

Program Announcement To DOE National Laboratories LAB 99-04

Human Genome Program Technological Advances

The Office of Biological and Environmental Research (OBER) of the Office of Science (SC), U.S. Department of Energy (DOE), hereby announces its interest in receiving proposals 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.

Under this announcement 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 centromeres 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 proposals 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. Proposals 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 centromeres 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. Proposals 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

DATES: Potential proposers are encouraged to submit a brief preproposal. All preproposals, referencing Program Announcement LAB99-04, should be received by DOE by 4:30 P.M., E.S.T., December 15, 1998. A response to the preproposals discussing the potential program relevance and encouraging or discouraging a formal proposal generally will be communicated within several days of receipt.

Formal proposals submitted in response to this announcement 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: Preproposals, referencing Program Announcement LAB99-04, should be sent preferable by E-mail to joanne.corcoran@oer.doe.gov, however, preproposals 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 preproposals, proposers may prepare formal proposals and send them to: U.S. Department of Energy, Office of Science, Office of Biological and Environmental Research, SC-72, 19901 Germantown Road, Germantown, MD 20874-1290, ATTN: Program Announcement LAB99-04. The above address for formal proposals also must be used for transmission by U.S. Postal Service Express Mail, any commercial mail delivery service, or when hand carried by the proposer. An original and seven copies of the proposal 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>.

Program Funding

It is anticipated that a total of \$2,000,000 will be available for awards in this area during FY 1999 and FY 2000, contingent upon availability of appropriated funds. Multiple year funding of 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.

Any recipient of an award from ER 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 instructions and format described below should be followed. Reference Program Announcement LAB 99-04 on all submissions and inquiries about this program.

OFFICE OF SCIENCE
GUIDE FOR PREPARATION OF SCIENTIFIC/TECHNICAL PROPOSALS
TO BE SUBMITTED BY NATIONAL LABORATORIES

Proposals from National Laboratories submitted to the Office of Science (SC) as a result of this program announcement will follow the Department of Energy Field Work Proposal process with additional information requested to allow for scientific/technical merit review. The following guidelines for content and format are intended to facilitate an understanding of the requirements necessary for SC to conduct a merit review of a proposal. Please follow the guidelines carefully, as deviations could be cause for declination of a proposal without merit review.

1. Evaluation Criteria

Proposals will be subjected to formal merit review (peer review) and will be evaluated against the following criteria which are listed in descending order of importance:

Scientific and/or technical merit of the project

Appropriateness of the proposed method or approach

Competency of the personnel and adequacy of the proposed resources

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, the uniqueness of the proposer's capabilities, and demonstrated usefulness of the research for proposals in other DOE Program Offices as evidenced by a history of programmatic support directly related to the proposed work.

2. Summary of Proposal Contents

Field Work Proposal Format (Reference DOE Order 5700.7C) (DOE ONLY)
Proposal Cover Page
Table of Contents
Abstract
Narrative
Literature Cited
Budget and Budget Explanation
Other support of investigators
Biographical Sketches
Description of facilities and resources
Appendix

2.1 Number of Copies to Submit

An original and seven copies of the formal proposal/FWP must be submitted.

3. Detailed Contents of the Proposal

Proposals must be readily legible, when photocopied, and must conform to the following three requirements: the height of the letters must be no smaller than 12 point with at least 2 points of spacing between lines (leading); the type density must average no more than 17 characters per inch; the margins must be at least one-half inch on all sides. Figures, charts, tables, figure legends, etc., may include type smaller than these requirements so long as they are still fully legible.

3.1 Field Work Proposal Format (Reference DOE Order 5700.7C) (DOE ONLY)

The Field Work Proposal (FWP) is to be prepared and submitted consistent with policies of the investigator's laboratory and the local DOE Operations Office. Additional information is also requested to allow for scientific/technical merit review.

Laboratories may submit proposals directly to the SC Program office listed above. A copy should also be provided to the appropriate DOE operations office.

