

**Office of Science**  
**Notice 00-20**

*Medical Applications Program*

**Department of Energy**  
**Office of Science**

**Office of Science Financial Assistance Program Notice 00-20; Medical Applications Program**

**AGENCY:** U.S. Department of Energy (DOE)

**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 grant applications to support one specific research area within the Medical Applications Program: Innovative approaches to cell-targeted ablation therapy for cancer with in vivo radiation techniques. The emphasis will be on the therapeutic use of ionizing radiation such as may be achieved with radionuclide therapy or dual step techniques such as boron neutron capture therapy. The specific goals include development of novel ligands and delivery techniques to target and treat cancer at the cellular level. Special consideration will be given to applications reflecting a well integrated, multidisciplinary team effort of scientists with skills to address such complex challenges as chemical ligand synthesis, tumor targeting, and dosimetry. Access to appropriate tumor models for pre-clinical testing will impact funding considerations. Applications for clinical trials using already developed compounds and techniques will not be considered.

**DATES:** Before preparing a formal application, potential applicants are encouraged to submit a brief pre-application. All pre-applications referencing Program Notice 00-20, should be received by DOE by 4:30 p.m., E.D.T., October 16, 2000. A response encouraging or discouraging the submission of a formal application will be communicated by electronic mail within approximately 2 weeks.

Formal applications submitted in response to this Notice must be received by 4:30 p.m., E.S.T., January 5, 2001, to be accepted for merit review and consideration of an award in Fiscal Year 2001.

**ADDRESSES:** Pre-applications referencing Program Notice 00-20, are to be sent, if possible, by E-mail or Fax to Ms. Sharon Betson (sharon.betson@science.doe.gov; Fax: 301-903-0567). Pre-applications will also be accepted if mailed to the following address: Ms. Sharon Betson, Office of Biological and Environmental Research, SC-73, 19901 Germantown Road, Germantown, MD 20874-1290.

Formal applications referencing Program Notice 00-20, should be forwarded to: U.S. Department of Energy, Office of Science, Grants and Contracts Division, SC-64, 19901 Germantown Road, Germantown, MD 20874-1290, ATTN: Program Notice 00-20. This address must also be used when submitting applications by U.S. Postal Service Express Mail or any other commercial overnight delivery service, or hand-carried by the applicant. An original and seven copies of the application must be submitted.

**FOR FURTHER INFORMATION CONTACT:** Peter T. Kirchner, MD, or Prem C. Srivastava, Ph.D., Office of Biological and Environmental Research, Medical Sciences Division (SC-73), U.S. Department of Energy, 19901 Germantown Road, Germantown, MD 20874-1290, telephone: (301) 903-3213, FAX: (301) 903-0567, E-mail: peter.kirchner@science.doe.gov or prem.srivastava@science.doe.gov. The full text of Program Notice 00-20 is available via the Internet using the following web site address: <http://www.sc.doe.gov/production/grants/grants.html>.

**SUPPLEMENTARY INFORMATION:** The Medical Applications Program supports directed nuclear medicine research in the areas of radiopharmaceutical development, molecular nuclear medicine and medical imaging to promote the use of radioisotopes for non-invasive diagnosis and therapy. Selective molecular targeting with radioligands will facilitate the analysis of cellular and tissue function and may enable purposeful disruption of specific cellular functions in tissues requiring therapy. The in-vivo distribution of radiopharmaceuticals and other cell-directed ligands may be defined and monitored with a variety of in-vivo imaging methods, such as the use of gamma cameras, positron emission tomographs (PET), fluorescent techniques and a variety of optical techniques. The development of in-vivo imaging techniques based on cell-targeting should assist reliable differentiation between normal and abnormal tissues at the molecular and/or metabolic levels, ideally leading to the development of more effective therapies and useful monitoring techniques for such therapies. Thus, highly selective substrate-binding molecules, when labeled with high energy-emitting radioisotopes or other noxious or pre-sensitizing agents, can become powerful tools for targeted molecular therapy of cancer.

