

National Advisory Council for Human Genome Research
May 15, 2023
Concept Clearance for PAR

Title: Developing novel theory and methods for understanding the genetic architecture of complex traits (R01/R21 Clinical Trial Not Allowed)

Purpose: The genetic architecture of complex traits is shaped by evolutionary forces including mutation, migration, and selection as well as the active and passive interactions of the individual with their physical and social environments. As noted in the NHGRI 2020 Strategic Vision, new approaches are needed to better account for this myriad of complexities and help deduce associations and interactions among genomic variants and environmental factors.

The goal of this NOFO is to support R01 and R21 applications for novel theory and methods development to better delineate how genetic and non-genetic factors contribute to complex trait variation across individuals, families, and populations. Approaches should go beyond current genetic association methods focused on the number, impact, and frequency of trait-associated alleles and include a more comprehensive characterization of direct and indirect, additive and non-additive, and main and interaction genetic and non-genetic effects. These methods should also account for interdependencies across scales of biological, social, and ecological organization that confound genetic association studies. We expect proposed frameworks to make extensive use of theory, simulations, and validation using available large-scale genetic and phenotypic datasets from populations with diverse environmental exposures, life experiences, demographics, and geographic histories. Special emphasis should be given to assembling interdisciplinary teams at the intersection of statistical, quantitative, and population genetics, evolutionary biology, behavioral ecology, epidemiology, sociology, econometrics, and the science of complex systems. The end result will be more comprehensive and holistic methods for understanding how and why people vary in their propensity for and presentation of diseases and traits.

New or renewal/modified initiative: New

Mechanism of Support: Research Project Grant / R01, R21