Office of Science
Financial Assistance
Funding Opportunity Announcement
DE-PS02-09ER09-18

Radiochemistry and Instrumentation Research

The Office of Biological and Environmental Research (BER) of the Office of Science (SC), U.S. Department of Energy (DOE) advances world-class biological and environmental research programs and scientific facilities for DOE missions in energy, environment, and basic research. BER hereby announce its interest in receiving applications for pilot research project grants in two topic areas, Radiochemistry and Radionuclide Imaging Instrumentation. **In the area of Radiochemistry**, BER invites applications for fundamental research involving particularly improvements in the synthetic methodology for incorporating the radioisotope in a wide range of organic molecules with techniques designed to allow dual or multiple labeling of the targeting molecule for dual energy or hybrid imaging techniques *in vivo*. **In the area of Radionuclide Imaging Instrumentation**, BER invites applications dealing with the design and development of new or improved radionuclide imaging instrumentation that can significantly increase the accuracy of quantitative assessments of the three dimensional spatial and temporal distribution of radiotracers in living systems with the aid of hybrid imaging techniques. Applications should focus on basic research that will significantly advance the current state of the science underpinning nuclear medicine research and applications.

Responses to this Funding Opportunity Announcement (FOA) should address the development and use of highly innovative radiotracer chemistry or instrumentation technologies for quantitative *in vivo* measurement of site-specific (*in situ*) chemical reactions, their spatial distributions and metabolic perturbations, and ensuing biological processes with a high degree of accuracy.

Program Funding

Total awards in **Fiscal Year 2009** are anticipated to be up to $7,000,000 for radiochemistry research and up to $3,000,000 for imaging instrumentation research. The number of awards will be contingent on satisfactory peer review, the availability of appropriated funds, and the size of the awards. Individual grants will be available as one time awards for pilot research projects that may extend to two-years. Award requests for projects that extend to two years should include one total budget (one budget page) for the entire project period. The total budget for a pilot research project is expected to be in the general range of $300,000 total costs (direct plus indirect) for one year, and $600, 000 for a two year project period. DOE is under no obligation to pay for any costs associated with the preparation or submission of an application. DOE reserves the right to fund, in whole or in part, any, all, or none of the applications submitted in response to this FOA.

PREAPPLICATIONS

Potential applicants are **strongly encouraged** to submit a brief preapplication, referencing Funding Opportunity Announcement DE-PS02-09ER09-18 for receipt by DOE by 4:30 p.m., Eastern Time, **April 20, 2009**.

Preapplications are limited to **three pages total**, including cover page. The cover page should include the title of the project, the institution or organization, principal investigator name, telephone number, fax number, and e-mail address. Preapplications should be sent as a text file without attachments or a single PDF file attachment via e-mail to: **radiochem@science.doe.gov with "Preapplication DE-PS02-09ER09-18 - [indicating Radiochemistry or Imaging Instrumentation]"** as the subject. No FAX or mail submission of preapplications will be accepted.

Preapplications will be reviewed for conformance with the guidelines presented in this FOA and suitability in the technical areas specified in this FOA. A response to the preapplications encouraging or discouraging formal applications will be communicated to the applicants by **April 24, 2009**. Applicants who have not received a response regarding the status of their preapplication by this date are responsible for contacting the program to confirm the status.

Preapplications should consist of no more than two pages of narrative stating the research objectives, describing the technical approach(s), and identifying the proposed team members and their expertise. No budget information or biographical data need be included, nor is an institutional endorsement necessary. The intent in requesting a preapplication is to save the time and effort of applicants in preparing and submitting a formal project application that may be inappropriate for the program.

