National Human Genome Research Institute

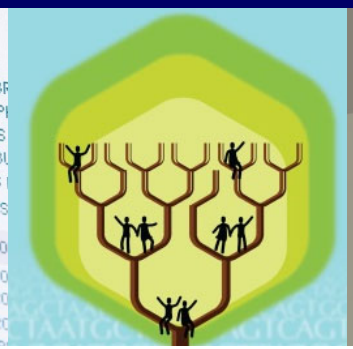
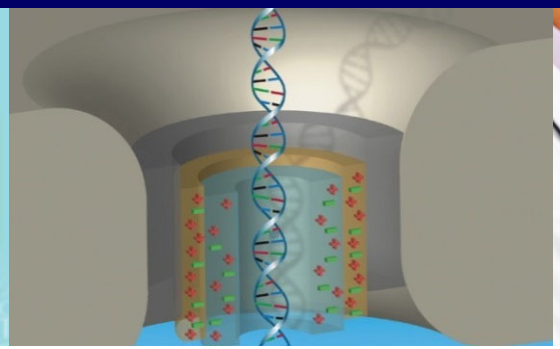
The Forefront of Genomics®

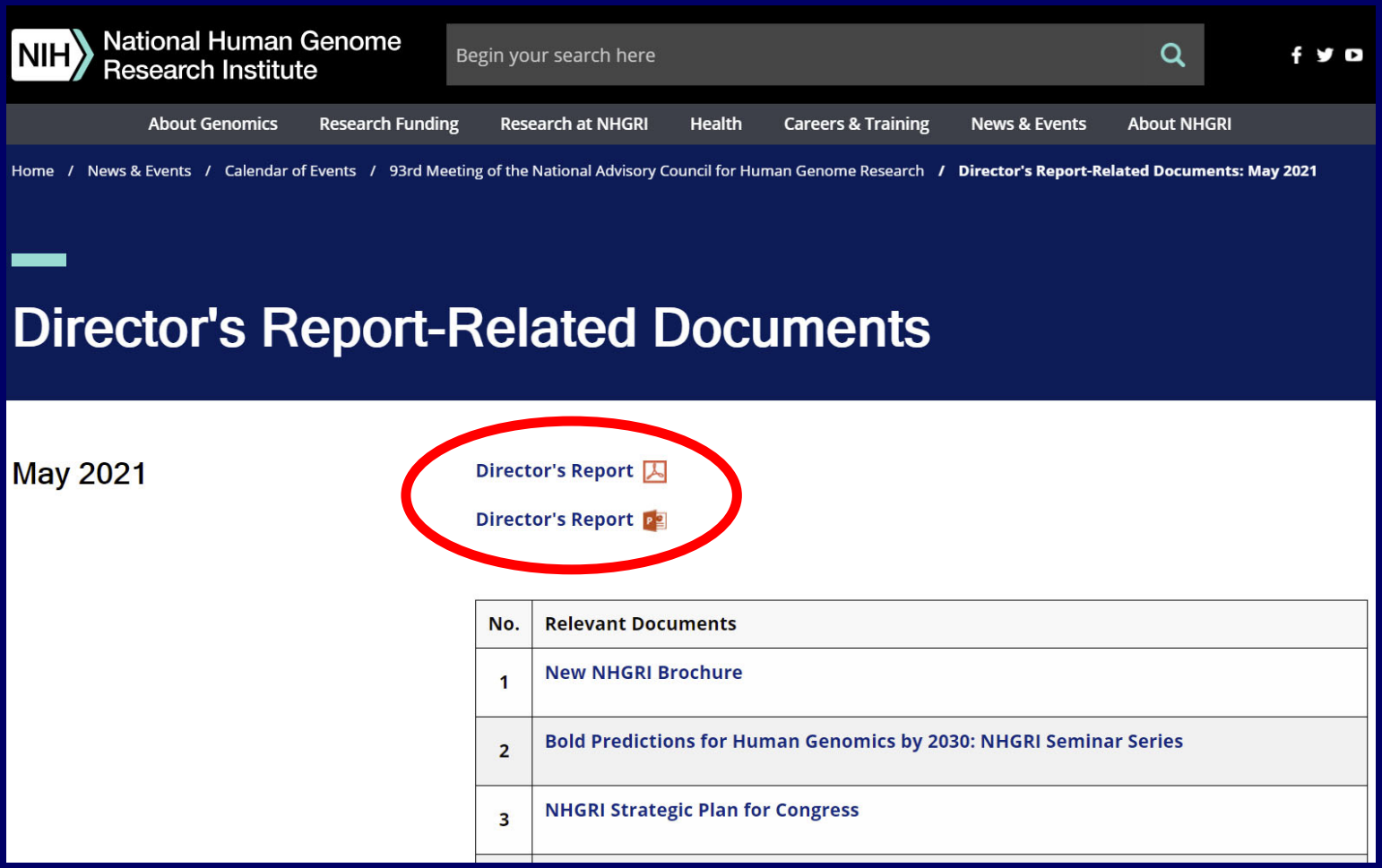
DIRECTOR'S REPORT

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

Director, NHGRI

May 2021



genome.gov/DirectorsReport

Document #

Open Session Presentations

Presentations:

Genomics & Society Working Group of NACHGR Annual Report
Steven Joffe

Genomic Medicine Working Group of NACHGR Annual Report
Teri Manolio

Open Session Presentations

Concept Clearances:

Supporting Talented Early Career Researchers in Genomics
Lisa Chadwick

Centers of Excellence in Genomic Science (CEGS) Program
Adam Felsenfeld

The Knockout Mouse Phenotyping Program
Colin Fletcher

Curriculum Development in Genomics, Genetics, or Genomic Informatics for Medical Students
Heather Colley

