Reported Genes for Sudden Arrhythmic Death: An Evidence-Based Evaluation of Gene Validity for Brugada Syndrome

S. Mohsen Hosseini, Raymond Kim, Sharmila Udupa, Gregory Costain, Rebekah Jobling, Eriskay Liston, Seema M. Jamal, Marta Szybowska, Chantal F. Morel, Sarah Bowdin, John Garcia, Melanie Care, Amy C. Sturm, Valeria Novelli, Michael J. Ackerman, James S. Ware, Ray E. Hershberger, Arthur A. M. Wilde, Michael H. Gollob
and on behalf of the NIH-Clinical Genome Resource Consortium



Document 19

Clinical Sequencing Evidence-Generating Research Program

Institution	Project	Study Population	% Racial and Ethnic Diversity	% Total Diversity
Baylor College of Medicine	KidsCanSeq	Children with cancer	75%	100%
ClinSeq*	ClinSeq A2	Adults, no specific phenotype	100%	100%
Kaiser Permanente	CHARM	Adults at risk for hereditary cancer	46%	64%
UNC	NCGENES 2	Children with unknown etiology for likely genetic conditions (developmental or neuromuscular disorders, dysmorphology)	70%	70%
Mount Sinai	NYCKidSeq	Children with suspected neurologic, immunologic, and cardiac genetic disorders	85%	85%
UCSF	P^3EGS	Children with severe developmental disorders, congenital anomalies; fetal structural anomalies	77%	77%
HudsonAlpha	South-Seq	Newborns with suspected genetic disorders	69%	69%

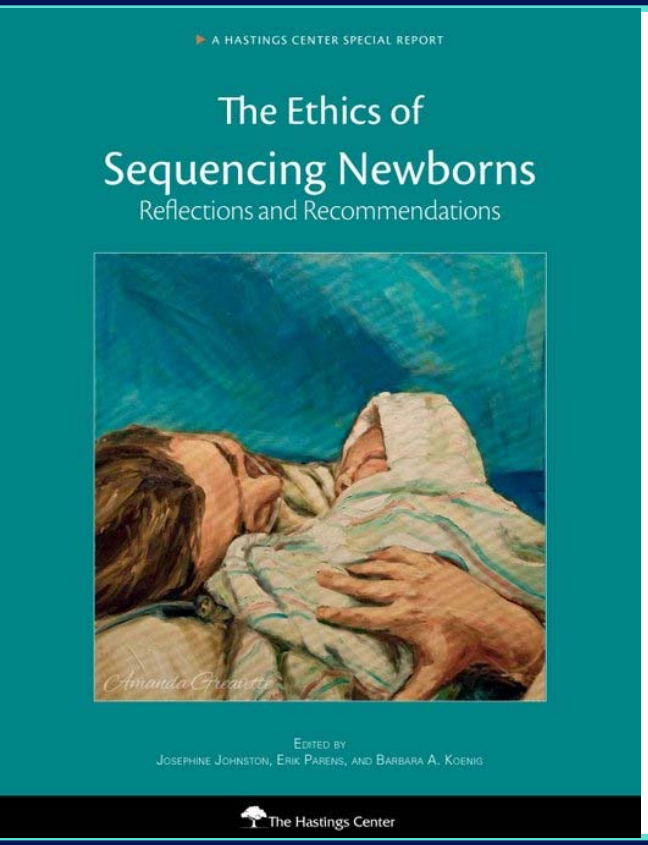
*** Additional African ancestry participants contributing to CSER**

Clinical Sequencing Evidence-Generating Research Program

Stakeholder Engagement Meeting

- Held with CSER in-person scientific meeting
- Convened investigator and stakeholder 'buddies'
- Explored participant and researcher perspectives on topics of interest (e.g., family communication, unmet needs from the healthcare system, and personal utility)
- Identified better ways to engage stakeholders across CSER

Newborn Sequencing In Genomic medicine and public HealTh (NSIGHT)



