

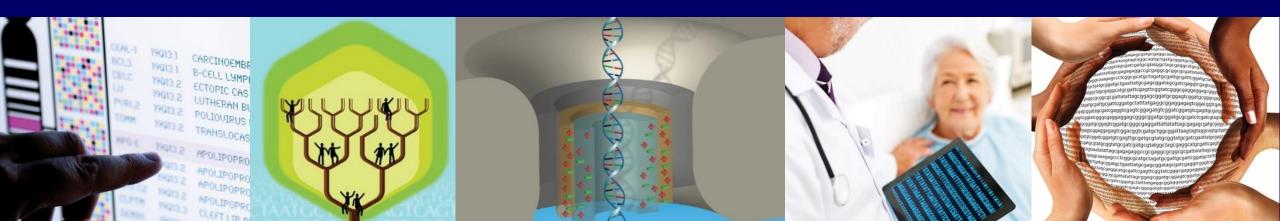


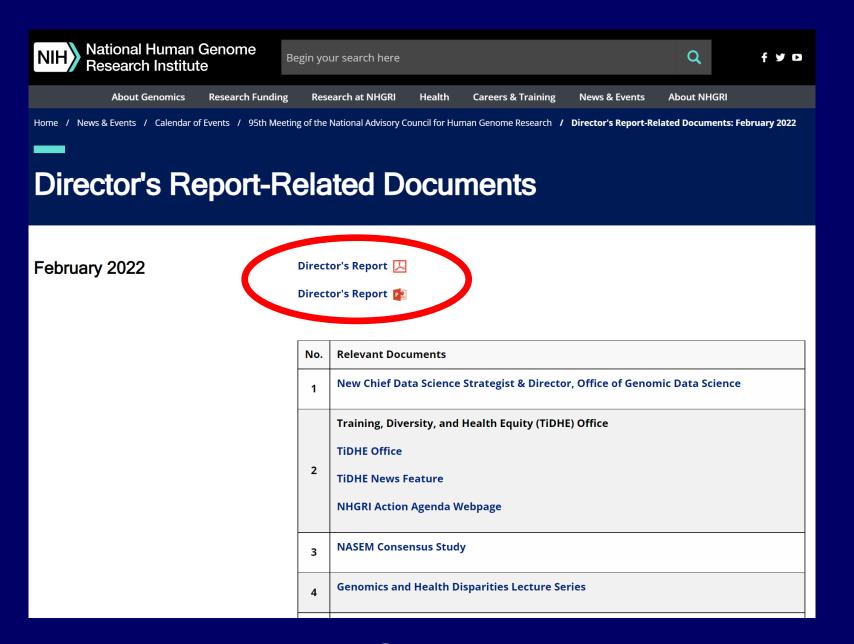


DIRECTOR'S REPORT

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

February 2022





genome.gov/DirectorsReport



Open Session Presentations

Presentations:

Expanding the Capacity to Conduct Gene x Environment Experiments

Rick Woychik

Future Directions of the NHGRI Analysis, Visualization, and Informatics Lab-space (AnVIL)

Marylyn Ritchie

Open Session Presentations

Concept Clearance:

Multi-Omics for Health and Disease Joannella Morales

Presentation:

Triennial Inclusion Report on Human Subjects Participation in NHGRI-Sponsored Research Christine Chang

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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Happy Institute'ness, NHGRI!



New Chief Data Science Strategist & Director, Office of Genomic Data Science



Valentina Di Francesco, M.S.

New Scientific Review Officer



Sarah Wheelan, M.D., Ph.D.

Training, Diversity, and Health Equity (TiDHE) Office



- Develop, support, and coordinate NHGRI programs that foster careers in genomics
- Advise divisions and branches about genomics workforce diversity and health equity
- Provide strategic programmatic leadership to reduce health disparities and advance health equity

Training, Diversity, and Health Equity (TiDHE) Office



Vence Bonham, J.D.



Faye Brown



Lorjetta Schools, M.B.A.



Jamil Scott, Ph.D.



Amber Jackson

New Lead Extramural Training Program Director



Lucia Hindorff, Ph.D., M.P.H.

New Health Equity and Workforce Diversity Program Director



Ebony Madden, Ph.D.

New Partnerships and Engagement Officer



Christina Daulton, M.A.

Industry Roundtables



- Two Industry Roundtables on diversifying the genomics workforce
- Strategies and methods of collaboration to attain a more diverse genomics workforce
- Meeting report forthcoming with objectives, themes, and next steps of engagement

NASEM Consensus Study

The National Academies of MEDICINE



- 14 NIH Institutes, Centers, Offices, & Programs co-sponsoring study (NHGRI as co-lead)
- Study committee announced on February 2
- Review existing methodologies, benefits, and challenges in the use of race and ethnicity and other population descriptors in genomics research
- Three public meetings planned
- **Final report in February 2023**

Genomics and Health Disparities Lecture Series



Alondra Nelson, Ph.D.

Deputy Director, Office of Science and Technology Policy | The White House

Presidential Rank Award



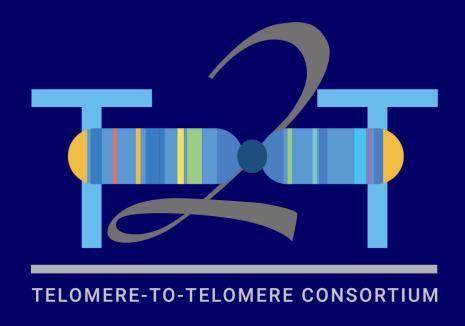
Teri Manolio, M.D., Ph.D.

