

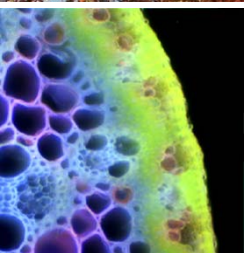
BERAC Meeting



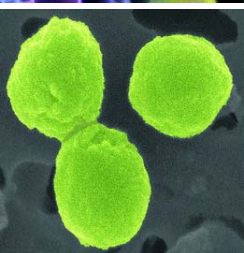
Biological Systems Science Division Update



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U.S. DEPARTMENT OF
ENERGY

Office
of Science

Office of Biological
and Environmental Research

Lab Science Focus Area Update

- BSSD Science Focus Areas (SFAs) include:
 - Genomic Science Fundamental Science
 - Genomic Science Biofuels
 - Low Dose
 - Radiochemistry and Instrumentation
- January 2009—Program plans approved
- May 2009—approved full Science Research plans received

Lab Science Focus Area Update

(continued)

- July 2009– external merit review by 31-member panel for
 - 1) overall scientific and technical merit
 - 2) appropriateness of the proposed method or approach
 - 3) competency of the personnel and adequacy of the resources
 - 4) reasonableness of the budget
 - 5) management and performance documentation
 - Unique capabilities of the national labs
- August 2009– summary findings and recommendations communicated to lab point of contact
 - accept, accept with revisions, revise and resubmit, reject

Updates on Division Solicitations

- **CLOSED SOLICITATIONS**

- 08-21 Low Dose Radiation Research - Integrated Program Projects
- 09-03 Joint USDA-DOE Plant Feedstock Genomics
- 09-08 Integrated Radiochemistry Research Projects of Excellence
- 09-18 Radiochemistry and Instrumentation Research

- **CURRENT SOLICITATIONS**

- 09-25 Biological Systems Research on the Role of Microbial Communities in Carbon Cycling

Human Subjects Protection Program Review of the Radiation Effects Research Foundation (RERF)

- The Radiation Effects Research Foundation (RERF) is a bi-national Japan-U.S. research organization dedicated to the study of health impacts of radiation in survivors of the atomic bombings in Hiroshima and Nagasaki.
- The RERF is funded jointly by the Japanese Ministry of Health, Labor, and Welfare and by DOE's Office of Health, Safety, and Security (DOE funding is \$14 M/year).
- DOE has an interest in understanding the health effects of radiation exposure for the purposes of protecting workers at DOE sites.
- BER has responsibility for overseeing the protection of human research subjects in **all research conducted at DOE institutions, supported with DOE funds, and conducted by DOE and DOE laboratory personnel**, and in this role, conducts periodic reviews of the human subjects protection programs at DOE labs and other institutions funded by DOE.

Human Subjects Protection Program Review of the Radiation Effects Research Foundation (continued)

BER conducted an on-site review of the RERF's program for the protection of humans research subjects in July 2009. Participants included Libby White (lead), Peter Kirchner, and David Thomassen plus 6 external reviewers with expertise in bioethics.

Summary of Findings:

- RERF has an exceptionally high level of commitment to the protection of the rights and welfare of its unique research population
- Overall practices meet or sometimes exceed U.S. and DOE HS protection requirements

Key Recommendations:

- Improvement in documentation of U.S. requirements
- Additional training of Institutional Review Board (IRB) members and RERF researchers
- Broader representation in IRB membership



Workshop on New Frontiers in Characterizing Biological Systems

- Workshop scope: What technical capabilities do we need to answer the most urgent scientific questions about biological and environmental systems relevant to the BER energy and environmental missions?
- BER lead organizers: Arthur Katz and Dean Cole
- Participants included experts in all types of imaging technologies and leading researchers in the BER mission areas.
- Key findings: Need technologies to: add dimensions to biological measurements; identify important events in *heterogeneous* environments; complete the “parts-list” of the cell; and integrate information for predictive understanding

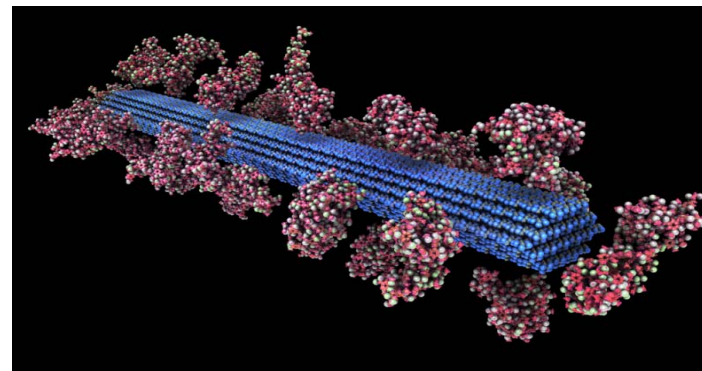
Largest Simulation Model of Lignocellulosic Biomass

