

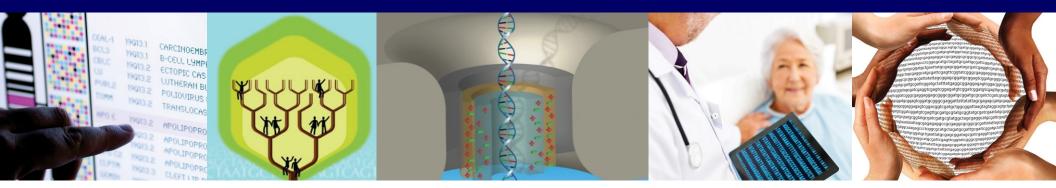
NIH National Human Genome Research Institute

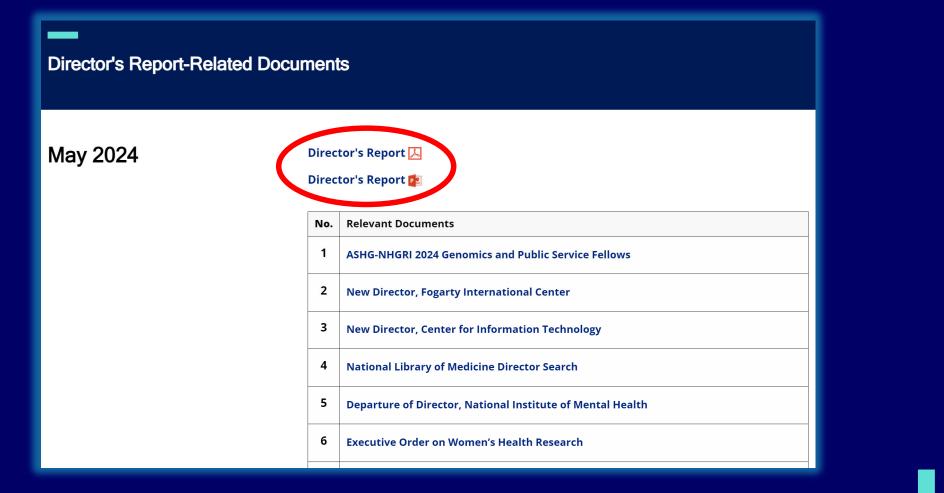


DIRECTOR'S REPORT

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

May 2024





genome.gov/DirectorsReport

Document #

Open Session Agenda

Presentation:

The NIAID Mission: Infectious Diseases and Beyond Jeanne Marrazzo

Concept Clearances:

Supporting Talented Early Career Researchers in Genomics Lisa Chadwick

Genome Research Experiences to Attract Talented Undergraduates into Genomic Fields to Enhance Diversity (GREAT) Ebony Madden

NHGRI Predoctoral to Postdoctoral Transition Award for a Diverse Genomics Workforce

Lucia Hindorff

Open Session Agenda

Presentations:

Bettie J. Graham Leadership Awards for Enhancing Diversity, Equity, Inclusion, and Accessibility in the Genomics Workforce Lucia Hindorff & Eric Green

Impact of Genomic Variation on Function (IGVF) Consortium Update Karen Mohlke & Jesse Engreitz

Genomics Research to Elucidate the Genetics of Rare Disease (GREGoR) Consortium Update Jennifer Posey

Open Session Agenda

Reports:

Workshop Report: Advances in the Genetic Architecture of Complex Human Traits Alexander Arguello & Nancy Cox

Overview of the NHGRI Small Business Program Renee Rider & Ian Nova

Presentation:

Revisions for Fellowship Applications and Simplified Review Framework for Research Applications Sarah Wheelan

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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New Deputy Director, Division of Extramural Operations



Issel Anne Lim, Ph.D.

New Extramural Program Director, Divisions of Extramural Operations & Genome Science



Kris Wetterstrand, M.S.

New Extramural Program Director, Division of Genomic Medicine



Nephi Walton, M.D., M.S.

New Extramural Program Director, Office of Genomic Data Science



Jean Gao, Ph.D.

