

**Program Announcement
To DOE National Laboratories
LAB 07-13**

Quantitative Microbial Biochemistry and Metabolic Engineering for Biological Hydrogen Production

SUMMARY: The Office of Biological and Environmental Research (BER) of the Office of Science (SC), U.S. Department of Energy (DOE), hereby announces its interest in receiving proposals for research that supports the Genomics: GTL research program (<http://www.genomicsGTL.energy.gov>). In this notice, proposals are solicited to develop and validate key technologies that support the systems-level study of regulatory and metabolic networks for microbial hydrogen production. These technologies must lead to substantial progress towards the characterization of the regulatory and metabolic pathways that influence and control hydrogen production, or the use of metabolic engineering to target and manipulate enzymatic, regulatory, or transport pathways that impact microbial hydrogen production.

DATES: Potential researchers are **required** to submit a brief preproposal, referencing **LAB 07-13 for receipt by DOE by 4:30 p.m., Eastern Time, January 4, 2007**. Preproposals will be reviewed for conformance with the guidelines presented in this Notice and suitability in the technical areas specified in this Notice. A response to the preproposals encouraging or discouraging formal proposals will be communicated to the researchers by **January 12, 2007**. Researchers who have not received a response regarding the status of their preproposal by this date are responsible for contacting the program to confirm this status.

Only those researchers that receive notification from DOE encouraging a formal proposal may submit a full proposal. **No other formal proposals will be considered.**

Potential researchers **must** submit a brief preproposal that consists of no more than three pages of narrative stating the research objectives, describing the technical approach(s), and identifying the proposed team members and their expertise. The intent in requesting a preproposal is to save the time and effort of researchers in preparing and submitting a formal project proposal that may be inappropriate for the program. Preproposals will be reviewed relative to the scope and research needs as outlined in the summary paragraph and in the **SUPPLEMENTARY INFORMATION**. The preproposal should identify, on the cover sheet, the title of the project, the institution or organization, principal investigator name, telephone number, fax number, and e-mail address. No budget information or biographical data need be included, nor is an institutional endorsement necessary.

Preproposals referencing LAB 07-13 should be sent as a text file or single PDF file attachments via e-mail to: **genomicsGTL@science.doe.gov** with "**Preproposal LAB 07-13 Biohydrogen Lastname Institution**" as the subject. No FAX or mail submission of preproposals will be accepted.

Eligibility: Researchers from FFRDCs (Federally Funded Research and Development Centers) or DOE National Laboratories. BER reserves the right to encourage, in whole or in part, any, all, or none of the preproposals submitted, and may issue further guidance on the scope of the full proposal submissions of those encouraged.

Formal proposals in response to this Notice should be submitted via ePMA and must be received by 8:00 pm Eastern Time, **March 8, 2007**.

This section pertains only to those proposers that have been encouraged to submit a full proposal. A complete formal FWP in a single Portable Document Format (PDF) file must be submitted through the DOE ePMA system (<https://epma.doe.gov>) as an attachment. To identify that the FWP is responding to this program announcement, please fill in the following fields in the "ePMA Create Proposal Admin Information" screen as shown:

Proposal Short Name:

Fiscal Year:

Proposal Reason:

Program Announcement Number: Lab 07-13 *

Program announcement Title: Quantitative Microbial Biochemistry and Metabolic Engineering for Biological Hydrogen Production *

Proposal Purpose:

Estimated Proposal Begin Date:

HQ Program Manager Organization:

* Please use the wording shown when filling in these fields to identify that the FWP is responding to this Program Announcement.

In order to expedite the review process, please submit a CD and three copies of the proposal using the following, by U.S. Postal Service Express Mail, any commercial mail delivery service, or when hand-carried to:

Ms. Joanne Corcoran
U.S. Department of Energy
Office of Biological and Environmental Research, SC-23.2
19901 Germantown Road
Germantown, MD 20874-1290
ATTN: Program Announcement LAB 07-13

FOR FURTHER INFORMATION CONTACT: Dr. Sharlene Weatherwax, phone: (301) 903-6165; E-mail: sharlene.weatherwax@science.doe.gov

SUPPLEMENTARY INFORMATION:

Background:

The Genomics: GTL program seeks to achieve a systems-level understanding of microbes (including fungi) directly relevant to DOE mission needs in energy (cleaner energy, biomass conversion, carbon sequestration) or the environment (cleanup of metals and radionuclides at DOE sites). The Hydrogen Fuel Initiative of 2003 encourages research and development of carbon-neutral hydrogen production technologies geared towards supplying the needs of a future hydrogen economy. In some specific cases, details of the biological processes linked to hydrogen metabolism and of the enzymes involved as essential catalysts have been investigated and are reasonably well known. However, efforts to understand the variety of organisms and the diversity of biochemical mechanisms that participate in this extensive biological hydrogen economy are still at an early stage. The emergence of tools for genomic analysis of microorganisms and for dissecting their interlocking metabolic functions presents an opportunity for extremely rapid progress in this promising area of research.

