

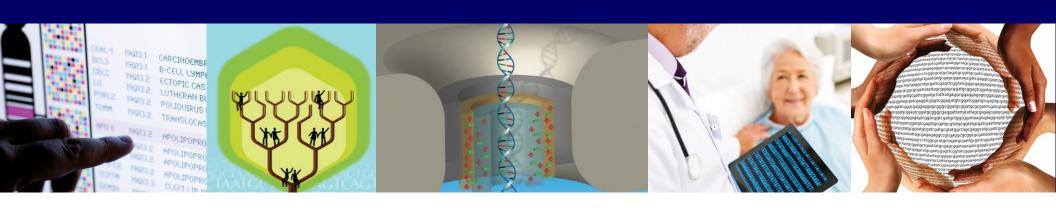


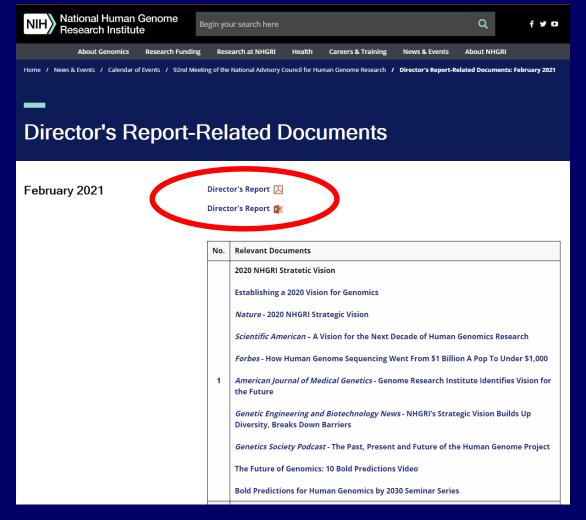


# DIRECTOR'S REPORT

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

February 2021





genome.gov/DirectorsReport



#### **Presentations:**

Final NIH Policy on Data Management and Sharing Carrie Wolinetz

Building a Diverse Genomics Workforce: An NHGRI Action Agenda

**Vence Bonham** 

#### **Concept Clearances:**

Genome Research Experiences to Attract Talented
Undergraduates into the Genomics Field to Promote
Diversity (GREAT Program)
Tina Gatlin

Grants for New Investigators to Promote Diversity in Genomics Research

Jyoti Dayal

#### **Concept Clearances:**

Non-Human Primate dGTEx

Jennifer Troyer

Computational Genomics and Data Science

Daniel Gilchrist

Molecular Phenotypes of Null Alleles in Cells Pilot Project
Adam Felsenfeld

#### **Presentation:**

Phenotypes and Exposures (PhenX) Toolkit Erin Ramos

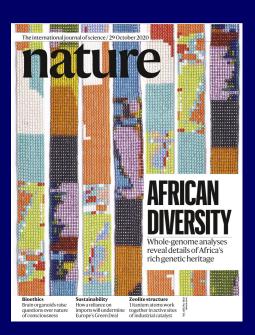
#### Director's Report Outline

- 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 Communications, Policy, and Education
- VII. NHGRI Intramural Research Program

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#### 2020 NHGRI Strategic Vision



#### Strategic vision for improving human health at The Forefront of Genomics

https://doi.org/10.1038/s41586-020-2817-4 lecelved: 30 June 2020

Accepted: 4 September 2020 Published online: 28 October 2020

Eric D. Green¹™, Chris Gunter¹, Leslie G. Biesecker¹, Valentina Di Francesco¹, Carla L. Easter¹, Elise A. Feingold<sup>1</sup>, Adam L. Felsenfeld<sup>1</sup>, David J. Kaufman<sup>1</sup>, Elaine A. Ostrander William J. Pavan¹, Adam M. Phillippy¹, Anastasia L. Wise¹, Jyoti Gupta Dayal¹, Britny J. Kish¹, Allison Mandich<sup>1</sup>, Christopher R. Wellington<sup>1</sup>, Kris A. Wetterstrand<sup>1</sup>, Sarah A. Bates<sup>1</sup>, Darryl Leja', Susan Vasquez', William A. Gahl', Bettie J. Graham', Daniel L. Kastner', Paul Liu', Laura Lyman Rodriguez<sup>1</sup>, Benjamin D. Solomon<sup>1</sup>, Vence L. Bonham<sup>1</sup>, Lawrence C. Brody<sup>1</sup>,