Objectives

- To develop new approaches to study the recalcitrance problem in biomass
- To advance scientific discovery through high performance computing
- To develop new algorithms and methods to enable longer time and larger lengthscale dynamics of biological systems

Approach

- Large-Scale Molecular Dynamics Simulation of up to 100 million atoms, simulating lignocellulosic biomass at 30ns/day using the ORNL “Jaguar” Cray XT5 supercomputer



Outcomes

- Largest and most detailed cellulosic biomass simulation performed to date
- The methods developed can be applied to overcoming biomass recalcitrance as well as to other biological systems

Multimillion-atom Molecular Dynamics simulation methodology scaling to the whole ORNL Jaguar machine (Schulz *et al* J. Chem. Theo. Comp. *in press*)

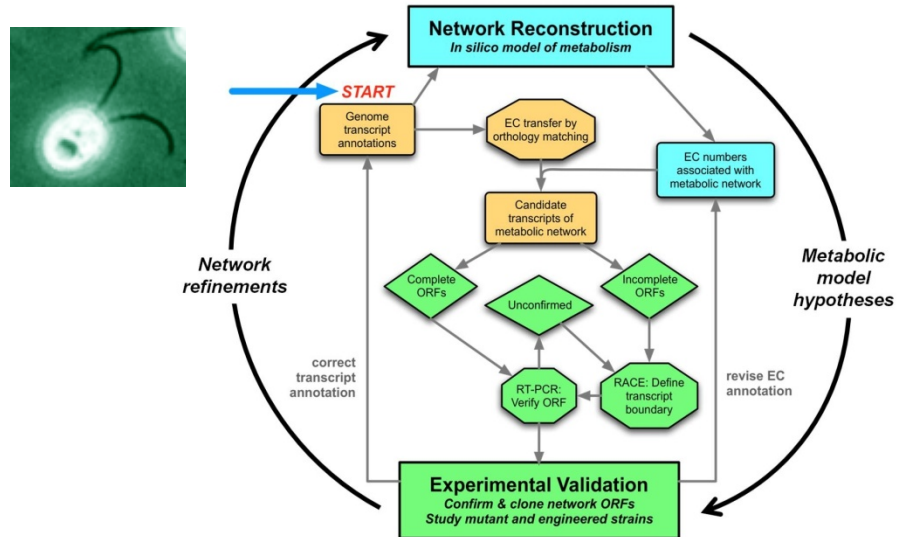
Integrated Approach to Metabolic Network Analysis and Annotation of Gene Function

Objectives

- Develop a systems biology approach bridging metabolic network analysis and experimental verification of gene function

Approach

- Iterative and integrative cycle
 - reannotation of the *Chlamydomonas reinhardtii* genome sequence
 - metabolic network reconstruction
 - experimental verification of network gene expression



Outcomes

- Enables new metabolic engineering approaches for enhancing algal biofuels production
- Provides a new systems-based method for metabolic network analysis and functional genome annotation, applicable to any sequenced organism.

Manichaikul et al. 2009. Nature Methods. 6:589-94

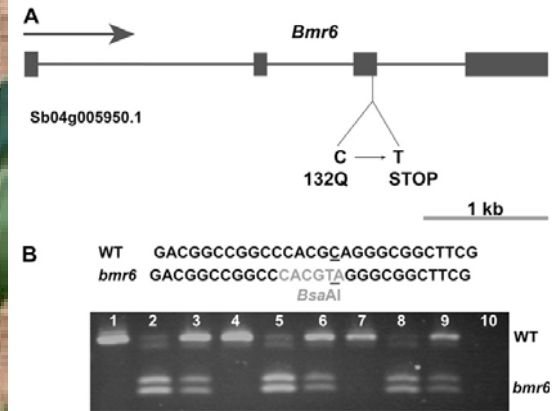
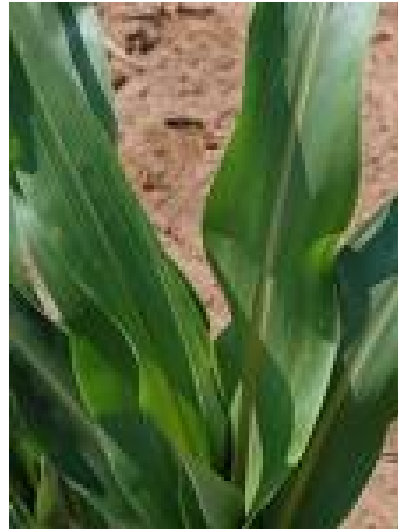
Identification of an important component of the Sorghum Lignin Biosynthetic Pathway

Objective

- *Bmr6* plants display reduced lignin content, with relatively little effect on overall plant fitness.
- Determine the role of the brown midrib (*bmr6*) gene on lignin biosynthesis in sorghum.