ASHG-NHGRI 2024 Genomics and Public Service Fellows





National Human Genome Research Institute

Genomics and Public Service Fellowship Program

Genetics Education & Engagement Fellow



Camerun Washington, M.S., C.G.C. Greenwood Genetic Center

Genetics & Public Policy Fellow

Genomics Communications Fellow



Elizabeth Roy, M.P.H. University of Pittsburgh



Jacqueline Cohen, M.P.H. University of Pittsburgh Document 1

ASHG-NHGRI 2024 Genomics and Public Service Fellows





National Human Genome Research Institute

Genomics and Public Service Fellowship Program

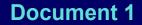
Post-Baccalaureate Genomics Analyst Fellows – ASHG-based



Maya Montgomery Duke University



Alison Wilcox St. Olaf College



ASHG-NHGRI 2024 Genomics and Public Service Fellows





National Human Genome Research Institute

Genomics and Public Service Fellowship Program

Post-Baccalaureate Genomics Analyst Fellows – NHGRI-based



Malia Jennings Fisk University



Mike Lopez New Mexico State University



Sofia Martin St. Edward's University



Jessica Reinach University of Michigan



Gabrielle Villard Southern California Univ. of Health Sciences

Director's Report Outline

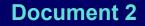
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New Director, Fogarty International Center



Kathleen Neuzil, M.D.





New Director, Center for Information Technology



NIH Center for Information Technology

Sean Mooney, Ph.D.

National Library of Medicine Director Search



- Search launched May 1
- Search committee co-chairs: Eric Green & Nora Volkow
- Applications due July 1



Departure of Director, National Institute of Mental Health





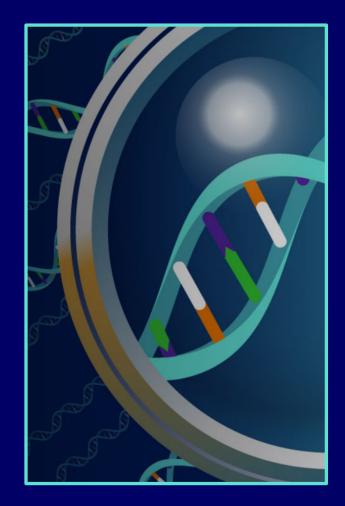
Joshua Gordon, M.D., Ph.D.

Executive Order on Women's Health Research

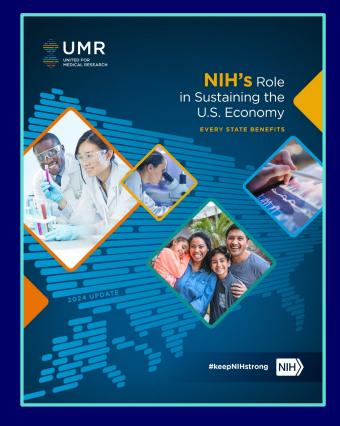


FDA Finalizes Rule for LDT Oversight and Regulation

- Medical devices to include LDTs
- Same oversight as other diagnostic products manufactured by industry
- Four-year phaseout of general enforcement discretion
- Implementation of targeted enforcement discretion of certain LDTs
- Some tests will be considered legacies and will not undergo the full FDA regulatory process
- LDTs offered prior to May 6, 2024, with no further modifications



NIH's Role in Sustaining the U.S. Economy



\$1 NIH funded research = \$2.46 economic activity

Fiscal Year 2024 Appropriations

Portion	FY 2024 Enacted Appropriation	FY 2023 Enacted Appropriation	FY 24-23 Difference \$	FY 24-23 Difference %
NIH (excluding ARPA-H)	\$47.08 B	\$47.68 B	-\$380 M	-0.8%
NHGRI	\$663.2 M	\$663.2 M	\$0	0%

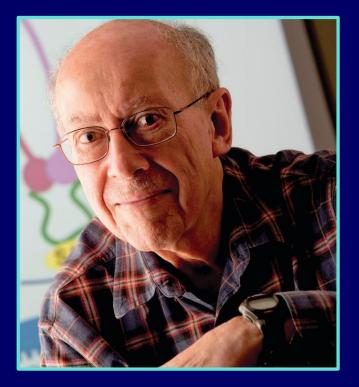
Fiscal Year 2025 Appropriations

Portion	FY 2025 President's Budget	FY 2024 Enacted L-HHS Appropriation	FY 2024 President's Budget	FY24 Enacted – FY24 President's Budget Difference \$	FY24 Enacted – FY24 President's Budget Difference %
NIH (excluding ARPA-H)	\$50.1 B	\$47.08 B	\$48.68 B	-\$1.4 B	-3%
NHGRI	\$664 M	\$663.2 M	\$663 M	+\$200,000	+0.03%

