

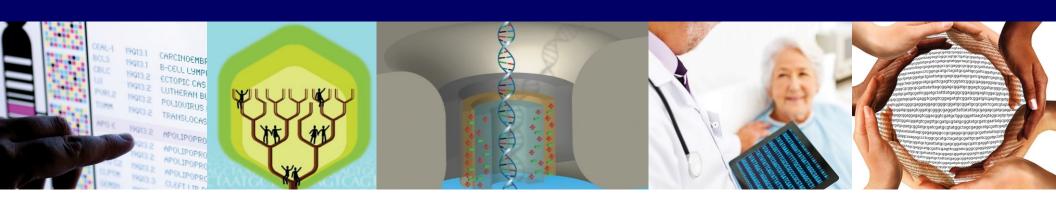


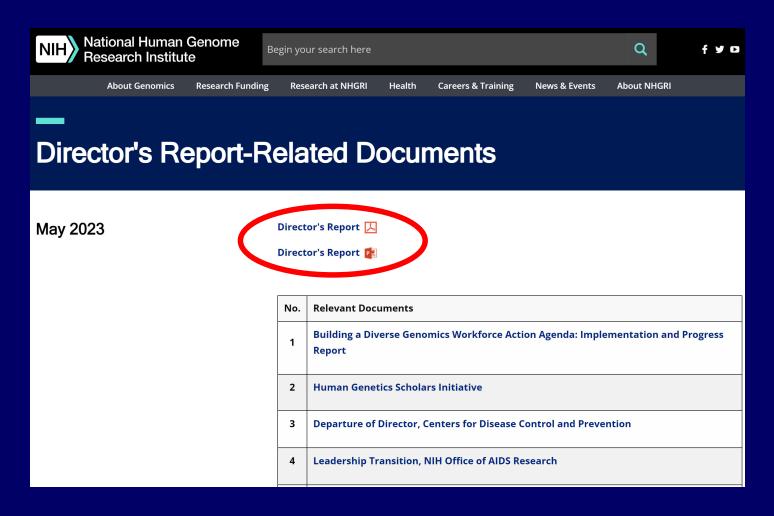


DIRECTOR'S REPORT

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

May 2023





genome.gov/DirectorsReport



Open Session Agenda

Presentations:

NHGRI Intramural Research Program Report Charles Rotimi

NHGRI Intramural Research Program Blue Ribbon Panel Report Gail Jarvik & Lynn Jorde

NASEM Report on the Use of Race, Ethnicity, and Ancestry as Population Descriptors

Aravinda Chakravarti & Charmaine Royal

Open Session Agenda

Presentation:

Update on the H3Africa Program Jennifer Troyer

Concept Clearances:

Genomic-Enabled Learning Health Systems
Robb Rowley

Developing Novel Theory and Methods for Understanding the Genetic Architecture of Complex Traits

Alexander Arguello

Director's Report Outline

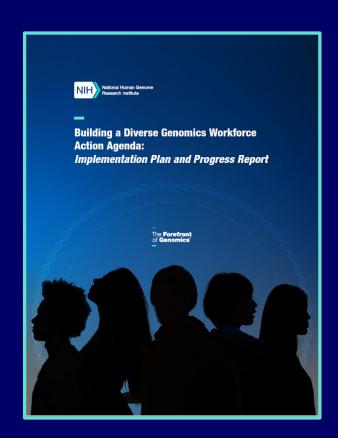
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- III. General Genomics Updates
- IV. NHGRI Extramural Research Program
- V. NIH Common Fund/Trans-NIH
- VI. NHGRI Communications, Policy, and Education
- VII. NHGRI Intramural Research Program

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Building a Diverse Genomics Workforce Action Agenda: Implementation and Progress Report

- Details programs, projects, initiatives, and engagements that have been enacted since release of Action Agenda in 2021
- Diversifying the genomics workforce cannot be achieved without support from the scientific community



Human Genetics Scholars Initiative





- >20 predoctoral, postdoctoral, and early-career scholars visited NHGRI
- Discussed research funding and career development opportunities
- NHGRI has supported this initiative since 2019

NHGRI Leadership: Director's Working Group



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Departure of Director, Centers for Disease Control and Prevention



Rochelle Walensky, M.D., M.P.H.



