Office of Science
Financial Assistance
Funding Opportunity Announcement
DE-PS02-09ER09-08

Integrated Radiochemistry Research Projects of Excellence

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 announces its interest in receiving applications for potential funding of **Integrated Radiochemistry Research Projects of Excellence** (Projects) to serve two important goals: 1) Integrated involvement of graduate-student and postdoctoral trainees in the fundamental research that seeks improvements in radiolabeling and radiotracer development chemistry in the following areas of interest to BER: a) Development of new chemical reactions for high specific activity probe synthesis, b) Models to study reactivity at the tracer mass scale, c) Nanoparticle platforms that can incorporate one or more imaging agents and d) Automation technology for radiotracer synthesis, and 2) Enhancement of training opportunities in radiochemistry to ensure the future availability of human resources for important radiochemistry applications. Such applications include the development of fundamental radiotracer methodologies for both BER mission-relevant biological research needs in the context of energy and environment, and for use in technological advances in nuclear medicine research. Applicant Projects must have access to existing advanced facilities and an interdisciplinary collaborative team of nuclear chemists, radiochemists, synthetic chemists and biochemists able to support a robust research training environment. Institutional settings should offer broad ranging research collaborations with other federally-funded and/or private sector-funded investigators to allow: i) opportunities to link radionuclide production research to incorporation of radioisotopes in a wide range of organic molecules for radiolabeled probe development, and ii) the use of these new probes and methodologies for quantitative *in vivo* measurement of site-specific (*in situ*) chemical reactions, their metabolic perturbations and the ensuing biological processes. For details, refer to supplementary information below.

Program Funding

It is anticipated that up to **$3,000,000 will be available for approximately 5 awards** to be made in Fiscal Year 2009, contingent on the availability of appropriated funds. Applicants may request project support for up to three years with annual budgets not to exceed $600,000/year total costs (direct plus indirect), with out-year support contingent on the availability of funds, progress of the research, and programmatic needs. 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 Announcement.

PREAPPLICATIONS

Potential applicants **are required to submit** a brief preapplication, referencing Funding Opportunity Announcement (FOA)
DE-PS02-09ER09-08 for receipt by DOE by 4:30 p.m., Eastern Time, **February 16, 2009**. Preapplications are limited to **three pages total**, including the 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.

Only those preapplicants that receive notification from DOE encouraging a formal application may submit full applications. No other formal applications will be considered.

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-PS02-09ER09-08 - [Integrated Radiochemistry Projects of Excellence]"** 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 Announcement and suitability in the technical areas of radiochemistry research and training, and availability of project supporting infrastructure including inter/or intra-institutional collaborations, personnel, equipment and facilities specified in this Announcement. A response to the preapplications encouraging or discouraging formal applications will be communicated to the applicants by **February 27, 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 this status.

Preapplications should consist of no more than two pages of narrative stating the project objectives, describing the technical approach(es) and radiochemistry training-supporting infrastructure, personnel and facilities, 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 not meet the program goals.

APPLICATION DUE DATE: April 2, 2009, 8:00 pm, Eastern Time

Applications must be submitted using Grants.gov, the Funding Opportunity Announcement can be found using the CFDA Number, 81.049 or the Funding Opportunity Announcement number, DE-PS02-09ER09-08. Applicants must follow the instructions and use the forms provided on Grants.gov.

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, one important focus of BER and its predecessor programs 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 radiotracer imaging technology innovations for use in biomedical research. This program has made major contributions to the advance of nuclear medicine technologies over the past several decades.

BER continues to support fundamental research in radiochemistry and radiotracer development activities which includes development of new methodologies for real-time, high-resolution imaging of dynamic biological processes in energy- and environment-relevant contexts, and encompasses applications of new innovative technologies for biological systems and nuclear medicine research use.

In the broader context of biological systems and nuclear medicine research, radionuclide imaging continues to stand out as a singular tool for studying living organisms in a manner that is highly quantitative, three dimensional, temporally dynamic, and non-perturbative of the natural biochemical processes under study. Radiotracer imaging methods provide new opportunities for quantitative measurement of *in situ* chemical reactions in living biological systems with a high degree of specificity. Such measurements extend to quantifying perturbation induced changes in these chemical reactions and the ensuing homeostatic processes.

This Announcement is to solicit applications for funding Integrated Radiochemistry Research Projects of Excellence (Projects) to fulfill the following important radiochemistry research and training needs.

A. Radiochemistry research needs

The applicant Projects must offer to address the challenges and opportunities in the following areas of radiochemistry research needs:

- Development of new chemical reactions that meet the demands and synthetic constraints of working with radioisotopes at high specific activity - All aspects of radiotracer imaging will benefit from an increased number and improved set of chemical reactions that can be used to label molecules of interest with a radioisotope. Radiotracer chemistry methods are needed which are versatile and easy to translate from molecule to molecule, and which will catalyze the use of radiotracer technology across a broad range of living biological systems.
- Utilization of physical chemistry to develop models that can predict and explain reactivity at the tracer mass scale - Models are needed for increasing our understanding of critical parameters of chemical reactions at tracer scale, and optimizing reaction methodologies for accelerated use of labeling protocols.