APPLICATION DUE DATE: May 20, 2009, 8:00 pm, Eastern Time

ATTENTION - CHANGE IN SUBMISSION REQUIREMENT EFFECTIVE March 12, 2009

The Office of Science is now requiring all financial assistance applications be submitted through the Department of Energy e-Center (IIPS) http://doe-iips.pr.doe.gov/. Applicants will still need to visit the Grants.gov website http://www.grants.gov/ to download the required Application Package (forms), by clicking on "Apply for Grants" and searching for the Funding Opportunity Announcement.

For Instructions on the Use of IIPS visit this web page, IIPS Instructions.
http://www.sc.doe.gov/grants/iips-Instructions.html

Registration Requirements: There are several one-time actions you must complete in order to submit an application (e.g., obtain a Dun and Bradstreet Data Universal Numbering System (DUNS) number, register with the Central Contract Registry (CCR), register with the credential provider, and register with Grants.gov). See http://www.grants.gov/GetStarted. Use the Grants.gov Organization Registration Checklist at http://www.grants.gov/assets/OrganizationRegCheck.doc to guide you through the process. Designating an E-Business Point of Contact (EBiz POC) and obtaining a special password called an MPIN are important steps in the CCR registration process. Applicants, who are not registered

with CCR and Grants.gov, should allow at least 21 days to complete these requirements. It is suggested that the process be started as soon as possible.

GENERAL INQUIRIES ABOUT THIS FOA SHOULD BE DIRECTED TO:

Scientific/Technical Program Contact:

Agency Contact:

Dr. Prem C. Srivastava
Phone: (301) 903-4071
Email: prem.srivastava@science.doe.gov

SUPPLEMENTARY INFORMATION:

For over 50 years, an important focus of BER and its predecessor offices has been to promote research advances in physics, chemistry, material sciences and high speed computing to translate our knowledge of radioactive-decay and its detection into innovative radiotracer imaging technology for use in biological and nuclear medicine research . The radiotracer and radionuclide imaging technologies already developed under this program have been used to solve critical problems in biology and nuclear medicine, and they constitute a large part of the scientific foundations of nuclear medicine today.

Along the way, advances in genomics, transgenic animal models and micro-imaging instrumentation technologies have prompted a paradigm shift from imaging human organ function to directly visualizing *in vivo* metabolic networks and regulatory systems, their interaction with molecular probes, and the chemical reactions in biological systems that underlay the functional differentiation of organs, tissues and specialized cell types.

Molecules that either direct or are subject to homeostatic controls in biological systems are convenient targets for specific molecular probes. Such target-directed molecular probes can be tailored to reflect a specific molecular interaction. Labeled with appropriate radioisotopes these molecular probes can be measured *in vivo*, in real time, on their way to, and in interaction with their targets *in vivo*. In other words, they allow the quantitative measurement of selected molecular interactions during normal tissue homeostasis and again after perturbations of the normal state. The *in vivo* quantification of radiolabeled molecules at various regional sites is accomplished by specialized radiation imaging instruments, such as single photon emission computed tomographs (SPECT) and positron emission computed tomographs (PET). This type of imaging has the capability of measuring biological processes at the molecular and the metabolic levels. **One limitation remains, however, and that relates to the correct spatial and tissue localization of the molecular and metabolic processes so measured. This can be substantially improved with hybrid imaging techniques as has been well demonstrated by PET-CT hybrid imaging. Hence, the development of efficient approaches dual labeling of molecular probes with maintenance of high specific activity for the radioactive label is highly desirable. Another advantage to dual labeling is the possibility of measuring two different biochemical or metabolic processes at the same time.**

Radiochemistry: Radiolabeled probes (radiotracers) can be detected at concentrations up to 1000-fold lower than those labeled with non-radioactive markers (e.g. MRI contrast agents). This remarkable sensitivity for the study of low abundance targets of biological interest requires a high specific activity of the radiolabeled molecular probe. High specific activity probes generally allow improved quantitative information about the target molecule and its binding capacity.

