

# **Program Announcement To DOE National Laboratories LAB 04-07**

## ***Microbial Genome Program***

**SUMMARY:** 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 for research in support of the Microbial Genome Program (MGP), focused on microbes of interest to the DOE, e.g., those involved in environmental processes, including waste remediation, carbon management, biomass conversion, and energy production. This announcement is focused on: 1) whole genome-based systems or functional biology of DOE mission relevant microorganisms; 2) bioinformatics tools for high-throughput microbial genome annotation focused on currently unannotated genes and sequences, and pathway/function modeling; and 3) technologies and approaches to assess consortia and environmental diversity of hard-to-culture microbes. Under this announcement, proposals to carry out sequencing of microbial genomes **will be ineligible**. A separate process is available for the nomination and prioritization of sequencing candidates for the DOE Joint Genome Institute. This announcement emphasizes the use of already sequenced genomes that address DOE mission needs.

**DATES:** Preproposals referencing Program Announcement LAB 04-07, should be received by January 29, 2004.

Formal proposals in response to this notice should be received by 4:30 p.m., E.D.T., April 15, 2004, to be accepted for merit review and funding in Fiscal Year 2004.

**ADDRESSES:** Preproposals referencing Program Announcement LAB 04-07, should be sent to Dr. Daniel W. Drell, SC-72/Germantown Building, U.S. Department of Energy, 1000 Independence Avenue, SW, Washington, DC 20585-1290. Email is strongly encouraged for submitting preproposals using the following address: kim.laing@science.doe.gov.

Formal proposals in response to Program Announcement LAB 04-07 are to be submitted as 2 paper copies of the proposal and one CD containing the proposal in PDF format. Color images should be submitted as a separate file in PDF format and identified as such. These images should be kept to a minimum due to the limitations of reproducing hardcopies. They should be numbered and referred to in the body of the technical scientific proposal as Color image 1, Color image 2, etc.

The 2 copies of the proposal and the CD, referencing Program Announcement LAB 04-07, should be sent to: Life Sciences Research Division, SC-72/Germantown Building, Office of Biological and Environmental Research, Office of Science, U.S. Department of Energy, 1000 Independence Avenue, SW, Washington, D.C. 20585-1290, ATTN: Program Announcement LAB 04-07.

When submitting by U.S. Postal Service Express Mail, any commercial mail delivery service, or when hand carried by the researcher, the following address must be used: Life Sciences Research Division, SC-72, Office of Biological and Environmental Research, Office of Science, U.S. Department of Energy, 19901 Germantown Road, Germantown, MD 20874-1290, ATTN: Program Announcement LAB 04-07.

**FOR FURTHER INFORMATION CONTACT:** Dr. Daniel W. Drell, SC-72/Germantown Building, U.S. Department of Energy, 1000 Independence Avenue, SW, Washington, DC 20585-1290, telephone: (301) 903-4742, Email: [daniel.drell@science.doe.gov](mailto:daniel.drell@science.doe.gov).

**SUPPLEMENTARY INFORMATION:** The Microbial Genome Program (MGP), a key element of the DOE Genomes to Life Program (<http://doegenomestolife.org>) supports key DOE missions by leveraging microbial DNA sequence information to further the understanding and application of microbiology relating to environmental processes, including waste remediation, carbon management, biomass conversion, and energy production. The determination of microbial genome sequences is a mission of the DOE Joint Genome Institute (JGI) and follows a separate process independent of this solicitation. Over the last nine years, sequencing of microorganisms that live in a variety of environments has provided a considerable information base for scientific research related not only to DOE missions but also to other Federal agency missions and U.S. industry. Proposals are now being sought in three complementary areas: whole-genome based systems and functional analyses; bioinformatics applied to extracting additional information from microbial genome sequences; and the characterization of the diversity of microbial consortia and/or hard-to-culture microbes that mediate processes of relevance to the DOE. Each proposal must clearly state which area is being addressed; if a researcher wishes to address more than one area, the proposal must clearly describe the expected advantages of an integrated approach.