Leadership Transition, NIH Office of AIDS Research



Maureen Goodenow, Ph.D.



Bill Kapogiannis, M.D.

New Director, NIH Tribal Health Research Office





Karina Walters, Ph.D., M.S.W.

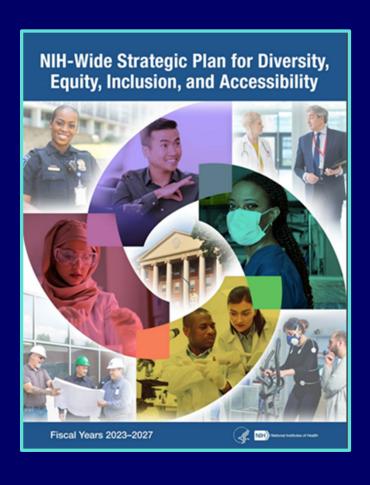
Departure of Senior Advisor, NIH Office of the Director



Carrie Wolinetz, Ph.D.



NIH-Wide Strategic Plan for Diversity, Equity, Inclusion, and Accessibility (DEIA)



- Fiscal Years 2023-2027
- NIH's role as a people-centered organization
- Encourages enhancing DEIA in operations, workforce, and research
- Crosscutting themes promoting transparency, communication, and engagement; fostering sustainable change; and harnessing data
- Roadmap for NIH-supported institutions

Recommendations for Improving National Research Service Award (NRSA) Fellowship Review

Recommendations for Improving NRSA Fellowship Review

Read the Request for Information on Recommendations for Improving NRSA Fellowship Review and Submit Comments



Submit Comments Online

Synopsis of Issue

NIH is recommending changes to the peer review of Ruth L. Kirschstein National Research
Service Award (NRSA) fellowship applications by restructuring the review criteria and modifying
some sections of the PHS Fellowship Supplemental Form that are specific to NRSAs. The goal of

RFI open through June 23, 2023

Request for Information (RFI) on Recommendations for Improving NRSA Fellowship Review

Notice Number:

NOT-OD-23-110

Key Dates

Release Date:

April 24, 2023

Response Date:

June 23, 2023

Fiscal Year 2024 Appropriations

	FY2022 (\$)	FY2023 (\$)	FY2024 PB (\$)	Increase (\$)	Increase (%)
NIH	\$46.178 billion *	\$49.178 billion *	\$51.098 billion *	\$1.92 billion	3.9%
NHGRI	\$636 million	\$661 million	\$661 million	\$0	0%

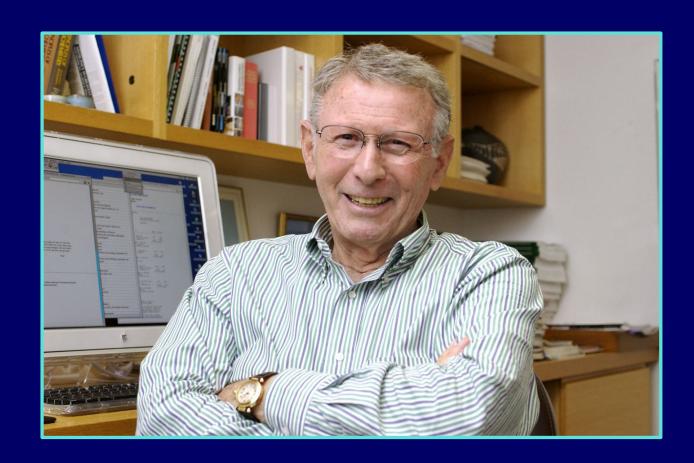
^{*} Includes appropriations for both NIH and ARPA-H

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Mourning the Loss of Paul Berg