Sequencing Newborns: *A Call for Nuanced Use of Genomic Technologies*

- Lessons for Sequencing from the Addition of Severe Combined Immunodeficiency to Newborn Screening Panels
- Eugenics Redux: *"Reproductive Benefit" as a Rationale for Newborn Screening*
- Are Parents Really Obligated to Learn as Much as Possible about Their Children's Genomes?
- What Genomic Sequencing Can Offer Universal Newborn Screening Programs
- Whose Odyssey Is It? *Family-Centered Care in the Genomic Era*
- A New Era, New Strategies: *Education and Communication Strategies to Manage Greater Access to Genomic Information*
- Families' Experiences with Newborn Screening: *A Critical Source of Evidence*
- My Diagnostic Odyssey - A Call to Expand Access to Genomic Testing for the Next Generation
- Single-Gene Sequencing in Newborn Screening: *Success, Challenge, Hope*
- The Legal Dimensions of Genomic Sequencing in Newborn Screening
- Commercial Interests, the Technological Imperative, and Advocates: *Three Forces Driving Genomic Sequencing in Newborns*
- Using Newborn Sequencing to Advance Understanding of the Natural History of Disease

Genomic Medicine XI: Research Directions in Genomic Medicine Implementation

Workshop Recommendations:

- Establish "CPIC"-style guideline development process for non-PGx genomic-medicine relevant genes
- Create registry of patients with genomic data to follow for outcomes
- Develop limited training program for majority of common, complex disorders; certify as genomic consultants
- Engage employers as key stakeholders

Genomic Medicine for Reproductive, Prenatal, and Neonatal Health Workshop

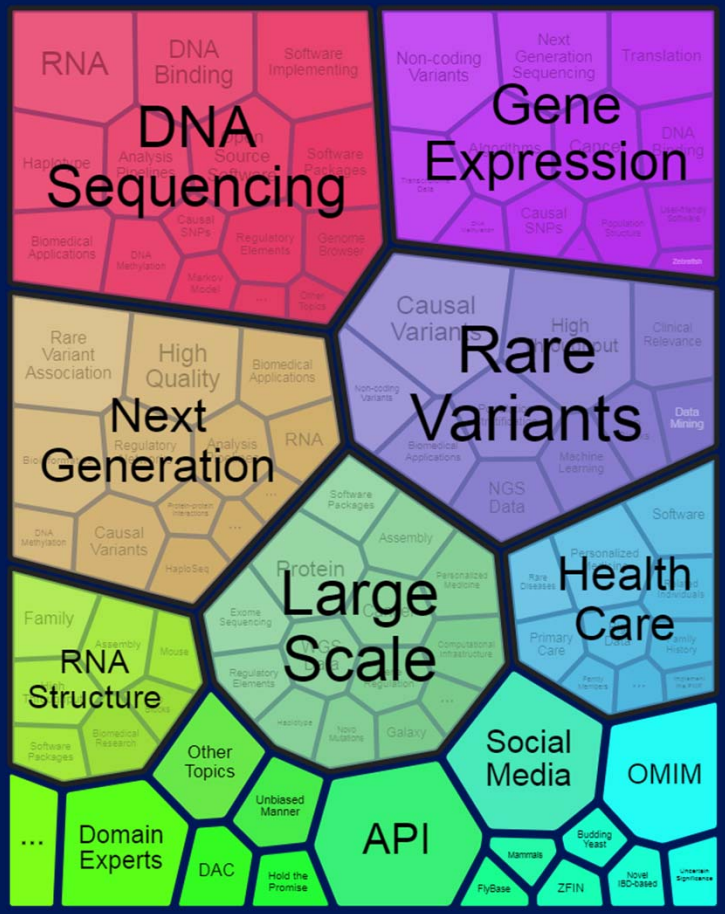
- What current technologies are ready for implementation in reproductive, prenatal, and neonatal health?
- What are the ethical, legal, and social implications of genomic medicine implementation?
- What are challenges to implementing genomic medicine in reproductive, prenatal, and neonatal health?

