

**Office of Energy Research**

**Notice 97-17**

***Human Genome Program***

***Technologies in Support of the DOE Joint Genome Institute***

**Department of Energy  
Office of Energy Research**

**Energy Research Financial Assistance Program Notice 97-17; Human Genome Program -  
Technologies in Support of the DOE Joint Genome Institute**

**AGENCY:** U.S. Department of Energy

**ACTION:** Notice inviting grant applications

**SUMMARY:** The Office of Health and Environmental Research (OHER) of the Office of Energy Research (ER), U.S. Department of Energy (DOE), hereby announces its interest in receiving applications for support of the Human Genome Program. This Program is a coordinated multidisciplinary research effort to develop creative, innovative resources and technologies that lead to a molecular level understanding of the human genome. As one aspect of this program, the DOE is establishing a "Joint Genome Institute" (JGI) to develop a DNA sequencing factory. The JGI will oversee a central sequencing facility that will initially have parallel production lines that use shotgun and transposon-based directed sequencing approaches. This dual approach is intended to evolve into an optimized and unified sequencing strategy within two to three years. This unified strategy will take advantage of technologies and expertise at the JGI and in the broader research community. An important aspect of developing this automated facility will be the establishment of external collaborations and partnerships aimed at technology development. The JGI's genomic sequencing program will also be coupled to a collection of experimental functional genomics approaches designed to provide a partial functional characterization of the genes as they are revealed by the sequencing. Here, the primary goal will be to develop cost-effective approaches that can yield worthwhile functional information. A related goal is to develop improved ways of integrating human genomics with the information coming from model organism genomics.

**DATES:** Preapplications referencing Program Notice 97-17 should be received by August 1, 1997. Formal applications in response to this notice must be received by 4:30 p.m., E.D.T., October 16, 1997, to be accepted for merit review and to permit timely consideration for award in FY 1998.

**ADDRESSES:** Preapplications referencing Program Notice 97-17 should be sent to Dr. Marvin E. Frazier, Office of Health and Environmental Research, ER-72, Office of Energy Research, U.S. Department of Energy, 19901 Germantown Road, Germantown, MD 20874-1290; e-mail is acceptable for submitting preapplications using the following address:

joanne.corcoran@oer.doe.gov. Formal applications referencing Program Notice 97-17 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 97-17. This address 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; however, applicants are requested not to submit multiple application copies using more than one delivery or mail service.

**FOR FURTHER INFORMATION CONTACT:** Dr. Marvin E. Frazier, ER-72, Office of Health and Environmental Research, Office of Energy Research, U. S. Department of Energy, 19901 Germantown Road, Germantown, MD 20874-1290, telephone: (301) 903-6488, e-mail: joanne.corcoran@oer.doe.gov.

**SUPPLEMENTARY INFORMATION:** The goal of this notice is to support technology development that serves the needs of the Department of Energy's (DOE) Joint Genome Institute (JGI). The DOE JGI is developing a high throughput DNA sequencing factory. This factory will take advantage of the complementing strengths of each of the three current DOE Genome Centers: Lawrence Berkeley National Laboratory (LBNL), Lawrence Livermore National Laboratory (LLNL), and Los Alamos National Laboratory (LANL). The JGI Sequencing Factory will be physically located in proximity to LLNL and LBNL. The Scientific Director of the DOE Human Genome Program, Dr. Elbert Branscomb, is the leader of the JGI. With respect to the JGI genomic sequencing task, the specific goals are: (1) to establish a cooperative technology development project with an outside entity that will produce, within two years, an automated DNA sequencing production line based on either shotgun or directed strategies; and (2) to develop and implement technologies for automated and advanced high-throughput DNA sequencing that can be integrated into the unified sequencing production strategy that is identified and implemented at the JGI.

