

HG-RFA-15-001

Applicant Webinar 2015

1:00-2:30 PM EST

Please email questions to
NHGRISequencingRFAWebinar@mail.nih.gov

Centers for Common Disease Genomics RFA-HG-15-001

Information for Potential Applicants

February 18, 2015



National Human Genome
Research Institute

CAVEAT

- *Read the RFA (and any amending Notices) carefully*
- *Read the review and funding criteria*
- *Read the Cooperative Agreement Terms and Conditions*

Major NHGRI Programs

Structure of
Genomes

Biology of
Genomes

Biology of
Disease

Science of
Medicine

Effectiveness of
Healthcare

**Genome
Function**

**Centers for
Mendelian
Genomics
RFA-HG-015-
002**

**Clinical
Applications
of Sequencing**

**Genome
Tech. Dev.**

**Centers for Common
Disease Genomics
RFA-HG-015-001**

Genome Informatics

Centers for Common Disease Genomics (CCDG)

- *Collaborative* large-scale genome sequencing effort
- *Comprehensively* identify rare risk and protective variants contributing to multiple common disease phenotypes
- *Explore a range of architectures and study designs:* multiple examples
- Understand the *general principles of genomic architecture* underlying common, complex inherited diseases
- Understand *general principles of how best to design* rare variant studies for common disease
- *Develop resources, informatics tools, and innovative approaches* for multiple disease research communities and the wider biomedical research community

CCDG: Multiple Objectives At Different Levels: “Scientific”

1. Specific lessons about each example: improved understanding of variants contributing to each individual example “disease”*; “comprehensive”
2. General lessons about identifying variants underlying common disease: e.g., design considerations, limits (e.g., when is a study “done”), etc. More than just quantitative.

This program must identify variants underlying specific common, complex diseases

CCDG: Multiple Objectives At Different Levels: “Foundational”

3. Improvements in ability to produce genome sequence data (e.g., cost, quality, etc.) to address the scientific questions (including adopting new platforms, if needed).
4. Improvements in analysis pipelines and methods
5. Developing data resources for the community
6. Ultimately developing and disseminating the “know-how”: design, methods, limitations

This program must also advance the state of the art in applying genome sequencing to identifying variants underlying common disease.

CCDG: Multiple Objectives At Different Levels: Additional

Additional features (also to be addressed in the application) that will aid in attaining the goals include:

1. Access to state-of-the-art genome sequencing platforms over the life of this program.
2. Capability to develop computational sequence analysis methods and pipelines in tandem with the data production.
3. Capability to work on multiple projects with different phenotypes, including access to multiple different sample sets, and ability to develop collaborations with multiple disease communities.
4. Flexibility to expand sequencing capacity significantly to accommodate emerging opportunities that may arise for the study of common disease.
5. Capability to undertake projects that are compelling and broadly useful, but may not be directly related to studies of a specific disease (e.g., population variation studies).
6. Potential to collaborate with other investigators to pursue more functional follow-up studies to enhance analysis and/or validate findings. This FOA provides only very limited funds for functional follow-up studies (see *Pilot Collaborations*).

CCDG: Multiple Objectives At Different Levels: Additional

7. Capability to bring to bear other technologies that are used in genomic analysis, and which could be directly relevant to disease variant analyses. It is expected that the great majority of data generation funded under this FOA will be genome sequence data produced from human samples, but some other, well-justified and limited studies may be proposed as an adjunct to genome sequencing studies.
8. Capabilities to use creative means to add value or take alternative, better approaches to identify variation underlying common disease; for example disease variant discovery in well-chosen non-human model organisms, or phenotypes that are not strictly disease phenotypes as an adjunct to genome sequencing studies on samples from humans.
9. Potential to identify other sources of funding or to otherwise increase the size or number (comprehensiveness) of studies that can be done under the broad intentions of this FOA. However, co-funding or cost-sharing is not a requirement.
10. Plans for and success in dissemination/deposition of genomic datasets, computational tools, project design "know-how", etc.