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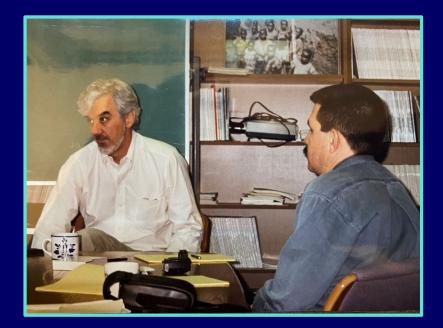
Mourning the Loss of Gary Felsenfeld





Mourning the Loss of Richard Cooper





New Chief Executive Officer, American Society of Human Genetics

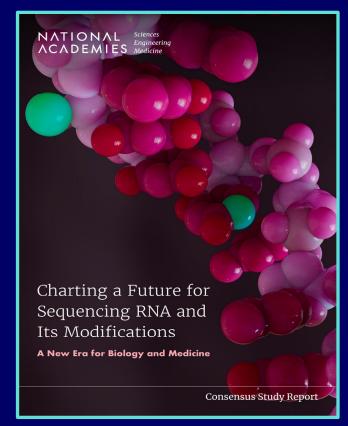


Amanda Perl

American Society of Human Genetics

NASEM Report: Charting a Future for Sequencing RNA and Its Modifications

- Reviews the impact of RNA base modifications
- Highlights critical gaps in existing RNA sequencing technologies
- Provides recommendations for standards, technologies, and regulatory agency tasks
- Sets 5, 10, and 15-year priorities and milestones



Elected to National Academy of Sciences



David J. Glass Todd R. Golub Thomas A. Kunkel Nipam H. Patel Steven A. Rosenberg Jenny Tung Joana Wysocka

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Molecular Phenotypes of Null Alleles in Cells (MorPhiC) Phase 1 MorPhiC



- Consortium Meeting in February 2024
- Focus on experimental design, data pipelines, individual scientific results, and progress updates
- Hackathon led by early career investigators

Identifying Research Priorities to Accelerate Genetic Diagnosis Meeting

Challenges, gaps, and opportunities:

Advance understanding of the genetic causes of Mendelian conditions

Increase rate of identifying genetic causes of rare genetic diseases

 Workshop recording and report will be available soon



Community Input on Genomic Variant Interpretation



- Testing and assessing function of individual genomic variants
- Testing and assessing function of genomic variants in context
- Technology development needs
- Predictive modeling
- Resource building

Educational Hub & Sites for Enhancing Diversity in Computational Genomics and Data Science



- The Hub will leverage cloud platforms to increase access to educational and research opportunities
- Partner Sites will develop educational content that makes uses cloudcomputing resources
- Applications are due on June 10

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





AnVIL collaborating with the NIH Cloud Platform Interoperability Program (NCPI) on four projects:



NATIONAL CANCER INSTITUTE Cancer Research Data Commons







Clinical Genome Resource (ClinGen)

10th Anniversary



DECIPH

Clinical Geno

2024



American College of Medical Genetics and Genomics (ACMG)



Curating the Clinical Genome (CCG)

PhenX Toolkit: Social Determinants of Health (SDOH)

The PhenX Toolkit: Recommended Measurement Protocols for Social Determinants of Health Research

Cataia L. Ives,¹ Michelle C. Krzyzanowski,¹ Vanessa J. Marshall,^{2,13} Keith Norris,³ Myles Cockburn,⁴ Keisha Bentley-Edwards,⁵ Dinushika Mohottige,⁶ Keshia M. Pollack Porter,⁷ Denise Dillard,⁸ Yochai Eisenberg,⁹ Monik C. Jiménez,¹⁰ Eliseo J. Pérez-Stable,² Nancy L. Jones,² Jyoti Dayal,¹¹ Deborah R. Maiese,^{1,12} David Williams,¹ Tabitha P. Hendershot,¹ and Carol M. Hamilton¹