Mourning the Loss of Casey Brown



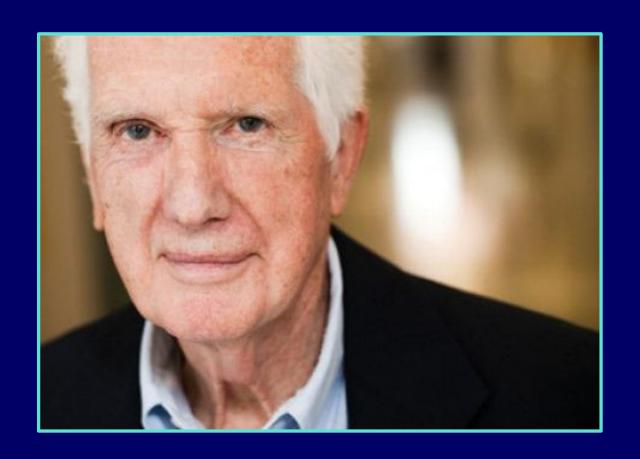


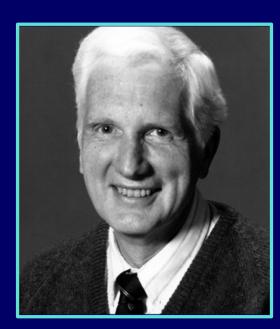
Mourning the Loss of Janet Sinsheimer





Mourning the Loss of Charles Scriver





New Director, Wellcome Sanger Institute



Matt Hurles, Ph.D.



Elected to National Academy of Sciences

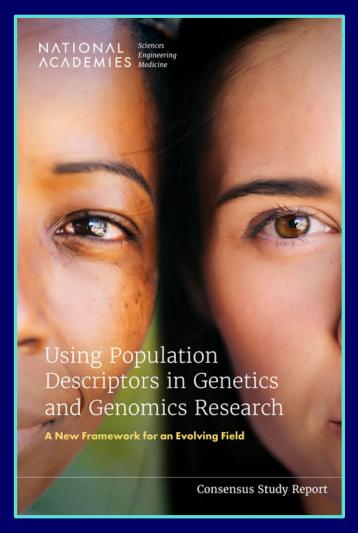


Spyros Artavanis-Tsakonas Claire Fraser Jo Handelsman Daphne Koller Leonid Kruglyak Xihong Lin

John O'Shea

Anna Marie Pyle
Richard Roberts
Yosef Shiloh
Alice Ting
Anne Yoder
Phil Zamore
Kenneth Zaret

NASEM Population Descriptors Report



- 14 NIH institutes, centers, and offices were co-sponsors
- NHGRI served as task co-leader with All of Us Research Program
- Past and current uses of population descriptors
- Proposes guiding principles and a new framework for the field
- Aravinda Chakravarti and Charmaine Royal will present later

NASEM Study: Toward Sequencing and Mapping RNA Modifications



- Public workshop held in March
- Facilitate additional community brainstorming and problemsolving

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Human Genome Reference Program (HGRP)



- Collection of high-quality reference human genome sequences
- Includes sequences from 47 people
- Four papers recently published



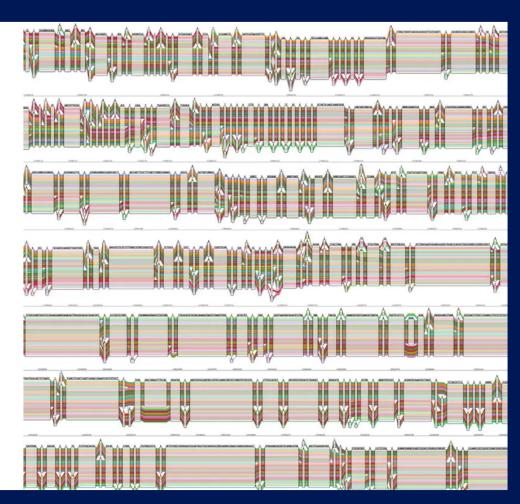
Human Genome Reference Program (HGRP)

The New York Times

Account

Scientists Unveil a More Diverse Human Genome

The "pangenome," which collated genetic sequences from 47 people of diverse ethnic backgrounds, could greatly expand the reach of personalized medicine.



Zoonomia Project



- Special issue in Science
- >150 researchers using comparative genomics to understand >240 species
- NHGRI-funded genome sequencing and analysis projects



Centers of Excellence in Genomic Science (CEGS)







PAR-23-098 CEGS Reissued
Next Receipt Dates: June 23, 2023; June 21, 2024

Molecular Phenotypes of Null Alleles in Cells (MorPhiC)

Data Production Reseach & Development Centers









PI: Paul Robson

PI: Danwei Huangfu

PI: Mazhar Adli

PI: Luke Gilbert

Data Resource & Administrative Coordinating Center



PI: Stephan Schürer

Data Analysis & Validation Centers

May 2023 Council

In-person meeting took place in January/February 2023

Document 21

Developmental Genotype-Tissue Expression (dGTEx)