Fundamental research into the molecular mechanisms underlying biological hydrogen production is the essential key to our ability to adapt, exploit, and extend what nature has accomplished for our own renewable energy needs. Microbial hydrogen production, through nitrogenase-mediated, fermentative, or biophotolytic pathways, must be understood well enough to model hydrogenase structure and function, regulatory and metabolic networks, and eventually entire organisms. Achieving this level of understanding will require basic research that investigates a greater range of hydrogen-producing enzymes and organisms, mechanisms of hydrogenase assembly, oxygen sensitivity of hydrogenase, electron-transfer rate limitations, and regulatory and metabolic processes that influence hydrogen production. Leveraging such knowledge against biotechnological innovation will be needed to engineer the ideal organism or consortial community to use in hydrogen bioreactors or the ideal enzyme-catalyst to use in bioinspired nanostructures for hydrogen production.

To this end, development of novel technologies is encouraged to support the characterization of the internal environment and subcellular architecture of microbes and to explore how these characteristics affect microbial metabolism and physiology with respect to biological hydrogen production.

A microbe's subcellular environment may be dictated by structural cytoskeletal components, partitioning and localization within a cell, proteins, concentrations, and subcellular dynamics are critically important parameters in determining its function, for identifying functional networks of proteins in a morphological context, and for expanding our understanding of whole-cell function. Thus, studies on the topological, physical, and chemical properties of cellular cytoplasm, their effects on protein dynamics, on flux rates of metabolites, on protein-protein and protein-ligand interactions, and ultimately, on protein function during microbial hydrogen production are needed.

Research is needed that furnishes information on the dynamic behavior of these various molecules as the "molecular machines" perform their functions and on the distribution, localization, movement, and temporal variations of the molecules and complexes inside individual microbes as they carry out hydrogen-producing reactions. Research is also needed to reconcile genomic information with cellular architecture and metabolic flux and to develop and validate computational algorithms designed to recognize regulatory networks or patterns of gene

expression under different circumstances. Molecular dynamic simulations are not encouraged for this solicitation.

Proposals are solicited to develop and validate key technologies that support the systems-level study of regulatory and metabolic networks for microbial hydrogen production, including but not limited to:

- Techniques to map the spatial distribution and concentrations of proteins and metabolites relevant to biological hydrogen production.
- Techniques to assess fluxes and changes in concentrations of key metabolites as a function of intracellular parameters and spatial location during biological hydrogen production.
- Techniques to effectively map the immediate environment surrounding specific proteins, protein complexes, or other structural components of microbial hydrogen production.
- Techniques to measure changes in enzyme-catalyzed reaction rates (catabolic and anabolic) and fluxes, as a function of the internal cell milieu, e.g., distance from the inner membrane surface, proton concentration, etc, relevant to biological hydrogen production.
- Techniques to quantitate intracellular protein-protein association/dissociation rates as a function of ion concentrations, dielectric constants, protein concentrations, small molecule (metabolite, cofactor, ligand, etc.) concentrations critical to biological hydrogen production.

Researchers must directly address how the selected key technologies selected will demonstrate substantial progress towards one or more of the following aims:

- Characterization of the regulatory and metabolic pathways that influence and control hydrogen production, including defining gene regulatory networks controlling the expression of genes involved in hydrogen production or cofactor synthesis.
- Metabolic engineering to target and manipulate enzymatic, regulatory, or transport pathways that impact microbial hydrogen production.

Proposals are not encouraged to pursue microbial fuel cell applications, biomimetic hydrogen production systems, or process improvements of industrial biohydrogen production from waste streams.

Data and results that are generated through these investigations that are appropriate to share with the broader community should be provided in timely, open, and machine-readable format where possible. Funded investigators are expected to contribute to and participate with the GTL working group on data management, and to adhere to the group's consensus on data sharing.

The Genomics:GTL program supports a combination of large, well integrated, multidisciplinary research teams and smaller, focused research projects. This solicitation will support smaller, focused research projects to develop new technologies, research strategies, or research resources needed by the Genomics:GTL program.

Information on the research projects currently funded by the Genomics: GTL program and a description of project goals and overall program organization can be found at:
<http://genomicsgtl.energy.gov/>.