Starting with the launch of the Human Genome Project three decades ago, and continuing after its completion in 2003, genomics has progressively come to have a central and catalytic role in basic and translational research. In addition, studies increasingly demonstrate how genomic information can be effectively used in clinical  $care. \, In \, the \, future, the \, anticipated \, advances \, in \, technology \, development, biological \,$ insights, and clinical applications (among others) will lead to more widespread integration of genomics into almost all areas of biomedical research, the adoption of genomics into mainstream medical and public-health practices, and an increasing relevance of genomics for everyday life. On behalf of the research community, the National Human Genome Research Institute recently completed a multi-year process  $of strategic\, engagement\, to\, identify\, future\, research\, priorities\, and\, opportunities\, in$  $human\,genomics, with\,an\,emphasis\,on\,health\,applications.\,Here\,we\,describe\,the$ highest-priority elements envisioned for the cutting-edge of human genomics going forward-that is, at 'The Forefront of Genomics'.

Beginning in October 1990, a pioneering group of international of biomedical research, medical practice, and society. The scope, scale researchers began an audacious journey to generate the first map and and pace of genomic advances so far were nearly unimaginable when sequence of the human genome, marking the start of a 13-year odyssey called the Human Genome Project began; even today, such advances are yielding scientific and clinical opportunities beyond our initial expectations, tion of the Project in 2003, which included parallel studies of a set of model organism genomes, catalysed enormous progress in genomics research. Leading the signature advances has been a greater than one million-fold reduction in the cost of DNA sequencing<sup>4</sup>. This decrease has allowed the generation of innumerable genome sequences, including Genome Project in 200315 and then again at the beginning of the last hundreds of thousands of human genome sequences (both in research and clinical settings), and the continuous development of assays to identify and characterize functional genomic elements36. These new tools, together with increasingly sophisticated statistical and computational methods, have enabled researchers to create rich catalogues of numan genomic variants<sup>78</sup>, to gain an ever-deepening understanding of the functional complexities of the human genome<sup>5</sup>, and to determine the genomic bases of thousands of human diseases<sup>510</sup>. In turn, the past from a large number of stakeholders, with the resulting input catalogued decade has brought the initial realization of genomic medicine<sup>11</sup>, as and synthesized using the framework depicted in Fig. 1. research successes have been converted into powerful tools for use in healthcare, including somatic genome analysis for cancer (enabling development of targeted therapeutic agents)<sup>12</sup>, non-invasive prenatal genetic screening<sup>13</sup>, and genomics-based tests for a growing set of naediatric conditions and rare disorders among others.

In essence, with growing insights about the structure and function of the human genome and ever-improving laboratory and computational technologies, genomics has become increasingly woven into the fabric

ing scientific and clinical opportunities beyond our initial expectations, with many more anticipated in the next decade.

Embracing its leadership role in genomics, the National Human Genome Research Institute (NHGRI) has developed strategic visions for the field at key inflection points, in particular at the end of the Human decade in 2011<sup>16</sup>. These visions outlined the most compelling opportuni-ties for human genomics research, in each case informed by a multi-year engagement process. NHGRI endeavoured to start the new decade with an updated strategic vision for human genomics research. Through a planning process that involved more than 50 events (such as dedicated workshops, conference sessions, and webinars) over the past two years (see http://genome.gov/genomics2020), the institute collected input

Unlike the past, this round of strategic planning was greatly influenced by the now widely disseminated nature of genomics across biomedicine. A representative glimpse into this historic phenomenon is illustrated in Fig. 2. During the Human Genome Project, NHGRI was the primary funder of human genomics research at the US National Institutes of Health (NIH), but the past two decades have brought a greater than tenfold increase in the relative fraction of funding coming from other parts of the NIH.

