# Office of Science
# Financial Assistance
# Funding Opportunity Announcement
# DE-PS02-07ER07-13

## *Quantitative Microbial Biochemistry and Metabolic Engineering for Biological Hydrogen Production*

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 applications for research that supports the Genomics: GTL research program ( http://www.genomicsGTL.energy.gov). In this Solicitation, applications 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.

**PREAPPLICATIONS**

Potential applicants are **required** to submit a brief preapplication, referencing **Program Solicitation DE-PS02-07ER07-13 for receipt by DOE by 4:30 p.m., Eastern Time, January 4, 2007.** Preapplications will be reviewed for conformance with the guidelines presented in this Solicitation and suitability in the technical areas specified in this Solicitation. A response to the preapplications encouraging or discouraging formal applications will be communicated to the applicants by **January 12, 2007.** 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.

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

Potential applicants **must** submit a brief preapplication 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 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. Preapplications will be reviewed relative to the scope and research needs as outlined in the summary paragraph and in the SUPPLEMENTARY INFORMATION. The preapplication 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.

Preapplications referencing Program Solicitation DE-PS02-07ER07-13 should be sent as a text file or single PDF file attachments via e-mail to: **genomicsGTL@science.doe.gov** with "Preapplication DE-PS02-07ER07-13 Biohydrogen Lastname Institution" as the subject. No FAX or mail submission of preapplications will be accepted.

**APPLICATION DUE DATE:** March 8, 2007, 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-PS02-07ER07-13. Applicants must follow the instructions and use the forms provided on Grants.gov.

**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.

Applications 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.

Applicants 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.

Applications 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/).

Posted on the Office of Science Grants and Contracts Web Site
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