3.2 Proposal Cover Page

The following proposal cover page information may be placed on plain paper. No form is required.

Title of proposed project
SC Program announcement title
Name of laboratory
Name of principal investigator (PI)
Position title of PI
Mailing address of PI
Telephone of PI
Fax number of PI
Electronic mail address of PI
Name of official signing for laboratory*
Title of official
Fax number of official
Telephone of official
Electronic mail address of official
Requested funding for each year; total request

Use of human subjects in proposed project:

If activities involving human subjects are not planned at any time during the proposed project period, state "No"; otherwise state "Yes", provide the IRB Approval date and Assurance of Compliance Number and include all necessary information with the proposal should human subjects be involved.

Use of vertebrate animals in proposed project:

If activities involving vertebrate animals are not planned at any time during this project, state "No"; otherwise state "Yes" and provide the IACUC Approval date and Animal Welfare Assurance number from NIH and include all necessary information with the proposal.

Signature of PI, date of signature

Signature of official, date of signature*

*The signature certifies that personnel and facilities are available as stated in the proposal, if the project is funded.

3.4 Abstract

Provide an abstract of no more than 250 words. Give the broad, long-term objectives and what the specific research proposed is intended to accomplish. State the hypotheses to be tested. Indicate how the proposed research addresses the SC scientific/technical area specifically described in this announcement.

3.5 Narrative

The narrative comprises the research plan for the project and is limited to 25 pages. It should contain the following subsections:

Background and Significance: Briefly sketch the background leading to the present proposal, critically evaluate existing knowledge, and specifically identify the gaps which the project is intended to fill. State concisely the importance of the research described in the proposal. Explain the relevance of the project to the research needs identified by the Office of Science. Include references to relevant published literature, both to work of the investigators and to work done by other researchers.

Preliminary Studies: Use this section to provide an account of any preliminary studies that may be pertinent to the proposal. Include any other information that will help to establish the experience and competence of the investigators to pursue the proposed project. References to appropriate publications and manuscripts submitted or accepted for publication may be included.

Research Design and Methods: Describe the research design and the procedures to be used to accomplish the specific aims of the project. Describe new techniques and methodologies and explain the advantages over existing techniques and methodologies. As part of this section, provide a tentative sequence or timetable for the project.

Subcontract or Consortium Arrangements: If any portion of the project described under "Research Design and Methods" is to be done in collaboration with another institution, provide information on the institution and why it is to do the specific component of the project. Further information on any such arrangements is to be given in the sections "Budget and Budget Explanation", "Biographical Sketches", and "Description of Facilities and Resources".

3.6 Literature Cited

List all references cited in the narrative. Limit citations to current literature relevant to the proposed research. Information about each reference should be sufficient for it to be located by a reviewer of the proposal.

3.7 Budget and Budget Explanation

A detailed budget is required for the entire project period, which normally will be three years, and for each fiscal year. It is preferred that DOE's budget page, Form 4620.1 be used for providing budget information*. Modifications of categories are permissible to comply with institutional practices, for example with regard to overhead costs.

A written justification of each budget item is to follow the budget pages. For personnel this should take the form of a one-sentence statement of the role of the person in the project. Provide a detailed justification of the need for each item of permanent equipment. Explain each of the other direct costs in sufficient detail for reviewers to be able to judge the appropriateness of the amount requested.

Further instructions regarding the budget are given in section 4 of this guide.

* Form 4620.1 is available at web site:

<http://www.er.doe.gov/production/grants/forms.html>

3.8 Other Support of Investigators

Other support is defined as all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors. Information on active and pending other support is required for all senior personnel, including investigators at collaborating institutions to be funded by a subcontract. For each item of other support, give the organization or agency, inclusive dates of the project or proposed project, annual funding, and level of effort devoted to the project.

3.9 Biographical Sketches

This information is required for senior personnel at the laboratory submitting the proposal and at all subcontracting institutions. The biographical sketch is limited to a maximum of two pages for each investigator.