Candidate microorganisms for study can comprise archaea, bacteria, algae or fungi or communities made up of bacteria, archaea, algae and/or fungi that mediate or catalyze metabolic events of energy or environmental importance. Preference will be given to those researchers using microbes, for which complete or near-complete genomic sequencing information in the public domain exists. (See <http://www.ornl.gov/microbialgenomes/progress.html> for a current list of microbes that have been and are being sequenced). Priority will be given to studies on those microbes or microbial consortia that can bioremediate metals and radionuclides, generate energy compounds (e.g., hydrogen or methane), convert biomass to intermediate or final energy products, or that are involved in environmental carbon management, e.g., fix CO<sub>2</sub>. For studies on microbes that are members of communities, at least one member should be a fully sequenced microbe. Strict or opportunistic pathogens or parasites will not be considered.

1) **Systems and Functional Analysis.** Even simple microbes are constituted from thousands of genome-derived proteins. Many of these proteins do not act alone; rather, they act as parts of protein complexes that carry out functions not mediated by the individual gene products themselves. Multi-protein complexes often are not static, they are dynamic in response to environmental influences, intracellular conditions and metabolic demands, and whether the cell is responding to a stress or preparing to divide. The DOE MGP is particularly interested in improved and high-throughput approaches to

functional characterization (e.g., transporters, environmental sensors, redox enzymes, cytoskeletal components, DNA repair systems, metal reductases, biodegradative enzymes, etc.) of the multi-protein complexes within sequenced microbes participating in processes related to the aforementioned mission areas. Coordinated expression of pathways and processes involved in the aforementioned areas of mission interest (e.g., bioremediation, carbon sequestration, and energy production) in response to environmental variations or experimental manipulations is also a priority.

2) **Bioinformatics.** By December 2003, completed genomic sequences of perhaps 145 archaea and bacteria had been completed and published, many as a direct result of DOE Microbial Genome Program funding. For several microbes, complete sequences of close evolutionary relatives now or will soon exist. Computational comparative genomics can illuminate evolutionary pathways to complement traditional phenotype-based analyses, provide data for the prediction of gene function between organisms, and contribute to modeling pathways. The value of such comparative functional analyses is highlighted by the remarkable frequency of novel open reading frames in microbial genome sequences (up to half the predicted genes in many cases) that currently lack any annotation. The evolutionary conservation of open reading frames and certain protein functions between microbes and more complex organisms (including human) emphasizes the value of microbial sequences for understanding the functions of uncharacterized microbial (and, potentially, human) genes. To this end, computational methods for high-throughput interspecies genomic comparisons are an area of particular interest for this solicitation. Proposals are requested that propose ways in which microbial sequence data from all sources can be analyzed, compared, annotated, and used to predict the function of homologous genes in both prokaryotic and eukaryotic organisms. Of particular interest are those approaches to predicting functions for currently unannotated open reading frames and approaches to predicting associations of genes in functional multi-protein complexes. Thus, this notice solicits proposals for research into:

- a) Novel computational tools to increase the value of microbial genome sequence information, such as improved approaches for identifying noncoding sequence elements that may participate in regulatory or genomic management (i.e., binding to intracellular scaffolding or membrane components) or that affects 3-D structure and chemistry of the genomic DNA;
- b) Computational tools to identify and model gene expression networks, or to identify likely participants in higher-order multi-protein complexes;
- c) Computational analyses to support existing techniques, such as (but not limited to) adjusting the BAC sequence size or primer walking, that would enable the more efficient finishing of draft sequences of microbial genomes. Proposals should identify those problems that require the most resources to finish a sequence and propose computational steps to reduce the time and effort involved.

Of special interest will be methods that use unique DOE resources in massively parallel, high- capacity supercomputers (machines in the multi-teraflop range). It is expected that computational tools developed under these awards will be widely distributed to the

scientific community (e.g., via a World Wide Website) and some level of user support will be available.

3) **Consortia and Hard-to-Culture Microbes.** Most of our current knowledge of microbiology is derived from individual species that either cause diseases or grow as monocultures under laboratory conditions and are thus easy to study. The preponderance of species in the environment does neither and is thus largely opaque to scientific study. Many are thought to grow as part of interdependent consortia in which one species supplies a nutrient necessary for the growth of another. Virtually nothing is known of the organization, membership, or functioning of these consortia, especially those involved in environmental processes in which DOE is interested. Technologies and approaches are sought that will enable genomic analyses of microbial consortia as well as analyses of the genomic information content and diversity of those species that have proven refractory to laboratory culture but are plentiful in environments challenged with metal and radionuclide wastes, or involved in carbon sequestration.