Genomic Medicine for Reproductive, Prenatal, and Neonatal Health Workshop

- Determine if reproductive, prenatal, and neonatal 'omics are good predictors of later health and disease
- Address barriers in linking medical records for reproductive, prenatal, and neonatal health
- Increase collaborations to improve implementation of new technologies in healthcare systems

Computational Genomics and Data Science Program

- Program Announcements released in July
- Support research interests of the informatics and data science community
- First due date: November 16, 2018
- Companion SBIR and STTR FOAs are in development



Computational Genomics and Data Science Program

Analysis, Visualization, and Informatics Lab-space (AnVIL)

- Cloud-based infrastructure and software platform
- Genomic datasets, phenotypes, and metadata
- Shared analysis and computing environment
- User training and outreach

BROAD INSTITUTE

JOHNS HOPKINS UNIVERSITY

11 Other Partner Institutions

Ethical, Legal, and Social Implications (ELSI) Research Program

ELSI Congress 2017

- Notice of Interest: Applications for Biennial ELSI Congress
- New RFA: Center for ELSI Resources and Analysis (CERA)

FAQs on the ELSI website

Application Deadline: November 8

Small Business Program Reauthorization

SBIR · STTR
America's Seed Fund™
POWERED BY SBA

- 'Direct to Phase II' reauthorized
- Technical assistance expanded
- Set-asides remain the same:

  SBIR – 3.2%

  STTR – 0.45%

Genomic Innovator Award

- Supports early-career researchers to do highly innovative work on important problems in genomics
- Part of the NIH set of R35 programs that focus on investigators
- NHGRI focusing on researchers involved in ‘team science’
- Annual receipt date October 30

NHGRI Extramural Research Highlights

nature genetics

ARTICLES

https://doi.org/10.1038/s41588-018-0102-3

Transcription factors operate across disease loci, with EBNA2 implicated in autoimmunity

John B. Harley[1,2,3,4,5,9*], Xiaoting Chen[1,9], Mario Pujato[1,9], Daniel Miller[1], Avery Maddox[1], Carmy Forney[1], Albert F. Magnusen[1], Arthur Lynch[1], Kashish Chetal[6], Masashi Yukawa[7], Artem Barski[4,7,8], Nathan Salomonis[4,6], Kenneth M. Kaufman[1,2,4,5], Leah C. Kottyan[1,4*] and Matthew T. Weirauch[1,3,4,6*]

NHGRI Extramural Research Highlights

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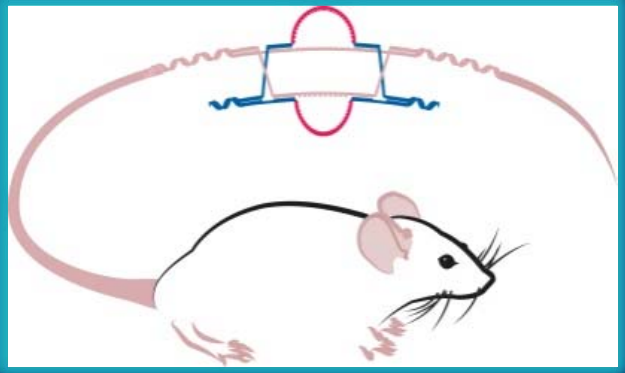
Knockout Mouse Phenotyping Project (KOMP2)