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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 NHGRI Brochure

- NHGRI's history, organization, values, and major research areas
- PDF and 'flipbook' versions available at genome.gov/brochure
- Printed copies will be available on request

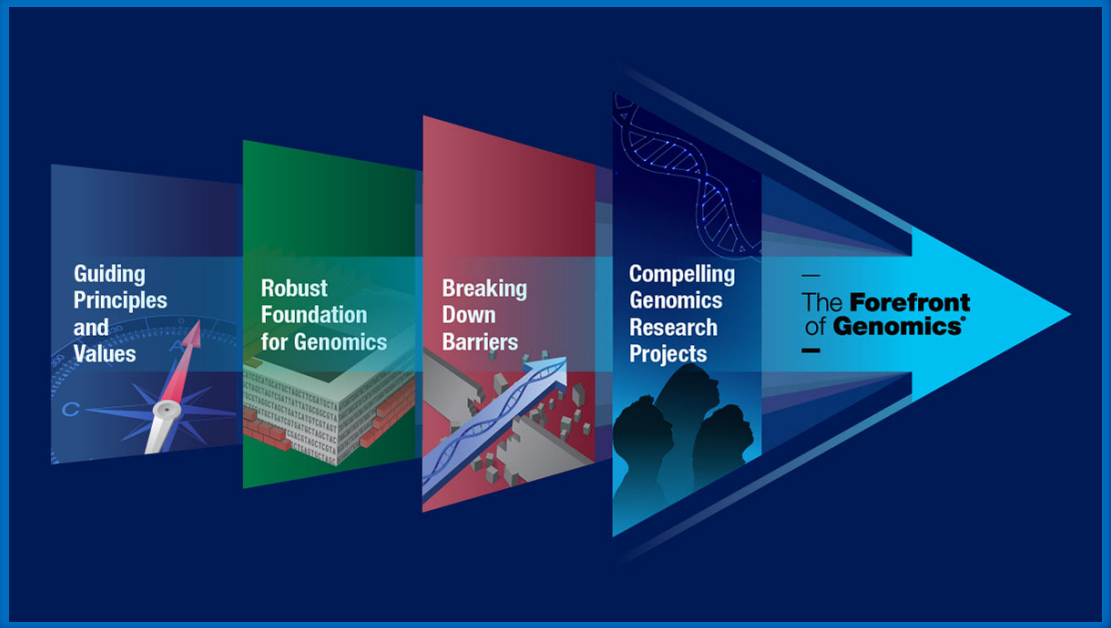
Document 1

Bold Predictions for Human Genomics by 2030

NHGRI Seminar Series

Document 2

NHGRI Strategic Plan for Congress



Perspective

Strategic vision for improving human health at The Forefront of Genomics

https://doi.org/10.1038/s41586-020-2817-4
Received: 30 June 2020
Accepted: 4 September 2020
Published online: 28 October 2020
Check for updates

Eric D. Green[✉], Chris Gunter[1], Leslie G. Biesecker[2], Valentina Di Francesco[3], Carla L. Easter[4], Elise A. Feingold[5], Adam L. Felsenfeld[6], David J. Kaufman[7], Elaine A. Ostrander[8], William J. Pavan[9], Adam M. Phillippy[9], Anastasia L. Wise[1], Jyoti Gupta Dayal[1], Britny J. Kish[1], Allison Mandich[1], Christopher R. Wellington[1], Kris A. Wetterstrand[1], Sarah A. Bates[1], Derryl Leja[1], Susan Vasquez[1], William A. Gahl[1], Bettie J. Graham[1], Daniel L. Kastner[1], Paul Liu[1], Laura Lyman Rodriguez[1], Benjamin D. Solomon[1], Vence L. Bonham[1], Lawrence C. Brody[1], Carolyn M. Hutter[1] & Teri A. Manolio[1]

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 researchers began an audacious journey to generate the first map and sequence of the human genome, marking the start of a 13-year odyssey called the Human Genome Project[1–3]. The successful and early completion 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[4]. This decrease has allowed the generation of innumerable genome sequences, including 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 elements[5,6]. These new tools, together with increasingly sophisticated statistical and computational methods, have enabled researchers to create rich catalogues of human genomic variants[7,8], to gain an ever-deepening understanding of the functional complexities of the human genome[9], and to determine the genomic bases of thousands of human diseases[10,11]. In turn, the past decade has brought the initial realization of genomic medicine[12], as research successes have been converted into powerful tools for use in healthcare, including somatic genome analysis for cancer (enabling development of targeted therapeutic agents)[13], non-invasive prenatal genetic screening[14], and genomics-based tests for a growing set of paediatric conditions and rare disorders[15], 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 of biomedical research, medical practice, and society. The scope, scale, and pace of genomic advances so far were nearly unimaginable when the Human Genome Project began; even today, such advances are yielding 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 Genome Project in 2003[16] and then again at the beginning of the last decade in 2011[17]. These visions outlined the most compelling opportunities 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 from a large number of stakeholders, with the resulting input catalogued and synthesized using the framework depicted in Fig. 1.

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.

National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, USA. ✉e-mail: egreen@nhgri.nih.gov

- NIH Institutes/Centers required to submit a plan every 5 years
- Companion document to go with 2020 NHGRI Strategic Vision
- Develop a framework for crafting next plan in 5 years

Document 3

NHGRI Staff Volunteer in Support of Unaccompanied Children's Program

ACF

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New Secretary, Department of Health and Human Services

Xavier Becerra, J.D.

Departure of Director, National Center for Advancing Translational Sciences

Chris Austin, M.D.