Nature | Vol 586 | 29 October 2020 | 683

#### The **Forefront** of **Genomics**®

Nature (2020)

#### 2020 NHGRI Strategic Vision

#### **Outreach and Media Coverage**





#### 2020 NHGRI Strategic Vision

#### Box 5

#### Bold predictions for human genomics by 2030

Some of the most impressive genomics achievements, when viewed in retrospect, could hardly have been imagined ten years earlier. Here are ten bold predictions for human genomics that might come true by 2030. Although most are unlikely to be fully attained, achieving one or more of these would require individuals to strive for something that currently seems out of reach. These predictions were crafted to be both inspirational and aspirational in nature, provoking discussions about what might be possible at The Forefront of Genomics in the coming decade.

- Generating and analysing a complete human genome sequence will be routine for any research laboratory, becoming as straightforward as carrying out a DNA purification.
- The biological function(s) of every human gene will be known; for non-coding elements in the human genome, such knowledge will be the rule rather than the exception.
- The general features of the epigenetic landscape and transcriptional output will be routinely incorporated into predictive models of the effect of genotype on phenotype.
- Research in human genomics will have moved beyond population descriptors based on historic social constructs such as race.
- 5. Studies that involve analyses of genome sequences and associated phenotypic information for millions of human participants will be regularly featured at school science fairs.
- The regular use of genomic information will have transitioned from boutique to mainstream in all clinical settings, making genomic testing as routine as complete blood counts.
- The clinical relevance of all encountered genomic variants will be readily predictable, rendering the diagnostic designation 'variant of uncertain significance (VUS)' obsolete.
- An individual's complete genome sequence along with informative annotations will, if desired, be securely and readily accessible on their smartphone.
- 9. Individuals from ancestrally diverse backgrounds will benefit equitably from advances in human genomics.
- Breakthrough discoveries will lead to curative therapies involving genomic modifications for dozens of genetic diseases.



# **Bold Predictions for Human Genomics by 2030**

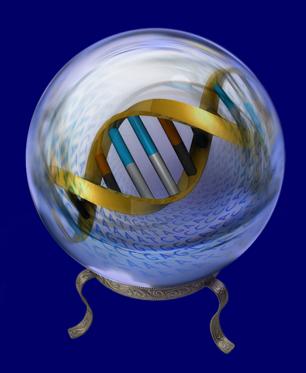
#### **NHGRI Seminar Series**

Bold Prediction #1: February 1

Evan Eichler, University of Washington Karen Miga, UC, Santa Cruz

Bold Prediction #2: March 8

Nancy Cox, Vanderbilt University Neville Sanjana, NY Genome Center



# Departure of Chief, Education and Community Involvement Branch



Carla Easter, Ph.D.

## **New Extramural Program Director**



Joannella Morales, Ph.D.

## 20<sup>th</sup> Anniversary of Publications Reporting Draft Human Genome Sequence







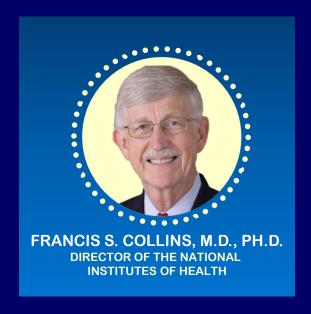
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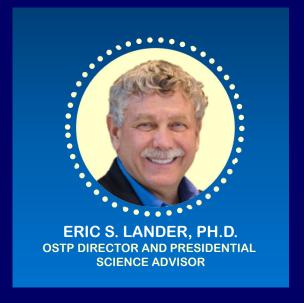
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#### **Members of White House Science Team**



PRESIDENT-ELECT BIDEN ANNOUNCES KEY
MEMBERS OF HIS WHITE HOUSE SCIENCE TEAM







# Leadership Changes at Centers for Disease Control (CDC) and Food and Drug Administration (FDA)



**New Director, CDC Rochelle Walensky M.D., M.P.H.** 







Acting Commissioner, FDA Janet Woodcock, M.D.