Program Funding: It is anticipated that up to \$4 million total will be available for multiple awards to be made in FY 2007 for Quantitative Microbial Biochemistry and Metabolic Engineering for Biological Hydrogen Production. The number of awards will be contingent on satisfactory peer review, the availability of appropriated funds, and the size of the awards. Multiple year funding is expected. Proposals may request project support for up to three years, with out-year support contingent on the availability of funds, progress of the research, and programmatic needs. Annual budgets are expected to range from \$250,000 to \$600,000 total costs. DOE is under no obligation to pay for any costs associated with the preparation or submission of a proposal. DOE reserves the right to fund, in whole or in part, any, all, or none of the proposals submitted in response to this Notice.

Submission Information

Full Proposal

The Department of Energy will accept Full Proposals by invitation only, based upon the evaluation of the preproposals. After receiving notification from DOE concerning successful preproposals, researchers may prepare formal proposals. The Project Description must not exceed 20 pages, including tables and figures, but exclusive of attachments. The proposal must contain an abstract or project summary, short vitae, and letters of intent from collaborators if appropriate.

Full proposals adhering to DOE Field Work Proposal format (Reference DOE Order 412.1) are to be prepared and submitted consistent with policies of the investigator's laboratory and the local DOE Operations Office. Laboratories may submit proposals directly to the SC Program Office listed above. A copy should also be provided to the appropriate DOE Operations Office.

The instructions and format described below should be followed. You must reference Program Announcement LAB 07-13 on all submissions and inquiries about this program.

OFFICE OF SCIENCE GUIDE FOR PREPARATION OF SCIENTIFIC/TECHNICAL PROPOSALS TO BE SUBMITTED BY NATIONAL LABORATORIES

Proposals from National Laboratories submitted to the Office of Science (SC) as a result of this program announcement will follow the Department of Energy Field Work Proposal process with additional information requested to allow for scientific/technical merit review. The following guidelines for content and format are intended to facilitate an understanding of the requirements necessary for SC to conduct a merit review of a proposal. Please follow the guidelines carefully, as deviations could be cause for declination of a proposal without merit review.

1. Evaluation Criteria

Proposals will be subjected to formal merit review (peer review) and will be evaluated against the following criteria which are listed in descending order of importance:

Scientific and/or technical merit of the project

Appropriateness of the proposed method or approach

Competency of the personnel and adequacy of the proposed resources

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 the Department's programmatic needs. 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 a proposal constitutes agreement that this is acceptable to the investigator(s) and the submitting institution.

2. Summary of Proposal Contents

- Field Work Proposal (FWP) Format (Reference DOE O 412.1A) (DOE ONLY)
- Proposal Cover Page
- Table of Contents
- Budget (DOE Form 4620.1) and Budget Explanation
- Abstract (one page)
- Narrative (main technical portion of the proposal, including background/introduction, proposed research and methods, timetable of activities, and responsibilities of key project personnel)
- Literature Cited
- Biographical Sketch(es)
- Description of Facilities and Resources
- Other Support of Investigator(s)
- Appendix (optional)

2.1 Number of Copies to Submit

This section pertains only to those proposers that have been encouraged to submit a full proposal. A complete formal FWP in a single Portable Document Format (PDF) file must be submitted through the DOE ePMA system (<https://epma.doe.gov>) as an attachment. To identify that the FWP is responding to this program announcement, please fill in the following fields in the "ePMA Create Proposal Admin Information" screen as shown:

Proposal Short Name:

Fiscal Year:

Proposal Reason:

Program Announcement Number: Lab 07-13 *

Program announcement Title: Quantitative Microbial Biochemistry and Metabolic

Engineering for Biological Hydrogen Production *

Proposal Purpose:

Estimated Proposal Begin Date:

HQ Program Manager Organization:

* Please use the wording shown when filling in these fields to identify that the FWP is responding to this Program Announcement.

In order to expedite the review process, please submit a CD and three copies of the proposal using the following, by U.S. Postal Service Express Mail, any commercial mail delivery service, or when hand-carried to:

Ms. Joanne Corcoran
U.S. Department of Energy
Office of Biological and Environmental Research, SC-23.2
19901 Germantown Road
Germantown, MD 20874-1290
ATTN: Program Announcement LAB 07-13

3. Detailed Contents of the Proposal

Adherence to type size and line spacing requirements is necessary for several reasons. No researcher should have the advantage, or by using small type, of providing more text in their proposals. Small type may also make it difficult for reviewers to read the proposal. Proposals must have 1-inch margins at the top, bottom, and on each side. Type sizes must be 10 point or larger. Line spacing is at the discretion of the researcher but there must be no more than 6 lines per vertical inch of text. Pages should be standard 8 1/2" x 11" (or metric A4, i.e., 210 mm x 297 mm).

