Office of Biological and Environmental Research

Biological Systems Science Division Update

Todd Anderson, Ph.D.
Director, Biological Systems Science Division,
Department of Energy, Office of Biological &
Environmental Research

April 20, 2017

Programmatic Activities

Completed Reviews/Activities

- Annual Genomic Sciences Program PI Meeting – (Feb 6-8)
- Annual JGI User Meeting - (Mar 20-23)
- Year 9 annual progress review of the Bioenergy Research Centers
- Review of applications submitted to the re-competition FOA for the Bioenergy Research Centers

Upcoming Reviews/Activities

- Panel Review of Biosystems Design FOA applications (next week)
- Panel Review of Plant Feedstocks for Bioenergy FOA applications (next week)
- Committee of Visitors review of BSSD (July 11-12)
- Lawrence Livermore National Laboratory SFA Review (July 18)
- Lawrence Berkeley National Laboratory SFA Review (Aug 1-2)
- New DOE Laboratory SFA Review (mid-Aug)
- DOE Systems Biology Knowledgebase review (Sept 26-27)
- Joint Genome Institute (JGI) triennial review (Dec 6-8)

Strategic Planning/Activities

Workshops

ASCR-BER Workshop on Exascale Computational Requirements

- Draft completed – out brief – this meeting (Dorothy Koch CESD, Ramana Madupu BSSD)

Technologies for Characterizing Molecular and Cellular Systems Relevant to Bioenergy and Environment

- Draft completed – out brief – this meeting (Paul Adams, Co-Chair, LBNL)

National Academy Studies

- ***"Developing a Research Agenda for Utilizing Gaseous Carbon Waste Streams."***
  Board on Chemical Sciences and Technology and the Board on Energy and Environmental Systems (BER, BES, ARPA-E, FE, EERE)
- ***"Biosecurity implications of gene editing tools"***
  Board on Life Sciences
- ***"Breakthroughs 2030: A Process for a 10-year Agenda for Food and Agricultural Research."***
  Board on Agricultural and Natural Resources

Funding Opportunities for FY 2017

Plant Feedstock Genomics for Bioenergy: A Joint Research Funding Opportunity Announcement USDA, DOE (DE-FOA-0001688)

- *Continues research on plant responses to pathogens*
- *Includes a focus on oil seed crops*

Panel review next week

Biosystems Design to Enable Next-Generation Biofuels and Bioproducts (DE-FOA-0001650)

- *Plant and microbial genome-scale design and engineering*
- *Expands its focus to biofuels and bioproducts*

Panel review next week

DOE National Laboratories Science Focus Area (SFA) Opportunity

- *Plant Systems Biology for Bioenergy*
- *Biosystems Design for Bioenergy*
- *Soil Microbiome Research*