15 new protocols added to the PhenX SDOH collections

- Examples of new individual measures: Discrimination in Healthcare & Internet Access
- Examples of new structural measures: Water Access, Sanitation, & Minimum Wage





Defining a Clinical Data Ecosystem for Genomic Health Workshop



- Define a data ecosystem, outlining paths of genomic data from laboratory to electronic health records to patient/clinician and across health systems
- Determine informatics standards to be adopted, systems to be built, and policies to be developed
- Identify research directions for optimizing genomic data integration and utilization in delivery of healthcare

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



ELSIcon2024: The 6th ELSI Congress Reimagining the Benefits of Genomic Science

SAVE THE DATE

June 10-12, 2024

New York City



Register now!

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

 NOT-HG-24-027: Building Partnerships and Broadening Perspectives to Advance Ethical, Legal and Social Implications (ELSI) Research (BBAER)

1) Transdisciplinary ELSI Research

2) Research Teams with Community Experts

3) ELSI Research Capacity Building

4) ELSI Workforce Development

 Eligible applicants: Domestic organizations in the U.S. receiving <\$30M per year in total NIH funding for last 3 years

9th Annual NHGRI Research Training and Career Development Meeting



- Held on April 7-9 in Seattle
- Hosted by Duke University
- >400 in-person attendees

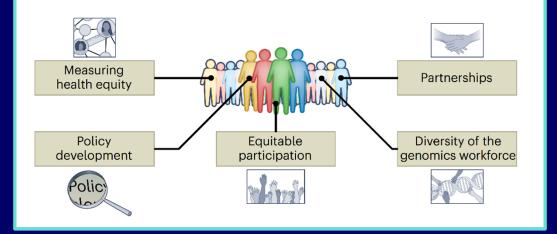
Publication of Genomics and Health Equity Paper

nature genetics

Perspective

Advancing genomics to improve health equity

Ebony B. Madden [©] ^[23], Lucia A. Hindorff¹, Vence L. Bonham¹, Tabia Henry Akintobi², Esteban G. Burchard ^{® 3}, Kellan E. Baker⁴, Rene L. Begay⁵, John D. Carpten⁶, Nancy J. Cox⁷, Valentina Di Francesco ^{® 1}, Denise A. Dillard⁶, Faith E. Fletcher⁹, Stephanie M. Fullerton ^{© 10}, Nanibaa' A. Garrison [©] ^{11/213}, Catherine M. Hammack-Aviran¹⁴, Vanessa Y. Hiratsuka^{® 15}, James E. K. Hildreth¹⁶, Carol R. Horowitz¹⁷, Chanita A. Hughes Halbert¹⁸, Michael Inouye ^{® 19}, Amber Jackson¹, Latrice G. Landry²⁰, Rick A. Kittles²¹, Jeff T. Leek²², Nita A. Limdi²², Nicole C. Lockhart¹, Elizabeth O. Ofili²⁴, Eliseo J. Pérez-Stable²⁵, Maya Sabatello^{36,27}, Loren Saulsberry ^{® 28}, Lorjetta E. Schools²⁹, Jennifer L. Troyer¹, Benjamin S. Wilfond³⁰, Geneviewe L. Wojcik ^{® 31}, Judy H. Cho^{® 17}, Sandra S.-J. Lee²⁷ & Eric D. Green¹



Population Descriptors for Legacy Genomic Data: Challenges and Future Directions Workshop May 28 - 29, 2024 (Virtual)



Register now!

- Leaders of genomic data science resources, researchers who use legacy data, & other partners
- Workshop objectives:
 - Summarize current approaches to the use of population descriptors in/for legacy data

Define and address challenges with harmonization, interoperability, and analysis

Develop recommendations that can be widely adopted

Identify opportunities for research and collaboration

Extramural Investigator-Initiated Highlights

Sex-specific genetic architecture of blood pressure

Min-Lee Yang, Chang Xu, Trisha Gupte, Thomas J. Hoffmann, Carlos Iribarren, Xiang Zhou & Santhi K. Ganesh

Nature Medicine 30, 818–828 (2024) Cite this article

3492 Accesses 58 Altmetric Metrics

ORIGINAL ARTICLE

PRENATAL DIAGNOSIS WILEY

Patient experiences with prenatal cell-free DNA screening in a safety net setting

