# Office of Science
# Notice DE-FG01-04ER04-07

## *Microbial Genome Program*

**Department of Energy**

**Office of Science Financial Assistance Program Notice DE-FG01-04ER04-07; Microbial Genome Program**

**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 (DOE), hereby announces its interest in receiving applications 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, applications 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:** Preapplications referencing Program Notice DE-FG01-04ER04-07, should be received by January 29, 2004.

Formal applications 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:** Preapplications referencing Program Notice DE-FG01-04ER04-07, 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 preapplications using the following address: kim.laing@science.doe.gov.

Formal applications referencing Program Notice DE-FG01-04ER04-07, must be sent electronically by an authorized institutional business official through DOE's Industry Interactive Procurement System (IIPS) at: http://e-center.doe.gov/. IIPS provides for the posting of solicitations and receipt of applications in a paperless environment via the Internet. In order to submit applications through IIPS, your business official will need to register at the IIPS website. **IIPS offers the option of using multiple files, please limit submissions to one volume and**

**one file if possible, with a maximum of no more than four PDF files.** The Office of Science will include attachments as part of this notice that provide the appropriate forms in PDF fillable format that are to be submitted through IIPS. Color images should be submitted in IIPS 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 them. They should be numbered and referred to in the body of the technical scientific grant application as Color image 1, Color image 2, etc. Questions regarding the operation of IIPS may be emailed to the IIPS Help Desk at: HelpDesk@pr.doe.gov, or you may call the help desk at: (800) 683-0751. Further information on the use of IIPS by the Office of Science is available at: http://www.sc.doe.gov/production/grants/grants.html.

If you are unable to submit an application through IIPS, please contact the Grants and Contracts Division, Office of Science at: (301) 903-5212 or (301) 903-3604, in order to gain assistance for submission through IIPS or to receive special approval and instructions on how to submit printed applications.

**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.

**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. Applications 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 application must clearly state which area is being addressed; if an applicant wishes to address more than one area, the application 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 applicants 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 CO2. 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. It is estimated that between three and six awards for a total of up to $1 million could be available for this area initiating in Fiscal Year 2004.

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. Applications 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 applications 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. Applications 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. It is anticipated that between three and six awards for a total of up to $1 million could be available for this area initiating in Fiscal Year 2004.

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. It is anticipated that between three and six awards totaling up to $1 million could be available for this area initiating in Fiscal Year 2004.

## Preapplicaitons

Potential applicants are strongly encouraged to submit a brief preapplication that consists of one to two pages of narrative describing the research objectives and technical approach(s). Preapplications 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. Preapplication 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 preapplication. A response to each preapplication discussing the potential programmatic relevance of a formal application will be communicated by Email to the Principal Investigator within 14 to 21 days of receipt. Any renewal applications must include a list of publications resulting from previous DOE Microbial Genome Program funding.

## Program Funding

It is anticipated that approximately $3 million will be available for all MGP awards in Fiscal Year 2004, with as many as fifteen awards anticipated, 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 applications 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 applications 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.

## Merit Review

Applications will be subjected to formal merit review (peer review) and will be evaluated against the following evaluation criteria which are listed in descending order of importance 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 will often be used, and submission of an application constitutes agreement that this is acceptable to the investigator(s) and the submitting institution.

The Office of Science (SC), as part of its grant regulations (10 CFR 605.11(b)) requires that a grantee funded by SC and performing research involving recombinant DNA molecules shall comply with the National Institutes of Health "Guidelines for Research Involving Recombinant DNA Molecules" (51 FR 16958, May 7, 1986), or such later 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 applicant, mailing address, phone, fax and Email listed. The application must include letters of intent from collaborators (briefly describing the intended contribution of each to the research), and short curriculum vitaes, consistent with the National Institutes of Health (NIH) guidelines, for the applicant and any co-PIs. To provide a consistent format for the submission, review and solicitation of grant applications submitted under this notice, the preparation and submission of grant applications must follow the guidelines given in the Application Guide for the Office of Science Financial Assistance Program 10 CFR Part 605. Access to SC's Financial Assistance Application Guide is possible via the World Wide Web at: http://www.sc.doe.gov/grants/grants.html.

**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/
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 Catalog of Federal Domestic Assistance number for this program is 81.049, and the solicitation control number is ERFAP 10 CFR Part 605.

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for Resource Management

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