Bold Predictions Seminar Series

Bold Predictions for Human Genomics by 2030: An NHGRI Seminar Series

- Two speakers discussed each Bold Prediction from the 2020 NHGRI Strategic Vision
- On average, 378 virtual attendees from 25 countries and 25 questions asked

Telomere-to-Telomere (T2T) Consortium



- Open, community-based effort to generate the first truly complete human genome sequence
- CHM13 sequence now complete
- Planning to complete additional, diverse human genome sequences and to help field transition to improved references

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Francis Collins Steps Down as Director, National Institutes of Health



Francis Collins, M.D., Ph.D.



Larry Tabak, D.D.S., Ph.D.



Dr. Francis Collins to step down as head of NIH





(CNN) — Dr. Francis Collins, the folksy, guitar-playing director of the National Institutes of Health (NIH), is planning to step down Tuesday as head of the gigantic research agency and return to

his previous job as the director of the National Human Genome Research Institute, the

Washington Post and Politico reported Monday night.





President Biden Visits NIH



Retirement of NIH Associate Director for Behavioral and Social Sciences Research



William Riley, Ph.D.



Christine Hunter, Ph.D., ABPP

NIH Genomic Data Sharing Policy

Request for Information on Proposed Updates and Long-Term Considerations for the NIH Genomic Data Sharing Policy

Notice Number:

NOT-OD-22-029

Key Dates

Release Date:

November 30, 2021

Response Date:

February 28, 2022

Responses due February 28, 2022

Fiscal Year 2022 Appropriations

	FY2022 House Labor-HHS Appropriation (passed)	Increase from FY2021	F2022 Senate Labor-HHS Appropriation (released)	Increase from FY2021
NIH	\$49.4 B	\$6.5 B * (15%)	\$47.9 B	\$5 B (12%)
NHGRI	\$646.3 M	\$30.5 M (5%)	\$634.6 M	\$18.8 M (3%)

^{*} House language designates that ARPA-H would receive \$3 billion of NIH's budget increase

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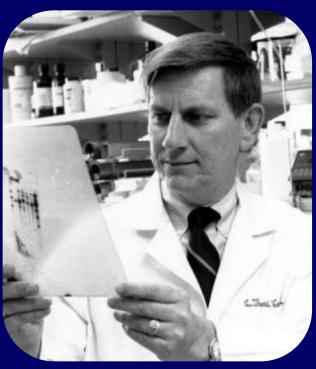
Mourning the Loss of Debbie Nickerson



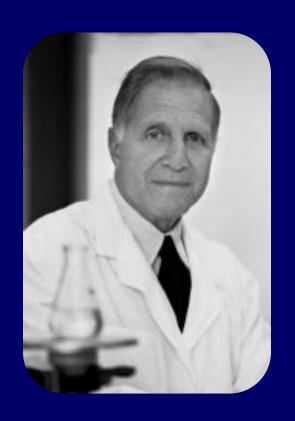


Mourning the Loss of Tom Caskey



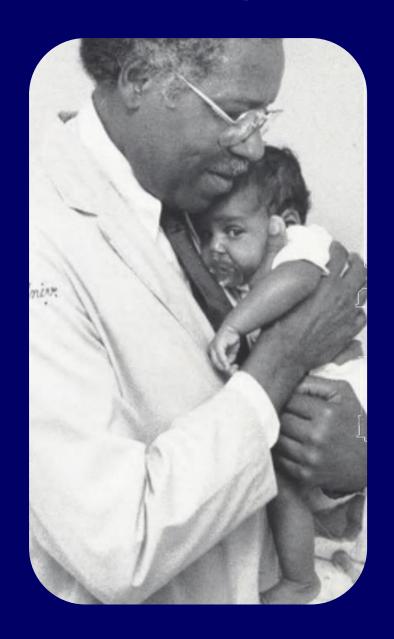


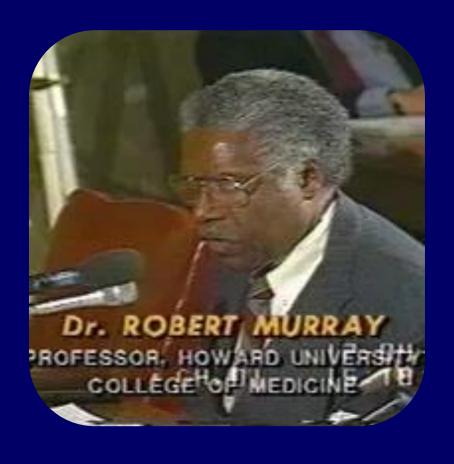
Mourning the Loss of Haig Kazazian





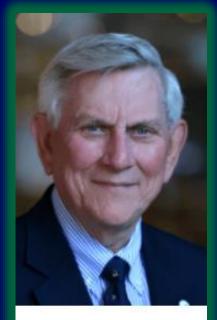
Mourning the Loss of Robert Murray





2021 American Society of Human Genetics Awards





C. Thomas Caskey, MD

Watch Award Lecture

2021 William Allan Award



Emmanouil Dermitzakis, PhD Watch Award Lecture 2021 Curt Stern Award



Wylie Burke, MD, PhD Watch Award Lecture 2021 McKusick Award



Sharon Terry, MA Watch Award Lecture 2021 Advocacy Award

Elected to National Academy of Medicine

Job Dekker
Paul Ginsburg
Vamsi Mootha

Marylyn Ritchie Sarah Tishkoff



Elected to AAAS

Christopher Austin
Yoav Gilad
Hopi Hoekstra
Tara Matise

Axel Meyer
Patrick Schloss
Kenneth Offit



New HHMI Investigators

Frederick Matsen
Dana Pe'er



New President, The Jackson Laboratory



Lon Cardon, Ph.D.