Kirsten A. Riggan¹ | Amelia Barwise¹ | Jane Q. Yap² | Niamh Condon³ |

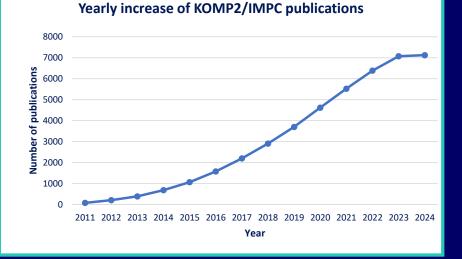
Megan A. Allyse^{1,4} 💿

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Resource impact demonstrated by >7,000 publications



 International Mouse Phenotyping Consortium (IMPC) Spring Meeting – April 2024

IMPC Virtual Workshop – May 2024

Bridge to Artificial Intelligence (Bridge2AI)





Goals:

Generate Al-ready datasets Create ethical Al best practices Train a future biomedical Al workforce All-Hands Conference and Al-Ready Data Open House April 2024

A of US RESEARCH PROGRAM

Article Open access Published: 19 February 2024

Genomic data in the All of Us Research Program

The All of Us Research Program Genomics Investigators

Nature 627, 340–346 (2024) Cite this article

115k Accesses 8 Citations 1097 Altmetric Metrics

Article Open access Published: 19 February 2024

Genetic drivers of heterogeneity in type 2 diabetes pathophysiology

Article Open access Published: 19 February 2024

The frequency of pathogenic variation in the *All of Us* cohort reveals ancestry-driven disparities

Eric Venner ^{CD}, Karynne Patterson, Divya Kalra, Marsha M. Wheeler, Yi-Ju Chen, Sara E. Kalla, Bo Yuan, Jason H. Karnes, Kimberly Walker, Joshua D. Smith, Sean McGee, Aparna Radhakrishnan, Andrew Haddad, Philip E. Empey, Qiaoyan Wang, Lee Lichtenstein, Diana Toledo, Gail Jarvik, Anjene Musick & Richard A. Gibbs on behalf of the All of Us Research Program Investigators

Communications Biology 7, Article number: 174 (2024) Cite this article

5365 Accesses | 2 Citations | 526 Altmetric | Metrics

Article | Open access | Published: 19 February 2024

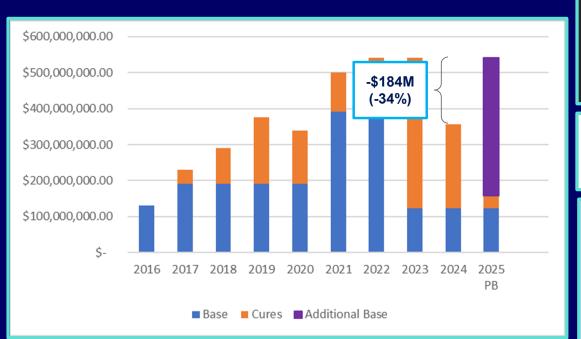
Selection, optimization and validation of ten chronic disease polygenic risk scores for clinical implementation in diverse US populations

Niall J. Lennon ¹²³, Leah C. Kottyan, Christopher Kachulis, Noura S. Abul-Husn, Josh Arias, Gillian Belbin, Jennifer E. Below, Sonja I. Berndt, Wendy K. Chung, James J. Cimino, Ellen Wright Clayton, John J. Connolly, David R. Crosslin, Ozan Dikilitas, Digna R. Velez Edwards, QiPing Feng, Marissa Fisher, Robert R. Freimuth, Tian Ge, The GIANT Consortium, The All of Us Research Program, Joseph T. Glessner, Adam S. Gordon, Candace Patterson, ... Eimear E. Kenny + Show authors

Nature Medicine 30, 480-487 (2024) Cite this article

27k Accesses | 5 Citations | 435 Altmetric | Metrics

A of US RESEARCH PROGRAM



SCIENCEINSIDER | FUNDING

Major budget cuts to two high-profile NIH efforts leave researchers reeling

Drop in 21st Century Cures Act funding will slow BRAIN and All of Us projects

From the *All of Us* CEO: Keeping Our Momentum Amidst Funding Uncertainties

April 23, 2024



Josh Denny

All of Us Research Program Chief Executive Officer

Bespoke Gene Therapy Consortium (BGTC)