Data Integration and Statistical Analysis Methods (DISAM) (U01 Clinical Trial Not Allowed)

U01 Research Project - Cooperative Agreements

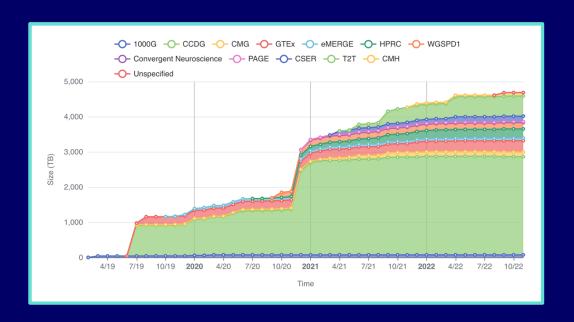




New Funding Opportunity Announcement:

- RFA-HG-23-005 Data Integration and Statistical Analysis Methods
- Develop methods for analyses of data from human and non-human primate dGTEx efforts
- Applications due Nov. 20, 2023

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





- Over 600,000 genomes and five petabytes of data
- AnVIL presented at AGBT Meeting in February 2023

Computational Genomics and Data Science (CGDS) Program

Genomic Community Resources

NHGRI Genomic Community Resources PAR-23-124

Due dates in 2023: May 25 and September 25

Trans-NIH Notice of Intent to Publish

Established Data Repositories and Knowledgebases NOT-OD-23-099

Early-stage Data Repositories and Knowledgebases NOT-OD-23-093

Earliest estimated application due date: Fall 2023

Genome-Wide Association Studies (GWAS) Catalog 15th Anniversary



- >515,000 curated associations from >6300 publications
- >60,000 user-submitted summary statistics
- >5,800 citations of the GWAS
 Catalog and associated papers



Credit: Jackie MacArthur

emerge network

ELECTRONIC MEDICAL RECORDS AND GENOMICS

Validate PRS in diverse populations

Combine with other forms of risk

Return results to patients and providers

Assess uptake of risk reduction recommendations

Genome-informed risk assessment (GIRA)

- □ PRS
- Monogenic risk
- **□** Family health history
- □ Clinical covariates

eMERGE has returned 753 results & 156 highrisk results

Marker paper published January 2023

ARTICLE

Returning integrated genomic risk and clinical recommendations: The eMERGE study



ARTICLE INFO

Article history:
Received 26 July 2022
Received in revised form
16 December 2022
Accepted 21 December 2022
Available online 6 January 2023

Keywords: Common variants Family history Genotyping Monogenic risks Polygenic risk scores

ABSTRACT

Purpose: Assessing the risk of common, complex diseases requires consideration of clinical risk factors as well as monogenic and polygenic risks, which in turn may be reflected in family history. Returning risks to individuals and providers may influence preventive care or use of prophylactic therapies for those individuals at high genetic risk.

Methods: To enable integrated genetic risk assessment, the eMERGE (electronic MEdical Records and GEnomics) network is enrolling 25,000 diverse individuals in a prospective cohort study across 10 sites. The network developed methods to return cross-ancestry polygenic risk scores, monogenic risks, family history, and clinical risk assessments via a genome-informed risk assessment (GIRA) report and will assess uptake of care recommendations after return of results.

Results: GIRAs include summary care recommendations for 11 conditions, education pages, and clinical laboratory reports. The return of high-risk GIRA to individuals and providers includes guidelines for care and lifestyle recommendations. Assembling the GIRA required infrastructure and workflows for ingesting and presenting content from multiple sources. Recruitment began in February 2022.

Conclusion: Return of a novel report for communicating monogenic, polygenic, and family history-based risk factors will inform the benefits of integrated genetic risk assessment for routine health care.

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Clinical Sequencing Evidence-Generating Research Program (CSER)



CSER at ACMG 2023: 10 oral presentations & 9 posters

Differences in genes implicated in disease comparing prenatal to pediatric patients (Sparks et al.)

Development and validation of new CSER-wide outcome measure to assess the impact of genomic sequencing on children and adults (Smith et al.)

Prenatal exome sequencing in an underrepresented population (Norton et al.)