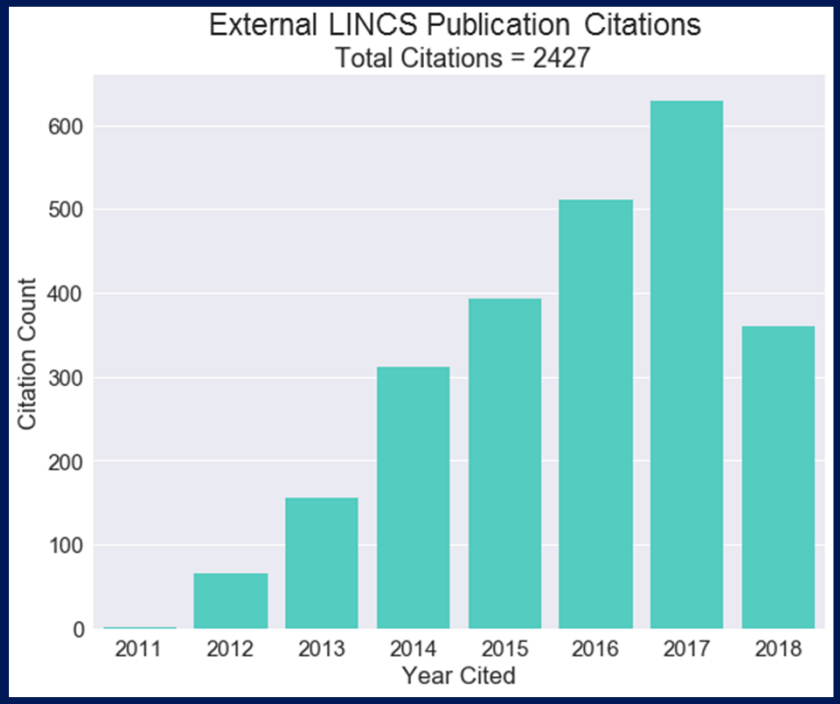
IMPC
International Mouse Phenotyping Consortium

- **KOMP2 Annual Meeting: Rockville, MD on Sept. 30 to Oct. 2, 2018**

  Last day will focus on collaborations with various human disease gene discovery programs

- **7 supplements awarded in Fiscal Year 2018**

Library of Integrated Network-based Cellular Signatures (LINCS) Program

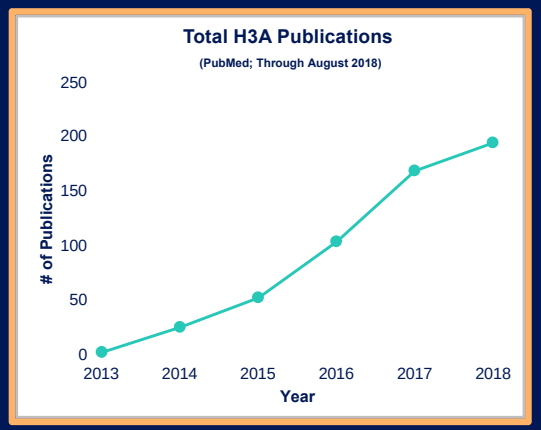


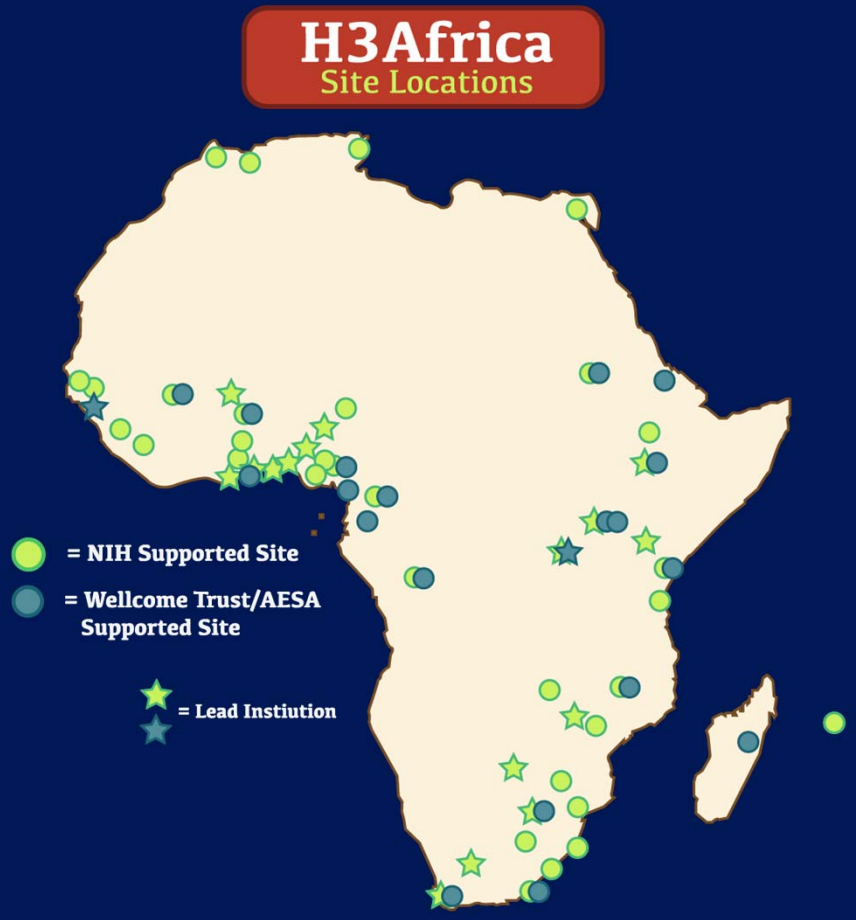
- **LINCS data usage continues to grow**
- **Outreach Activities:**