#### **VIPs Visit NIH**



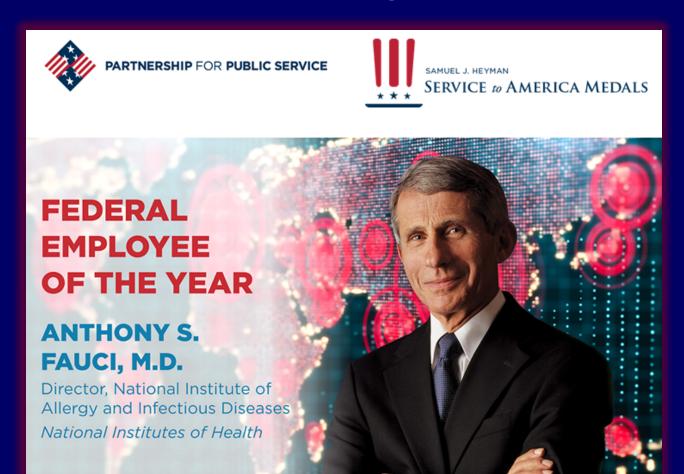
Vice President Kamala Harris President Joe Biden





First Lady Dr. Jill Biden

### 2020 Federal Employee of the Year



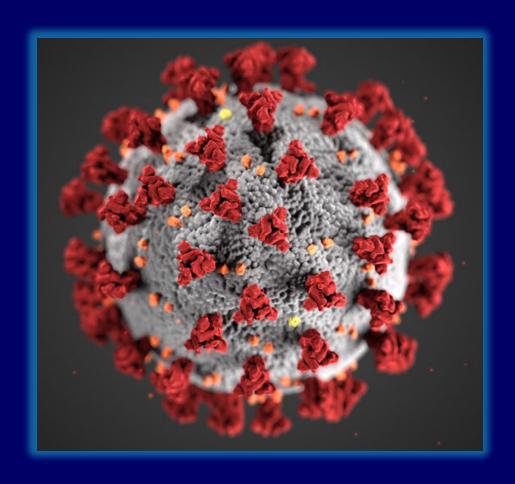
#### Judith Greenberg Retires as Deputy Director, National Institute of General Medical Sciences



Judith Greenberg, M.D., Ph.D.



#### **NIH COVID-19 Information Resources**



# Fiscal Year 2021 Appropriations

|       | Fiscal Year<br>2020<br>Labor-HHS<br>Appropriation | Fiscal Year<br>2021<br>Labor-HHS<br>Appropriation | \$<br>Increase | %<br>Increase |
|-------|---|---|----------------|---------------|
| NIH   | \$41.68 B   | \$42.93 B   | \$1.25 B       | 2.99%         |
| NHGRI | \$606.35 M  | \$615.78 M  | \$9.43 M       | 1.56%         |

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# **Mourning the Loss of Marvin Frazier**



## Mourning the Loss of Gertjan van Ommen





#### 2020 American Society of Human Genetics Awards







Education Awardee Kenneth Lange, PhD

University of California Los Angeles



Early-Career Awardee
Benjamin Neale, PhD

Massachusetts General Hospital



#### **Elected to National Academy of Medicine**



Judy Cho
Wendy Chung
Levi Garraway
Joel Hirschhorn
David Liu
Consuelo Hopkins Wilkins