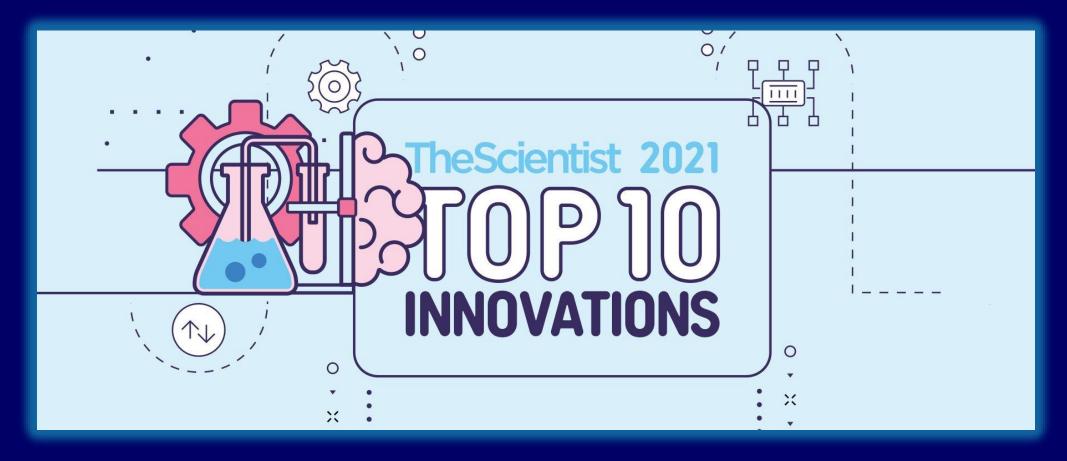
Science's 2021 Breakthrough of the Year & Runners Up





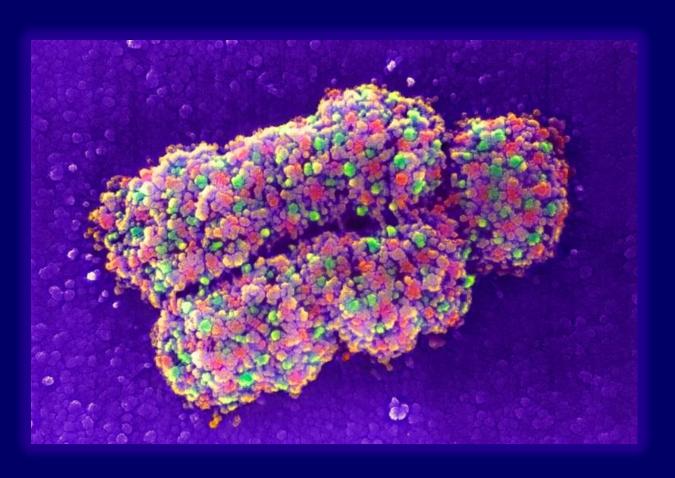


The Scientist's Top Technical Advances of 2021



Spatial genomics tools
Instruments for single-cell analysis
CRISPR-based SNP chip

Nature's Seven Technologies to Watch in 2022



- 1. Fully finished genomes
- 2. Protein structure solutions
- 3. Quantum simulation
- 4. Precise genome manipulation
- 5. Targeted genetic therapies
- 6. Spatial multi-omics
- 7. CRISPR-based diagnostics

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Genome Sequencing Program (GSP)

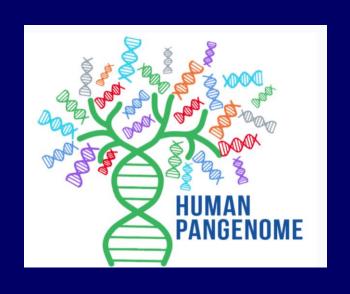
Centers for Mendelian Genomics Final Publication



Samantha M. Baxter, Jennifer E. Posey, Nicole J. Lake, Nara Sobreira, Jessica X. Chong, Steven Buyske, Elizabeth E. Blue, Lisa H. Chadwick, Zeynep H. Coban-Akdemir, Kimberly F. Doheny, Colleen P. Davis, Monkol Lek, Christopher Wellington, Shalini N. Jhangiani, Mark Gerstein, Richard A. Gibbs, Richard P. Lifton, Daniel G. MacArthur, Tara C. Matise, James R. Lupski, David Valle, Michael J. Bamshad, Ada Hamosh, Shrikant Mane, Deborah A. Nickerson, Centers for Mendelian Genomics Consortium, Heidi L. Rehm, Anne O'Donnell-Luria

- Final publication slated for Genetics in Medicine
- Article available in medRxiv

Human Genome Reference Program (HGRP)



TOWARDS A
COMPLETE
REFERENCE OF
HUMAN GENOME
DIVERSITY

- Generate ≥350 high-quality reference genome sequences; data from phased diploid genomes from 100 individuals released
- Annual HGRP meeting:

Embedded ELSI component

Multi-genome graph representation results are promising

International outreach: GA4GH, H3Africa

Comparative Genomics

Enabling Discovery through GEnomics (EDGE) Program





NHGRI-funded EDGE Awards:

Yang Da, University of Minnesota

Nadav Ahituv, UCSF

Lars Steinmetz, Stanford







- January 2022 Awardee meeting
- Next EDGE proposal due date: February 17, 2022

Technology Development Program



 Transformative Nucleic Acid Sequencing Technology Innovation and Early Development Next due date: March 1, 2022

 Advanced Genomic Technology Development Meeting

Hosted by the Technology Development Coordinating Center at the Jackson Laboratory

Small Business Program

- ~\$16.5 million in Fiscal Year 2021
- 10 Phase I Proof of Principle awards
- 15 Phase II Pre-Commercialization awards to companies including:



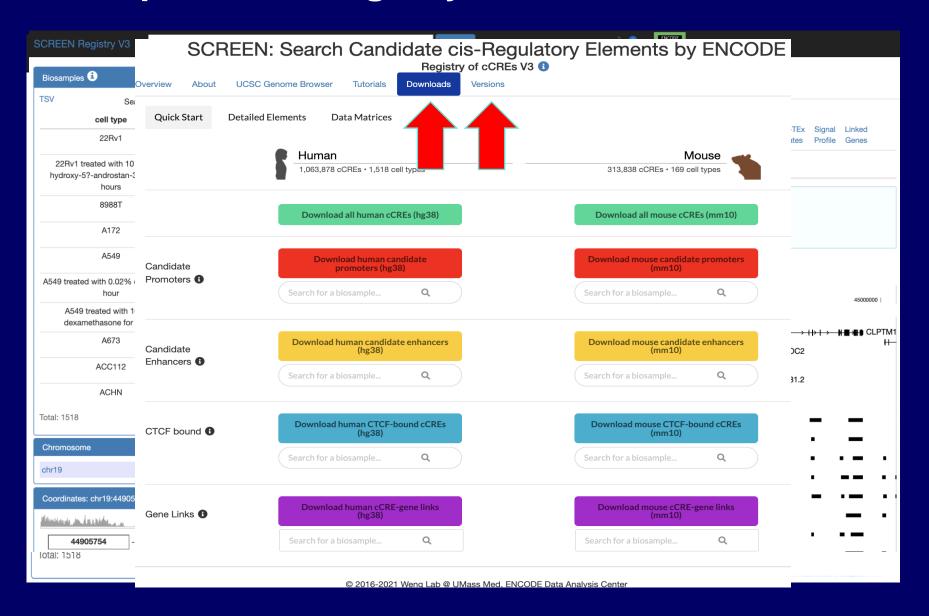








ENCyclopedia of DNA Elements (ENCODE)Updates to Registry of cCREs & SCREEN



ENCyclopedia of DNA Elements (ENCODE)

Highlights of cCRE Findings in 2021 Papers Funded by ENCODE



Volume 184, Issue 24, 24 November 2021, Pages 5985-6001.e19



Resource

A single-cell atlas of chromatin accessibility in the human genome

Kai Zhang ^{1, 6, 8}, James D. Hocker ^{1, 2, 3, 8}, Michael Miller ⁴, Xiaomeng Hou ⁴, Joshua Chiou ^{3, 5}, Olivier B. Poirion ⁴, Yunjiang Qiu ¹, Yang E. Li ^{1, 6}, Kyle J. Gaulton ^{5, 7}, Allen Wang ⁴, Sebastian Preissl ⁴, Bing Ren ^{1, 4, 6, 7, 9} $\stackrel{\triangle}{\sim}$

Article Published: 29 July 2021

Direct characterization of *cis*-regulatory elements and functional dissection of complex genetic associations using HCR–FlowFISH

Steven K. Reilly , Sager J. Gosai, Alan Gutierrez, Ava Mackay-Smith, Jacob C. Ulirsch, Masahiro Kanai, Kousuke Mouri, Daniel Berenzy, Susan Kales, Gina M. Butler, Adrianne Gladden-Young, Redwan M. Bhuiyan, Michael L. Stitzel, Hilary K. Finucane, Pardis C. Sabeti & Ryan Tewhey

Nature Genetics 53, 1166–1176 (2021) | Cite this article

7154 Accesses | 1 Citations | 62 Altmetric | Metrics

Genome-wide enhancer maps link risk variants to disease genes

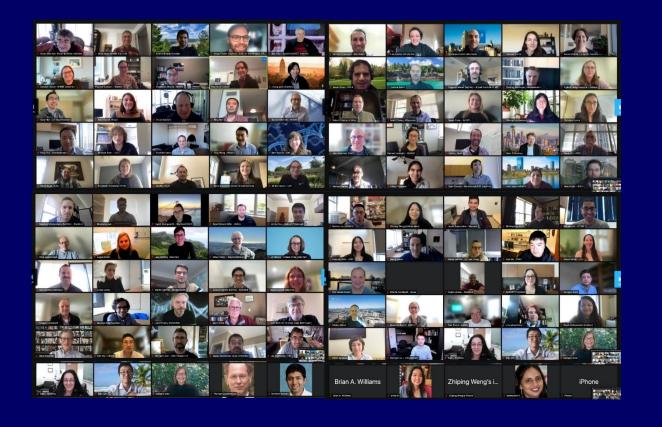
Joseph Nasser, Drew T. Bergman, Charles P. Fulco, Philine Guckelberger, Benjamin R. Doughty, Tejal A. Patwardhan, Thouis R. Jones, Tung H. Nguyen, Jacob C. Ulirsch, Fritz Lekschas, Kristy Mualim, Heini M. Natri, Elle M. Weeks, Glen Munson, Michael Kane, Helen Y. Kang, Ang Cui, John P. Ray, Thomas M. Eisenhaure, Ryan L. Collins, Kushal Dey, Hanspeter Pfister, Alkes L. Price, Charles B. Epstein, Anshul Kundaje, Ramnik J. Xavier, Mark J. Daly, Hailiang Huang, Hilary K. Finucane, Nir Hacohen, Eric S. Lander