				Comment
Disease Type	Disease Name	Affected Gene	Lea	
Ocular	Congenital Hereditary Endothelial Dystrophy	enital Hereditary SLC4A11 Univer facilitating develo	The Bespoke Gene Therapy Cor facilitating development of AAV therapies for rare diseases	
	Retinal Degeneration	NPHP5	Uı	* P. J. Brooks, Timothy M. Miller, Frédéric Revah, Junghae Suh, Bradley R. Garrison, Lawrence C. Starke, Timothy K. MacLachlan, Edward G. Neilan, Gopa Raychaudhur
	Retinitis pigmentosa 45	CNGB1		Sadik H. Kassim, Jean Dehdashti & Joni L. Rutter A public – private partnership managed by the FNIH aims to address biological, manufacturing Av-based in vivo gene therapy
Neurological	Multiple Sulfatase Deficiency	SUMF1	Childr	and regulatory challenges to the development remain a number of challenges: to fgene therapies for rare diseases. gene therapy safer, more effect to some of these challenges will standing of AVS as viruses and for therapeutic use.
	Charcot-Marie-Tooth Disease Type 4J	FIG4	Elpida	According to recent estimates, there are more than 10,000 known human diseases that are considered rare - defined as affecting fewer than 200,000 people in the USA'. Collectively, these diseases affect upwards of 450 million people worldwide'. About 80% of rare diseases are monogenic, in which known alterations in a single gene are respon- sible for the clinical manifestations that result in significant morbidity and mortality. Monogenic diseases are protential candidates for gene transduction biology and two
	Spastic Paraplegia 50	AP4M1	Elpida	therapies because the defective gene can be corrected or replaced, thereby restoring gene function to levels that show clinical benefit and arresting or reversing the disease state. Adeno associated virus (AAV) gene therapies have the potential to provide long term benefit ICAAD SOULLINVESLEIII
Systemic	Propionic Acidemia	PCCB	Nationa	Il Human Genome Research Institute
	Mucopolysaccharidosis IVA (Morquio A Syndrome)	GALNS	Ne	mours Children's Health

https://doi.org/10.1038/d41573-024-00020-8

Gene Therapy Consortium: elopment of AAV are diseases

Revah, Junghae Suh, Bradley R. Garrison, chlan, Edward G. Neilan, Gopa Raychaudhu i L. Rutter naged by the into the brain - with relatively le tion compared with lentiviral v nanufacturing AAV-based in vivo gene therapy levelopment remain a number of challenges t gene therapy safer, more effect to some of these challenges wil standing of AAVs as viruses and for therapeutic use. than 10.000 known To enhance the fundame ed as affecting fewer released two requests for prop these diseases affect AAV gene expression and transo t 80% of rare diseases tigating and/or developing way ngle gene are respon-production. Through these fur significant morbidity porting eight discovery research candidates for gene transduction biology and two o rrected or replaced. tary Table 1), For example, two show clinical benefit intracellular trafficking of AAV eno-associated virus not fully understood. A couple of

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NIH Common Fund Program to Support Clinical Research in Primary Care Settings

- Establish clinical research network focused on primary care
- All institute/center mission areas but also disease agnostic
- Integrate innovative research with routine clinical care in real-world settings
- Create foundation for engagement with underrepresented communities

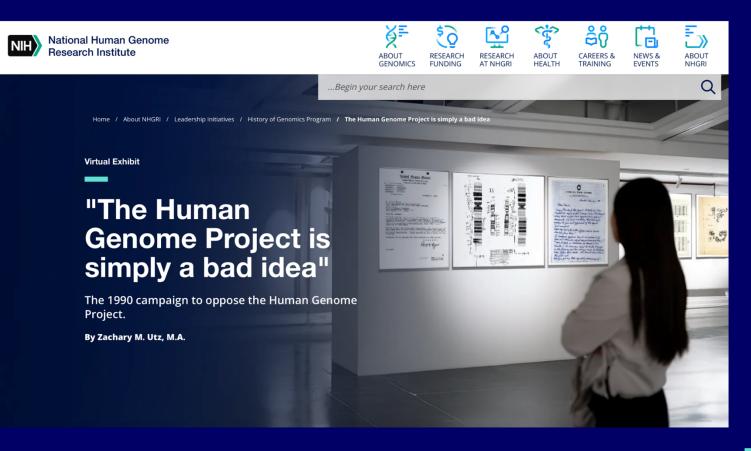


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NHGRI History of Genomics Program