  Community challenge improved query speed December outreach event

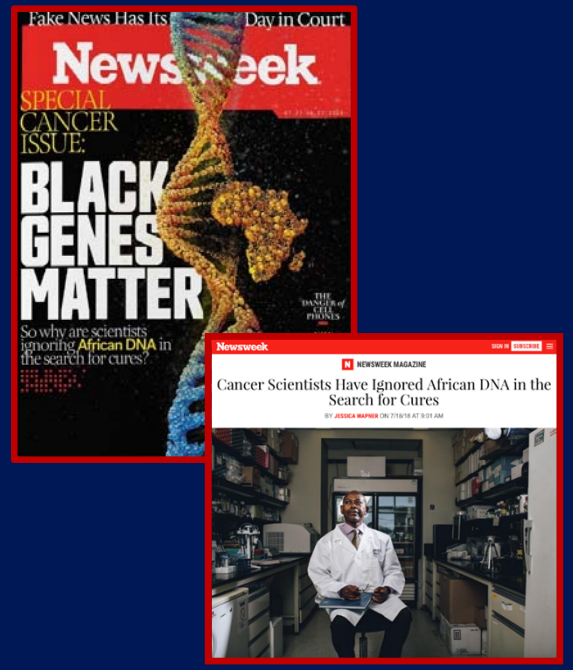
Human Heredity and Health in Africa (H3Africa)

H3Africa Biorepository Program





H3ABioNet
Pan African Bioinformatics Network for H3Africa



Document 31

Human Heredity and Health in Africa (H3Africa)

- 12th H3Africa Consortium Meeting & 11th Annual African Society of Human Genetics (AfSHG) Meeting - September 2018 (Kigali, Rwanda)
- New H3Africa ELSI awards (Uganda, Nigeria, & Ghana)

Undiagnosed Diseases Network (UDN)

Undiagnosed Diseases Network | New sites for Phase II of the UDN!

New Clinical Sites

- Children's Hospital of Philadelphia and the University of Pennsylvania
- University of Miami School of Medicine
- University of Utah
- University of Washington School of Medicine and Seattle Children's Hospital
- Washington University in St. Louis

Follow us on social media for real-time research updates.