Clinical Sequencing Evidence-Generating Research Program (CSER)

Lessons Learned and Challenges

Research during the COVID-19 pandemic

> Am J Med Genet A. 2023 Feb;191(2):391-399. doi: 10.1002/ajmg.a.63033. Epub 2022 Nov 7.

Conducting clinical genomics research during the COVID-19 pandemic: Lessons learned from the CSER consortium experience

Stephanie A Kraft ¹ ², Heidi Russell ³, Jeannette T Bensen ⁴, Katherine E Bonini ⁵, Jill O Robinson ⁶, Nuriye Sahin-Hodoglugil ⁷, Kathleen Renna ⁸ ⁹, Lucia A Hindorff ⁸, Dave Kaufman ⁹, Carol R Horowitz ¹⁰, Margaret Waltz ¹¹, Jamilyn M Zepp ¹², Sara J Knicht ¹³

Designing and implementing research in underrepresented populations

> Contemp Clin Trials. 2023 Feb;125:107063. doi: 10.1016/j.cct.2022.107063. Epub 2022 Dec 22.

Lessons learned while starting multi-institutional genetics research in diverse populations: A report from the Clinical Sequencing Evidence-Generating Research (CSER) consortium

Heidi Russell ¹, Hadley Stevens Smith ², Jeannette T Bensen ³, Priyanka Murali ⁴, Bart S Ferket ⁵, Candice Finnila ⁶, Lucia A Hindorff ⁷, Nurive Sahin-Hodoglugil ⁸



Clinical Genome Resource (ClinGen)

International Collaborations

H3Africa Workshop Participation



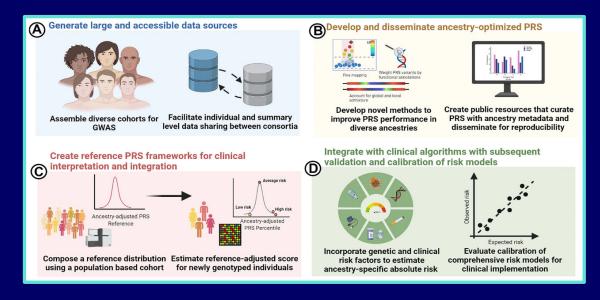
Variant Curation Interface Workshop, India 2022



Polygenic RIsk MEthods in Diverse Populations (PRIMED) Consortium



PRIMED publications (~32)



- Methods Review Working Group → Methods Development Working Group
- Joint meeting with eMERGE





Global Genomic Medicine Consortium (G2MC)

7th International Conference



- Campus Biotech in Geneva
- Genomic Medicine for Everyone
- Themes:

Implementation of Genomic Medicine

Collaboration

Diversity, Equity, & Inclusion (DEI) in Genomics

Registration now open

Advancing Genomic Medicine Research (AGMR)



Notice of Intent to Publish a Notice of Funding Opportunity for Advancing Genomic Medicine Research (R01/R21 Clinical Trial Optional)

Notice Numbers: NOT-HG-23-034, NOT-HG-23-035

Topics funded:

Undiagnosed diseases

EHR integrated tools

Evidence for clinical & economic value

Newborn screening

Promoting access for underserved populations

Technology Development Program

Virtual Outreach Series



- Direct RNA Sequencing & Base Modifications
- Single-Molecule Protein Sequencing
- Advances in Single-Cell Analysis
- Genome-Scale Regulatory Mechanisms

All events are free, virtual, and open to the public

Registration is required

Small Business Program

Transition Grant Opportunity

- Funding for early-career academic scientists interested in transitioning to entrepreneurship while supporting technology transfer
- Unique fast-track mechanism: Phase I STTR → Phase II SBIR



- Mentorship required and entrepreneurship training provided
- Partnership with NCI, NIBIB, and NIDA
- Applications due August 21, 2023

Training and Career Development Program









- 8th Annual Training Meeting
- Hosted by Duke University and held in Salt Lake City
- 300 in-person attendees and 50 virtual attendees

Genomics Workforce Diversity Programs

Notices of Funding Opportunities



 PAR-23-123: Entry-Level Modules (ELM) for Training the Genomics Research Workforce

Receipt date: June 1

 PAR-23-137: NIH Science Education Partnership Award (SEPA)