3.1 Field Work Proposal Format (Reference DOE O 412.1A) (DOE ONLY)

The Field Work Proposal (FWP) is to be prepared and submitted consistent with policies of the investigator's laboratory and the local DOE Operations Office. Additional information is also requested to allow for scientific/technical merit review. Laboratories may submit proposals directly to ePMA.

3.2 Proposal Cover Page

The following proposal cover page information may be placed on plain paper. No form is required.

Title of proposed project
SC Program announcement title
Name of laboratory
Name of principal investigator (PI)
Position title of PI

Mailing address of PI
Telephone of PI
Fax number of PI
Electronic mail address of PI
Name of official signing for laboratory*
Title of official
Fax number of official
Telephone of official
Electronic mail address of official
Requested funding for each year; total request
Use of human subjects in proposed project:
If activities involving human subjects are not planned at any time during the proposed project period, state "No"; otherwise state "Yes", provide the IRB Approval date and Assurance of Compliance Number and include all necessary information with the proposal should human subjects be involved.
Use of vertebrate animals in proposed project:
If activities involving vertebrate animals are not planned at any time during this project, state "No"; otherwise state "Yes" and provide the IACUC Approval date and Animal Welfare Assurance number from NIH and include all necessary information with the proposal.
Signature of PI, date of signature
Signature of official, date of signature*

*The signature certifies that personnel and facilities are available as stated in the proposal, if the project is funded.

3.3 Table of Contents

Provide the initial page number for each of the sections of the proposal. Number pages consecutively at the bottom of each page throughout the proposal. Start each major section at the top of a new page. Do not use unnumbered pages and do not use suffices, such as 5a, 5b.

3.4 Budget and Budget Explanation

A detailed budget is required for the entire project period and for each fiscal year. It is preferred that DOE's budget page, Form 4620.1 be used for providing budget information*. Modifications of categories are permissible to comply with institutional practices, for example with regard to overhead costs.

A written justification of each budget item is to follow the budget pages. For personnel this should take the form of a one-sentence statement of the role of the person in the project. Provide a detailed justification of the need for each item of permanent equipment. Explain each of the other direct costs in sufficient detail for reviewers to be able to judge the appropriateness of the amount requested.

Further instructions regarding the budget are given in section 4 of this guide. * Form 4620.1 is available at web site: <http://www.science.doe.gov/grants/budgetform.pdf>

3.5 Abstract

Provide an abstract of less than 400 words. Give the project objectives (in broad scientific terms), the approach to be used, and what the research is intended to accomplish. State the hypotheses to be tested (if any). At the top of the abstract give the project title, names of all the investigators and their institutions, and contact information for the principal investigator, including e-mail address.

3.6 Narrative (main technical portion of the proposal, including background/introduction, proposed research and methods, timetable of activities, and responsibilities of key project personnel)

The narrative comprises the research plan for the project and is limited to 20 pages (maximum). It should contain enough background material in the Introduction, including review of the relevant literature, to demonstrate sufficient knowledge of the state of the science. The major part of the narrative should be devoted to a description and justification of the proposed project, including details of the methods to be used. It should also include a timeline for the major activities of the proposed project, and should indicate which project personnel will be responsible for which activities.

If any portion of the project is to be done in collaboration with another institution (or institutions), provide information on the institution(s) and what part of the project it will carry out. Further information on any such arrangements is to be given in the sections "Budget and Budget Explanation", "Biographical Sketches", and "Description of Facilities and Resources".

3.7 Literature Cited

Give full bibliographic entries for each publication cited in the narrative.

3.8 Biographical Sketches

This information is required for senior personnel at the institution submitting the proposal and at all subcontracting institutions (if any). The biographical sketch is limited to a maximum of **two pages** for each investigator.

To assist in the identification of potential conflicts of interest or bias in the selection of reviewers, the following information **must be provided in each biographical sketch**.

Collaborators and Co-editors: A list of all persons in alphabetical order (including their current organizational affiliations) who are currently, or who have been, collaborators or co-authors with the investigator on a research project, book or book article, report, abstract, or paper during the 48 months preceding the submission of the proposal. Also include those individuals who are currently or have been co-editors of a special issue of a

journal, compendium, or conference proceedings during the 24 months preceding the submission of the proposal. If there are no collaborators or co-editors to report, this should be so indicated.