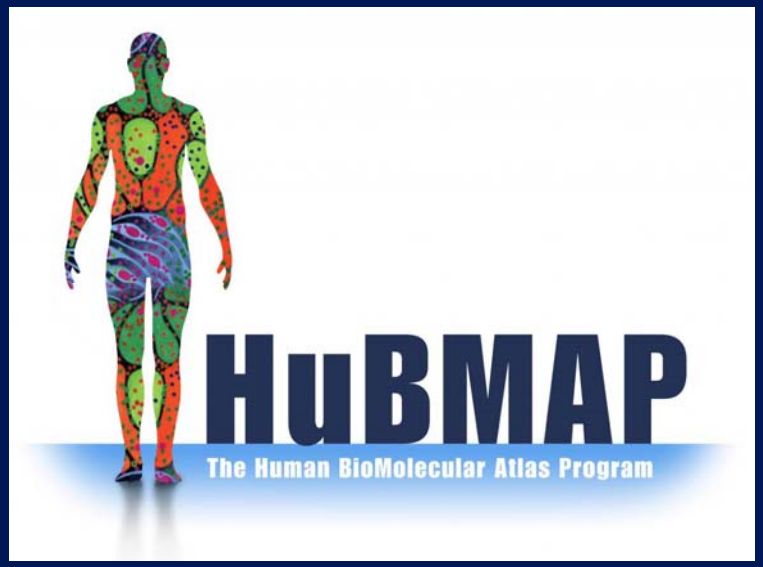
udnconnect and @UDNconnect

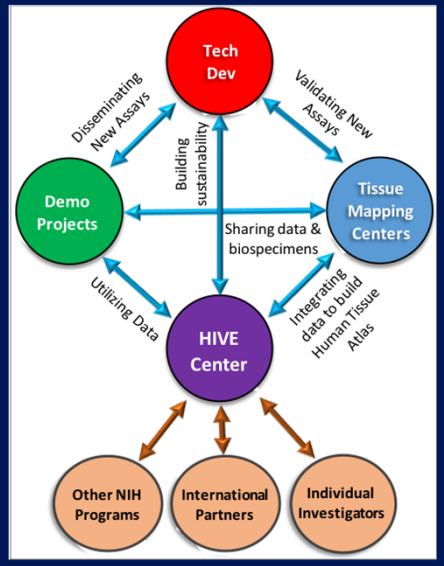
New Metabolomics Core - Mayo Clinic

New Model Organisms Screening Center - Washington University in St. Louis

APPLY

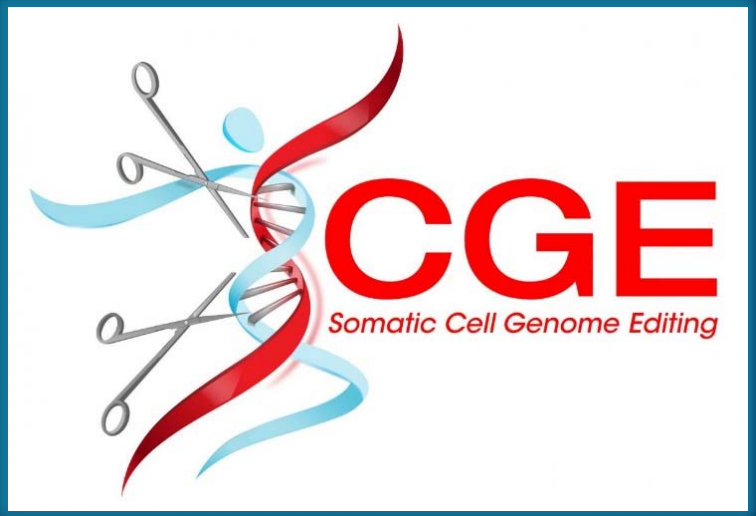
Human Biomolecular Atlas Program (HuBMAP)





- **Awards will soon be announced for Tissue Mapping Centers, Transformative Technology Development Groups, and HuBMAP Integration, Visualization, and Engagement (HIVE)**
- **HuBMAP Consortium kick-off meeting in November 2018**