Comprehensiveness

Why? Because we want to understand the scientific and practical limits, and piecemeal studies will not tell us this.

What do we mean?
As an ideal, at least:

" The identification of all associated (risk-raising and protective) variants (coding and noncoding) down to a specified but arbitrary low frequency and effect size, in a representative set of diverse human populations, for a particular phenotype, including replication. Identification of associations will require statistical analyses, and may require computational functional analysis (for example, to cluster implicated genes by function). "

Over multiple different examples, multiple designs, multiple populations.

Comprehensiveness

We recognize this is an IDEAL. We want applicants to tell us how far they can take projects towards this definition, considering the scientific and practical factors discussed in the RFA.

If you think we have listed the wrong considerations, you should refine them and address them in your application.

Recent RFA Changes

“Leveraging resources”:

NOT-HG-015-020

<http://grants.nih.gov/grants/guide/notice-files/NOT-HG-15-020.html>

“Diversity Action Plan”:

<http://grants.nih.gov/grants/guide/pa-files/PAR-13-063.html>

A clarification Notice will be published very soon

Core Genome Sequencing Program Additions

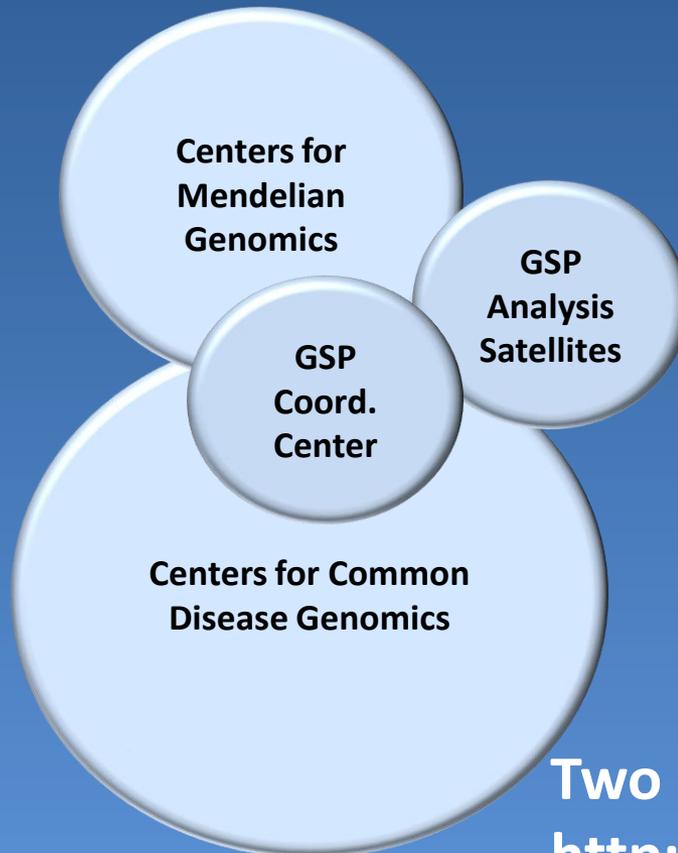
Structure of
Genomes

Biology of
Genomes

Biology of
Disease

Science of
Medicine

Effectiveness of
Healthcare



Two new "Concepts"

<http://www.genome.gov/27560312>

FAQ's

I. Goals

II. Format of application

III. Eligibility and Funding

Contacts

Adam Felsenfeld (felsenfa@mail.nih.gov): Overall program, RFA-HG-015-001, new Concepts

Lu Wang (wanglu@mail.nih.gov): RFA-HG-015-002

Bettie Graham (grahambj@exchange.nih.gov): Questions about the Diversity Action Plan (DAP)

Rudy Pozzatti (pozzatr@exchange.nih.gov): Questions about Review

Cheryl Chick (chickc@mail.nih.gov): Administrative questions about budget