Approach

- Candidate gene approach
- Homology search of sorghum genome with known lignification genes from other plants.
- Follow up genetic analysis.
- Cloning to isolate the *bmr6* gene.



Outcomes

- Identification of a key gene in sorghum lignin biosynthesis will greatly facilitate development of new strategies for the conversion of grass feedstocks to biofuels.

Sattler et al (2009), Plant Physiol 150:584-595
Saballos et al (2009), Genetics 181:783-795

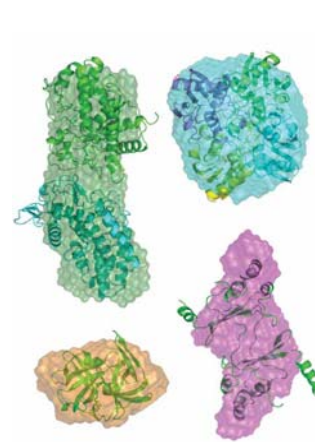
New Synchrotron Technologies Enhance Chemical Understanding of Cellular Function

Objectives

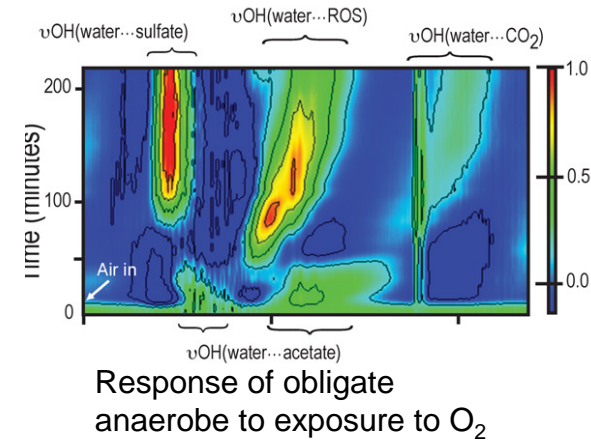
- Expand capabilities for identifying key chemical species and their roles in cellular processes
- Expand insights into the changes induced in living cells by changes in their environments

Approach

- **High-throughput small-angle x-ray scattering (SAXS)** rapidly identifies shapes of proteins and protein complexes, providing clues to their functions
- **Synchrotron Infrared spectromicroscopy** follows changes in chemical species in living microbes under stress, revealing cellular processes



SAXS-derived structures



Outcome

- Enhanced understanding of chemical species involved in functional processes of interest for applications such as biofuels production
- New non-destructive ways to study changes in living cells when the surrounding environment is perturbed

G. Hura, et al., *Nature Methods* **6**, 606 (2009)

H-Y. N. Holman, et al., *PNAS*, **106**:12599 (2009)

New Evidence for Differences in Radiation-Induced Gene Expression

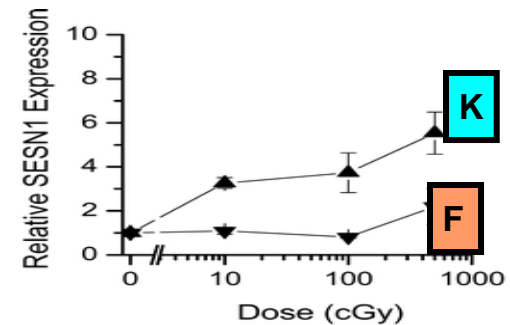
Objectives

- Validate the use of neonatal foreskin tissue model
- Test whether different cell types within the same tissue show differential gene expression after low dose exposures

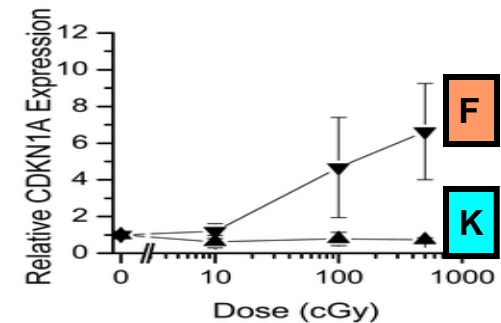
Approach

- Compare gene expression from different human skin isolates
 - F** • Primary **Fibroblasts**
 - K** • Primary **Keratinocytes**
- Gene expression profiling by
 - Microarray expression analysis
 - Quantitative PCR