Joni Rutter, Ph.D.

Document 5

NIH UNITE Initiative

U — Understanding stakeholder experiences through listening and learning
N — New research on health disparities, minority health, and health equity
I — Improving the NIH culture and structure for equity, inclusion, and excellence
T — Transparency, communication, and accountability with our internal and external stakeholders
E — Extramural research ecosystem: changing policy, culture, and structure to promote workforce diversity

Document 6

NIH COVID-19 Information Resources

- **NOT-OD-21-106: Continuation of Temporary Extension of Eligibility for the NIH K99/R00 Pathway to Independence Award During the COVID-19 Pandemic**
- **RFA-OD-21-009: RADx-UP - Social, Ethical, and Behavioral Implications Research on Disparities in COVID-19 Testing among Underserved and Vulnerable Populations**

OPEN MIKE

Helping connect you with the NIH perspective, and helping connect us with yours.

Fiscal Year 2022 Appropriations

	Fiscal Year 2021 Enacted	Fiscal Year 2022 President's Budget Outline	$ Increase	% Increase
HHS	$108.6 B	**$133.7 B**	$25.1 B	**23.1%**
NIH	$41.7 B	**$51.0 B**	**$9.0 B** *	21.6%
NHGRI	$606.3 M	TBD	TBD	TBD

*** ARPA-H would receive $6.5 billion of the $9 billion increase for NIH**

NIH Feline-in-Chief and Head NIH Zoom Bomber

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Mourning the Loss of Mark Boguski

Document 9

Elected to National Academy of Sciences

Katherine High

Kenneth Lange

David Liu

Olufunmilayo Olopade

Elected to American Academy of Arts & Sciences

Charles Rotimi

Sarah Tishkoff

Document 11

2021 ACMG David L. Rimoin Lifetime Achievement Award in Medical Genetics

ACMG Foundation for Genetic and Genomic Medicine

Better Health Through Genetics™

Ada Hamosh, M.D., M.P.H, FACMG

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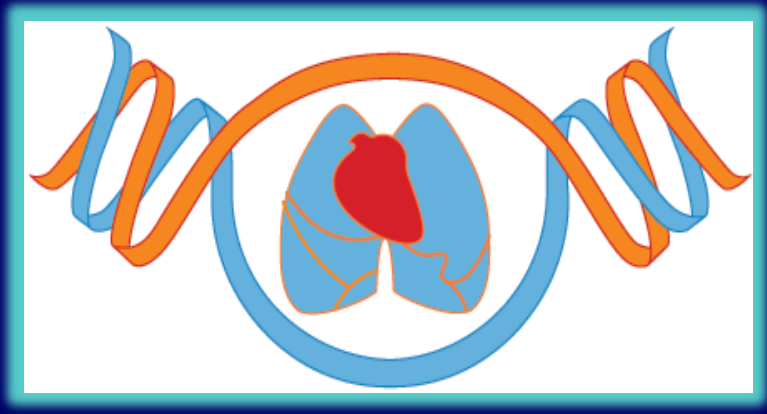
Genome Sequencing Program

Final GSP datasets in AnVIL

Joint GSP-TOPMed Workshop

- Data sharing
- Data analysis



Comparative Genomics

Notice of Intent to Publish a Funding Opportunity Announcement for Non-Human Primate Developmental Genotype-Tissue Expression (NHP dGTEx) Project (U24 Clinical Trials Not Allowed)

Notice Number:

NOT-HG-21-027

- **Study gene-expression patterns in non-human primates and compare to humans**
- **Expected due date: Summer 2021**

Technology Development Program

Funding Opportunities:

Notice of Special Interest: Advancing Genomic Technology Development for Research and Clinical Application

- NOT-HG-21-018

Transformative Nucleic Acid Sequencing Technology Innovation and Early Development

- RFA-HG-21-007 (R01, also linked R21 and R43/44)
- First due date: June 25, 2021

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

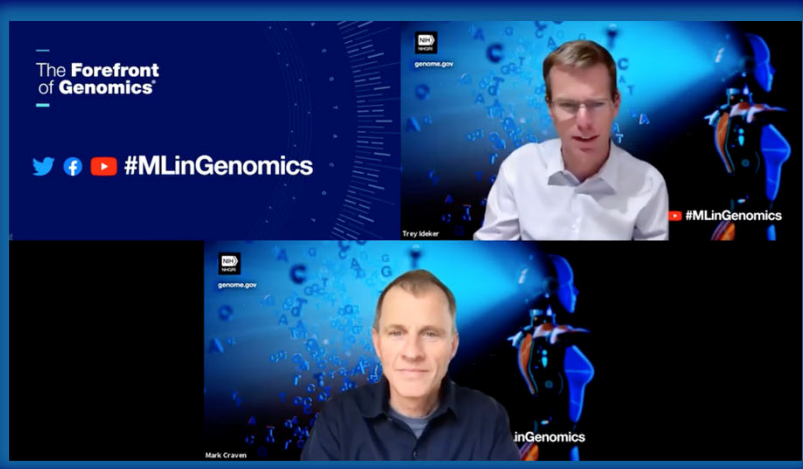
Genomic Data Science Community Network

- Partnerships from diverse spectrum of institutions
- Develop curricula for undergraduate students

Virtual Applied Data Science Training Institute

- Free eight-week training series
- AnVIL-led session on cloud computing

NHGRI Genomic Data Science Working Group



- Define key areas in genomics for machine learning analysis and NHGRI's role in machine learning research for both genomic medicine and genomic sciences
- Nearly 1,800 participants
- Video recordings and presentations available on workshop webpage