In support of the first goal, the grantee will form a close collaboration with the JGI aimed at technology co-development and transfer for high throughput production DNA sequencing. A critical success factor for this effort will be the construction of a new, highly automated pilot DNA sequencing production line at the JGI within 6 to 9 months of the project's start. The grantee, working in conjunction with the JGI, will help build and maintain automated devices as appropriate for this pilot line (e.g., those for DNA purification, DNA sequencing, and automated finishing). It is anticipated that this pilot DNA sequencing production line may use, in significant part, technology supplied by the grantee. The second phase of the project, to be completed within two years, will be the development of a high throughput DNA sequencing production line. It is anticipated that this production line will lead current technology in automation and the minimization of human labor and will ultimately produce 100-200 Mb of finished human genomic sequence per year. It is also expected that, in close cooperation with the JGI, the grantee will use the technology being supplied to perform a significant amount of DNA sequencing on targets that support the DOE effort. This would be designed to drive the technology development and to permit modifications in technology between the pilot and production phases to be evaluated and validated under high throughput conditions. It is estimated that one major award, for a total of approximately \$4 million in FY 1998, will be made.

In support of the second sequencing goal, technology developments aimed at improving the constituent technologies and overall performance of the JGI DNA sequencing production line are sought. These could include: innovative instrumentation and automated systems that offer the potential for rapid, cost-effective sequencing of approximately a million bases per day; for non-gel techniques and direct imaging approaches; for development of applied genome informatics software for use in DNA sequencing and functional interpretation, including information retrieval; for user interfaces compatible with Genome Data Base (GDB), Genome Sequence DataBase (GSDB), and GenBank; and for communications, software engineering, and data management. Improved algorithms and hardware for DNA sequence annotation, including identification of homologies, regulatory sites, and protein coding regions can also be included. It is anticipated that between 2-4 awards for a total of up to \$1 million could be made in FY 1998.

With respect to the functional genomics and model organism goals, projects in the following program areas are solicited: 1) strategies for full-length cDNA clone generation and sequencing and for economically and accurately determining transcript lengths and types; 2) strategies for expression mapping, sub-cellular localization, and pathway tracing; 3) economical approaches for revealing single base pair polymorphisms and for characterizing their haplotypes; and 4) affordable approaches for using model organisms to systematically relate phenotype information to anonymous genes discovered in the human genome. It is anticipated that between 2-4 awards for pilot and proof-of-principle studies, for a total of up to \$1 million could be made in FY 1998.

Potential applicants are strongly encouraged to submit a brief preapplication that consists of two to three pages of narrative describing the research objectives and methods of accomplishment. Preapplications will be reviewed relative to the scope and research needs of the DOE Human Genome Program, as outlined in the summary paragraph and in the SUPPLEMENTARY INFORMATION. Principal investigator address, telephone number, FAX number, and e-mail address are required as part of the preapplication. A response to each preapplication discussing the potential programmatic relevance of a formal application generally will be communicated to the Principal Investigator within 21 days of receipt. ER's preapplication policy can be found on ER's Grants and Contracts Web Site at: <http://www.er.doe.gov/production/grants/preapp.html>.

It is anticipated that approximately \$6 million will be available for grant awards during FY 1998, contingent upon availability of appropriated funds. Multiple year funding of grant awards is expected, with out-year funding also contingent upon the availability of appropriated funds, progress of the research, and programmatic needs. It is expected that most awards will be from one to three years and that there will be one award for approximately \$4 million per year (total costs) with the remaining 4-6 awards in the \$200 thousand to \$400 thousand per year (total costs) range. The dissemination of materials and research data in a timely manner is essential for progress towards the goals of the DOE Human Genome Program. OHER requires the timely sharing of resources and data. Applicants should, in their applications, discuss their plans for disseminating research data and materials which may include, where appropriate, putting cell lines, probes, sequence data, etc., into public repositories. Funds to defray the costs of disseminating materials or submitting data to repositories are allowable; however, such requests must be adequately justified.

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.

Information about development and submission of applications, eligibility, limitations, evaluation, selection process, and other policies and procedures may be found in the ER Application Guide for the Office of Energy Research Financial Assistance Program 10 CFR Part 605, which is available on the World Wide Web at:

<http://www.er.doe.gov/production/grants/grants.html>. The ER, as part of its grant regulations, requires at 10 CFR 605.11(b) that a grantee funded by ER and 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" (51 FR 16958, May 7, 1986), 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  
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for Resource Management  
Office of Energy Research

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