

Program Announcement LAB 98-13
Molecular Biology Research Program
Microbial Genome Research

The Office of Biological and Environmental Research (OBER) of the Office of Energy Research (ER), U.S. Department of Energy (DOE), hereby announces its interest in receiving peer-reviewable proposals for research in support of the Molecular Biology Research Program. This Program is a coordinated multidisciplinary research effort to leverage progress in the Microbial Genome Program and develop creative, innovative approaches to exploit the rich diversity of microbes for environmental, energy, or commercial applications.

Funding is available for research that uses broad, interdisciplinary approaches and that takes advantage of the unique resources and capabilities of the national laboratories to understand complex biological processes. Special consideration will be given to research that includes significant collaborations with other national laboratories and/or with university or industrial partners although a few outstanding single investigator initiated proposals will also be considered. Proposals should include a description of how the National Laboratory is uniquely suited to carry out the proposed research.

Research proposals should address one of the following areas: (1) microbial diversity, (2) novel, more efficient strategies for determining the sequence of microbes for which the complete sequence of a very closely related microbe is known, and (3) novel strategies and tools for characterizing, manipulating, and modeling entire reaction pathways or regulatory networks of microbes or groups of microbes. Each proposal must clearly state which area is being addressed. If more than one area is being addressed, the proposal must clearly describe the expected advantages of an integrated approach.

1. Microbial Diversity

The majority of the biomass on earth is microbial. Microbial forms first appeared on earth approximately 3.7 billion years ago and all present-day life evolved from them. The recent confirmation of the Archaeal lineage (C. J. Bult, et al., Science, 273: 1058-1073, 1996) underscores that hitherto unsuspected microorganisms exist which possess many interesting and unique properties. Many of these offer considerable potential for commercial or industrial exploitation. Additionally, microbial life has been isolated from numerous "extreme" environments characterized by extremes in temperature, salinity, acidity, barometric pressure, or other unusual properties such as high metal or radionuclide concentrations.

This program seeks proposals to characterize the diversity of microbial species that can be identified in extreme environments, with a particular emphasis on environments of potential importance to DOE missions. These include, but are not limited to, environments contaminated by high concentrations of toxic chemicals, metals, and radionuclides or combinations of these contaminants. Other environments of interest include those likely to contain microbes with metabolic or biochemical properties of potential utility for DOE's missions in waste remediation, clean up mission, and energy production. Finally, techniques that allow characterization of microbes (including genomic sequencing) without prior cultivation are of interest.

2. Leveraged sequencing strategies

The most reasonable cost of sequencing genomic DNA, whether microbial or from other organisms, is currently estimated to be less than or equal to \$0.50 per base pair. Even if sequencing costs drop by a factor of 10, we will only be able to afford to sequence the genomes of a limited number of microorganisms. As the number of microbes whose genomes have been sequenced continues to increase, it is increasingly clear that having complete genomic sequence information on large numbers of microbes, more than we are likely to be able to afford to sequence, is going to be an invaluable resource for a wide variety of future applications. Microbial species are grouped in a number of ways based on shared properties, sequence, and forms. Very closely related microbial species often have dramatically different and useful properties. However, determining, de novo, the sequence of closely related microbial species is costly and inefficient.

This program seeks proposals to develop new strategies that use a previously determined microbial genomic sequence to rapidly, accurately, and cost effectively determine the entire genomic sequence of a related species. Approaches that use subtractive hybridization or chip hybridization have previously been suggested. Proposals of these or other novel approaches are encouraged that will enable rapid sequence determination. Proposals are also sought that will generate useful information for determining the phylogenetic "distance" between a previously sequenced reference organism and an organism whose sequence is being determined. Methods that are automatable and scalable are highly desired.

3. Reaction Pathways/Regulatory Networks

The analysis of complex systems requires an identification and an understanding of their elements, their interconnections, and, ultimately, their system properties. Understanding and exploiting the biological capabilities and potential of microbes will require strategies involving single genes and large networks of genes that are coordinately regulated. This information will be useful in efforts to engineer microbes

that produce or modify materials of interest to DOE. It will also be useful for determining the functions of unknown genes identified in microbial sequencing projects. Up to 67% of predicted genes in the 13 bacteria sequenced to date are unknown based on their lack of similarity to previously identified genes.