Nature 593, 238–243 (2021) | Cite this article**

31k Accesses | 20 Citations | 255 Altmetric | Metrics**

Impact of Genomic Variation on Function (IGVF) Consortium Kick-Off Meeting: November 2021

Team Science Working Groups **Kick Off** Meeting Steering **Major Goals** Committee



Developmental Genotype-Tissue Expression (dGTEx) Project



Biospecimen Procurement Center (BPC)

National Disease Research Interchange

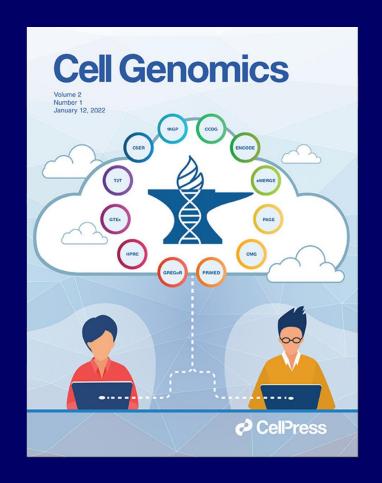
Laboratory, Data Analysis, and Coordinating Center (LDACC)

Broad Institute Yale University

Non-Human-Primate dGTEx applications reviewed in October 2021

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

- Future Directions of the NHGRI AnVIL Workshop (October 2021)
- Marker paper "Inverting the Model of Genomics Data Sharing with the NHGRI AnVIL" in Cell Genomics (January 2022)



Phenotypes and Exposures (PhenX) Toolkit



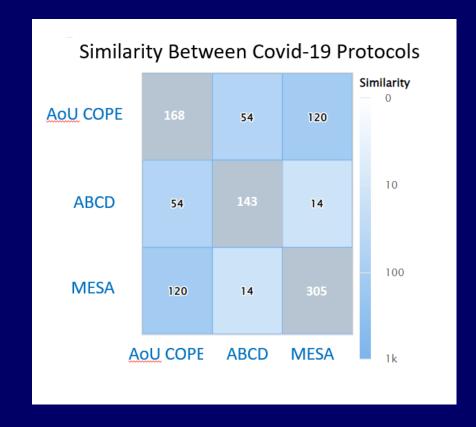
Sickle Cell Disease Curative Therapies

13 protocols released in August 2021

Funding: NHLBI

COVID-19 Variable Compare Tool

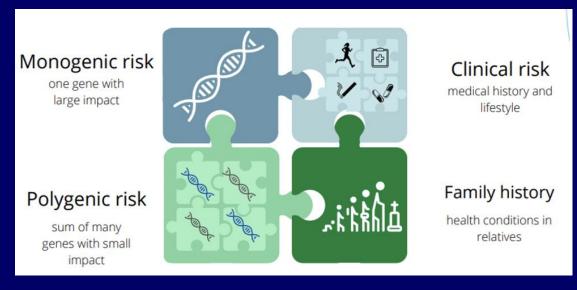
- 39 protocols
- Assesses content of COVID-19 protocols at the variable level



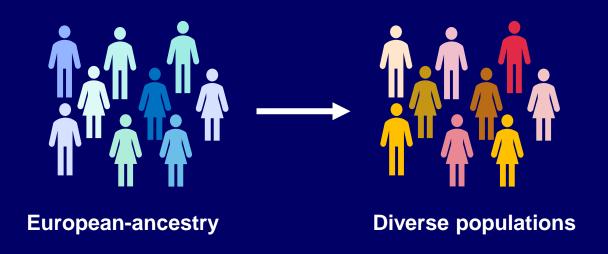




Received single Institutional Review Board approval



Combine monogenic risk, clinical risk, polygenic risk, and family history

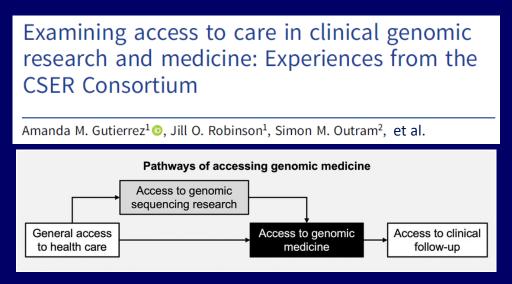


Research ways to apply Europeanancestry derived PRSs in diverse populations

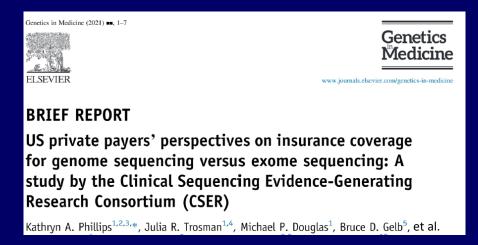
Begin enrolling 25,000-participant cohort in Spring 2022