Alondra Nelson
Aviv Regev
Pardis Sabeti
Louis Staudt
Hannah Valantine

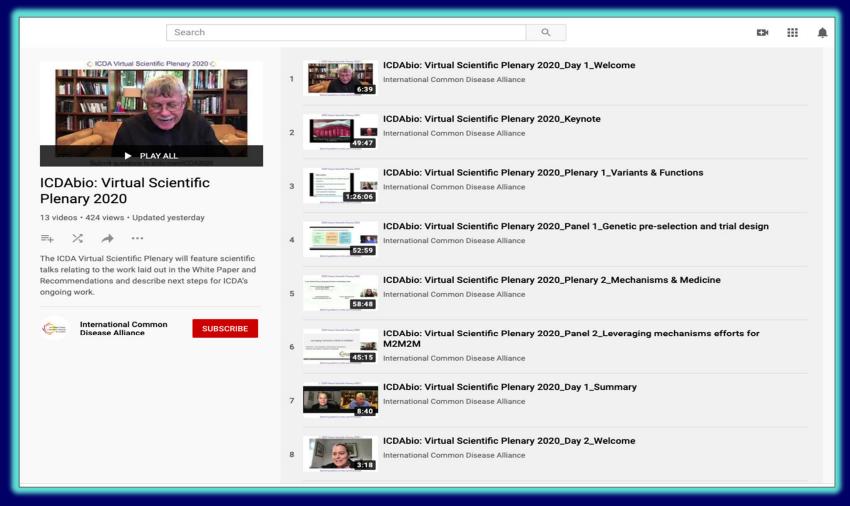
#### **Elected to AAAS**

Lisa Brooks
R. Alta Charo
Dana Crawford
Ronald Davis

Pui-Yan Kwok
Matthew Meyerson
William Murphy
Len Pennacchio

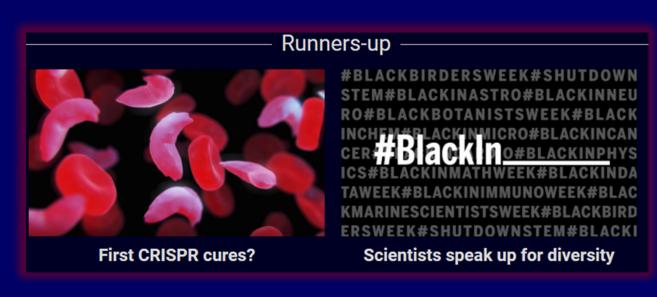


#### **International Common Disease Alliance (ICDA)**



## Science 2020 Breakthrough of the Year Runners Up





#### The Scientist Top Technical Advances of 2020



DNA assembly and amplification Single cell gene expression Spatial gene expression Digital genome engineering

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#### **Human Genome Reference Program**

TOWARDS A
COMPLETE
REFERENCE OF
HUMAN GENOME
DIVERSITY

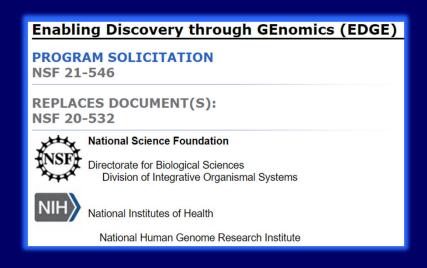
- Generate ≥350 high-quality reference genome sequences
- Year 1 data released
- HGRP and T2T joint meeting (September 2020)
- Human pangenome video

#### **Comparative Genomics**

Notice of NIH Participation in the National Science Foundation Enabling Discovery through GEnomics (EDGE) Program

**Notice Number:** 

NOT-HG-21-014



Enabling Discovery Through GEnomics (EDGE)

Functional Genomic Tools Track
Complex Multigenic Traits Track

Applications due: March 16, 2021

#### **Technology Development Program**

#### **Funding Opportunities**

Notice of Special Interest (NOSI): Advancing Genomic Technology Development for Research and Clinical Applications

NOT-HG-21-018

Standard due dates start February 5, 2021

Novel Synthetic Nucleic Acid Technology Development

RFA-HG-20-014 (R01, also linked R21 and R43/44)

Applications due March 9, 2021

Notice of Intent to Publish: Transformative Nucleic Acid Sequencing Technology Innovation and Early Development

NOT-HG-21-016

#### **Technology Development Program**

#### **Advanced Genomic Technology Development Meetings**

- New colloquia (Fall 2020)
- Virtual annual meeting
   May 25-27, 2021
   Northeastern University



