

National Advisory Council for Human Genome Research

September 19, 2022

Concept Clearance for RFA

Investigator-Initiated Research in Genomics and Health Equity

Purpose: The purpose of this initiative is to support investigator-initiated research in genomics and health equity, with the ultimate goal of developing approaches, generating and disseminating data, and implementing metrics or interventions that will advance the equitable use of genomics to improve health in U.S. populations. Awardees will conduct innovative and generalizable research in genomics and health equity spanning across NHGRI's scientific areas and will incorporate a plan for strategies to facilitate inclusive and diverse perspectives.

Background

Although advances in genomic discovery and technology have fueled the application of genomics to improve understanding of human health and disease, not all groups have benefitted equitably. Lack of diverse representation in genomic research and the genomic workforce impedes equitable access to and application of genomics. For example, the persistent underrepresentation of non-European ancestry participants in genome-wide association studies (despite contributing disproportionately greater proportions of statistically significant associations¹) has led to poorer predictive performance of polygenic risk scores². This unevenness in access to genomic technology, resources and clinical testing impacts health disparities disproportionately among underrepresented populations. The [NHGRI Strategic Vision](#) includes a bold prediction that individuals from ancestrally diverse backgrounds will benefit equitably from advances in human genomics. NHGRI held a virtual public workshop in April 2022 to understand the gaps in genomic research and identify research directions that will help to alleviate health disparities and advance health equity, with over 300 attendees. Recommendations received from this workshop are described in the [workshop report](#) and form the basis for the scope and objectives of these RFAs.

Scope and objectives.

Health equity is relevant across all aspects of NHGRI's research portfolio. Proposed RFAs will solicit applications to conduct research that addresses health equity in any of the areas in genomics that are related to NHGRI's mission. The proposed research could draw from multi-disciplinary approaches, such as conceptual frameworks, technology development, methods development, data generation, data analysis, or genomic implementation. Applicants are encouraged to include populations or communities that experience health disparities, such as racial or ethnic minorities, socioeconomically disadvantaged populations, underserved rural populations, individuals with disabilities, women, and sexual and gender minorities, as relevant to the scientific question to be investigated. Efforts for rigorous community engagement preceding or as part of the research are encouraged. However, the application must go beyond simple inclusion of an underrepresented population and show evidence that the research will address health equity. As related to genomics, health equity evidence could include availability of high quality genomic information which is

comprehensive in its inclusion of diverse populations; access to genomic testing; quality of treatment and management of genomic findings; and acceptability of genomic approaches and interventions. Examples of possible research areas in genomics and health equity include, but are not limited to:

- Using multi-omic data to better understand how lack of diversity impacts health equity across populations
- Improving prediction of molecular variation from genetic variation in admixed populations, accounting for biological and social determinants of health
- Developing approaches to maximize the utility of genomic, social, and environmental data for studies of health and disease in underrepresented populations, especially when sample sizes are limiting
- Developing and implementing genomic technology for under-resourced laboratories and clinics
- Addressing challenges to data sharing or data science that impact health equity, including inequities related to sources of data, data governance, access to data, and utilization of data in under-resourced settings
- Distinguishing the utility of race and other socially defined descriptors from genomic information in determining laboratory reference values and clinical algorithms
- Identifying the gaps between the prognostic and diagnostic properties that genomic tests need to have to impact health disparities, and the current properties of genomic tests; designing strategies to address those gaps
- Identifying and overcoming barriers that limit participation in and benefit from genomic research, particularly barriers stemming from structural and social inequities
- Conducting decision science, economic or healthcare utilization studies around genomic testing that impact allocation of clinical resources
- Developing and applying metrics of health equity in genomic research that are acceptable and useful to communities, participants, and researchers

Applicants are encouraged to utilize Social Determinants of Health (SDOH) measures in the [PhenX Toolkit](#), as relevant. Applicants will also incorporate and evaluate measures of health equity in implementing the proposed research.

In addition, applicants will also be required to have a plan that would advance the scientific and technical merit of the proposed project through inclusivity. Examples of strategies to be incorporated are: inclusion of diverse personnel; enhancement of engagement of research participants from diverse groups; team science approaches for equitable contributions to research and publication, or enhancing career development for junior investigators. This plan will be integrated with a specific research objective or objectives.

An annual meeting of grantees is proposed to exchange analytic approaches and results, allowing for independent but synergistic efforts among grantees and promoting rapid sharing of lessons learned.

Relationship to ongoing studies.

If approved, these RFAs will be NHGRI's first initiative focused on genomics and health equity. They will follow similar models of other NHGRI RFAs that solicit investigator-initiated applications and develop a collaborative community of investigators through annual

meetings, such as the [Advancing Genomic Medicine Research \(AGMR\)](#); [New Investigators to Promote Workforce Diversity in Genomics, Bioinformatics, or Bioengineering and Biomedical Imaging Research](#); and [Technology Development for Single-Molecule Protein Sequencing and Single-Cell Proteome Analysis](#) RFAs. The emphasis on workforce diversity for two of the four proposed RFA (see Mechanism of support below) aligns programmatically with the [New Investigators to Promote Workforce Diversity in Genomics, Bioinformatics, or Bioengineering and Biomedical Imaging Research FOA](#). However, this FOA has a specific scientific focus on health equity. The programmatic goals of these RFAs are also similar to the Common Fund-led initiative [Transformative Research to Address Health Disparities and Advance Health Equity at Minority Serving Institutions](#) in addressing health equity approach, but will focus on genomics.

Mechanism of support.

Two sets of inter-related RFAs are proposed, one set for R01 and one set for R21 applications. For each set, there will be one general RFA, and one RFA for New and Early Stage investigators from diverse backgrounds. Diversity will be defined according to the NIH's Interest in Diversity ([NOT-OD-20-031](#)).

Funds Anticipated. Applicants may request up to \$500K DC per year for up to 5 years for R01 applications, and up to \$250K DC per year for up to 2 years for R21 applications. For each receipt date, up to 4 R01 applications and 2 R21 applications will be funded, with half of the awards dedicated to New and Early Stage Investigators from diverse backgrounds. Total costs: FY24, \$3.6M; FY25, \$7.2M; FY26, \$10.2M; FY27, \$9.6M; FY28, \$9M; FY29, \$6M; FY30, \$3M.

References

1. Morales, et al. *Genome Biol* 2018; 19(1): 21. PMID 29448949.
2. Martin, et al. *Nat Genet* 2019; 51(4): 584. PMID 30926966.

Appendix: definitions

- [Health equity](#): the attainment of the highest level of health for all people. Achieving health equity requires valuing everyone equally with focused and ongoing societal efforts to address avoidable inequalities, historical and contemporary injustices, and the elimination of health and health care disparities.
- [Diversity in genomics research](#) will be considered at the level of ancestral diversity as well as other aspects of diversity, such as rural or underserved status, disability, women, sexual and gender minorities, or disadvantaged backgrounds.
- [Diversity in the genomics workforce](#) refers to individuals from diverse backgrounds who work or train in basic, translational and clinical research, as well as healthcare professionals.