### **Preapplicaitons**

Potential researchers are strongly encouraged to submit a brief preproposal that consists of one to two pages of narrative describing the research objectives and technical approach(s). Preproposals will be reviewed relative to the scope and research needs of both the BER Microbial Genome Program, as well as the Genomes to Life Program into which the Microbial Genome Program will become fully integrated in Fiscal Year 2008. Preproposal review criteria are more fully outlined in the summary paragraph and in the SUPPLEMENTARY INFORMATION. Principal investigator telephone number, Fax number, and Email address are required as part of the preproposal. A response to each preproposal discussing the potential programmatic relevance of a formal proposal will be communicated by Email to the Principal Investigator within 14 to 21 days of receipt. Any renewal proposals must include a list of publications resulting from previous DOE Microbial Genome Program funding.

### **Program Funding**

It is anticipated that approximately \$1 million will be available for MGP awards in Fiscal Year 2004, contingent on availability of appropriated funds in Fiscal Year 2004, and the size of the awards. Multiple year funding is expected up to a maximum of three years, also contingent on availability of funds and progress of the research. **At the end of three years, the Microbial Genome Program will transition fully into the DOE Genomes to Life Program and proposals for continuation of ongoing research started under this Program will not be accepted.** Awards are expected to range from \$150,000 to \$450,000 per year, total costs, with terms of one to three years. Reasonable increases in second and third year budget periods can be requested. DOE is under no obligation to pay for any costs associated with the preparation or submission of proposals if an award is not made.

Each response to this solicitation will be evaluated for relevance to: a) the successful completion of the BER long term measure to characterize the multiprotein complexes (or the lack thereof) involving a scientifically significant fraction of a microbe proteins; b) the development of

computational models to direct the use and design of microbial communities to clean up waste, sequester carbon, or produce hydrogen; or c) to develop science-based solutions for the cleanup and long term monitoring of DOE contaminated sites.

Any recipient of an award from the Office of Science, performing 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/rdna-apr98.pdf>, (59 FR 34496, July 5, 1994), or such later revision of those guidelines as may be published in the Federal Register.

The Project Description must be 20 pages or less, exclusive of attachments. It must contain an abstract or project summary on a separate page with the name of the principal investigator (PI), mailing address, phone, fax and Email listed. The proposal must include letters of intent from collaborators (briefly describing the intended contribution of each to the research), and short curriculum vitae, consistent with the National Institutes of Health (NIH) guidelines, for the PI and any co-PIs.

**Other useful web sites include:**

MGP Home Page - <http://www.ornl.gov/sci/microbialgenomes/>  
DOE Genomes to Life Program: <http://DOEGenomestoLife.org>  
DOE Joint Genome Institute Microbial Web page: [http://www.jgi.doe.gov/JGI\\_microbial/html/](http://www.jgi.doe.gov/JGI_microbial/html/)  
GOLD Microbial Genome Database: <http://wit.integratedgenomics.com/GOLD/>  
GenBank Home Page - <http://www.ncbi.nlm.nih.gov/>  
Human Genome Home Page - <http://www.ornl.gov/hgmis>

The instructions and format described below should be followed. Reference Program Announcement LAB 04-07 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 (FWP) 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**

Formal proposals in response to Program Announcement LAB 04-07 are to be submitted as 2 paper copies of the proposal and one CD containing the proposal in PDF format. Color images should be submitted as a separate file in PDF format and identified as such. These images should be kept to a minimum due to the limitations of reproducing hardcopies. They should be numbered and referred to in the body of the technical scientific proposal as Color image 1, Color image 2, etc.

## **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 10 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.

### **3.3 Table of Contents**

Provide the initial page number for each of the sections of the proposal. Number pages consecutively at the bottom of each page throughout the proposal. Start each major section at the top of a new page. Do not use unnumbered pages and do not use suffices, such as 5a, 5b.

### **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 5 pages per task. 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.sc.doe.gov/production/grants/Forms-E.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 \$25,000 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.