Clinical Sequencing Evidence-Generating Research (CSER) Program



- Among 5 sites, ~19% of CSER participants experienced barriers
- Evaluation and improvement strategies
- Example: patient, family and provider interviews to identify barriers in accessing follow-up care



- Group interview of 12 payers
- Opportunities to advance coverage

Genome vs. exome sequencing

Methods for evidence generation

Consistency among labs

Implementation and care delivery



Clinical Genome Resource (ClinGen)

Grantees

PI Team	Institutions
Jonathan Berg	UNC Chapel Hill
Sharon Plon, Aleks Milosavljevic, Teri Klein	Baylor College of Medicine Stanford University
Heidi Rehm, Christa Martin, Erin Riggs	Broad Institute Geisinger

~\$14.5M per year (FY21-FY25)

Renewal Themes

- Engage relevant communities including patients, healthcare systems, scientific experts, and genetics professionals
- Increase scale and impact of ClinGen tools and curation results
- Expand diversity of curation workforce and databases



Clinical Genome Resource (ClinGen) ClinGen and GeT-RM Collaborative Project





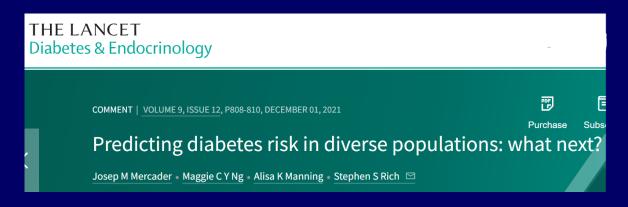


Expert Curated Variant List:

- Nominations from 36 ClinGen Expert Panels
- 546 variants in 84 genes, including 29 genes on ACMG Secondary Findings v3.0 List
- Heritable cancers, inborn errors of metabolism, cardiomyopathy, diabetes, and immune disorders

Polygenic Risk Methods in Diverse Populations (PRIMED) Consortium

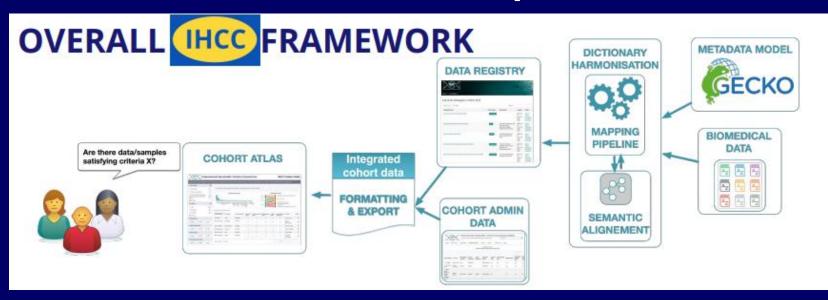


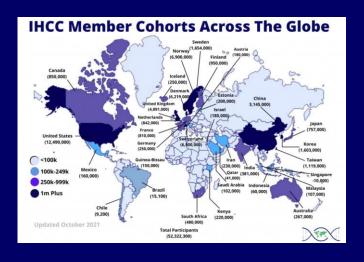


- New study site will be led by Iftikhar Kullo (Mayo Clinic)
- Broad Institute's D-PRISM study site publication about improving use of PRSs for assessing diabetes risk in diverse populations
- PRIMED website and Twitter now accessible to public

International 100K+ Cohort Consortium (IHCC)

IHCC Cohort Atlas Workshop





2021 Q4 IHCC Virtual Members Workshop



Workshop on Ethical, Legal, and Social Implications of Gene-Environment Interaction Research



- Community partnership throughout
- Communication on myriad downstream implications
- Importance and new challenges of data sharing
- Incorporating hypotheses on social determinants of health

Supporting Talented Early Career Researchers in Genomics

Supporting Talented Early Career Researchers in Genomics (R01 Clinical Trial Optional)

Activity Code

R01 Research Project Grant

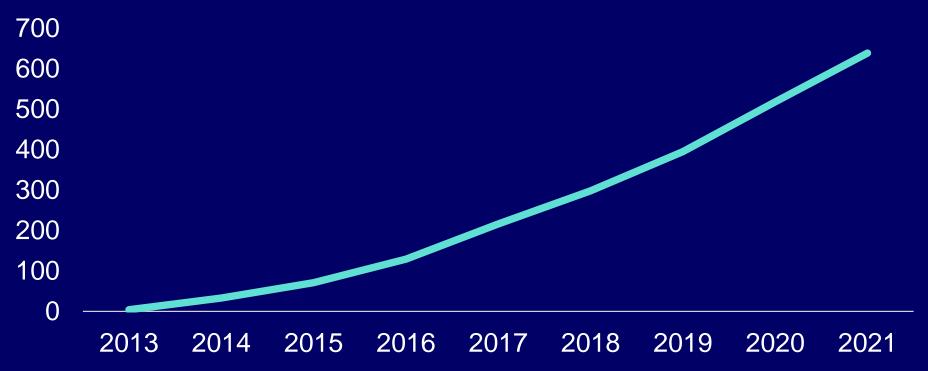
- RFA-HG-22-001
- Early-Stage Investigator (ESI) status
- First receipt date: March 4, 2022
- Additional receipt dates: Feb 2023 & Feb 2024

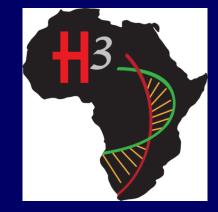
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Human Heredity & Health in Africa (H3Africa)