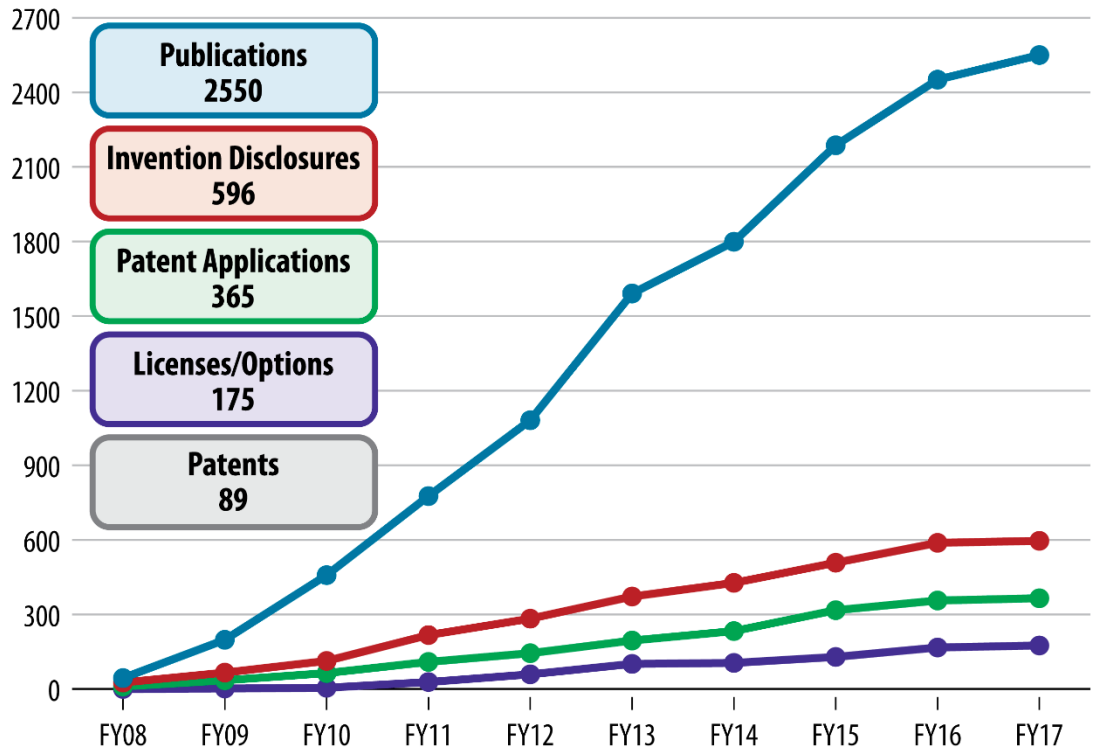
Systems Biology for Bioenergy FOA

- *Posting TBD*

Bioenergy Research Centers - 10th Year!!

Multidisciplinary fundamental science guided by milestones & deliverables, targeted to key areas needed to improve production of biofuels from renewable biomass.

- **BioEnergy Science Center** (Oak Ridge National Laboratory)
- **Great Lakes Bioenergy Research Center** (Univ. of Wisconsin, Michigan State Univ.)
- **Joint BioEnergy Institute** (Lawrence Berkeley National Laboratory)



BESC
BioEnergy Science Center

Key traits leading to reduced recalcitrance remain stable following three years of field trials

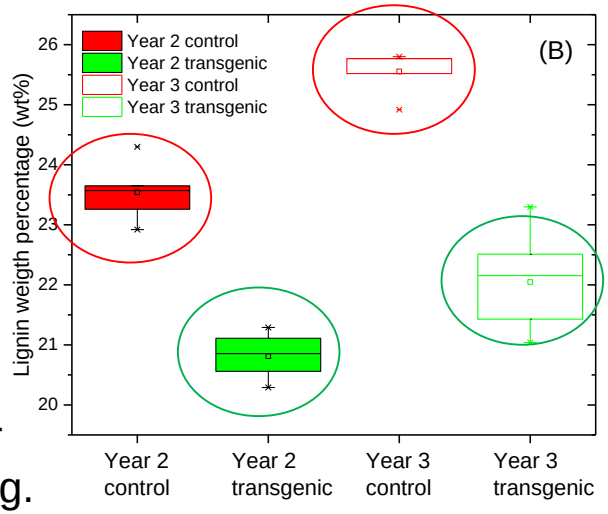
Objective Evaluate retention of lignin-altered traits in field trials of lignin altered switchgrass.

Approach

- Chemical composition, cellulose crystallinity and degree of polymerization and cellulose accessibility were measured in down-regulated COMT switchgrass following growth in the field for two and three seasons.

