**CONCEPT CLEARANCE FOR RFA**

**Clinical Sequencing Exploratory Research Program Coordinating Center**

**National Advisory Council for Human Genome Research**

**February, 2012**

## Purpose

The goal of this proposed RFA is to provide centralized support and infrastructure for the network of Clinical Sequencing Exploratory Research (CSER) grantees funded under RFA HG-10-017, who will explore, within an active clinical setting, the application of genomic sequence data to the care of patients, including the ethical and psychosocial implications relating to the return of results from sequencing data. This Coordinating Center (CC) awardee will: 1) facilitate the work of the CSER Consortium through scientific coordination as well as logistical and administrative activities; 2) accelerate the generation and dissemination of findings and best practices by applying appropriate scientific expertise to the communication of Consortium findings and outputs to the broader community; and 3) support interactions and potential collaborative activities with research groups conducting investigations related to those of the CSER Consortium, as appropriate, to promote synergy and consistency among projects of this nature.

## Background

In late 2010, NHGRI broadened the focus of its Genome Sequencing Program to include a new CSER Program, and solicited proposals for research projects to investigate the infrastructure, methods and issues that will need to be addressed to make routine interrogation of a patient's genomic sequence a fundamental aspect of her/his medical care. The RFA called for grantees to develop and apply methods to integrate sequencing into the clinic, as well as to study relevant ethical, legal and psychosocial issues involved in responsibly applying personal genomic sequence data to medical care. Using the U01 cooperative agreement mechanism, applicants would work together to facilitate Consortium goals, create a forum for the dissemination of innovative and best practices in this area, and interact with other related consortia where opportunities arise. Each proposal was to include three interdependent projects: Project 1, clinical study; Project 2, sequencing, analysis, and interpretation, and Project 3, ethical and psychosocial research.

In December 2011 and January 2012, six applications were funded:

| Institution | PI | Disease focus |
|---|---|---|
| Baylor College of Medicine* | Sharon Plon and Will Parsons | Childhood cancer |
| Brigham and Women's Hospital | Robert Green | Familial hypertrophic cardiomyopathy |
| Children's Hospital of Philadelphia | Ian Krantz and Nancy Spinner | Pediatric disorders |
| Dana Farber Cancer Institute | Levi Garraway | Cancer |
| University of North Carolina-Chapel Hill | James Evans, Gail Henderson, Karen Weck-Taylor, Kirk Wilhelmsen, and Jonathan Berg | Broad range of disorders |
| University of Washington* | Gail Jarvik | Colorectal cancer |

* Cofunded by NCI

These grants span a range of diseases and will enroll and sequence many hundreds of patients over the project period. To leverage opportunities to synergize and build on existing resources, several proposed working groups have already been formed within the Consortium: Informed Consent, Return of Results (to include assessment of actionable variants), Sequencing Standards, Phenotype Measures and Analysis, and Electronic Reports / Medical Records. Other working groups are likely to be established as the Consortium matures. Furthermore, those investigators involved in Project 3 of each grant, which is focused on the ethical and psychosocial aspects of returning results, will also participate in the larger NHGRI Return of Results (RoR) Consortium. The RoR Consortium includes investigators from nine other grants who are working on related issues, promoting synergy among all NHGRI-funded projects in this area. Also, funds permitting, the CSER RFA is to be reissued with an expectation to make 2 to 4 additional awards in FY13.

The similarities in purpose among the funded grants suggest that facilitating cross-study activities would increase the efficiency and reach of the Consortium as a whole. In this light, NHGRI proposes to establish a Coordinating Center (CC) to work collaboratively with the CSER investigators, the investigators in the related RoR Consortium and other relevant NHGRI programs, as well as NHGRI staff to facilitate a comprehensive program of research to promote incorporation of genomic information into clinical care. The proposed CC would interact with all CSER participants to determine issues that have broad applicability, within and external to the CSER Consortium; accelerate the resolution of these issues; and disseminate methods, tools and best practices. The CC would also be responsible for key logistical and administrative aspects of the program, including meeting planning, generating and distributing documents, and facilitating Consortium-wide communication.

Within the context of the 2011 NHGRI Strategic Plan, the CSER Program will have an important role in defining key challenges and opportunities and exploring approaches to merging genomic sequence data with the complexities underlying the practice of medicine and a complicated healthcare system. Similar efforts are ongoing at other academic medical institutions; the research and insight generated by this Program will benefit the entire field by developing and widely disseminating methods and best practices and, where appropriate, interacting with these other efforts.

**Research scope and objectives**

To meet the primary goal of this RFA to provide centralized support and infrastructure to the CSER investigators, the awardee is expected to propose and demonstrate the capability to implement action plans in multiple areas of scientific and administrative coordination. The CC will work with the CSER Steering Committee and NHGRI to identify and implement key coordination activities, such as facilitating and tracking generation and release of data and tools for promoting the use of sequencing in clinical care. The CC will assist in the packaging and submission of phenotypic and genomic data sets to data repositories; will inventory and, as appropriate, harmonize psychosocial research instruments and data across studies; will serve as an archive for Consortium documents, and will act as a liaison between the Consortium and the external scientific and clinical communities. The CC also will contribute scientific expertise and leadership as needed within the Consortium to facilitate cross-study activities and accelerate the development of best practices. Such expertise might include any and/or all areas encompassed by the CSER Program, such as study design or methods of genotype-phenotype analysis; genomic sequence analysis, including variant calling; policy compliance; harmonization of phenotype and psychosocial measures; coordination with other activities and facilitating consensus with regards to "actionability" of genetic variants; evaluation of approaches to returning genomic sequence results; psychosocial implications and other effects (disease-centered, patient-centered, physician-centered and/or cost-related); integration of information into electronic health records, and development of clinical decision support tools. Where needed, the CC will provide direct assistance to Study Investigators, help to develop common methods and tools, and evaluate cross-study approaches. The CC will also work closely with NHGRI staff and the CSER Steering Committee to manage the logistical and administrative aspects of the Consortium, such as scheduling calls and meetings, planning network meetings, preparing meeting minutes and tracking projects. Because the CSER Program will continue to evolve as the science matures, the CC should be flexible in response to its needs, and applicants should describe the expertise that makes them uniquely qualified to meet these evolving needs.

**Mechanism of support**

- One award will be made using the U01 cooperative agreement mechanism. This RFA is open to all applicants and will not be restricted to existing or to-be-funded CSER awardees.

**Funds available**

- A maximum of $800,000 total costs per year, beginning in FY2013, with an award period of 4 years, will be made available.