Receipt date: July 14

Extramural Investigator-Initiated Highlights

Multi-ancestry transcriptome-wide association analyses yield insights into tobacco use biology and drug repurposing

Fang Chen, Xing

Khunsriraksakul,

Allison E. Ashley

Bis, John Blange

Chuang, Adolfo

A cis-regulatory lexicon of DNA motif combinations mediating cell-type-specific gene regulation

Laura K.H. Donoh Poornima H. Neel and Paul A. Khaya

"Extremely slow and capricious": A qualitative exploration of genetic researcher priorities in selecting shared data resources



M. Grace Trinidad¹, Kerry A. Ryan², Chris D. Krenz², J. Scott Roberts^{2,3}, Amy L. McGuire⁴, Raymond De Vries^{1,2,5}, Brian J. Zikmund-Fisher^{2,3}, Sharon Kardia⁶, Erica Marsh⁵, Jane Forman⁷, Madison Kent⁸, David Wilborn⁹, Kayte Spector-Bagdady^{2,5,*}

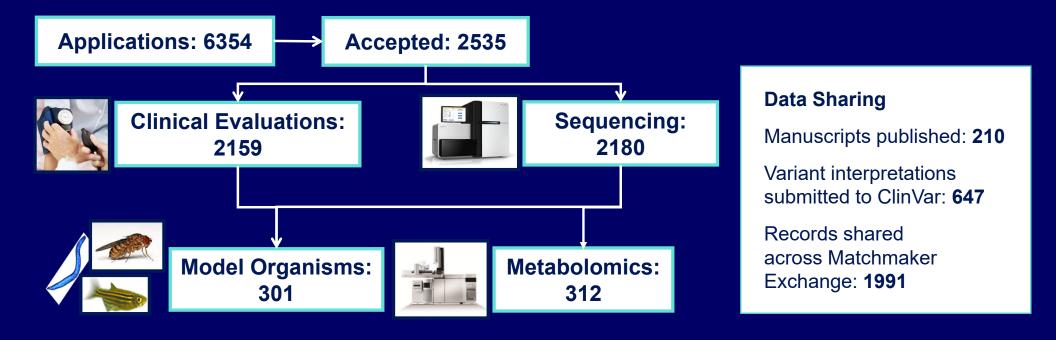
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Undiagnosed Diseases Network



Solving Medical Mysteries Through Team Science



Diagnosed: 679

Undiagnosed Diseases Network



- Transition from NIH Common Fund support to Trans-NIH support Led by NINDS and supported by 16 NIH institutes and centers:
 - NCATS, NCCIH, NCI, NEI, NHGRI, NHLBI, NIA, NIAID, NIAMS, NICHD, NIDCD, NIDCR, NIDDK, NIEHS, NIGMS, NLM
- Vision: evolve into a larger, self-sustained network to provide expert diagnostic services for undiagnosed patients and to foster scientific discovery
- Data Management Coordinating Center (Fiscal Year 2023-2027)
 Awarded to Harvard Medical School (PI: Kohane)
- Diagnostic Centers of Excellence

Bridge to Artificial Intelligence (Bridge2AI)

Four Centers:

Functional genomics

Voice as a biomarker of disease

AI/ML in acute care

Human health restoration after disease

- Bridge Center for cross-program coordination and dissemination
- First Bridge2Al in-person consortium meeting in April





Somatic Mosaicism Across Human Tissues (SMaHT)

Tissue Procurement Center



Data Analysis Center



Organizational Center



Genome Characterization Centers

Baylor College of Medicine
Broad Institute
New York Genome Center
Seattle Children's Hospital
Washington University

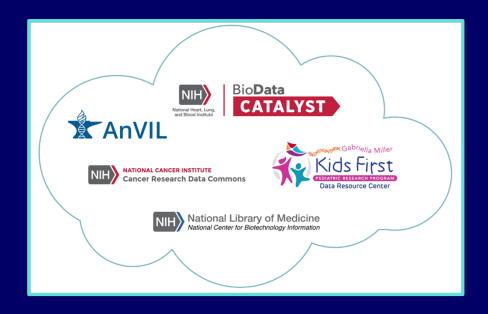
Tools and Technology Development Awards



- Release of nearly 250,000 whole-genome sequences
- 45% of data from people who identify as a member of a group underrepresented in medical research



NIH Cloud Platform Interoperability (NCPI)