Results/Impact

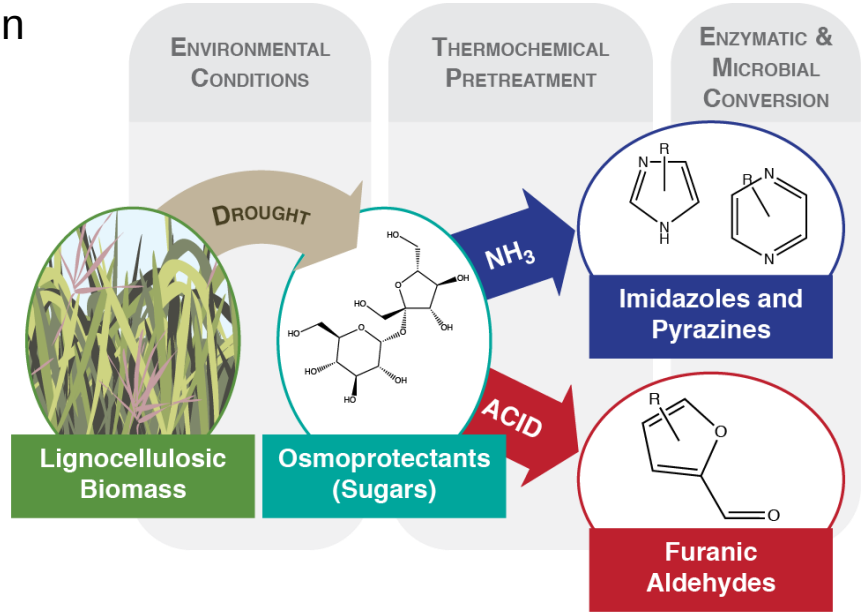
- Reduced lignin content and resultant reduced biomass recalcitrance remained stable in field-grown trials for at least three seasons.
- The findings are consistent with the originally reported improvements in cellulose accessibility via down-regulation of COMT in switchgrass.
- Demonstrates the long(er) term stability of introduced traits for improved biofuel production in bioenergy crops in a field setting.



Li, M. et.al., "Study of traits and recalcitrance reduction of field-grown COMT down-regulated switchgrass" ***Biotechnol Biofuels*** (2017). DOI: 10.1186/s13068-016-0695-7

Inhibition of microbial biofuel production in drought stressed switchgrass hydrolysate

Objective Examine impact of variable precipitation on biomass hydrolysate composition and fermentation



Approach

- Corn stover and switchgrass samples collected from field sites over a 3-year period
- Time period included a major drought year and two years of average precipitation
- Biomass samples were analyzed for hydrolysate composition, and fermentative performance.

Result/Impacts

- Growth of yeast was completely inhibited in hydrolysate made from drought stressed switchgrass and contained elevated levels of pyrazines and imidazoles
- Environmental variation can have significant effects on biomass hydrolysate properties
- Knowledge of how these factors impact biofuel production can guide pretreatment and biocatalyst choices to mitigate these inhibitory effects.

Ong, R. G. *et al.* Inhibition of microbial biofuel production in drought stressed switchgrass hydrolysate. ***Biotechnology for Biofuels*** (2016) DOI: 10.1186/s13068-016-0657-0

jbei
Joint BioEnergy Institute

On-chip integration of droplet microfluidics with nanostructure initiator mass spectrometry for enzyme assay

Objective

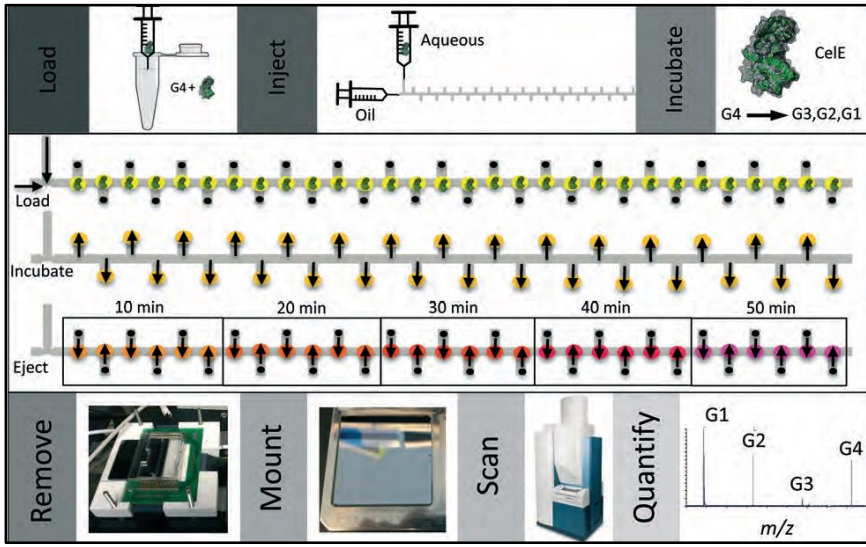
Develop new high throughput technologies for rapid screening of enzyme activity