- Construction of nanoparticle platforms that can incorporate one or more imaging agents and targeting moieties - Such particles may be ideal for dual-modality applications. There is a significant opportunity and need for the development of methods for highly efficient radiolabeling and purification techniques able to separate labeled and unlabeled macromolecules, proteins, and nanoparticles, thus increasing their specific activity.
- Creation/improvement of automation technology for radiotracer synthesis that is adaptable in a variety of reaction scenarios through modular or "kit-like" construction - Reliable kit-like labeling and purification protocols and versatile automated systems, which can potentially bridge the gap that exists in translating radiotracer technologies into new research areas, are needed.

B. Areas of research applications

Listed below are applications that include development of fundamental radiotracer methodologies for both BER mission-relevant biological research needs in the context of energy and environment, and for use in technological advances in nuclear medicine research.

- **Radiolabeled probes for imaging mRNA transcripts and gene expression in real time in tissue culture and living biological systems:** These are to 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.
- **Radiolabeled molecular probes for targeting protein structures:** These include new radiolabeled molecular probes for targeting protein sites and mutations critical in mediating cellular signaling and abnormal cell function and growth as well as for *in vivo* measurement and understanding of developmental pathways to wayward genes.
- **Radiotracers for imaging 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 and also for measuring cell-to-cell communications, cell behavior and fate, and repopulation of highly specialized cell types in important biological processes.

Addressing these specific areas of research opportunities will allow development of new techniques for radiolabeling of molecular probes of biological importance, with radionuclides currently available, with specific activities that approach the theoretical maximum for these specific probes. These new radiolabeling techniques should allow incorporation of preventive measures to protect the probe from auto-radiolysis in vitro and *in vivo*. These new labeling techniques can be applicable to molecular probes for either PET or SPECT, or for multimodality imaging (e.g. two different radionuclides or one fluorescent- and one radio-label at two different sites of the same molecular probe) for simultaneous quantitative assessment of two different biochemical reactions that may reflect two different functional characteristics or a combination of structural and functional information.

C. The applicant projects must offer graduate- and postdoctoral level training that is integrated with the fundamental radiochemistry research outlined in this application.

- Ideally a Project will support four radiochemistry trainees including up to three graduate research students (enrolled towards Ph.D. degree) and up to two postdoctoral fellows.
- The radiochemistry training of graduate-student and postdoctoral trainees is to be integrated with the four research areas outlined above through active participation of these trainees in these BER specific research projects.

D. Projects must have easy access to existing advanced facilities and an interdisciplinary collaborative team of nuclear chemists, radiochemists, synthetic (organic and inorganic) chemists and biochemists to produce radionuclides for incorporation into molecular probes and to quantify and characterize the behavior of radiolabeled molecular probes in biological systems of interest.

E. Institutional settings are to offer broad ranging intra - or inter-institutional research collaborations with other federally-funded and or private sector-funded investigators and allow: a) opportunities to link separately funded programs in radionuclide production and/or nuclear chemistry to the preparation of precursors for the synthesis of radiolabeled probes, and b) utilization of these new probes in the investigation of biological processes and new radiopharmaceutical research applications stemming from programs supported by other sources.

F. Projects must be in an academic environment, existing independently or in a partnership with a National Laboratory. They are required to have easy access to multispecialty capabilities such as strong departments or programs in nuclear-, radio- and radiolabeling-chemistry, physics, and biological imaging.

- Required resources include cyclotron, reactor, or generator-based facilities for the production, isolation, and purification of radionuclides and radiolabeled chemical probes and radionuclide imaging capabilities such as positron emission tomography (PET) and single photon emission computed tomography.
- The research environment should be robust and multi-disciplinary, able to offer training opportunities that interlink the radiochemistry applied to radiolabeled probe development with both nuclear chemistry for production and use of radioisotopes and applications research for use of radiolabeled probes in advancing biological and nuclear medicine imaging. The academic institution(s) should possess strong programs in chemistry, physics, and medical imaging with well-supported basic research in technology applications and/or translational research programs.
- The projects should be embedded in a multidisciplinary institutional setting with the opportunity to attract other federally funded training grants in the radiochemistry allied fields of nuclear chemistry and nuclear medicine research.

G. The Applicant Projects must provide a timeline/schedule of anticipated milestones and performance (deliverables) for both the proposed radiochemistry research and the training of Ph.D. students and post-doctoral researchers. These schedules should provide criteria against which to measure the progress and productivity of the projects on an annual basis for the duration of the project.

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 Methods and/or Approach;
3. Competency of the Research Team and Adequacy of Available Resources;
4. Reasonableness and Appropriateness of the Proposed Budget (Justification of the Proposed Budget); and
5. Likelihood that the research can contribute to the achievement of an extrinsic goal that is outside the research field itself and thereby serve as a basis for new or improved technology or assist in the solution of other national needs.

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
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