Graduate and Postdoctoral Advisors and Advisees: A list of the names of the individual's own graduate advisor(s) and principal postdoctoral sponsor(s), and their current organizational affiliations. A list of the names of the individual's graduate students and postdoctoral associates during the past 5 years, and their current organizational affiliations.

3.9 Description of Facilities and Resources

Facilities to be used for the conduct of the proposed research should be briefly described. Indicate the pertinent capabilities of the institution, including support facilities (such as machine shops), that will be used during the project. List the most important equipment items already available for the project and their pertinent capabilities. Include this information for each subcontracting institution (if any).

3.10 Other Support of Investigators

Other support is defined as all financial resources, whether Federal, non-Federal, commercial, or institutional, available in direct support of an individual's research endeavors. Information on active and pending other support is required for all senior personnel, including investigators at collaborating institutions to be funded by a subcontract. For each item of other support, give the organization or agency, inclusive dates of the project or proposed project, annual funding, and level of effort (months per year or percentage of the year) devoted to the project.

3.11 Appendix

Information not easily accessible to a reviewer may be included in an appendix, but **do not use the appendix to circumvent the page limitations of the proposal**. Reviewers are not required to consider information in an appendix, and reviewers may not have time to read extensive appendix materials with the same care they would use with the proposal proper.

The appendix may contain the following items: up to five publications, manuscripts accepted for publication, abstracts, patents, or other printed materials directly relevant to this project, but not generally available to the scientific community; and letters from investigators at other institutions stating their agreement to participate in the project (do not include letters of endorsement of the project).

4. Detailed Instructions for the Budget

(DOE Form 4620.1 "Budget Page" may be used)

4.1 Salaries and Wages

List the names of the principal investigator and other key personnel and the estimated number of person-months for which DOE funding is requested. Proposers should list the number of postdoctoral associates and other professional positions included in the proposal and indicate the number of full-time-equivalent (FTE) person-months and rate of pay (hourly, monthly or annually). For graduate and undergraduate students and all other personnel categories such as secretarial, clerical, technical, etc., show the total number of people needed in each job title and total salaries needed. Salaries requested must be consistent with the institution's regular practices. The budget explanation should define concisely the role of each position in the overall project.

4.2 Equipment

DOE defines equipment as "an item of tangible personal property that has a useful life of more than two years and an acquisition cost of \$25,000 or more." Special purpose equipment means equipment which is used only for research, scientific or other technical activities. Items of needed equipment should be individually listed by description and estimated cost, including tax, and adequately justified. Allowable items ordinarily will be limited to scientific equipment that is not already available for the conduct of the work. General purpose office equipment normally will not be considered eligible for support.

4.3 Domestic Travel

The type and extent of travel and its relation to the research should be specified. Funds may be requested for attendance at meetings and conferences, other travel associated with the work and subsistence. In order to qualify for support, attendance at meetings or conferences must enhance the investigator's capability to perform the research, plan extensions of it, or disseminate its results. Consultant's travel costs also may be requested.

4.4 Foreign Travel

Foreign travel is any travel outside Canada and the United States and its territories and possessions. Foreign travel may be approved only if it is directly related to project objectives.

4.5 Other Direct Costs

The budget should itemize other anticipated direct costs not included under the headings above, including materials and supplies, publication costs, computer services, and consultant services (which are discussed below). Other examples are: aircraft rental, space rental at research establishments away from the institution, minor building alterations, service charges, and fabrication of equipment or systems not available off-the-shelf. Reference books and periodicals may be charged to the project only if they are specifically related to the research.

a. Materials and Supplies

The budget should indicate in general terms the type of required expendable materials and supplies with their estimated costs. The breakdown should be more detailed when the cost is substantial.

b. Publication Costs/Page Charges

The budget may request funds for the costs of preparing and publishing the results of research, including costs of reports, reprints page charges, or other journal costs (except costs for prior or early publication), and necessary illustrations.

c. Consultant Services

Anticipated consultant services should be justified and information furnished on each individual's expertise, primary organizational affiliation, daily compensation rate and number of days expected service. Consultant's travel costs should be listed separately under travel in the budget.

d. Computer Services

The cost of computer services, including computer-based retrieval of scientific and technical information, may be requested. A justification based on the established computer service rates should be included.

e. Subcontracts

Subcontracts should be listed so that they can be properly evaluated. There should be an anticipated cost and an explanation of that cost for each subcontract. The total amount of each subcontract should also appear as a budget item.

4.6 Indirect Costs

Explain the basis for each overhead and indirect cost. Include the current rates.