Clinical Genome Resource (ClinGen)

nature

Perspective | Published: 10 March 2021

Improving reporting standards for polygenic scores in risk prediction studies

Hannah Wand, Samuel A. Lambert, Cecelia Tamburro, Michael A. Iacocca, Jack W. O'Sullivan, Catherine Sillari, Iftikhar J. Kullo, Robb Rowley, Jacqueline S. Dron, Deanna Brockman, Eric Venner, Mark I. McCarthy, Antonis C. Antoniou, Douglas F. Easton, Robert A. Hegele, Amit V. Khera, Nilanjan Chatterjee, Charles Kooperberg, Karen Edwards, Katherine Vlessis, Kim Kinnear, John N. Danesh, Helen Parkinson, Erin M. Ramos, Megan C. Roberts, Kelly E. Ormond, Muin J. Khoury, A. Cecile J. W. Janssens, Katrina A. B. Goddard, Peter Kraft, Jaqueline A. L. MacArthur, Michael Inouye & Genevieve L. Wojcik ✉ -Show fewer authors

Nature **591**, 211–219(2021) | Cite this article

6887 Accesses | **322** Altmetric | Metrics

Complex Disease Working Group publishes reporting standards for polygenic scores

Includes guidance for:

- **Score development**
- **Describing study populations**
- **Score evaluation**
- **Clinical applications**

Curating the Clinical Genome (CCG)

ClinGen and DECIPHER Host Annual Conference

Topics included:

- Polygenic risk scores across populations
- Estimating penetrance
- Non-invasive prenatal testing
- Precision oncology
- Sharing data and associated clinical phenotypes

Clinical Sequencing Evidence-Generating Research Program

Usual care minimal checklist

- ✓ Client-centered
- ✓ Respectful
- ✓ Culturally informed
- ✓ Empathetic
- ✓ Obtains personal and family history information
- ✓ Tailors education
- ✓ Discusses testing recommendations/option
- ✓ Provides guidance for follow-up
- ✓ Value-based decision making
- ✓ Identifies coping resources
- ✓ Promotes psychological well-being

- Phillips et al.: affordability and value are key to precision medicine implementation
- Biesecker et al.: definition of "usual care" in genetic counseling
- ACMG 2021: challenges and strategies for reporting findings in young patients

Document 19

Implementing Genomics in Practice (IGNITE)

GUARDD-US assesses knowledge of *APOL1* variants on blood pressure management

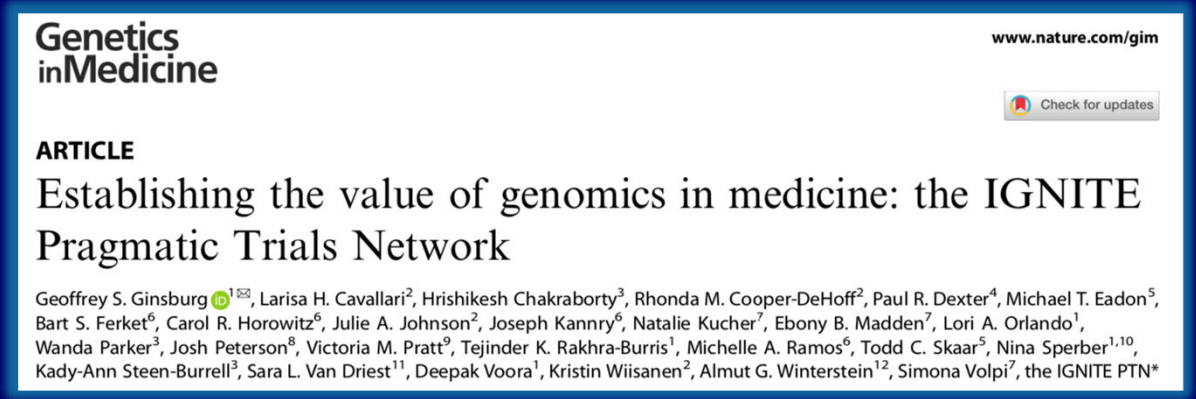
- **Over 1,850 of 5,435 participants enrolled**

GUARDD-US
Genetic testing to Understand and Address Renal Disease Disparities across the US

ADOPT PGx investigates genotype-guided therapy on acute pain, chronic pain, and depression

