Office of Science
Notice 99-04

Human Genome Program - Technological Advances

Department of Energy
Office of Science

Office of Science Financial Assistance Program Notice 99-04: Human Genome Program - Technological Advances

Agency: U.S. Department of Energy

Action: Notice inviting grant applications.

SUMMARY: The Office of Biological and Environmental Research (OBER) of the Office of Science (SC), U.S. Department of Energy, hereby announces its interest in receiving grant applications in support of the DOE Human Genome Program (HGP). This program is a coordinated, multidisciplinary, goal-oriented research effort to obtain a detailed understanding of the human genome at the molecular level. High throughput sequencing is now a major focus of the program, but needs for supporting resources and technologies remain in several areas.

DATES: Potential applicants are encouraged to submit a brief preapplication. All preapplications, referencing Program Notice 99-04, should be received by DOE by 4:30 P.M., E.S.T., December 3, 1998. A response to the preapplications discussing the potential program relevance and encouraging or discouraging a formal application generally will be communicated within several days of receipt.

Formal applications submitted in response to this notice must be received by 4:30 P.M., E.S.T., February 23, 1999, in order to be accepted for merit review and to permit timely consideration for award in FY 1999.

ADDRESS: Preapplications, referencing Program Notice 99-04, should be sent preferable by E-mail to joanne.corcoran@oer.doe.gov, however, preapplications will also be accepted if mailed to the following address: Ms. Joanne Corcoran, Office of Biological and Environmental Research, SC-72, U.S. Department of Energy, 19901 Germantown Road, Germantown, MD 20874-1290, or transmitted by facsimile to (301) 903-8521.

After receiving notification from DOE concerning successful preapplications, applicants may prepare formal applications and send them to: U.S. Department of Energy, Office of Science, Grants and Contracts Division, SC-64, 19901 Germantown Road, Germantown, MD 20874-1290, ATTN: Program Notice 99-04. The above address for formal applications also must be used for transmission by U.S. Postal Service Express Mail, any commercial mail delivery service, or when hand carried by the applicant. An original and seven copies of the application must be submitted.

FOR FURTHER INFORMATION CONTACT: Dr. Marvin Stodolsky if referencing topics (1-4) and Dr. Daniel Drell if referencing topic (5) and Ms. Joanne Corcoran for general program information. Their email addresses are marvin.stodolsky@oer.doe.gov, daniel.drell@oer.doe.gov and joanne.corcoran@oer.doe.gov with telephone exchange (301) 903 and respective extensions 4475, 4742 and 6488. E-mail communications are preferred. General HGP information can also be obtained with Internet browsers at: **http://www.er.doe.gov/production/ober/hug_top.html**, **http://www.ornl.gov/TechResources/Human_Genome/home.html**, and sites linked to these WWW pages. The solicitation topics are in accordance with the 1998 revision of the 5-year goals of the U.S. HGP. It is published in the October 21, 1998 issue of the journal, Science, volume 282 and is available on the Internet at: **http://www.ornl.gov/hg5yp**. The full text of Program Notice 99-04 is available via the Internet using the following web site address: **http://www.er.doe.gov/production/grants/grants.html**.

SUPPLEMENTARY INFORMATION: Under this solicitation near term resource development or improvements are sought in: (1) large insert DNA clone libraries and their characterization; (2) chemistries and biochemistries for DNA sequencing; (3) protocols and reagents for full length messenger RNA to cDNA production and sequencing; (4) characterizing exceptional chromosomal regions including those near telomeres and centromers by sequencing and/or other relevant methodologies; and (5) computational processing of sequence information including viewing, curating, and integrating. Instrumentation development complementary to these topics was sought under a separate solicitation and is specifically excluded from this call.

Topic Details

The goal of (1), large insert DNA clone libraries and their characterization, is to provide additional resources in support of human and mouse genomics, and perform characterizations supportive of genomic sequencing. The vectors for the libraries should be of the generic BAC (bacterial artificial chromosomes) type, supporting stable maintenance of their inserts in bacterial hosts. For a mouse library, the C57Bl/6J strain should be the source of the DNA, with a 10-15 fold genome coverage

sought. There should be two sub-libraries, with DNA fragments generated by different restriction nucleases to diminish representation biases. Also to diminish representation biases, DNA breakage by shearing only is a desired substitute to breakage by restriction. If this improvement can be implemented quickly, both mouse and human libraries produced from sheared DNAs are sought. Companion quality control analyses must be specified. Separate applications are sought for more extensive characterization of the BACs by restriction fingerprinting, end sequencing of inserts, cDNA mapping onto BACs and/or other high throughput methodologies supportive of genomics projects.