## High-Throughput Molecular and Cellular Phenotyping Opportunity

Notice of Special Interest (NOSI): High-throughput Molecular and Cellular Phenotyping

Notice Number:
NOT-HG-21-004

Key Dates

Release Date:

December 3, 2020

First Available Due Date:

February 05, 2021

**Expiration Date:** 

January 10, 2024

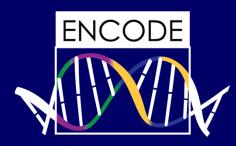
#### **ENCyclopedia of DNA Elements**

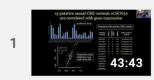


ENCODE 2020 Research Applications & Users Meeting

Encode 2020 Research Applications & Users meeting is virtual September 30th - October 2nd

**Meeting materials** available on the **ENCODE** portal





Aravinda Charkravati: Sequence-based studies of regulatory control

National Human Genome Research Institute



Stephanie Morris: ENCODE: The **Encyclopedia of DNA Elements** 

National Human Genome Research Institute



Paul Flicek: Comparative regulatory genomics approaches to

National Human Genome Research Institute



John Stamatoyannopoulos: Highresolution maps of regulatory DNA:

National Human Genome Research Institute



5

Neva Durand: Juicebox Hands-on Session - September 30, 2020

National Human Genome Research Institute

#### **Computational Genomics and Data Science Program**

#### **Machine Learning in Genomics Workshop**

Genomic Data Science Working Group April 13-14, 2021





**Algorithm development** 



**Data and resource needs** 





**Clinical applications** 



#### Clinical Genome Resource (ClinGen)

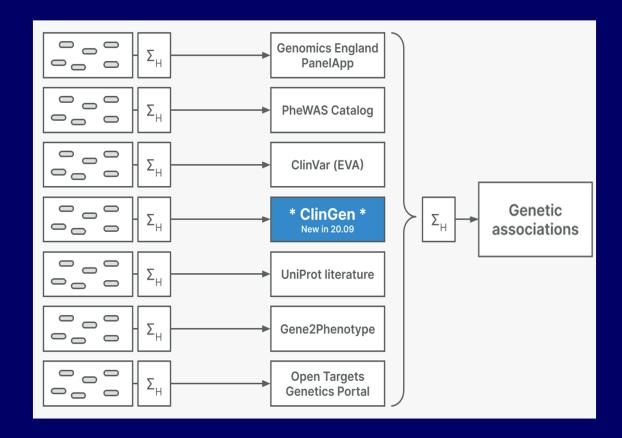
#### ClinGen Validity Curations Integrated into Open Targets Platform



#### **OPEN TARGETS PLATFORM**

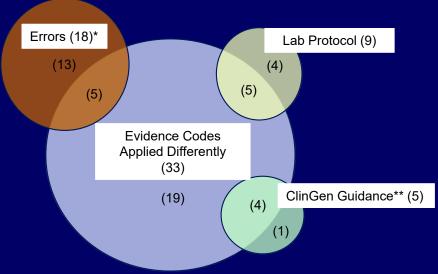
## Introducing ClinGen's Gene Validity Curations

Learn how the Open Targets Platform integrates and scores ClinGen's Gene-Disease Validity curation data to enhance rare disease associations





# Clinical Sequencing Evidence-generating Research (CSER) Program





- "Variant bake-off 2.0" of ACMG secondary findings genes
- Concordance rate of 84%
- CSER sites adapted to COVID-19 challenges through telemedicine



## International 100K+ Cohort Consortium (IHCC)

The International Hundred Thousand Plus Cohort Consortium: integrating large-scale cohorts to address global scientific challenges



- Exploring the Role of Genetically Determined BMI in Infancy, Childhood, and Early Adulthood on Colorectal Cancer Development in Later Life
- High-throughput Metabolomic Biomarker Measures in Diverse Ancestries
- Opioid Cohort Consortium (OPICO) to Investigate the Effects of Regular Opioid Use on Mortality and on Cancer Development
- Global Mental Health Impact of the COVID-19 Pandemic
- Strengthening biospecimen collection for Global Longitudinal Population Studies in the COVID-19 era
- Novel coronavirus host susceptibility study in South Africa (COVIGen-SA)

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

Launch of ELSIhub

Curated by the Center for ELSI Resources and Analysis (CERA)

- ELSI publications database
- Scholar directory
- Research tools database
- Policy resources
- ELSI funding opportunities











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

**ELSI Friday Forum & ELSI Conversations** 



Gail Geller, ScD, MH

Rhea Boyd.