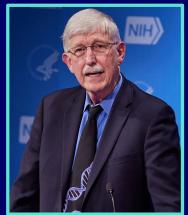
- Establish a trans-NIH, cloud-based, federated data ecosystem
- NCPI Administrative Coordinating Center
- Solicitations for interoperability projects

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2023 Genomics Anniversaries















New NHGRI Videos on GenomeTV/YouTube



Purifying Strawberry DNA



Sequencing a Genome

Human Genome Project 'G5' Virtual Reunion



Genome: Unlocking Life's Code Exhibition Pieces Now on Display at NIH



- Opened in 2013, traveled to 12 U.S. states and Canada
- Attracted millions of visitors over the last 10 years
- Five pieces of the exhibition now on display at NIH

Genomics Featured in National History Day

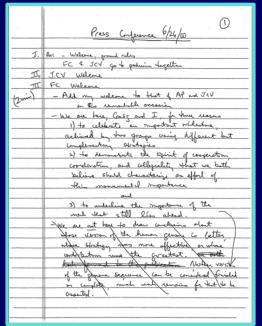


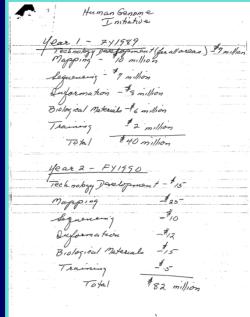


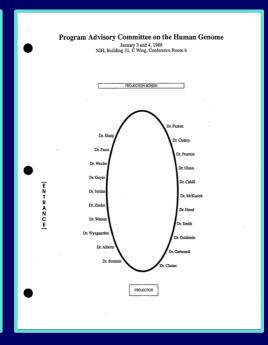
The Human Genome Project

NHGRI History of Genomics Program

Archive Highlight







Report of the International Strategy Meeting on Human Genome Sequencing held at the Princess Hotel, Southampton, Bermuda, on 25th-28th February 1996

Aims of the Meeting
To discuss mechanisms to co-ordinate, compare and evaluate different strategies for human genome mapping and sequencing.
To consider the potential role of new technologies in sequencing and informatics and to discuss different scenarios for data release.

Summary
The following principles were endorsed by all participants. These included officers from, and scientias supported by, the Welkome Frust, the UR. Medical Research Cosmici, the NHT NCHGR (Neticoal Institute of Fleth), National Center for Human Genome Project of Papara. It was noted that some centers may find it difficult to implement these principles because of logal constraints and it was, therefore, important that funding agencies were urged to fonter these policies.

Primary genomic sequences should be in the public domains.

It was agreed that all human genomic sequence information, generated by centres for large-scale human sequencing, should be freely available and in the public domain in order to encourage further research and development and to manistine the benefit to society.

Primary genomic sequences should be relaxed as soon as possible; in some centres, assembles of greater than 14 would be released as soon as possible; in some centres, assembles of greater than 15 would be refused as soon as possible; in some centres, assembles of greater than 15 would be refused as soon as possible; in some centres, assembles of greater than 15 would be refused as soon as possible; in some centres, assembles of greater than 15 condition for the public databases.

It was agreed that these principles should be publicated immediately to the public databases.

It was agreed that these principles should be good in order to recover sequences sequence center, funded for the public good, in order to prevent such centres establishing a privileged position in the exploitation and control of human s

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



ISCC-PEG 12th Annual Meeting

New Chief, Education and Community Involvement Branch



Beth Tuck, M.A.

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Samuel J. Heyman Service to America Medal Finalists





American Society of Human Genetics 2022 Presidential Address



ASHG AWARDS AND ADDRESSES

2022 ASHG presidential address— One human race: Billions of genomes

Charles N. Rotimil,*

This article is based on the address given by the author at the 2022 meeting of The American Society of Human Genetics (ASHG) in Los Angeles, California, The video of the original address can be found at the ASHG website.