This FOA is to solicit applications for grants in the radiochemistry topic area to support development of new techniques for dual labeling of molecular probes (including nanoparticles) of biological importance, both with radionuclides in high specific activities and with contrast agents for CT, MRI, or a variety of indicators for optical imaging. These new labeling techniques can be applicable to molecular probes for either PET or SPECT imaging. The two different molecular labels may include also. two different radionuclides with or without additional labels for CT, MRI or Optical Imaging at different sites of the same molecular probe in order to reflect two different functional characteristics or a combination of structural and functional information through the use of multimodality/hybrid instruments such as PET/MRI, PET/CT or PET combined with an Optical detector system.

Radionuclide Imaging Instrumentation

There is an urgent need for **design and development of new or improved radionuclide imaging instrumentation that can significantly increase the accuracy of quantitative assessments of the three dimensional spatial and temporal distribution of radiotracers in living systems with the aid of hybrid imaging techniques. This need is particularly applicable to small animal imaging.**

To achieve these goals, improvements in instrumentation are needed to accurately quantify radiotracers present in low concentrations in small tissue volumes that can be accurately defined in 3D space. In order to accomplish this goal, new developments, improvements or radical changes **are needed in the fundamental detector components that are necessary for simultaneous measurement of spatial, metabolic and biochemical data. Proposals may include significant improvements or radical design changes for effective combinations of signal detectors (scintillators, or solid-state detectors), electronics, signal processing and display systems,** and reconstruction and noise-reduction algorithms.

This FOA solicits applications for grants to support development of new advanced hybrid instruments which can provide accurate spatial localization and quantitative measurement of metabolic and biochemical processes in 1 mm cubed target volumes throughout the entire field of view and have sensitivities the same or significantly higher than currently available high-resolution MicroPET or MicroSPECT systems.

General Requirement - Potential Applications and Benefits of Radiochemistry and Imaging Instrumentation in Biology Underpinning Major Advances in Nuclear Medicine: Within the context of the current mission, scope and focus of BER, the programmatic goal of this FOA is to provide, through basic research, the Radiochemistry and Instrumentation capabilities for quantitative measurement, detection and study of *in situ* perturbations of homeostatic reactions

and biological processes underlying the functional differentiation of organs, tissues and specialized cell types. It is anticipated that new radiotracer and new imaging instrumentation technologies will provide invaluable tools to investigators for advancing the biological applications of nuclear medicine.

Applications should address hypothesis-driven research to define and/or understand the key physical, chemical, and biological problems influencing the need for the proposed technological advances. Furthermore, these applications should discuss and detail the scientific basis for the development of new, innovative radiochemistry or imaging instrumentation technologies. **Applications should address the applicability of the proposed research to DOE's stated investments in science and technology and describe how the proposed research will contribute to the advancement of nuclear medicine.**

Biological targets included for the proof of concept to study potential applications of the investigative technologies under this FOA are listed below.

Endogenous Genes: Radiotracer technologies to image mRNA transcripts in real time in tissue culture and in animal models. These include new generation of radioligand molecules that will interact with the macromolecular nucleic acid structures *in vivo*, and technologies which will significantly improve the signal to background ratio and will make *in vivo* visualization of *in situ* chemical reactions and the effects of their perturbations feasible. Successful projects should contribute to the goal of imaging specific gene expression in real time *in vivo*.

Protein Structures: Radiolabeled molecular probes for targeting protein structures including mutations critical in mediating cellular signaling and developmental pathways to carcinogenesis and abnormal cell growth. Such radiolabeled probes would be unique tools for *in vivo* measurement of specific biological pathways, and for understanding the mechanism of action of target specific new drugs.

Cellular Targets of Low Abundance: Radiotracers for *in vivo* targeting and imaging sites in and/or on cells that allow those cells to respond to external or environmental stimuli including cell to cell communications, and to study behavior, fate and repopulation of highly specialized cell types in important biological processes.

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.

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

Posted on the Office of Science Grants and Contracts Web Site
April 3, 2009.