

Office of Energy Research

Notice 98-16

Genome Instrumentation Research Program

Department of Energy
Office of Energy Research

Energy Research Financial Assistance Program Notice 98-16; Genome Instrumentation Research Program

Agency: U.S. Department of Energy

Action: Notice inviting research grant applications.

SUMMARY: The Office of Biological and Environmental Research (BER) of the Office of Energy Research (ER) of the U.S. Department of Energy (DOE), hereby announces its interest in receiving applications in Instrumentation Research supporting the Human Genome Program. Applications are sought from a broad range of scientists with backgrounds in biology, chemistry, physics, and engineering including those not presently involved in the Human Genome Program. Both substantive improvements to current systems and novel and creative new strategies are needed in preparation for the needs of biology in the next century. New instrumentation and technical approaches are sought for DNA sequencing, automation and integration of DNA sequencing systems, validation of DNA sequencing accuracy, and the determination of gene function of newly sequenced DNA. The goals are to reduce costs and increase the throughput while maintaining accuracy for production DNA sequencing and related analyses.

DATES: Potential applicants are strongly encouraged to submit a brief preapplication. All preapplications should be received by DOE by 4:30 P.M., E.D.T., June 8, 1998. Early submissions are encouraged. A response encouraging or discouraging a formal application will be communicated to the applicant within two weeks of receipt.

Formal applications, in response to this notice, must be received by 4:30 p.m., E.D.T., August 19, 1998, in order to be accepted for merit review and to permit timely consideration for award in Fiscal Year 1999.

ADDRESS: Preapplications, referencing Program Notice 98-16, should be forwarded to: Dr. Charles G. Edmonds, Medical Applications and Biophysical Research

Division, ER-73, U.S. Department of Energy, 19901 Germantown Road, Germantown, MD 20874-1290, Attn: Program Notice 98-16. Preapplications will also be accepted by Fax and E-mail: Fax number: (301) 903-0567 and E-mail: charles.edmonds@oer.doe.gov.

Formal applications, referencing Program Notice 98-16, should be forwarded to: U.S. Department of Energy, Office of Energy Research, Grants and Contracts Division, ER-64, 19901 Germantown Road, Germantown, MD 20874-1290, Attn: Program Notice 98-16. This address also must be used when submitting applications by U.S. Postal Service Express Mail, or any commercial mail delivery service, or when hand-carried by the applicant. An original and seven copies of the application must be submitted.

FOR FURTHER INFORMATION CONTACT: Dr. Charles G. Edmonds, Medical Applications and Biophysical Research Division, ER-73, 19901 Germantown Road, Germantown, MD 20874-1290; telephone: (301) 903-0042; E-mail: charles.edmonds@oer.doe.gov. The full text of Program Notice 98-16 is available via the Internet using the following web site address:
<http://www.er.doe.gov/production/grants/grants.html>

SUPPLEMENTAL INFORMATION: The Office of Biological and Environmental Research of the U. S. Department of Energy and the National Human Genome Research Institute of the National Institutes of Health are participating in a coordinated international program to "determine the complete sequence of the human genome, discover all the human genes and render them accessible for further biological study." As this program continues, improvement of sequencing technology is essential to complete the sequence of the 3 billion subunits of the human genome by the target year of 2005. Functional analyses of the displayed genes and their encoded proteins will continue long thereafter.

In December of 1997 a DOE-sponsored review of the DOE Human Genome Program was published by the JASON Program Office of the MITRE Corporation. A summary and related discussion has been printed: Science, 279(5347), (1998) 36-37; Science, 279(5347), (1989) 23; and Science, 279(5354), (1989) 1115-1116. The full report can be accessed on the Internet using the following web address:

<http://www.ornl.gov/hgmis/publicat/miscpubs/jason/index.html>. A more general discussion of the Human Genome Program may be found in Primer on Molecular Genetics available on the Internet using the following web address:
http://www.ornl.gov/TechResources/Human_Genome/publicat/primer/intro.html.

These documents and companion references will be particularly useful to scientists and engineers less knowledgeable regarding current genomic technologies and projected needs.

Production scale sequencing has been initiated based largely on gel electrophoresis with data acquisition by laser induced fluorescence. Additionally, sequence comparison tasks are performed using "sequencing by hybridization" technologies. However, it may not be possible to achieve the desired goal within the available budget and project period without substantial improvements in speed and reliability of sequencing methods and other techniques currently in widespread use. Continuing developments of existing approaches to address the necessities of the production environment will be required.

Further, with an eye to the future, basic research is also needed that will substantially speed and enhance genomic analyses in the years following the projected completion of the human genome in the year 2005. After this date, the need for fast and cost-effective determination of DNA sequence for the comparison of sequences among human individuals and also for the determination of the genomes of numerous organisms of biomedical and commercial interest will be ongoing. Additionally, with the continuing acquisition of this remarkable base of biological data, high throughput experimental tools will be required to assist conversion into a practical and useful understanding of the function for the encoded gene products.

Both substantial evolutionary improvements in current systems and also revolutionary technologies for the post-2005 era are sought under this solicitation.