- **Over 50 of 4,500 participants enrolled**

ADOPT-PGx
A Depression and Opioid Pragmatic Trial in Pharmacogenetics



Genetics inMedicine

www.nature.com/gim

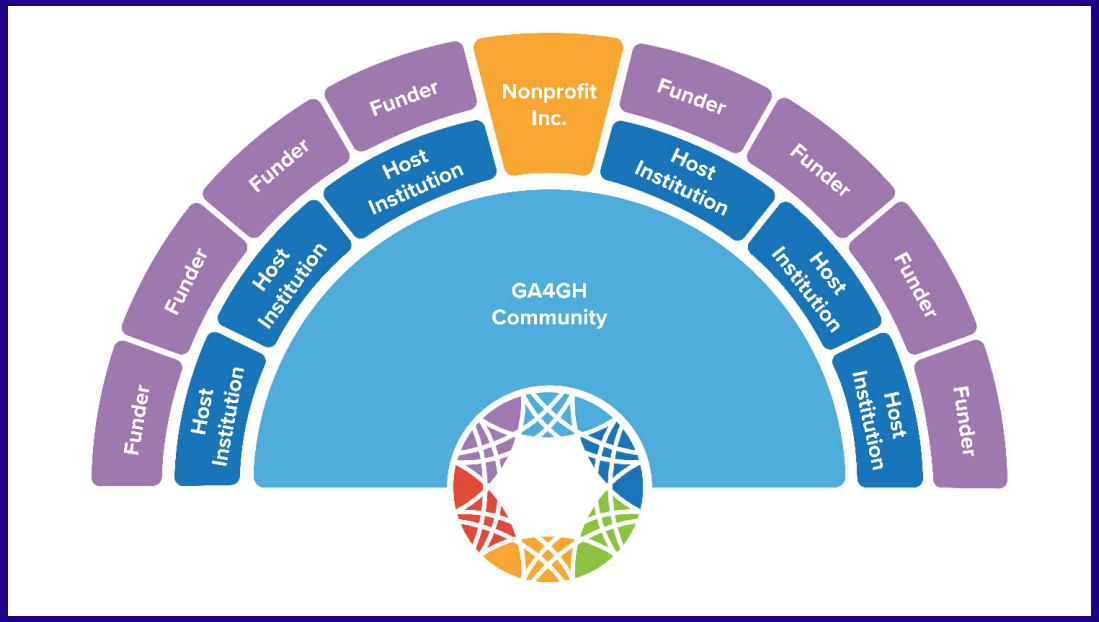
Check for updates

ARTICLE

Establishing the value of genomics in medicine: the IGNITE Pragmatic Trials Network

Geoffrey S. Ginsburg[1], Larisa H. Cavallari[2], Hrishikesh Chakraborty[3], Rhonda M. Cooper-DeHoff[2], Paul R. Dexter[4], Michael T. Eadon[5], Bart S. Ferket[6], Carol R. Horowitz[6], Julie A. Johnson[2], Joseph Kannry[6], Natalie Kucher[7], Ebony B. Madden[7], Lori A. Orlando[1], Wanda Parker[3], Josh Peterson[8], Victoria M. Pratt[9], Tejinder K. Rakhra-Burris[1], Michelle A. Ramos[6], Todd C. Skaar[5], Nina Sperber[1,10], Kady-Ann Steen-Burrell[3], Sara L. Van Driest[11], Deepak Voora[1], Kristin Wiisanen[2], Almut G. Winterstein[12], Simona Volpi[7], the IGNITE PTN*

Genomics in Healthcare: GA4GH in 2025



- Incorporated as not-for-profit “GA4GH, Inc.”
- U24 Community Resource (NHGRI, NCI, NHLBI, All of Us, ODSS)
- NIH Cloud Commons adopting GA4GH standards

Genomic Medicine Meeting XIII

Developing a Clinical Genomic Informatics Research Agenda

To develop a research strategy for using genomic-based clinical informatics tools and resources to improve the detection, treatment, and reporting of genetic disorders in clinical settings

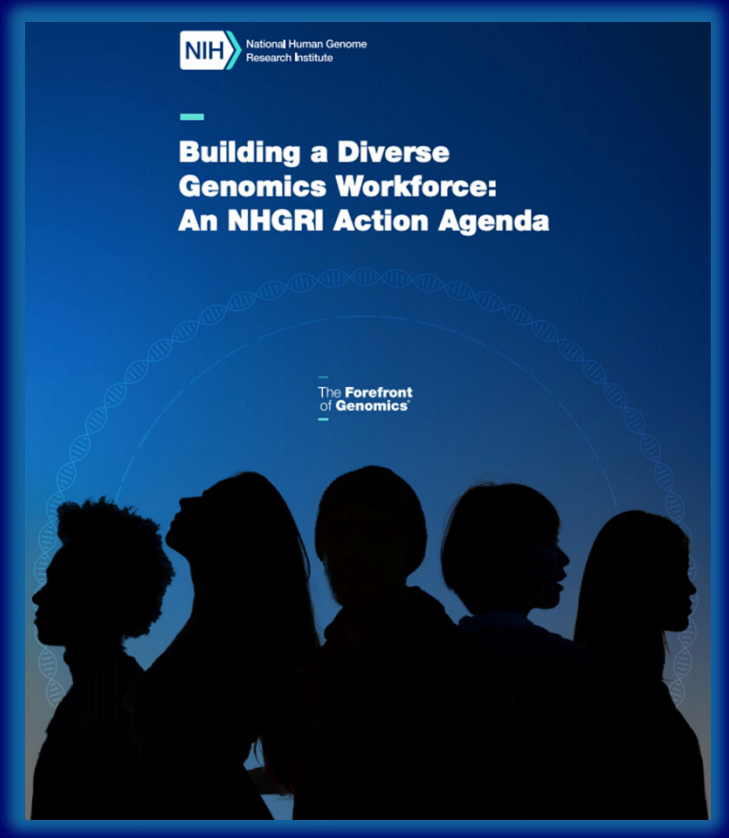
Key recommendations included:

- Incorporate an implementation component within the overall clinical informatics research framework
- Advance research to better understand the interface between human cognition and information technology
- Develop methods to identify and mitigate inherent and pervasive biases

Document 22

Training and Career Development

Enhancing the Diversity of the Genomics Workforce



New FOAs:

- **PAR-21-143**
  F99/K00 – NHGRI Predoctoral to Postdoctoral Transition Award to Promote Diversity
- **PAR-21-214**
  K18 – Short-term Mentored Research Career Enhancement Award to Promote Diversity

FOAs Under Development:

- **R01 – Grants for New Investigators to Promote Diversity in Genomics Research**
- **R25 – Genome Research Experiences to Attract Talented Undergraduates into the Genomics Field to Promote Diversity (GREAT)**

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Undiagnosed Diseases Network (UDN)

Solving Medical Mysteries Through Team Science

Article | Open Access | Published: 12 February 2021

Commonalities across computational workflows for uncovering explanatory variants in undiagnosed cases