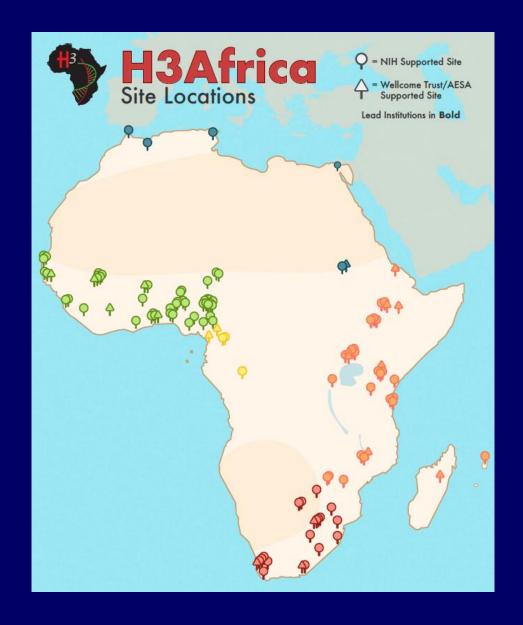






- 600+ publications to date
- Continued involvement in COVID-19 response
- 18th Consortium Meeting

Human Heredity & Health in Africa (H3Africa)



 H3Africa investigators received new awards

PRIMED





DS-I Africa

NIH and others

Final year of program

Publications

Finale Consortium Meeting



4D Nucleome (4DN)

Bonora et al. Genome Biology (2021) 22:279 https://doi.org/10.1186/s13059-021-02432-w

Genome Biology

ANALYSIS

https://doi.org/10.1038/s41592-021-01248-7



RESEARCH **Open Access**



OPEN

Systematic evaluation of chromosome conformation capture assays

Betul Akgol Oksuz^{1,10}, Liyan Yang^{1,10}, Sameer Abraham ⁰², Sergey V. Venev¹, Nils Krietenstein Christine M. Disteche^{5,6,12*} Krishna Mohan Parsi 604,5, Hakan Ozadam^{1,6}, Marlies E. Oomen 601, Ankita Nand 601, Hui Mao^{4,5}, Ryan M. J. Genga^{4,5}, Rene Maehr^{10,4,5}, Oliver J. Rando^{10,3}, Leonid A. Mirny^{10,2,7,8}, Johan H. Gibçus^{11,23}

configuration and gene expression during

Giancarlo Bonora¹, Vijay Ramani², Ritambhara Singh^{3,4}, He Fang⁵, Dana L. Jackson¹, Sanjay Srivatsan¹, Ruolan Qiu¹, Choli Lee¹, Cole Trapnell^{1,6,7}, Jay Shendure^{1,6,7,8}, Zhijun Duan^{9,10}, Xinxian Deng^{5*}, William S. Noble^{1,11*} and

Cell-type specialization is encoded by specific chromatin topologies

stem cell differentiation and X inactivation



Article

RNA promotes the formation of spatial compartments in the nucleus

Sofia A. Quinodoz, Joanna W. Jachowicz, Prashant Bhat, 1,2,5 Noah Ollikainen, 1,5 Abhik K. Banerjee, 1,3,6 Isabel N. Goronzy, 1,2,6 Mario R. Blanco, 1 Peter Chovanec, 1 Amy Chow, 1 Yolanda Markaki, 4 Jasmine Thai, 1 Kathrin Plath, 4 and Mitchell Guttman 1,7,8



Check for updates

https://doi.org/10.1038/s41586-021-04081-2 Received: 4 August 2020 Accepted: 30 September 2021 Published online: 17 November 2021 Open access

Warren Winick-Ng^{1,22 ⋈}, Alexander Kukalev^{1,22}, Izabela Harabula^{1,2,22}, Luna Zea-Redondo^{1,2,22} Dominik Szabó^{1,2,22}, Mandy Meijer³, Leonid Serebreni^{1,16}, Yingnan Zhang⁴, Simona Bianco⁵, Andrea M. Chiariello⁵, Ibai Irastorza-Azcarate¹, Christoph J. Thieme¹, Thomas M. Sparks¹, Sílvia Carvalho^{1,6,7,8}, Luca Fiorillo⁵, Francesco Musella⁵, Ehsan Irani^{1,9}, Elena Torlai Triglia^{1,17} Aleksandra A. Kolodziejczyk^{10,11,18}, Andreas Abentung^{12,19}, Galina Apostolova¹², Eleanor J. Paul^{13,20,21}, Vedran Franke¹⁴, Rieke Kempfer^{1,2}, Altuna Akalin¹⁴, Sarah A. Teichmann^{10,11}, Georg Dechant¹², Mark A. Ungless¹³, Mario Nicodemi^{5,9}, Lonnie Welch⁴, Gonçalo Castelo-Branco^{3,15} & Ana Pombo^{1,2,9} ⊠

A of US RESEARCH PROGRAM

Chief Engagement Officer



Karreim Watson, D.H.Sc.

Chief Medical and Scientific Officer



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

Chief Cohort Development Officer



Holly Garriock, Ph.D.