Gene 1



Gene 2



Outcome

- The two cell types displayed minimal overlap in gene response to ionizing radiation
- Observe differential changes in primarily p53-regulated gene expression between different cell types

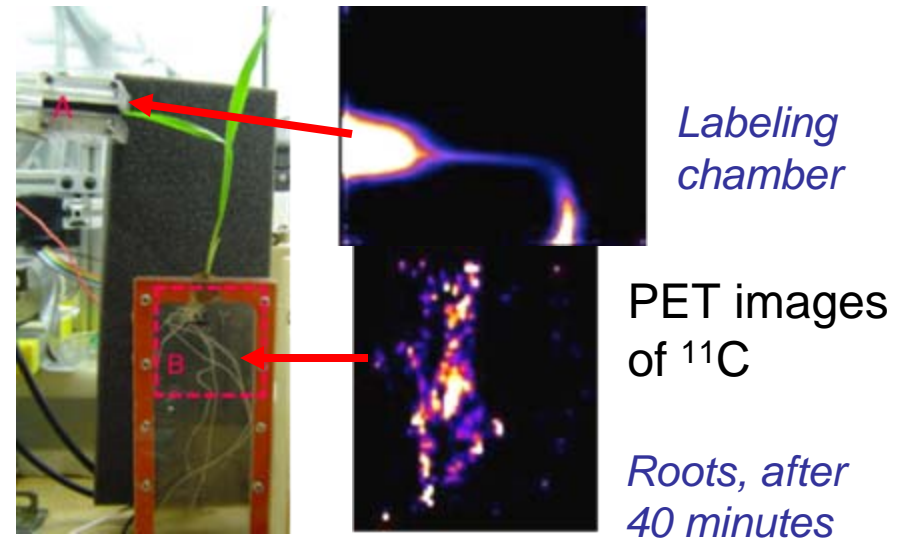
Positron Emission Tomography (PET) Detector Development for Plant Biology

Objectives

- Develop limited angle PET tomography for application in plant biology research
- Apply the technology to studying dynamics of CO₂ transport in plants

Approach

- Configure two PET systems using scintillator arrays coupled to position sensitive photomultiplier tubes to image ¹¹C
- Evaluate system in ¹¹CO₂ uptake studies in barley plants, showing transport from leaves to roots



Outcome

- A new technique is available for imaging rapid processes involving carbon in plants
- Potential for many applications in research into optimizing plant productivity for DOE missions in energy and environment

DOE Bioenergy Research Centers



- Second year on-site progress reviews
 - GLBRC—September 9-10, 2009
 - JBEI—September 30 – October 1, 2009
 - BESC—October 14-15, 2009
- External review team will evaluate:
 - science and management
 - progress against stated milestones

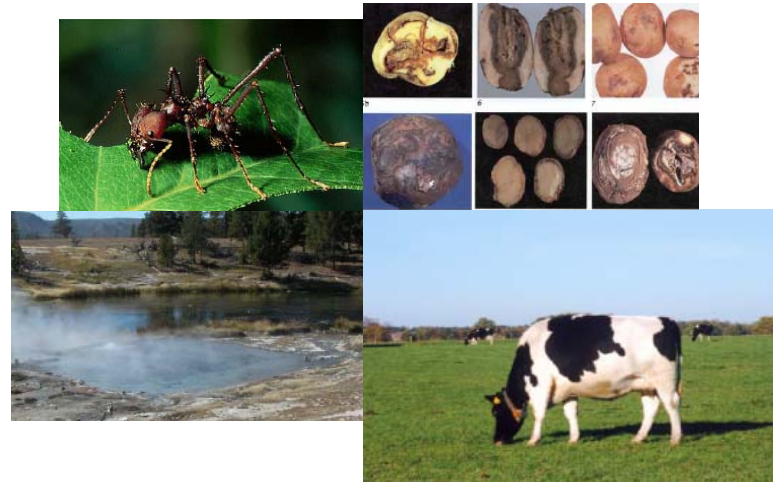
An Improved Multiplex Expression Screen for the Discovery of Biomass-degrading Enzymes

Objective

- Develop rapid screening technique for discovering new biomass-degrading enzymes in environmental microbial samples.

Approach

- Improved and patent pending random shotgun expression cloning system
- Newly-developed enzymatic screening process to dramatically improve the discovery of cellulytic enzymes



Outcomes

- Enzyme screening time now ~100 times faster
- New technology for identification of metabolic bottlenecks impeding synthesis of biofuel compounds.