Shilpa Nadimpalli Kobren, Dustin Baldridge, Matt Velinder, Joel B. Krier, Kimberly LeBlanc, Cecilia Esteves, Barbara N. Pusey, Stephan Züchner, Elizabeth Blue, Hane Lee, Alden Huang, Lisa Bastarache, Anna Bican, Joy Cogan, Shruti Marwaha, Anna Alkelai, David R. Murdock, Pengfei Liu, Daniel J. Wegner, Alexander J. Paul, Undiagnosed Diseases Network, Shamil R. Sunyaev & Isaac S. Kohane

Genetics in Medicine (2021) | Cite this article

- Investigated commonalities across genome-sequencing processing workflows
- Advances in structural variant detection, noncoding variant interpretation, and integration of additional biomedical data promising for solving undiagnosed cases

February 25, 2021

Machine Learning of Patient Characteristics to Predict Admission Outcomes in the Undiagnosed Diseases Network

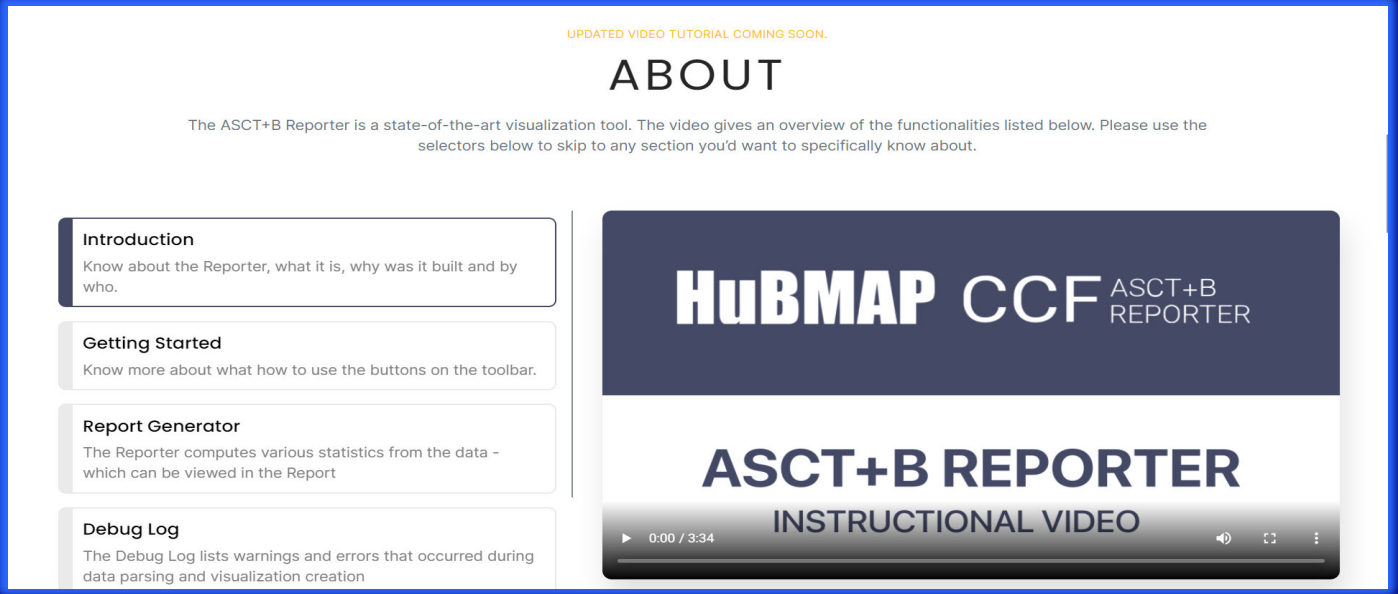
Hadi Amiri, PhD[1,2]; Isaac S. Kohane, MD, PhD[1]; for the Undiagnosed Diseases Network

» Author Affiliations | Article Information

JAMA Netw Open. 2021;4(2):e2036220. doi:10.1001/jamanetworkopen.2020.36220

- Developed and evaluated machine learning model to prioritize evaluation of patients with undiagnosed diseases by retrospective and prospective validation
- Predictive model may reduce the processing time for accepted applications by two thirds

Human Biomolecular Atlas Program (HuBMAP)



Community effort to relate anatomical structures and cell types to ontologies

Opportunities for trainees and early career investigators:

- **Student Genome Internship Program for Undergraduates**
- **Jump Start Program for Junior Investigators**

Bridge to Artificial Intelligence (Bridge2AI)

New NIH Common Fund Program

Notice of Intent to Publish a Funding Opportunity Announcement for Research Opportunity Announcement for the Data Generation Projects of the NIH Bridge to Artificial Intelligence (Bridge2AI) Program (OT2)

Notice Number:

NOT-RM-21-022

Notice of Intent to Publish a Funding Opportunity Announcement for NIH Bridge2AI Integration, Dissemination, and Evaluation (BRIDGE) Center (U54 Clinical Trial Not Allowed)

Notice Number:

NOT-RM-21-021

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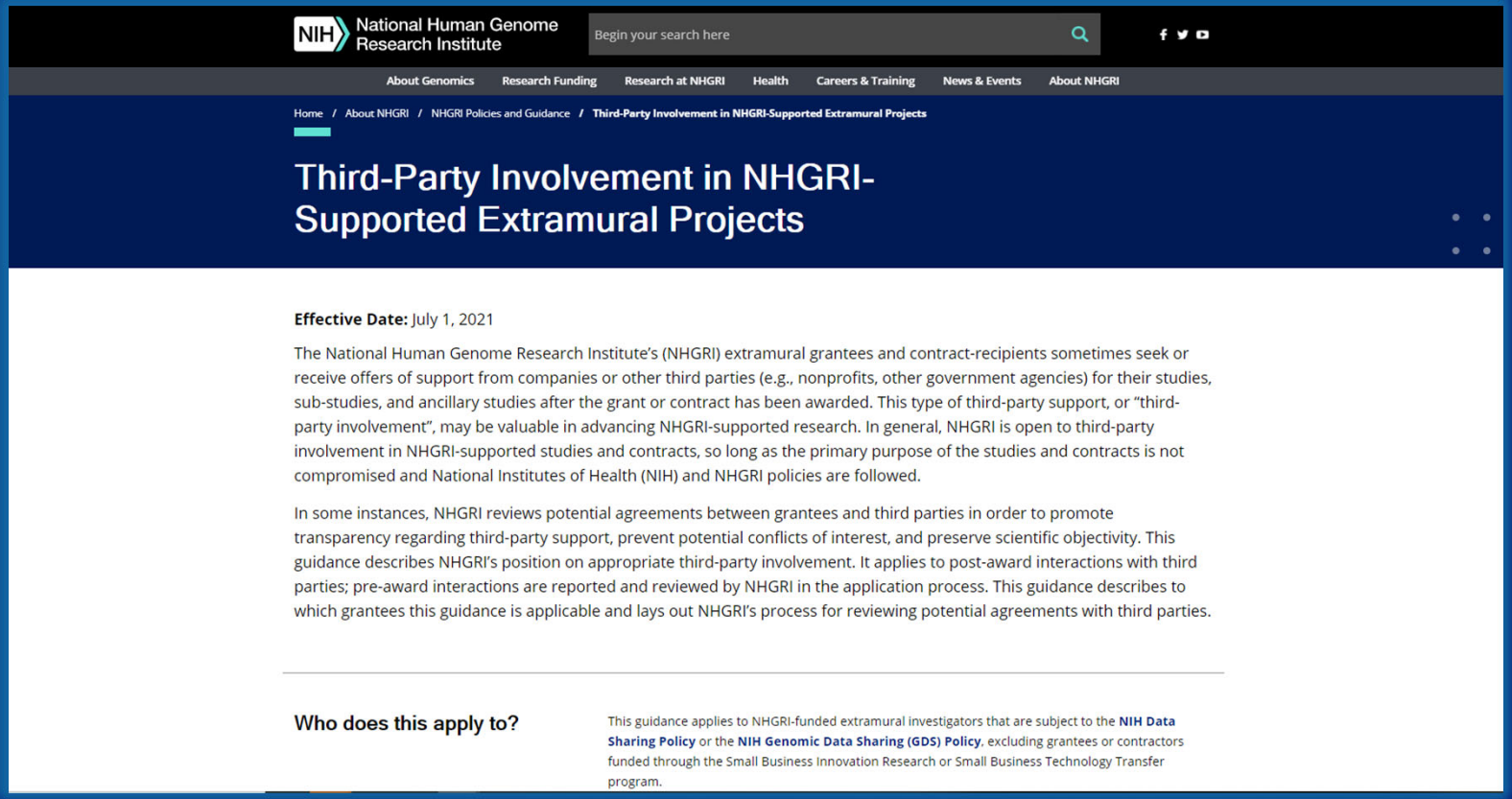
NHGRI Guidance for Third-Party Involvement in Extramural Research



NIH National Human Genome Research Institute

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Home / About NHGRI / NHGRI Policies and Guidance / Third-Party Involvement in NHGRI-Supported Extramural Projects

Third-Party Involvement in NHGRI-Supported Extramural Projects

Effective Date: July 1, 2021

The National Human Genome Research Institute's (NHGRI) extramural grantees and contract-recipients sometimes seek or receive offers of support from companies or other third parties (e.g., nonprofits, other government agencies) for their studies, sub-studies, and ancillary studies after the grant or contract has been awarded. This type of third-party support, or "third-party involvement", may be valuable in advancing NHGRI-supported research. In general, NHGRI is open to third-party involvement in NHGRI-supported studies and contracts, so long as the primary purpose of the studies and contracts is not compromised and National Institutes of Health (NIH) and NHGRI policies are followed.

In some instances, NHGRI reviews potential agreements between grantees and third parties in order to promote transparency regarding third-party support, prevent potential conflicts of interest, and preserve scientific objectivity. This guidance describes NHGRI's position on appropriate third-party involvement. It applies to post-award interactions with third parties; pre-award interactions are reported and reviewed by NHGRI in the application process. This guidance describes to which grantees this guidance is applicable and lays out NHGRI's process for reviewing potential agreements with third parties.

Who does this apply to?

This guidance applies to NHGRI-funded extramural investigators that are subject to the **NIH Data Sharing Policy** or the **NIH Genomic Data Sharing (GDS) Policy**, excluding grantees or contractors funded through the Small Business Innovation Research or Small Business Technology Transfer program.

