Energy Biosciences Institute

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UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN
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1206 WEST GREGORY DRIVE, MC-195, URBANA, IL 61801
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Biosciences and Bio-Engineering Call for Preproposals

The Energy Biosciences Institute (EBI) has funding available from Shell to support research in the area of Biosciences & Bio-Engineering to address fundamental questions in the area of energy transition. We expect to initiate project funding in August 2017. Currently we are interested in the interconversion of CO_2 or CH_4 into chemicals for advanced energy storage, dense energy carriers, or high value chemicals. These reactions may be mediated by biological or hybrid biochemical-chemical processes. As such, biological sciences including but not limited to synthetic biology, biochemistry, and biomimicry are important areas of specific interest. In an effort to narrow down our target scope, we are requesting principal investigators (PIs) at UC Berkeley, Lawrence Berkeley National Laboratory and the University of Illinois, Urbana-Champaign to submit brief pre-proposals that outline ideas for in-depth studies that include both a landscaping document and an empirical research component. We expect to fund up to five studies for a duration of three years with annual budgets of up to $300k. After the first 6 months, the funded studies should have an output of a single landscaping document that critically evaluates one or more of the different areas of interest outlined below.

Based on the outcome of this document, funding will be provided for a subsequent two and a half years (30 months) of empirical research. The landscaping studies should address fundamental questions that underpin the different potential routes for the conversion of CO_2 or CH_4 by biologically derived systems. Proposals focused on CO_2 fixation and conversion by land-based biomass will not be considered in this program. Rather the focus is on processes mediated by single cellular species, organelles, or enzymes that can be readily scaled in a predictable manner. Because the problems posed are complex, we envision that some of the proposals will involve multiple investigators who will contribute complementary expertise to a team approach. However, each proposal should have a single PI who can serve as a point person for the interaction between EBI and the team. PI's are encouraged to reach out to the Shell scientific liaison Rob Lee (r.lee@energybiosciencesinstitute.org) to establish a collaborative proposal. Please direct broader operational (non-technical) inquiries to EBI administration at ebiadmin@berkeley.edu.

The preproposals will be evaluated by a scientific committee appointed by the EBI leadership. The PIs of proposals considered novel and promising will be asked to submit detailed full proposals later in the year.

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The EBI will not provide copies of reviews of preproposals to proposers. The pre-proposals should use the online template and include:

i. A description of the proposed study, including goals and expected outcomes
ii. A summary of how many full-time investigators would be supported by the award, if funded, and the proposed duration of the project

In addition, a two-page vita of the principal investigators is requested. Any images provided will not count against the page limit. **Preproposals are due on Sunday, June 4, 2017 and should be submitted at https://webportalapp.com/appform/bio-preproposal.**

Structure for each of the Landscaping Studies

Before initiating specific projects to tackle empirical research, a detailed landscaping study of the underlying fundamental technical issues is needed to guide the decision process. The landscaping study may include postulated solutions yet to be proven as it is recognized that the technical answer to a problem may be currently unknown. The study should identify problems that may be addressed, in part, by the development of a technical analysis and critical evaluation of existing literature and markets, and distinguish them from problems that may require the acquisition of new empirical datasets.

Landscaping studies should include the following:

- Incorporation of some type of biological system (wholly non-biological systems are not part of this landscaping)
- Within an area of interest outlined below, the study should provide a complete mapping of the current landscape with an assessment of the benefits and failings of the known routes identified, in addition to any newly proposed routes to allow for reliable evaluation (routes/ideas/options that are currently known – 'knowns')
- Within an area of interest, the study should provide a sketch of "beyond the horizon" (postulated options still to be proven – 'postulates').
- Knowns and postulates should be technically evaluated
  - -Using a common set of criteria outlined below-
  - -Incorporating a qualitative assessment of the relative difficulty of improving the *vis a vis* the evaluation criteria
- An outline of an experimental plan for determining the tractability/intractability of the technical hurdles in 'knowns'
- An outline of an experimental plan for finding/proving/disproving 'postulates'

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Areas of interest:

1) ***Capture and utilization of photon reductive potential in biological systems.***

Known routes include (but in the study are not limited to):

a) Direct photon capture and conversion by proteins in cells (e.g. photosynthesis in cyanobacteria)
b) Enhanced microbial metabolism by direct photon capture and conversion using inorganic or artificial photon capturing and conversion techniques that can be incorporated into cellular environments in a non-toxic manner (e.g active CdS nano-particle catalysts displayed on microbial envelope surfaces).
c) Bioelectrochemical metabolism in which photon capture and conversion is mediated in a non-biological system (such as PV) and then either directly or indirectly transferred via an electron carrier (e.g. H_2) to a biocatalyst (an enzyme, an organelle, or whole cell).