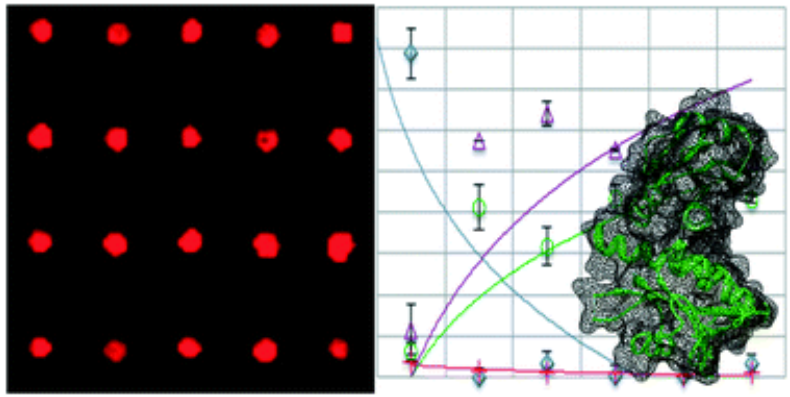
Approach

- Designed microfluidics chip for assaying enzyme activity with 1000x fold reduction in reagent consumption.
- Integrated microfluidics with NIMS to establish a new screening platform

Result/Impacts

- Device can manipulate150 nl droplets with subsequent deposition onto the NIMS surface, achieving a significant decrease in reagent use
- Disruptive technology based on a grid of 50 µm resolution that enables >100 000 pads per 5 cm2 NIMS array when scaling the current design
- Potential significant impact on enzyme engineering, DNA manipulation, microbial screening for bioenergy applications





Heinemann *et al.* (2017) "On-chip integration of droplet microfluidics and nanostructure-initiator mass spectrometry for enzyme screening". ***Lab Chip***. doi, 10.1039/c6lc01182a

Microbial Community Interactions Drive Methane Consumption in Lakes

Objective Evaluate methane metabolism in lake sediments

Image courtesy of iStock

Approach

- Assembled a microbial community consisting of methanotrophs and co-occurring non-methanotrophic bacteria found in lake sediments
- Used community-scale meta-omics analyses of shifts in gene expression to track metabolism of associated microbes during methane-driven growth

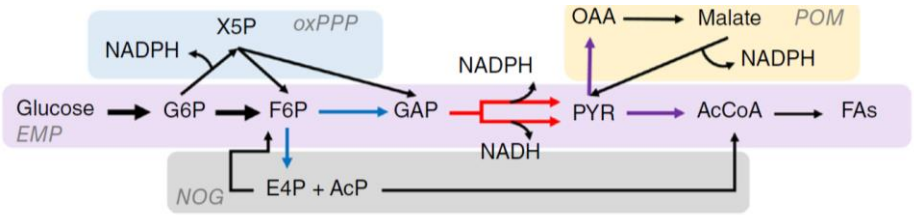
Results/Impact

- In the co-culture system, presence of non-methanotrophs altered the gene expression and metabolism of the methanotrophs to convert a portion of the available methane to methanol
- Methanol served as an energy source for the non-methanotrophs suggesting a cross-feeding mechanism
- Beneficial partner-induced changes in gene expression has implications for understanding the microbial interactions occurring in complex environments

SMB Krause et al. 2017. "Lanthanide-dependent cross-feeding of methane-derived carbon is linked by microbial community interactions." ***PNAS*** [DOI: 10.1073/pnas.1619871114]