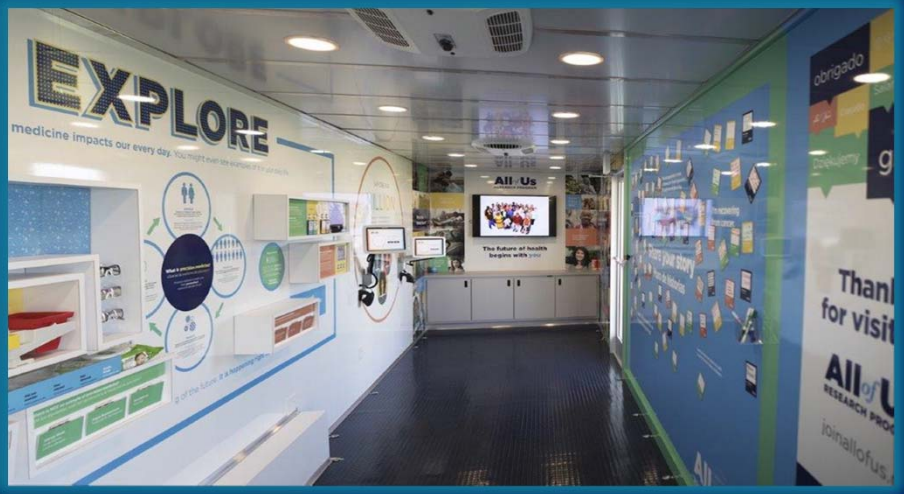
Somatic Cell Genome Editing (SCGE)



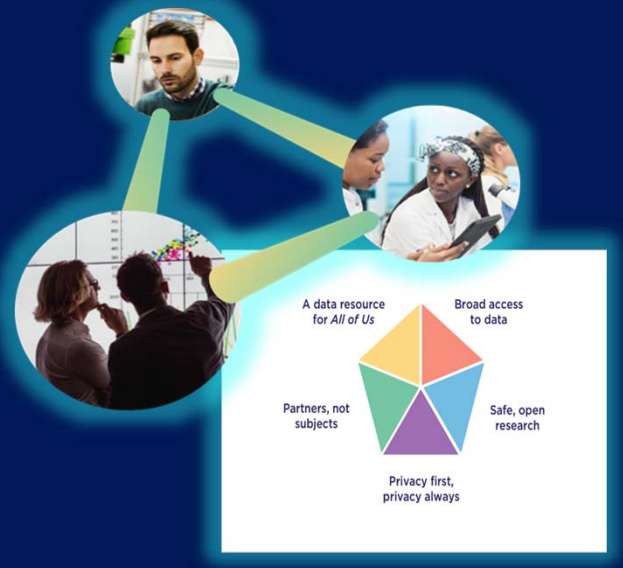
- Develop quality tools to perform effective and safe genome editing in human patients
- First round application reviews are complete and awards are being issued
- Kickoff meeting - December 10-11, 2018

All of Us RESEARCH PROGRAM

All of Us Journey



All of Us Research Hub



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All of Us
RESEARCH PROGRAM

Kelly Gebo, M.D., M.P.H.