The goal of (2), chemistries and biochemistries for DNA sequencing, is to further bring speed and economies to DNA sequencing through improvements in reagents such as enzymes, their substrates, reporting labels and related protocols.

The goal of (3), protocols and reagents for full length messenger RNA to cDNA production and sequencing, is to address outstanding needs in characterizing messenger RNA populations of tissues, as represented by more stable derivative libraries of cDNAs. Particularly for human sources, obtaining mRNAs with minimal degradation remains troublesome. For longer mRNAs, faithful conversion to cDNAs is problematic. Within completed libraries, identifying optimal representatives for complete sequencing is still time consuming and expensive. For cDNAs in the few kilobase size range, full length sequencing does not yet have the economies of sequencing longer DNAs. Applications which address these problem areas are sought. Reports on recent workshops on cDNAs can be accessed on the Internet through the WWW site **http://www.ornl.gov/meetings/wccs/index.html**.

The goal of (4), characterizing exceptional chromosomal regions including those near telomeres and centromers by sequencing and/or other relevant methodologies, recognizes that current sequencing strategies may prove inadequate for chromosomal regions which are troubled by abundant repeat structures, or are the boundaries of heterochromatin and euchromatin regions. Applications addressing these problem areas specifically as they apply to chromosomes 5, 16 and 19 are sought.

The goal of (5) computational processing of sequence information including viewing, curating, and integrating, seeks ways to more efficiently and more accurately assemble partial DNA sequences, to identify regions of biological significance, and to more efficiently utilize previously determined DNA sequence to identify polymorphisms and to characterize related but not yet sequenced DNA. An additional interest is identification of useful standards, which may include (but is not limited to) controlled vocabularies, data types, and annotation types. Standards development must proceed with user community input. A report on a May, 1998 workshop on informatics needs can be accessed on the Internet at:

http://www.ornl.gov/TechResources/Human_Genome/publicat/hgn/v9n3/02doenih.html.

Program Funding

It is anticipated that a total of $5,000,000 (Changed from $7,000,000 to $5,000,000 in correction to notice published in the Federal Register December 10, 1998, Vol. 63, No. 237, page 68262) will be available for grant awards in this area during FY 1999 and FY 2000, contingent upon availability of appropriated funds. Multiple year funding of grant awards is expected, and is also contingent upon availability of funds, progress of the research, and continuing program need. Projected awards will be in the range of $50,000 per year up to $1,000,000 per year with terms of 2 to 3 years.

Applications will be subjected to scientific merit review (peer review) and will be evaluated against the following evaluation criteria listed in descending order of importance as codified at 10 CFR 605.10(d):

1. Scientific and/or Technical Merit of the Project,
2. Appropriateness of the Proposed Method or Approach,
3. Competency of Applicant's Personnel and Adequacy of Proposed Resources,
4. Reasonableness and Appropriateness of the Proposed Budget.

The evaluation will include program policy factors such as the relevance of the proposed research to the terms of the announcement and an agency's programmatic needs. Note, external peer reviewers are selected with regard to both their scientific expertise and the absence of conflict-of-interest issues. Non-federal reviewers may be used, and submission of an application constitutes agreement that this is acceptable to the investigator(s) and the submitting institution.

Information about the development and submission of applications, eligibility, limitations, evaluation, selection process, and other policies and procedures may be found in 10 CFR Part 605, and in the Application Guide for the Office of Science Financial Assistance Program. Electronic access to the Guide and required forms is made available via the World Wide Web at: **http://www.er.doe.gov/production/grants/grants.html**. The Project Description must be 25 pages or less, exclusive of attachments. The application must contain an abstract or project summary, letters of intent from collaborators, and short curriculum vitaes consistent with NIH guidelines.

The Office of Science, as part of its grant regulations, requires at 10 CFR 605.11(b) that a recipient receiving a grant to perform research involving recombinant DNA molecules and/or organisms and viruses containing recombinant DNA molecules shall comply with the National Institutes of Health "Guidelines for Research Involving

Recombinant DNA Molecules", which is available via the world wide web at: **http://www.niehs.nih.gov/odhsb/biosafe/nih/nih97-1.html**, (59 FR 34496, July 5, 1994), or such later revision of those guidelines as may be published in the Federal Register.

The Catalog of Federal Domestic Assistance Number for this program is 81.049, and the solicitation control number is ERFAP 10 CFR part 605.

John Rodney Clark
Associate Director of Science
for Resource Management

Published in the Federal Register November 24, 1998, Volume 63, Number 226, Pages 64944-64946.