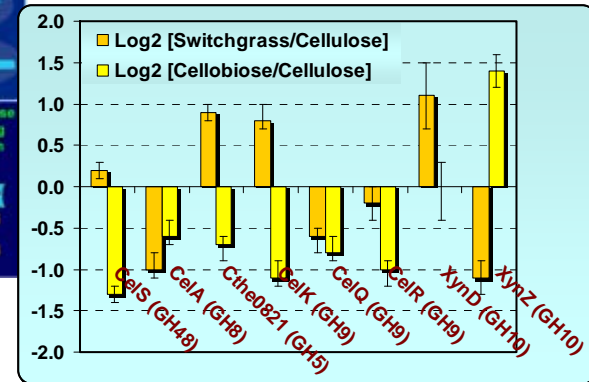
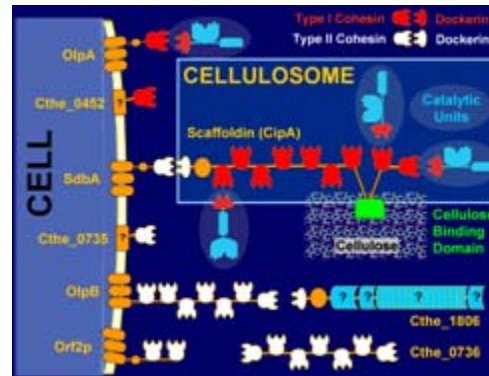
Substrate-specific changes in *C. thermocellum* cellulosome composition

Objective

Investigate global changes in composition of *C. thermocellum* biomass hydrolysis machinery, the cellulosome, during growth on different plant biomass constituents.

Approach

- Grow *C. thermocellum* on different model substrates
- Use proteomics to identify and quantitate different cellulosome components



Outcome

- First study of a biomass-degrading enzyme system under “real-world conditions”
- Enables new bioengineering approaches to construct designer biomass-degrading enzymes with “plug in” components.

Raman B, et al. (2009) Impact of Pretreated Switchgrass and Biomass Carbohydrates on *Clostridium thermocellum* ATCC 27405 Cellulosome Composition: A Quantitative Proteomic Analysis. PLoS ONE 4(4): e5271.

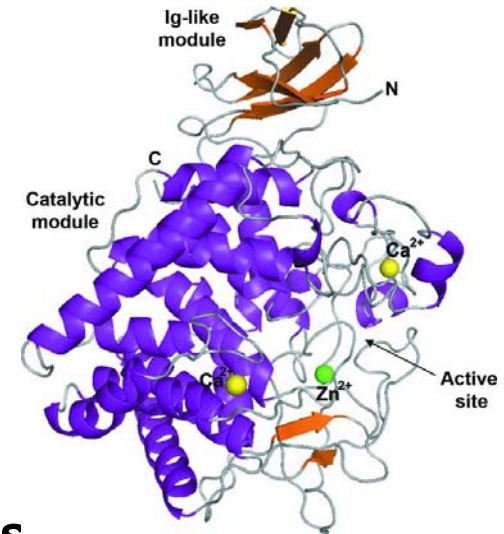
Structural Characterization of a Heat- and Acid-Tolerant Cellulase Enzyme

Objective

- Understand the catalytic actions of cellulase enzymes to improve the biomass conversion process through engineering or selection.

Approach

- The crystal structure of a cellulase, Cel9A from *Alicyclobacillus acidocaldarius*, was determined. The bacterium thrives in high-temperature and acidic environments.



Outcomes

- Catalytic activity was shown to depend on specific interaction of two structural modules.
- New platform for engineering requisite catalytic properties in key biomass degrading enzymes.

Structure of endoglucanase Cel9A from the thermoacidophilic *Alicyclobacillus acidocaldarius*

Acta Crystallographica Section D; Volume 65, Issue 8: 744-750; Pereira, J. H. et al

Joint Genome Institute

- Follow up from December 2008 Science and Operations Review
- Key recommendations:
 - Improve informatics capabilities
 - Establish standard operating procedures to facilitate project and data management
 - Consolidate funding to single point of responsibility

- ~~Community Sequencing Program 2010 Update~~

Bacteria & Archaea	Bacterial Resequencing	EST	Eukaryotic	Eukaryotic resequencing	Metagenomes
20	8	2	15	6	20

- Strategic Planning update

A look ahead for BSSD

- Principal investigator meetings
 - Genomic Sciences
 - Radiochemistry and Imaging Instrumentation
 - Joint USDA-DOE Plant Feedstock Genomics (PAG)
- Future workshops
 - Supercomputing 2009
 - Plant and Animal Genome XVIII