Archival Spotlight



NHGRI History of Genomics Program Oral History Update



Beth Shapiro, Ph.D. Chief Scientific Officer, Colossal Biosciences

NHGRI History of Genomics Program

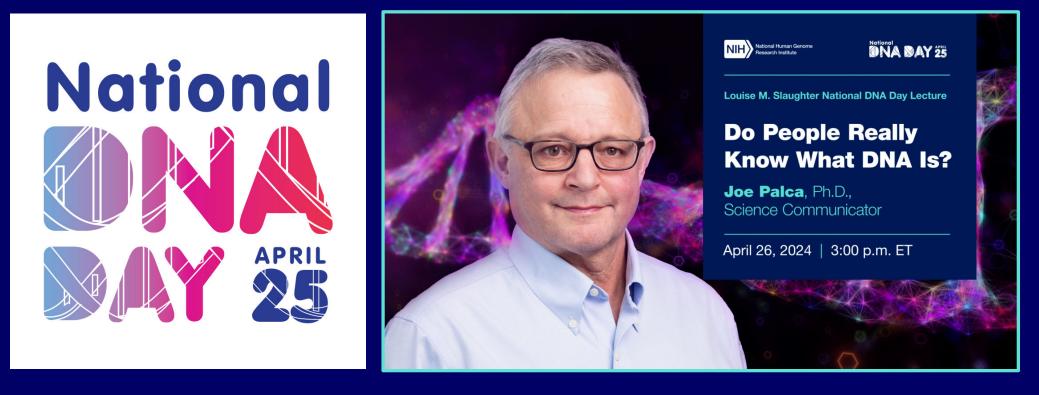
Virtual Symposium





- July 17-18, 2024
- Exploring the many dimensions of sex and gender in the genomics era: Clarifying complexities in light of social and genomic advances and their histories

Louise M. Slaughter National DNA Day Lecture



National DNA Day: "The Ladder" Dedication



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



13th Annual Meeting

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2024 Edward Novitski Prize



Elaine Ostrander, Ph.D.



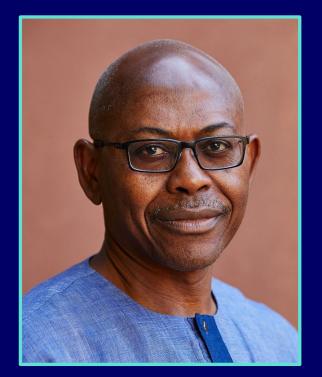
2023 George M. Kober Medal



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



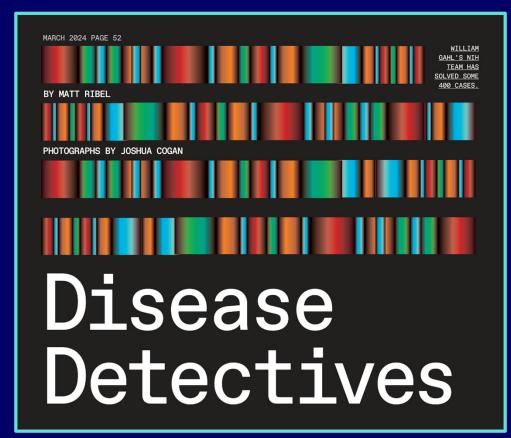
2023 Arthur S. Flemming Award



Charles Rotimi, Ph.D.



Washingtonian Magazine: Disease Detectives





NHGRI Intramural Research Highlights





Lipodystrophy in methylmalonic acidemia associated with elevated FGF21 and abnormal methylmalonylation





The variation and evolution of complete human centromeres





Vitamin B12 status and folic acid supplementation influence mitochondrial heteroplasmy levels in mice

'One-Stop-Shop' to Stay Connected

genome.gov/stayconnected







Thanks!



Special Thanks!