Basic research in molecular biology has provided new insights to the molecular basis of human disease and its potential molecular targets. DOE's current Molecular Nuclear Medicine Program encourages development of new technologies for

molecular delivery of radioisotopes to disease target sites with a high degree of molecular precision, recognition, and target selectivity. The availability of new technology for high resolution imaging of small animals should facilitate the evaluation of new molecular ligands for their potential value and subsequent use in human trials of cancer therapy.

This Notice is to solicit grant applications for developing innovative approaches to cell-targeted ablation therapy for tumors with in vivo radiation techniques. A well integrated team effort by scientists from overlapping disciplines of chemistry, radiopharmaceutical chemistry, cellular and molecular biology, and biological and nuclear medicine imaging will be judged important in the evaluation of submitted research applications. Methodological approaches that can be adapted to deliver more than one type of radiation or more than one radioisotope to the target sites are encouraged. It will be important for each application to consider also the following objectives:

- 1) Techniques to ensure highly selective tumor targeting by the proposed ligands;
- 2) Efficient screening techniques for selecting candidate ligands for in-vivo testing;
- 3) Preliminary data indicating reasonable likelihood of success for in-vivo targeting of primary tumors and their metastases in pre-clinical animal trials;
- 4) Reliable approaches for dosimetry calculations to normal tissues and to tumor sites based on 3-dimensional modeling;
- 5) Measurement techniques for accurately assessing the success of tumor targeting in vivo;
- 6) Measurement techniques for assessing therapy effects in vivo at the molecular, cellular and metabolic levels.

### **Program Funding**

It is anticipated that up to \$2 million will be available for multiple awards in Fiscal Year 2001 contingent upon the availability of appropriated funds and the scientific merit of the submitted applications. Previous awards have ranged from \$200,000 to \$400,000 per year (direct plus indirect costs) with terms lasting up to three years. Similar award sizes are anticipated for new grants. Applications may request project support up to three years, with out-year support contingent on the availability of

appropriated funds, satisfactory progress in the research proposed, and programmatic needs.

## **Pre-applications**

A brief pre-application should be submitted. The cover sheet of the pre-application should list the title of the project, the institution, and the principal investigator's name, address, telephone, fax, and E-mail address. The pre-application should not exceed two pages (in addition to the cover sheet). It should identify and describe the research objectives, the methods proposed for accomplishment of the research, and the key members of the scientific team responsible for this effort. Pre-applications will be evaluated relative to the scope and objectives of this solicitation.

## **Merit Review**

Applications will be subjected to 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 Approach and Methods
3. Competency of the Research Team and Adequacy of Available Resources
4. Justification 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 the agency's programmatic needs. It should be noted that external peer reviewers are selected on the basis of 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 review process is acceptable to the investigator(s) and the submitting institution.

## **Submission Information**

Information about the development, submission of applications, eligibility, limitations, evaluation, the selection process, and other policies and procedures may be found in 10 CFR Part 605, and in the Application Guide for the Office of Science Financial Assistance Program. Electronic access to the Guide and required forms is made available via the World Wide Web at: <http://www.sc.doe.gov/production/grants/grants.html>. DOE is under no obligation to pay for any costs associated with the preparation or submission of applications if an award is not made. In addition, in response to this Notice, the Project Description must be 25 pages or less, exclusive of attachments, and the application must contain a table of contents, an abstract or project summary, letters of intent from collaborators

(if any), and short curriculum vitae, consistent with National Institutes of Health guidelines. Block 15 of the SC grant face page (form DOE F4650.2) should list the PI's phone number, fax number, and E-mail address.

DOE policy requires that potential applicants adhere to 10 CFR 745 "Protection of Human Subjects" or such later revision of those guidelines as may be published in the Federal Register.

The Office of Science as part of its grant regulations requires at 10 CFR 605.11(b) that a recipient receiving a grant and performing research involving recombinant DNA molecules and/or organisms and viruses containing recombinant DNA molecules shall comply with NIH "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 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 of Science  
for Resource Management

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