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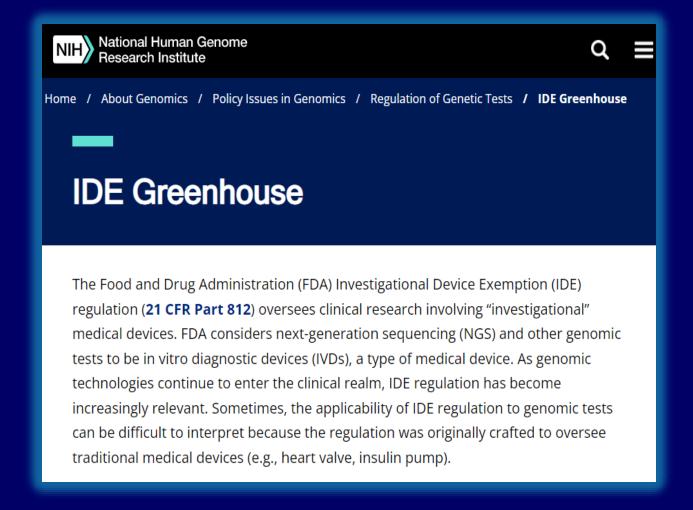
New Informed Consent Information



Two New Fact Sheets
 The informed consent process
 Why is informed consent required?

Informed Consent Resource
 Required Elements of Informed Consent
 Considerations for Genomics Research
 Sample Informed Consent Forms

Investigational Device Exemption (IDE) Greenhouse



New educational resource with reference application documents

New and Refreshed NHGRI Fact Sheets





Introducing The Forefront of Genomics Newsletter



NHGRI History of Genomics Program

The Meaning of Eugenics: Historical and Present-Day Discussions of Eugenics and Scientific Racism



- Examined the history of eugenics, scientific racism, and complex legacies in the modern health sciences
- Over 1400 registered attendees

UNITED STATES HOLOCAUST MEMORIAL MUSEUM



NHGRI History of Genomics Program Eugenics and Scientific Racism Fact Sheet & Timeline





Fact Sheet

Timeline

Family Health History Social Media Campaign #FamilyHealthDay2021





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



Lisa Ferrand, MSA, CRNA, APRN



Abimbola Oladayo, B.D.S., M.P.H.

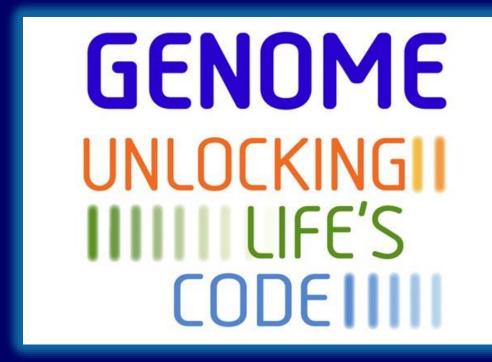


Katharine Press (KP) Callahan, M.D.



Sarah Roth, M.A.

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





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New Chair, National Cancer Advisory Board



John Carpten, Ph.D.

History of Population Descriptors in Genetics

ARTICLE

Evolving use of ancestry, ethnicity, and race in genetics research—A survey spanning seven decades

Yen Ji Julia Byeon,^{1,3} Rezarta Islamaj,² Lana Yeganova,² W. John Wilbur,² Zhiyong Lu,² Lawrence C. Brody,^{4,*} and Vence L. Bonham^{3,*}

Human geneticists curb use of the term 'race' in their papers

Field still struggles with how to accurately describe populations, study finds

2 DEC 2021 · 5:30 PM · BY RODRIGO PÉREZ ORTEGA

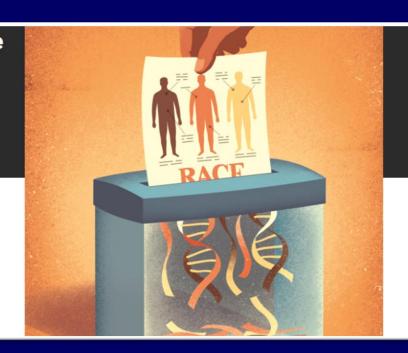
SHARE:





f

Human geneticists have mostly abandoned the word "race" when describing populations in their papers, according to a new study of research published in a leading genetics journal. That's in line with the current scientific understanding that race is a social construct, and a welcome departure from research that in the past has often conflated genetic variation and racial categories, says Vence Bonham, a social scientist at the National Human Genome Research Institute who led the study.



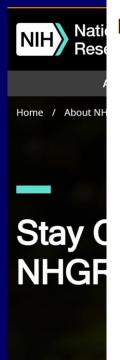
High-Profile Intramural Research Program Highlights



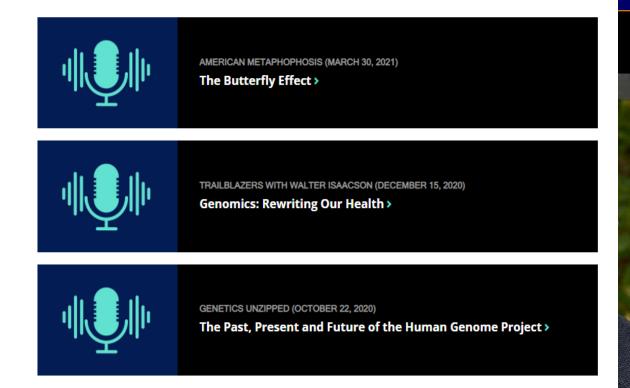




'One-Stop-Shop' to Stay Connected genome.gov/stayconnected



Podcasts



There are ma of the major :

Op-Eds/Commentaries

An Anti-racist Action Plan for Studying the Human Genome

The Hill, September 16, 2021

A Vision for the Next Decade of Human Genomics Research

Scientific American, October 28, 2020



Thanks!





Special Thanks!