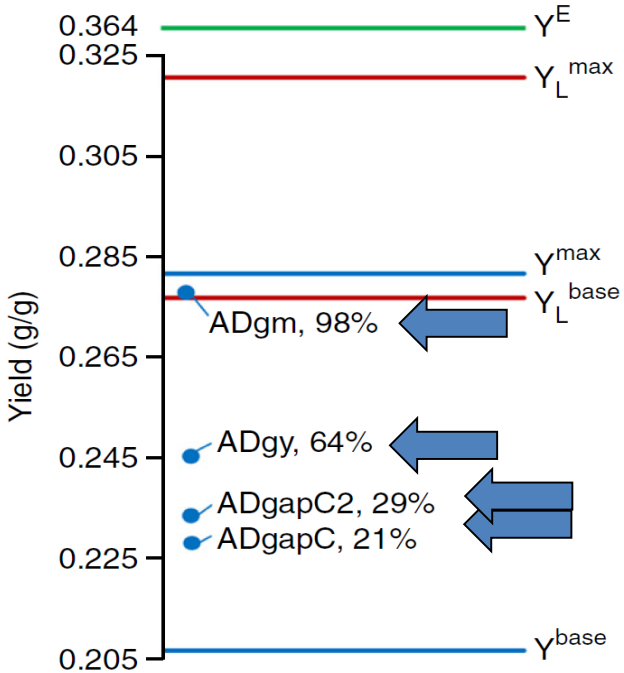
Engineering Oleaginous Yeast for High Productivity of Biodiesel from Sugars

Objective Engineer *Yarrowia lipolytica* for high oil production yield



Approach

- Model results identified a metabolic bottleneck in oil biosynthesis pathway
- Introduced heterologous yeast and bacterial genes to convert NADH into NADPH, required for lipid biosynthesis.
- Increased oil production by overexpressing a bacterial malic enzyme (MCE2)



Results/Impact

- Lipid production in the engineered *Y. lipolytica* increased 25% relative to control strains.
- Approach could be optimized for converting plant biomass into biofuel precursors and other DOE-relevant bioproducts.

K. Qiao, T. Wasylenko, K.Zhou, P.Xu & G. Stephanopoulos, "Lipid production in *Yarrowia lipolytica* is maximized by engineering cytosolic redox metabolism." ***Nature Biotechnology*** 35, 173 (2017)

Phosphate Stress and Immunity Systems in Plants are Orchestrated by the Root Microbial Community

Objective: Evaluate how plant immune systems coordinate microbial recognition with nutritional cues during microbiome assembly.

Approach

- Mutants of *Arabidopsis thaliana* with altered phosphate starvation response (PSR) to test impact of genes controlling PSR on normal root microbiome assembly

Results/Impact

- PSR regulation and pathogen defense are coordinated, providing insight into the coordinated interchange of plant response to nutritional stress, the plant immune system, and the root microbiome
- Provides a foundational basis for using the soil microbiome to enhance phosphate use efficiency in plants.

Castrillo *et al* "Root microbiota drive direct integration of phosphate stress and immunity." ***Nature*** 543, 513-518 (2017). [10.1038/nature21417]

Populus trichocarpa encodes small, effector-like secreted proteins that are highly induced during mutualistic symbiosis