Chief Medical and Scientific Officer

Director's Report Outline

I. General NHGRI Updates

II. General NIH Updates

III. General Genomics Updates

IV. NHGRI Extramural Research Program

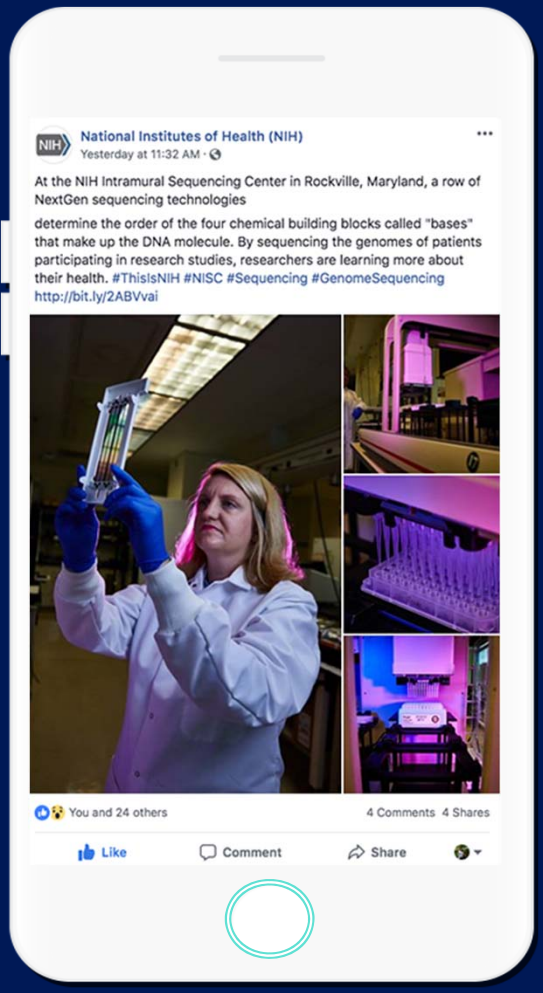
V. NIH Common Fund/Trans-NIH

VI. NHGRI Division of Policy, Communications, and Education

VII. NHGRI Intramural Research Program

New Synthetic Biology Resource

#ThisIsNIH Social Media Takeover



- Highlighted NHGRI programs, staff, and genomics research breakthroughs
- Engaged with 900,000 NIH followers
- Reached >8 million people using #ThisIsNIH

NHGRI Summer Outreach Programs

Capitol Hill Maker Faire®

Dr. Ben Busby (NCBI) and
Rep. Mark Takano (D-CA)

Prince George's County
Youth Career Connect Program

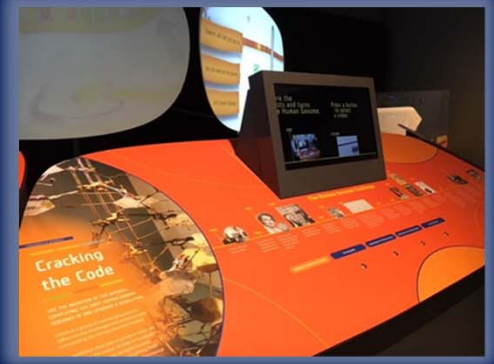
NHGRI Short Course in Genomics

Tribal Colleges Consortium on Genomics Training (TCCGT) Workshop

T C C G T

Tribal Colleges Consortium on Genomics Training

Genome: Unlocking Life's Code Exhibition
Travel Schedule



- **Fall 2018**

  Orange County History Museum, Orlando, FL

- **Winter 2019**

  McWane Science Center, Birmingham, AL

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International Summit in Human Genetics and Genomics

- Five-year initiative (2016-2020)
- Help developing nations build expertise in genetics and genomics
- 2018 Summit: 26 participants from countries across the globe

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NHGRI Intramural Research Highlights

nature immunology

Hyperactivated PI3Kδ promotes self and commensal reactivity at the expense of optimal humoral immunity

PLOS | BIOLOGY

A direct link between MITF, innate immunity, and hair graying

Annals of Internal Medicine®

Is It Ethical to Use Genealogy Data to Solve Crimes?

Sign up for The Genomics Landscape email updates

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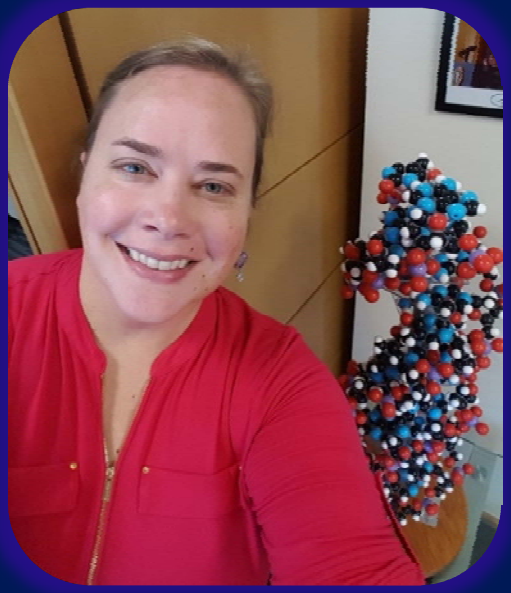
National Human Genome Research Institute

Thanks!



Special Thanks!


The Forefront
of Genomics®