This program seeks proposals for novel or improved strategies to characterize, model, or manipulate entire biochemical or gene regulatory pathways. DOE has particular interest in pathways and networks associated with biocatalysis of organics, oxidation/reduction of metals, bioaccumulation of metals and radionuclides, fuel bioprocessing, biotransformation of DOE wastes, and pathways relevant to global carbon management. One entirely new opportunity for the rapidly growing amount of microbial genomic information that is becoming available is an area that can be termed Genome Engineering. For the first time the new knowledge enables us to conceive of transferring entire batteries of genes from one microbe to another in order to engineer new properties into these organisms. This is the next natural step beyond the single gene transfers and the recombinant organisms we are familiar with today.

DATES: Potential applicants are encouraged to submit a brief preproposal, consisting of a two to three page narrative describing the research project objectives and methods of accomplishment. Preproposals, referencing announcement LAB 98-13, should be sent by E-mail to: joanne.corcoran@oer.doe.gov no later than February 13, 1998. These will be reviewed relative to the scope and research needs of the DOE Molecular Biology Research Program. Telephone, telefax numbers, and Electronic mail addresses are required parts of the preproposals. A response to the preproposals will be provided by E-mail no later than February 19, 1998.

Formal proposals submitted in response to this notice must be received by 4:30 p.m., E.D.T., April 6, 1998, to be accepted for merit review and to permit timely consideration for award beginning in Fiscal Year 1999. Formal proposals must be sent to: Ms. Joanne Corcoran, ER-72, Mail Stop F-237, Office of Biological and Environmental Research, Office of Energy Research, U.S. Department of Energy, 19901 Germantown Road, Germantown, MD 20874-1290, Attn: Announcement 98-13, this address must also be used when submitting by U.S. Postal Service Express Mail, any commercial mail delivery service, or when hand carried.

FOR FURTHER INFORMATION CONTACT: Dr. Daniel Drell, telephone: (301) 903-4742 or Dr. David Thomassen, telephone: (301) 903-9817, Office of Biological and Environmental Research, ER-72, Office of Energy Research, U.S. Department of Energy, 19901 Germantown Road, Germantown, MD 20874-1290.

Molecular biological research on industrially important microorganisms and on microorganisms that live in extreme environments (including the deep subsurface,

geothermal environments, hypersaline environments, frozen environments, and toxic waste sites) is a developing area of great scientific promise that will impact many DOE missions, other federal agency missions, and U.S. industry. The Microbial Genome Program (MGP) supports key DOE business areas by providing microbial DNA sequence information that will further the understanding and application of microbial biology relating to energy production, chemical and materials production, and environmental cleanup. The current focus of the Microbial Genome Program is on microbial genomic sequencing. This solicitation represents an expansion of the current program to exploit information generated by the program and to anticipate future program and DOE needs.

It is anticipated that up to \$2.0 million will be available for awards during FY 1999, contingent upon the availability of funds.

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 announcement LAB 98-13 on all submissions and inquiries about this program.

**OFFICE OF ENERGY RESEARCH
GUIDE FOR PREPARATION OF SCIENTIFIC/TECHNICAL PROPOSALS
TO BE SUBMITTED BY NATIONAL LABORATORIES**

Proposals from national laboratories submitted to the Office of Energy Research (ER) as a result of this program announcement, will undergo scientific/technical merit review. The following guidelines for content and format are intended to facilitate an understanding of the requirements necessary for ER 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 applications 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 Cover Sheet (DOE ONLY)
- Face 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 type in this paragraph meets the guidelines); 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 Cover Sheet (DOE ONLY)

The Field Work Proposal (FWP) Cover Sheet is to be prepared and submitted consistent with policies of the investigator's laboratory and the local DOE Operations Office.

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

3.2 Face Page

The face page is to include the following information.

Title of proposed project
ER 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 ER 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 Energy Research. 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.