Research applications are invited:

- To develop approaches to more rapidly, accurately, and economically determine DNA sequence. Cost-effective approaches that increase current maximum read lengths of 800-1000 bases by at least a factor of 2.5, i.e., to at least 2000-2500 bases, are particularly desired.
- To develop instrumentation that integrates and more thoroughly automates the current steps of DNA sequence determination, e.g., sample preparation, sample loading, sample analysis, and data analysis. A priority will be placed on approaches that emphasize miniaturization and micro fabrication.
- To develop approaches that (1) verify the accuracy of a previously determined DNA sequence without having to redetermine its entire sequence and (2) provide economical error checking and proofreading of newly determined DNA sequence.
- To develop tools that enable the efficient comparison of a known DNA sequence with a related but previously undetermined DNA sequence.
- To develop techniques for determining the functions of large numbers of genes in parallel. Techniques that match the speed and volume of DNA sequence determination are particularly desired.

The success of devices, methods or techniques for DNA sequencing is dependent on downstream data technologies. Where appropriate, applications should account for the necessary link to current information technology and existing data sets in their plans to address the technical challenges enumerated above.

Program Funding

It is anticipated that up to a total of \$2,000,000 will be available for multiple awards to be made in Fiscal Year 1999 funding grants for the new Genome Instrumentation Research Program, contingent on the availability of appropriated funds. Award sizes are expected to be on the order of \$100,000-600,000 per year for total project costs for a typical three-year grant with out-year support contingent on the availability of funds, progress of research and programmatic needs. Collaborative projects involving several research groups or more than one institution may receive larger awards if merited. A similar announcement is being simultaneously issued to the DOE National Laboratories.

Collaboration

Applicants are encouraged to collaborate with researchers in other institutions, such as universities, industry, non-profit organizations, federal laboratories and federally funded research and development centers (FFRDCs), including the DOE National Laboratories, where appropriate, and to incorporate cost sharing and/or consortia wherever feasible.

Collaborative research applications may be submitted in several ways:

(1) When multiple private sector or academic organizations intend to propose collaborative or joint research projects, the lead organization may submit a single application which includes another organization as a lower-tier participant (subaward) who will be responsible for a smaller portion of the overall project. If approved for funding, DOE may provide the total project funds to the lead organization who will provide funding to the other participant via a subcontract arrangement. The application should clearly describe the role to be played by each organization, specify the managerial arrangements and explain the advantages of the multi-organizational effort.

(2) Alternatively, multiple private sector or academic organizations who intend to propose collaborative or joint research projects may each prepare a portion of the application, then combine each portion into a single, integrated scientific application. A separate Face Page and Budget Pages must be included for each organization participating in the collaborative project. The joint application must be submitted to

DOE as one package. If approved for funding, DOE will award a separate grant to each collaborating organization.

(3) Private sector or academic organizations who wish to form a collaborative project with a DOE FFRDC may not include the DOE FFRDC in their application as a lower-tier participant (subaward). Rather, each collaborator may prepare a portion of the proposal, then combine each portion into a single, integrated scientific proposal. The private sector or academic organization must include a Face Page and Budget Pages for its portion of the project. The FFRDC must include separate Budget Pages for its portion of the project. The joint proposal must be submitted to DOE as one package. If approved for funding, DOE will award a grant to the private sector or academic organization. The FFRDC will be funded, through existing DOE contracts, from funds specifically designated for new FFRDC projects. DOE FFRDCs will not compete for funding already designated for private sector or academic organizations. Other Federal laboratories who wish to form collaborative projects may also follow guidelines outlined in this section.

Preapplications

A brief preapplication may be submitted. The preapplication should identify, on the cover sheet, the institution, Principal Investigator name, address, telephone, fax and E-mail address, title of the project, and the field of scientific research. The preapplication should consist of a two to three page narrative describing the research project objectives and methods of accomplishment. These will be reviewed relative to the scope and research needs described in this Notice.

Preapplications are strongly encouraged but not required prior to submission of a full application. Please note that notification of a successful preapplication is not an indication that an award will be made in response to the formal application.

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

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

The evaluation will include program policy factors such as the relevance of the proposed research to the terms of the announcement and an agency's programmatic needs. Note, external peer reviewers are selected with regard to both their scientific

expertise and the absence of conflict-of-interest issues. Non-federal reviewers may be used, and submission of an application constitutes agreement that this is acceptable to the investigator(s) and the submitting institution.

Information about development and submission of applications, eligibility, limitations, evaluation, selection process, and other policies and procedures may be found in 10 CFR Part 605 and in the Application Guide for the Office of Energy Research Financial Assistance Program. Electronic access to the Guide and required forms is made available via the World Wide Web at:

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

Energy Research, as part of its grant regulations, requires at 10 CFR 605.11(b) that a recipient receiving a grant to perform research involving recombinant DNA molecules and/or organisms and viruses containing recombinant DNA molecules shall comply with the National Institutes of Health "Guidelines for Research Involving Recombinant DNA Molecules," which is available via the World Wide Web at: ***<http://www.niehs.nih.gov/odhsb/biosafe/nih/nih97-1.html>***, (59 FR 34496, July 5, 1994), or such later revision of those guidelines as may be published in the Federal Register.

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

John Rodney Clark
Associate Director
for Resource Management
Office of Energy Research

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