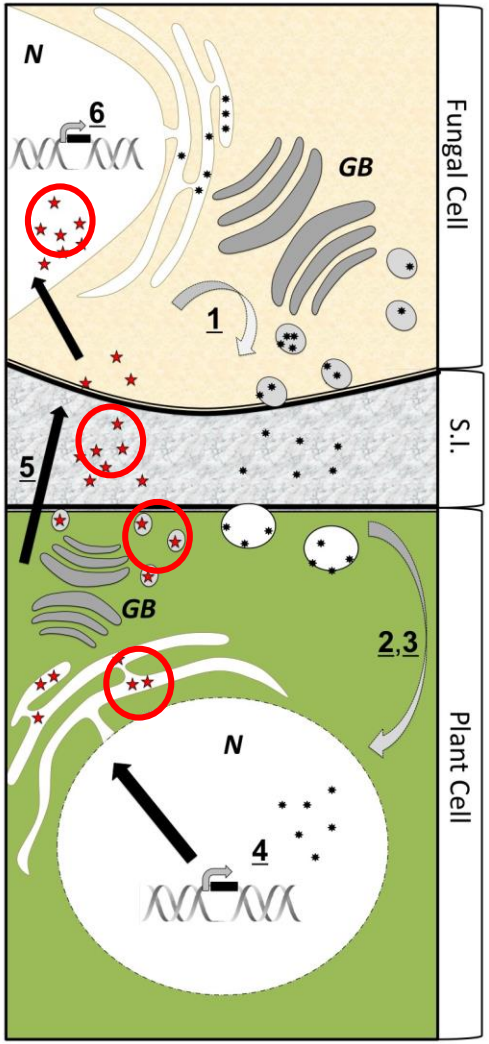
Objective Evaluate plant-microbe interactions in a *Populus-Laccaria* system

Approach

- Computational analysis of the *Populus* transcriptome identified 2,819 protein-encoding genes that exhibited differential transcript abundance during mycorrhizal root tip development during symbiosis with *L. bicolor*.
- Of these, 417 were predicted to be small secreted proteins or SSPs (≤250 aa in length).
- A subset of SSPs were able to enter *L. bicolor* hyphae and accumulate in the nucleus altering development of multiple ectomycorrhizal and pathogenic fungi.

Results/Impact

- This study demonstrates that SSPs in *Populus* can be secreted and function as effector proteins during symbiotic interactions.
- This study highlights a novel avenue by which plants communicate with (or control) their mutualistic microbial partners.



Plett J.M. *et al*. (2017). *Populus trichocarpa* encodes small, effector-like secreted proteins that are highly induced during mutualistic symbiosis. ***Nature Scientific Reports***

Deep Annotation of Protein Function across Diverse Bacteria from Mutant Phenotypes

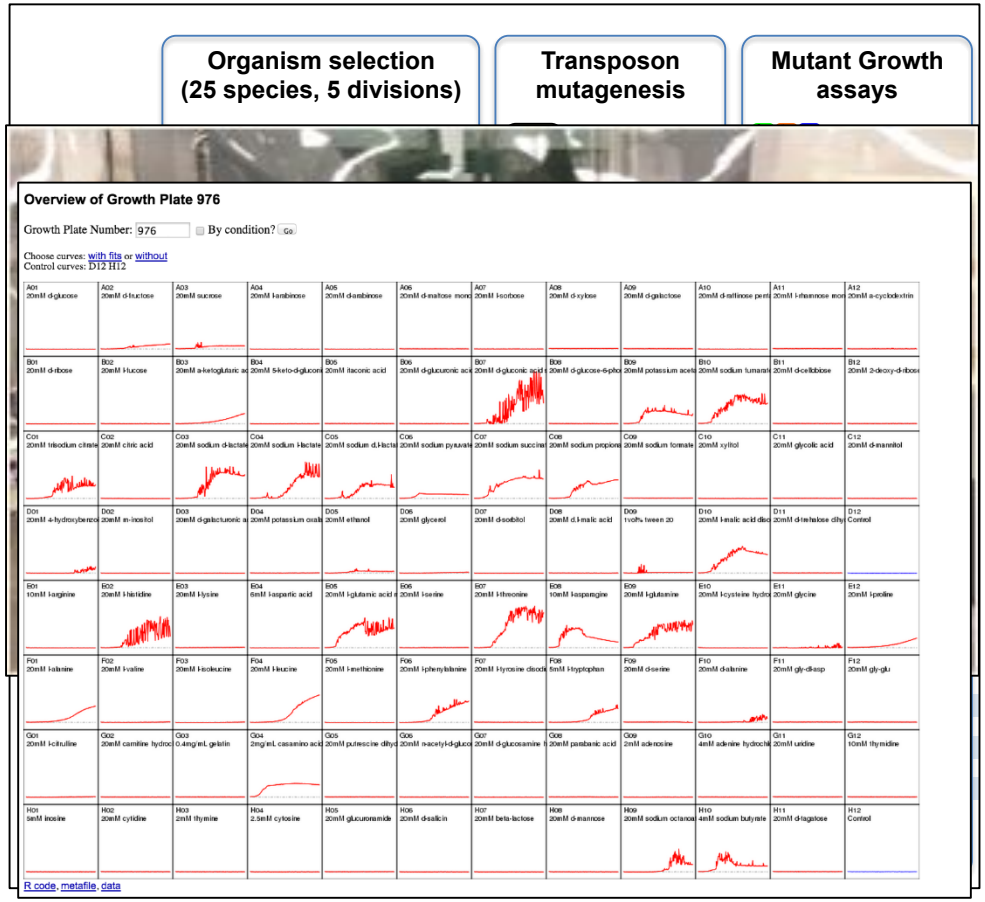
Objective Improve the annotation of genes of unknown function in bacterial genomes.