Fridays at 12:00 pm ET on ELSIhub

Sara Katsanis, MS

Northwestern University

Vera Eidelman, JD

#### **Training and Career Development**

#### Response to Training Task Force Recommendations

Mentored Research Experiences for Genetic Counselors (R25) PAR-21-074

Research Experience in Genomic Research for Data Scientists (R25)
PAR-21-075

- Release date: December 9, 2020
- Applications due: May 25, 2021

#### **FOAs Under Development:**

- F99/K00 NHGRI Predoctoral to Postdoctoral Transition Award to Promote Diversity
- K18 Short-term Mentored Research Career Enhancement Award to Promote Diversity

  Document 25

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### **Genotype-Tissue Expression (GTEx) project**



September 2020:GTEx Version 8 data release





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



>700 attendees



### Human Heredity and Health in Africa (H3Africa)

#### **Growing Publication Record**

#### 440+ publications to date

Article Open Access | Published: 28 October 2020

### High-depth African genomes inform human migration and health

Ananyo Choudhury, Shaun Aron, Laura R. Botigué, Dhriti Sengupta, Gerrit Botha, Taoufik Bensellak, Gordon Wells, Judit Kumuthini, Daniel Shriner, Yasmina J. Fakim, Anisah W. Ghoorah, Eileen Dareng, Trust Odia, Oluwadamilare Falola, Ezekiel Adebiyi, Scott Hazelhurst, Gaston Mazandu, Oscar A. Nyangiri, Mamana Mbiyavanga, Alia Benkahla, Samar K. Kassim, Nicola Mulder, Sally N. Adebamowo, Emile R. Chimusa, Donna Muzny, Ginger Metcalf, Richard A. Gibbs, TrypanoGEN Research Group, Charles Rotimi, Michèle Ramsay, H3Africa Consortium, Adebowale A. Adeyemo , Zané Lombard & Neil A. Hanchard . Show fewer authors

Nature **586**, 741–748(2020) | Cite this article

27k Accesses | 2 Citations | 688 Altmetric | Metrics





#### Human Heredity and Health in Africa (H3Africa)

#### **Continued International Collaborations**

Virtual Consortium Meeting: >150 attendees



ClinGen and H3Africa Rare Disease Working Group

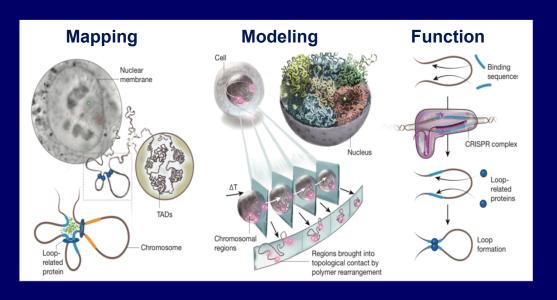








#### **4D Nucleome (4DN)**



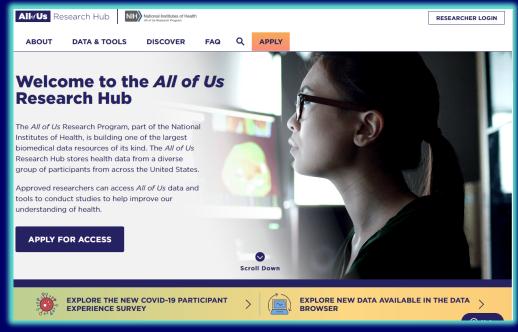
#### 30 Awards:

- Chromatin dynamics and function
- Data integration, modeling, and visualization
- Nuclear organization in human health and disease
- New investigator projects in human health and disease
- Data center and organizational hub

Phase II kickoff meeting in December 2020

# A of US RESEARCH PROGRAM





# A of US RESEARCH PROGRAM



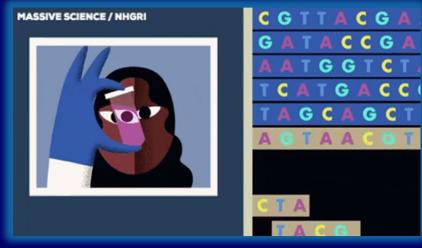
Due Date: April 6, 2021

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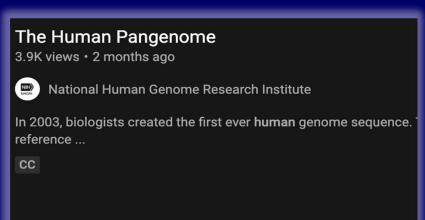
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### Human Pangenome Video

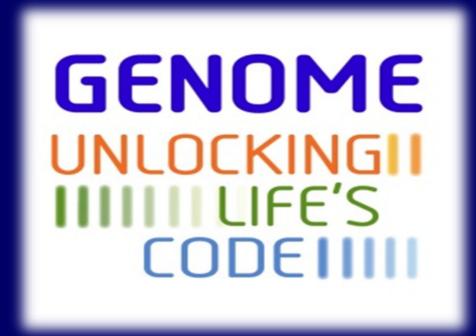








## Genome: Unlocking Life's Code Exhibition's Return to the Smithsonian





### Family Health History Social Media Campaign









### **New ISCC-PEG Scholars Program**

#### **A Genomics Education Opportunity**



Samantha Bailey, Pharm.D., Ph.D.



Rene Begay, M.P.H.



Kelsey Ellis, M.S.



Katherine Robinson, Pharm.D.

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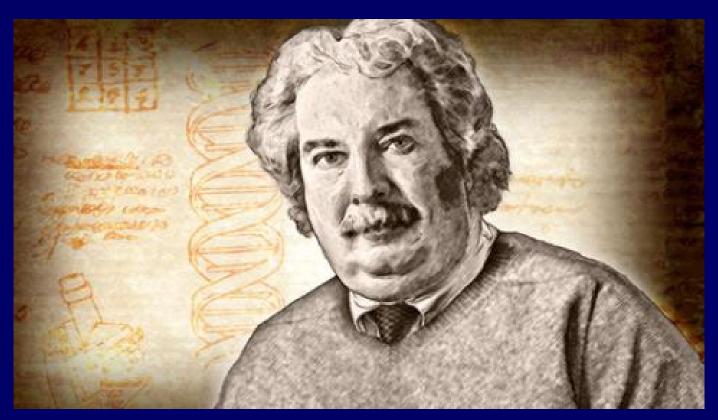
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## New Genomic Science and Health Equity Fellowship Program



- Use genetic, genomic, and pharmacogenomic approaches to advance minority health and health equity
- Research methodology and medical product development processes that facilitate delivery of drugs, biologics, and devices
- First fellow will start Summer/Fall 2021

### Retirement of NHGRI Intramural Investigator



Alec Wilson, Ph.D.

### **New NHGRI Intramural Investigator**



Neil Hanchard, M.D., Ph.D.

### Royal Swedish Academy of Sciences' Crafoord Prize



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

#### **NHGRI Scientific Director Search**

- Dan Kastner will step down as NHGRI Scientific Director
- Search for the next NHGRI Scientific Director begins in mid-March



#### **NHGRI Director on Twitter**





#### **Email Updates**

Sign up to receive National Human Genome Research Institute (NHGRI) updates and stay informed about our latest science, research, news, upcoming events and website content.

**Email Address** 



### Thanks!



**Special Thanks!** 