3.10 Description of Facilities and Resources

Describe briefly the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe pertinent capabilities, including support facilities (such as machine shops) that will be used during the project. List the most important equipment items already available for the project and their pertinent capabilities. Include this information for each subcontracting institution, if any.

3.11 Appendix

Include collated sets of all appendix materials with each copy of the proposal. Do not use the appendix to circumvent the page limitations of the proposal. Information should be included that may not be easily accessible to a reviewer.

Reviewers are not required to consider information in the Appendix, only that in the body of the proposal. Reviewers may not have time to read extensive appendix materials with the same care as they will read the proposal proper.

The appendix may contain the following items: up to five publications, manuscripts (accepted for publication), abstracts, patents, or other printed materials directly relevant to this project, but not generally available to the scientific community; and letters from investigators at other institutions stating their agreement to participate in the project (do not include letters of endorsement of the project).

4. Detailed Instructions for the Budget

(DOE Form 4620.1 "Budget Page" may be used)

4.1 Salaries and Wages

List the names of the principal investigator and other key personnel and the estimated number of person-months for which DOE funding is requested. Proposers should list the number of postdoctoral associates and other professional positions included in the proposal and indicate the number of full-time-equivalent (FTE) person-months and rate of pay (hourly, monthly or annually). For graduate and undergraduate students and all other personnel categories such as secretarial, clerical, technical, etc., show the total number of people needed in each job title and total salaries needed. Salaries requested must be consistent with the institution's regular practices. The budget explanation should define concisely the role of each position in the overall project.

4.2 Equipment

DOE defines equipment as "an item of tangible personal property that has a useful life of more than two years and an acquisition cost of \$5000 or more." Special purpose equipment means equipment which is used only for research, scientific or other technical activities. Items of needed equipment should be individually listed by description and estimated cost, including tax, and adequately justified. Allowable items ordinarily will be limited to scientific equipment that is not already available for the conduct of the work. General purpose office equipment normally will not be considered eligible for support.

4.3 Domestic Travel

The type and extent of travel and its relation to the research should be specified. Funds may be requested for attendance at meetings and conferences, other travel associated with the work and subsistence. In order to qualify for support, attendance at meetings or conferences must enhance the investigator's capability to perform the

research, plan extensions of it, or disseminate its results. Consultant's travel costs also may be requested.

4.4 Foreign Travel

Foreign travel is any travel outside Canada and the United States and its territories and possessions. Foreign travel may be approved only if it is directly related to project objectives.

4.5 Other Direct Costs

The budget should itemize other anticipated direct costs not included under the headings above, including materials and supplies, publication costs, computer services, and consultant services (which are discussed below). Other examples are: aircraft rental, space rental at research establishments away from the institution, minor building alterations, service charges, and fabrication of equipment or systems not available off-the-shelf. Reference books and periodicals may be charged to the project only if they are specifically related to the research.

a. Materials and Supplies

The budget should indicate in general terms the type of required expendable materials and supplies with their estimated costs. The breakdown should be more detailed when the cost is substantial.

b. Publication Costs/Page Charges

The budget may request funds for the costs of preparing and publishing the results of research, including costs of reports, reprints page charges, or other journal costs (except costs for prior or early publication), and necessary illustrations.

c. Consultant Services

Anticipated consultant services should be justified and information furnished on each individual's expertise, primary organizational affiliation, daily compensation rate and number of days expected service. Consultant's travel costs should be listed separately under travel in the budget.

d. Computer Services

The cost of computer services, including computer-based retrieval of scientific and technical information, may be requested. A justification based on the established computer service rates should be included.

e. Subcontracts

Subcontracts should be listed so that they can be properly evaluated. There should be an anticipated cost and an explanation of that cost for each subcontract. The total amount of each subcontract should also appear as a budget item.

4.6 Indirect Costs

Explain the basis for each overhead and indirect cost. Include the current rates.