

SOLICITATIONS FROM THE OFFICE OF POPULATION GENOMICS, 2006-2008

1. RFA-HG-06-008: Public Consultation to Inform the Design of Possible Large-Scale Studies of Genes and Environment in Common Disease (U01) (in collaboration with NHGRI ELSI Program)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-06-008.html>

Goal: To conduct a pilot public consultation study to obtain wide societal input to inform the design and implementation of one or more possible large U.S. population-based studies, including a longitudinal cohort study, of the role of genes and environment in health and disease.

Objectives: To obtain preliminary vital input relevant to the design and implementation of a longitudinal cohort study, by methodologies such as surveys, focus groups, and public meetings with participants who reflect the broad demographic makeup of the U.S., to:

- Assess public attitudes regarding this type of population research
- Identify preconceptions and concerns
- Define expectations about privacy protections, return of results, and other matters
- Inform full-scale efforts for public consultation with the specific communities selected for study, should such an initiative eventually be launched
- Help develop educational and recruitment materials for subjects in such research.

Awarded in September 2006; 1.55M total over FY06 and FY07

2. RFA-HG-06-014: Genome-wide Association Studies in the Genes and Environment Initiative – Genotyping Facilities (U01)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-06-014.html>

3. RFA-HG-06-032: Genome-wide Association Studies in the Genes and Environment Initiative – Coordinating Center (U01)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-06-032.html>

4. RFA-HG-06-033: Genome-wide Association Studies in the Genes and Environment Initiative - Study Investigators (U01)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-06-033.html>

Goal: To conduct genome-wide association (GWA) genotyping and/or replication studies using data and samples from human subjects on whom information is available for conditions/traits of public health importance and relevant environmental exposures.

Objectives:

- Assess quality of phenotypic and exposure data and DNA samples proposed for genotyping
- Support initial GWA genotyping for ~ 15 complex diseases or traits and deposition of resulting data in open and controlled access portions of dbGaP
- Support genotyping of initial strongly associated variants in replication samples

- Promote standardization and harmonization of phenotypic and environmental exposure data to permit cross-study analyses
- Support analysis efforts within and across studies

Awarded in August 2007, \$54.4M total over four years (including re-issuance of HG-06-033)

5. RFA-HG-07-005: Genome-Wide Studies in Biorepositories with Electronic Medical Record Data (U01) (with funding from NHGRI ELSI Program and NIGMS)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-07-005.html>

Goal: To develop and apply approaches for using U.S. biorepositories with EMR systems for large-scale, high-throughput genomic research.

Objectives: To determine, for each participating biorepository:

- Completeness, validity, and reliability of available phenotypic and exposure data for use in genome-wide studies
- Adequacy of existing consent for high-throughput genome-wide technologies such as GWA genotyping or sequencing, and for sharing data
- Needs for additional consent and/or consultation with biorepository participants, investigators, and other relevant groups
- Best practices for IRB interactions, participant consent, and results reporting, and for collecting, formatting, documenting, and sharing data
- Representativeness and diversity of individuals participating in the biorepository in relation to the source population from which they are drawn
- Associations of genome-wide data with specific EMR-derived phenotype(s)

Awarded in September 2007, \$30.2M total over four years

6. RFA-HG-07-006: High-Priority Phenotype and Exposure Measures for Cross-Study Analysis in Genome-Wide Association Studies (U01)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-07-006.html>

Goal: To identify, develop, and disseminate readily standardized and implemented phenotypic and environmental exposure measures of public health significance suitable for addition to planned or ongoing genome-wide association (GWA) studies.

Objectives:

- Define 15-20 high priority phenotypic and exposure domains for GWA studies, such as cancer, pulmonary disease, anthropometrics, lifestyle factors, or medication use
- For each domain, identify standardized measures available or under development and recommend 10-15 high priority measures to consider for inclusion in GWA studies
- Disseminate the recommendations broadly to research communities involved in genome-wide and related studies

Awarded in September 2007, \$6.9M total over three years.

7. RFA-HG-07-012: Genome-wide Association Studies in the Genes, Environment, and Health Initiative - Study Investigators (U01)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-07-012.html>

Reissuance of RFA-HG-06-033 for 2-4 additional awards, with increased emphasis on potential for addressing minority health and health disparities relevant to the U.S. population

Applications received October 18, 2007; anticipated award July 2007 of \$3.3M total over two years plus associated genotyping and data management costs.

8. RFA-HG-07-014: Epidemiologic Investigation of Putative Causal Genetic Variants—Study Investigators (U01)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-07-014.html>

9. RFA-HG-07-015: Epidemiologic Investigation of Putative Causal Genetic Variants—Coordinating Center (U01)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-07-015.html>

Goal: To investigate, in well-characterized population studies, of genetic variants identified as potentially causally associated with complex diseases in genome-wide association (GWA) and other genetic studies, with the aim of widespread sharing of the resulting population-based descriptive and association data to accelerate the understanding of genes related to complex diseases.

Objectives: To utilize existing population-based cohort studies and clinical trials, and the investigators most familiar with their intricacies, to:

- Determine the population-based profile, or “epidemiologic architecture,” of putative causal variants, including prevalence in racial and ethnic subgroups of relevance to the U.S. population and magnitude of disease risk and associations with other health characteristics
- Identify modifiers of gene-trait associations, particularly lifestyle factors or medication use
- Identify potential clues to the biological basis of an association by studying the relationship of the putative causal variants to phenotypic characteristics such as laboratory measures or imaging findings

Applications received November 19, 2007; anticipate 3-5 awards in July 2007 for \$32.2M total over four years.

Affiliated RFAs (Genes, Environment, and Health Initiative, GEI)

10. RFA-HL-07-010: Methods of Analysis of Gene-Environment Interactions in Complex Diseases: The Genes and Environment Initiative (R01)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-07-010.html>

Goal: To develop and test innovative, informative, and cost-effective study designs and analytical strategies for identifying gene and environment interactions in genome-wide association (GWA), sequencing, linkage, or candidate gene studies in complex diseases.

Objectives:

- Develop analytical tools and approaches to identify environmental components or covariates of complex diseases and their interactions with genes in linkage, candidate gene, sequencing, or genome-wide association studies
- Develop and subsequently validate algorithms and new computational approaches to help identify individuals at highest risk for developing a specific disease or dysfunction based on both their exposure patterns and genetic risk profiles
- Emphasize methods that allow integration of new exposure assessment tools as developed in the Exposure Biology GEI initiatives into whole genome association studies such as those developed from GEI-GWA

Awarded in September 2007, \$6.0M total over three years.

11. RFA-MH-08-040: Methods of Statistical Analysis of DNA Sequence Data for Studies Relating Variation to Disease (R01)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-08-040.html>

Goal: To develop statistical methods for designing sequencing studies, for analyzing the data to find associations with phenotypes, to narrow down and prioritize regions for further study, and to provide information on possible functional roles of the variation.

Objectives:

- To develop methods that statistically analyze the sequence data to identify sets of associated variants that contain functional variants
- To provide clues about function that will guide the choice of sets of variants for later functional studies and the types of functional studies to be done

Applications due January 8, 2008; anticipate 6 awards in September 2008 for \$6.0M total over three years.