Technical criteria for evaluating the routes should include (at a minimum – other criteria to be agreed with the PI):

i. Photon efficiency (from sunlight to reductive agent (e.g. e^- or H_2))
    a. Current efficiencies observed
    b. Max theoretical
    c. Maximum practical
ii. Photon capture density
    a. Current
    b. Maximum theoretical
    c. Maximum practical
iii. Reductive agent efficiency ("on a consistent basis" – recognizing that the paths may be different)
    a. Current efficiencies observed
    b. Maximum theoretical
    c. Maximum practical

iv. Heterologous interfaces between photon and cell usable reductive potential (for example a leaf is a single interface – single point capture and utilization by the cell proteins, whereas PV to H_2 to hydrogenase in a cell has 4 interfaces: photon to electron in Si, electron to water, water converted to hydrogen

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gas, hydrogen gas dissolved back in water (and thereby accessible to water based cell)
- a. Number of interfaces
- b. Types of interfaces (solid/liquid, gas/liquid etc)
- c. Reductive density change at interface (order of magnitude) (e.g. photon to electron in a wire a huge increase, hydrogen gas to dissolved hydrogen in water, massive drop)
- d. Current ability to manipulate interface
- e. Future ability to manipulate interface

2) *Capture and utilization of CO_2 in an optimized (natural or engineered) biological system*.

Known routes include (but in the study are not limited to):

a) Optimized capture and conversion of CO_2 by phototrophs (e.g. cyanobacteria)

b) Bioelectrosynthesis in which the energy needs for CO_2 capture and conversion by chemotrophs (e.g. homoacetogens) is provided electrochemically

c) Capture and conversion of CO_2 mediation by cell-free proteins or organelles

Technical criteria for evaluating the routes should include (at a minimum – other criteria to be agreed with the PI):

i. Mass transfer rate from gaseous CO_2 to protein bound CO_2
- a. Current
- b. Maximum theoretical
- c. Maximum practical

ii. Energy required on a per molecule basis from gaseous CO_2 to protein bound CO_2
- a. Current
- b. Maximum theoretical
- c. Maximum practical

iii. Energy required on a per molecule basis from protein bound CO_2 to acetate
- a. Current
- b. Maximum theoretical

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c. Maximum practical

3) ***Methane activation and chain elongation in biological system*****.**
Traditional methane activation and conversion in biological systems is rate limited and environmentally sensitive. Limitations in the biocatalyst can be potentially negated through selective genetic modification and protein engineering. Within this area of interest possible routes include:

a. Methanotroph synthetic biology for pathway optimization
b. Protein engineering of key enzymes such as methane monooxygenases (MMOs), methyl-coenzyme M reductase (MCRs), methane di-oxygenase, methylsuccinate synthase, methane dehydrogenase, or methane carboxylase
c. Biomimicry of key enzyme catalysts

Technical criteria for evaluating the different metabolic routes for activation of methane and subsequent elongation to butanol should include (at a minimum – other criteria to be agreed with the PI):

i. Energetics (include current proven and maximum)
    a. Overall Energy efficiency
    b. Overall Carbon efficiency
    c. Overall extra reductive agents required (e.g. e^-)
    d. Overall extra oxidative requirement (e.g O_2 or CO_2)
ii. Usability
    a. Tractable host (temperature tolerance, atmosphere, transformability, growth rate & biomass yields if known)
    b. Metabolic routes work in a tractable host
    c. Metabolic proteins have been successfully modified
    d. Methane capturing and activation enzymes shown/found in land-based methane seep microbes
iii. Freedom of Action
    a. How many existing patents covering that route
    b. How many still active

4) ***Upscaling and optimization.***
Successful large scale microbial processes utilizing CO_2 or CH_4 will be dependent on robust biocatalysts to allow for readily scalable, continuous processes.

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For those systems that use microbial cells it is important to identify the ideal host at an early stage in the program development. Possible hosts range from *Escherichia coli* to *Yarrowia lipolytica* but also include "genome minimized" *Vibrio natrigens* or "codon reduced" *E. coli*. While each of these have their own technical merits, they also have several failings as the basis of a robust large scale advanced energy catalysts and are often susceptible to culture contamination, gene loss, or genetic variation.

Technical criteria for evaluating possible hosts should include (at a minimum – other criteriamto be agreed with the PI):

i. Hazard class
ii. Temperature and pH tolerance
iii. Atmosphere (anaerobe/aerobe, obligate/facultative)
iv. Transformability
    a. Genomic gene deletion ability/tools
    b. Genomic gene removal ability/tools
    c. Genomic gene integration ability/tools
    d. Integration stability
v. Susceptibility to phage attack
vi. Freedom of action
    a. Patented?
    b. License to use required?
vii. Industrially used?
    a. products
    b. tonnage
viii. Cellular dynamics
    a. Growth rate (μ) (/h)
    b. Biomass yield (g/g.h)
    c. Maintenance (g/g.h)
    d. Any specific nutritional requirements required for growth
    e. Ability to thrive when immobilized (in water or gel systems)
    f. Ability to thrive immobilized in air
    g. Ability to resist culture contamination

ix. Mass and energy yield (include current proven and maximum) from to:
    a. Ethanol (as simplest dense energy carrier)
    b. Butanol (smallest dense energy carrier with simple separation)
    c. Hexadecanoic acid

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x. Freedom of Action – how many existing patents for that host for metabolic path to:
    a. Ethanol
    b. Butanol
    c. Hexadecanoic acid

Preproposals should be submitted at the following URL:
https://webportalapp.com/appform/bio-preproposal