and to engaging in discussions on research findings and as the president was made infinitely easier by the dedicamittees who volunteer to serve our society. My sincere gratitude to all

draw your attention to two upcoming events. (1) the Prespopulations with the resulting well-documented global idential Symposium on exciting dialogue about what African genomics is and is becoming. The symposium will scientists that are engaged in genomic sciences. As has highlight the profoundly dynamic and diverse continent's been acknowledged by me and others, if not urgently tific leadership, exciting investment in technology infrastructure, and more; how can and will genomics in Africa 'spread its wings," and what areas are most exciting? Join a global community for an exciting dialogue about what African genomics is-and is becoming-this Thursday, October 27, 2022, at 8:30 a.m. (2) The Interna- organizations, including the World Health Organization, tional Congress on Human Genetics is taking place the National Human Genome Research Institute at NIH. February 22 -26, 2023 in beautiful Cape Town, South Africa; the theme of the conference is "Coming Home," which acknowledges our common origin in the geographical region called Africa today. I do sincerely hope that you will join us in person because it is difficult if not impossible to "Come Home" virtually.

I will begin my address with an acknowledgement of the wonderful progress the global scientific community is making towards fulfilling the promise of how understanding the information coded in human genomes will revolutionize our appreciation of who we are, where our genetic ancestors come from, and why there is differential susceptibility or resistance to disease in diverse environmental contexts. The developing understanding of the evolutionary history and function of the about 4% of the modem human genome that came from interbreeding with archaic humans including Neanderthals and Denisovans I am excited to welcome you in person to Los Angeles for is a clear demonstration of the power of genomics. I use our 2022 annual meeting. I look forward to reconnecting this opportunity to congratulate our colleague, Svante with as many colleagues as possible in the coming days Pääbo, who was awarded this year's Nobel Prize in Physiology or Medicine for his discoveries concerning the gehow we move human genetics forward globally. I want nomes of extinct hominins and human evolution. Collecto thank all of you for placing your trust in me to serve tively, progress in human genetics and related fields is as your president this year. Performing my responsibilities moving us closer to the full integration of genomic understanding of biology into the day-to-day practice of medition and professionalism of the ASHG staff and my colleagues on the board of directors and on the various comof cancers, and gene-editing to cure sickle cell disease.

However, genomics-driven scientific and medical inno-Before I go into my presidential address, I would like to vations are currently not shared equitably by all human challenge of lack of diversity in both the participants and major advances, new directions and goals, emerging scien-and systematically addressed, these challenges will likely compromise our goal and vision that "people everywhere realize the benefits of human genetics and genomics research." While more work is needed. I am encouraged by efforts underway in Africa, the Middle East, Asia, and North and South America and the call to action by several the International Common Disease Alliance, the Global Alliance for Genomics and Health, and our society.

ASHG is contributing to achieving the promise of geno mics in a variety of ways, including (1) serving the research community by providing a forum where scientists present and share transformative approaches and technologies in

NHGRI Intramural Research Highlights



Biological Psychiatry

The impact of Mmu17 non-Hsa21 orthologous genes in the Ts65Dn mouse model of Down syndrome: the "gold standard" refuted



Science Advances

The dogs of Chernobyl: Demographic insights into populations inhabiting the nuclear exclusion zone

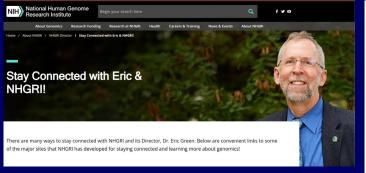


nature biotechnology

Telomere-to-telomere assembly of diploid chromosomes with Verkko

'One-Stop-Shop' to Stay Connected

genome.gov/stayconnected





Evolore the official website of the National Human Genome Research Institute.



The Genomics Landscape> Subscribe to Dr. Eric Green's monthly newsletter summarizing NHGRI and genomics highlights.



Dr. Eric Green on Twitter> Follow Dr. Fric Green on Twitter @NHGRI Director.



2020 NHGRI Strategic Vision> Read NHGRI's strategic vision for improving



Learn more about NHGRI and the institute's portfolio, and various other programs.

NHGRI Brochure



Genomic Terms> Gain a better understanding of hundreds of genetics and genomics terms and concepts using this educational NHGRI resource.





Building a Diverse Genomics Workforce>

Read about NHGRI's plans to increase the number of individuals from diverse backgrounds in the genomics workforce



GenomeTV

Watch GenomeTV, a vast collection of NHGRI videos, including live event coverage, scientific seminars, and educational films.



NHGRI's Oral History Collection>

View video interviews of those with perspectives and experiences in genomics programs and other NHGRI endeavors







Thanks!



Special Thanks!