Document 27

NHGRI Data Sharing Expectations: Sharing Quality Metadata and Phenotypic Data

NHGRI-funded and -supported researchers are expected to:

- **Share metadata and phenotypic data associated with the study**
- **Use standardized data-collection protocols and survey instruments for capturing data, as appropriate**
- **Use standardized notation for metadata to enable the harmonization of datasets for secondary research analyses**

NHGRI Communications Video Wins Journalism Award

NHGRI science writer Prabarna Ganguly wins DCSWA Newsbrief Award for “The Human Pangenome” video

Credit: Massive Science/NHGRI

The D.C. Science Writers Association
DCSWA

Genomics and the **Media**

Apoorva Mandavilli
Reporter (Science and Global Health), The New York Times

May 20, 2021

Dorothy Roberts
Professor of Law and Sociology, Civil Rights, University of Pennsylvania; Author, *Fatal Invention*

November 4, 2021

Magdelena Skipper
Editor in Chief, Nature; Chief Editorial Advisor, Nature Research

May 25, 2022

John Inglis
Executive Director, Cold Spring Harbor Laboratory Press; Co-founder, bioRxiv, medrXiv

July 28, 2021

Elizabeth Wayne
Associate Professor of Chemistry, Carnegie Melon University; Co-host, PhDivas Podcast

January 20, 2022

Amy Harmon
National Correspondant (Science and Society), The New York Times

September 20, 2021

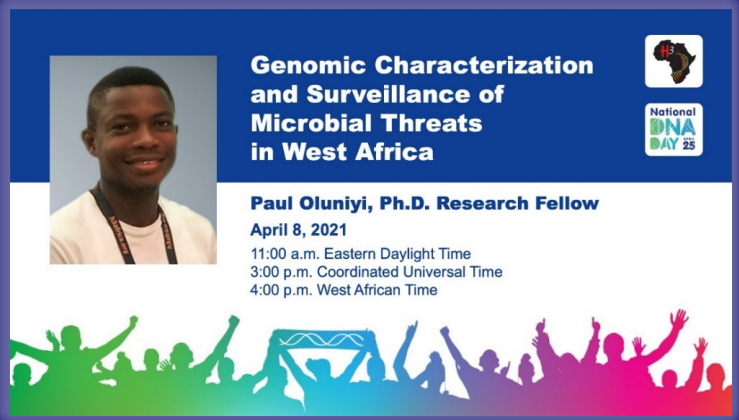
Joe Palca
Science Correspondent, NPR

March 2022

Conversations with trailblazing science communicators

Document 30

National DNA Day 2021



Document 31

Inter-Society Coordinating Committee for Practitioner Education in Genomics

10th "In-Person" Meeting

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Genome Sequencing on Prime-Time TV

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Somatic Mutations in *UBA1* and Severe Adult-Onset Autoinflammatory Disease

D.B. Beck, M.A. Ferrada, K.A. Sikora, A.K. Ombrello, J.C. Collins, W. Pei, N. Balanda, D.L. Ross, D. Ospina Cardona, Z. Wu, B. Patel, K. Manthiram, E.M. Groarke, F. Gutierrez-Rodrigues, P. Hoffmann, S. Rosenzweig, S. Nakabo, L.W. Dillon, C.S. Hourigan, W.L. Tsai, S. Gupta, C. Carmona-Rivera, A.J. Asmar, L. Xu, H. Oda, W. Goodspeed, K.S. Barron, M. Nehrebecky, A. Jones, R.S. Laird, N. Deuitch, D. Rowczenio, E. Rominger, K.V. Wells, C.-C.R. Lee, W. Wang, M. Trick, J. Mullikin, G. Wigerblad, S. Brooks, S. Dell'Orso, Z. Deng, J.J. Chae, A. Dulau-Florea, M.C.V. Malicdan, D. Novacic, R.A. Colbert, M.J. Kaplan, M. Gadina, S. Savic, H.J. Lachmann, M. Abu-Asab, B.D. Solomon, K. Retterer, W.A. Gahl, S.M. Burgess, I. Aksentijevich, N.S. Young, K.R. Calvo, A. Werner, D.L. Kastner, and P.C. Grayson

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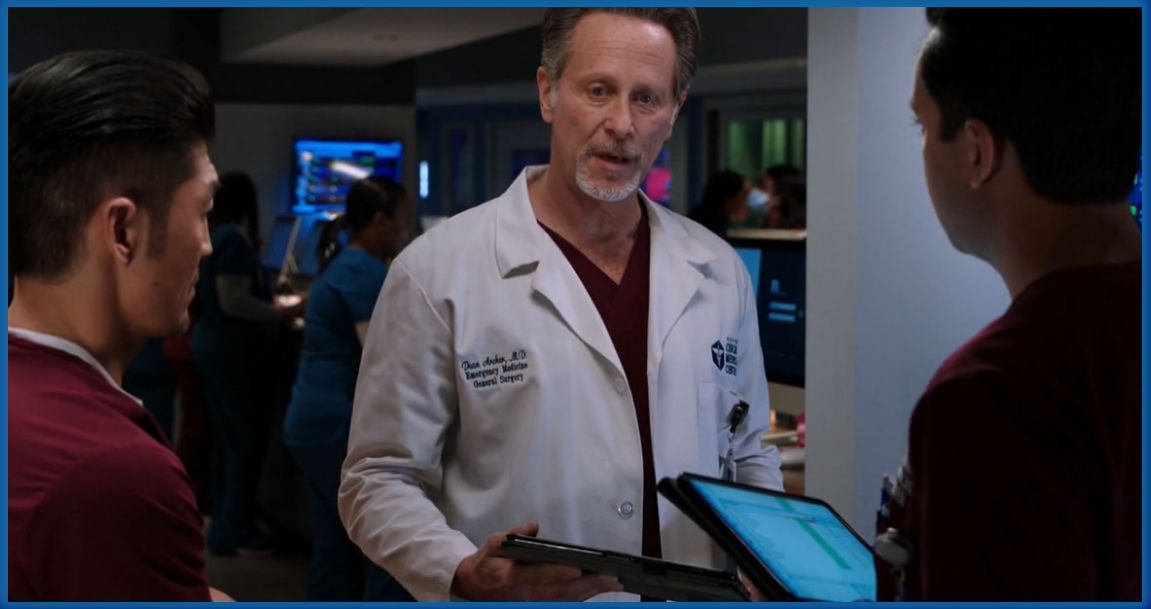

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