Approach

Assay transposon mutant libraries from 25 diverse bacteria across hundreds of distinct conditions

Results/Impact

- From 3,903 mutant fitness assays, 14.9 million gene phenotype measurements were collected & the mutant phenotypes for 8,487 proteins with previous unknown functions were identified
- Demonstrates utility of high-throughput genetics for large-scale annotation of bacterial proteins
- Provides a large collection of experimentally-determined protein functions across diverse bacteria



Price et al. "Deep Annotation of Protein Function across Diverse Bacteria from Mutant Phenoypes" (in review)

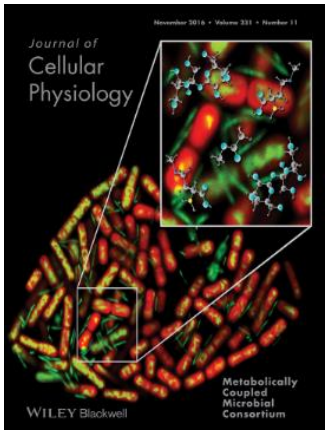
Computational Biosciences

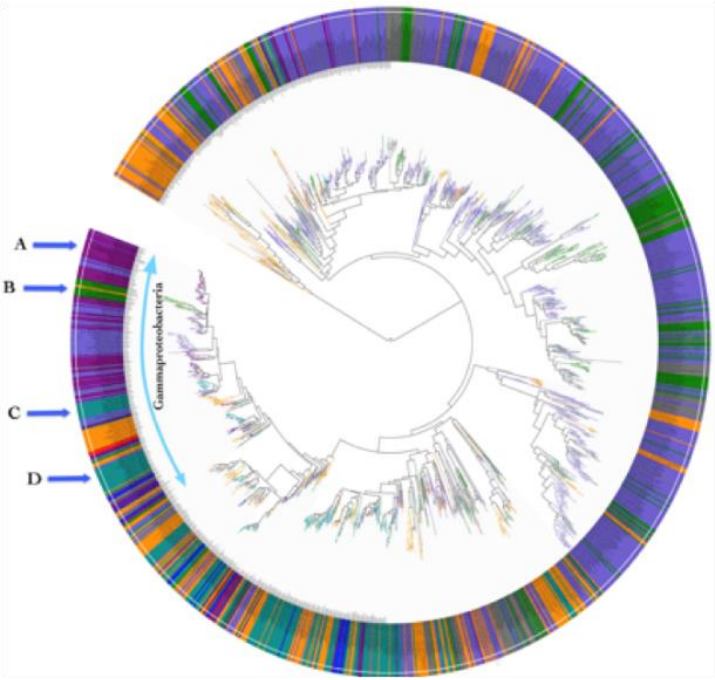
KBase
PREDICTIVE BIOLOGY

What's new In KBase?

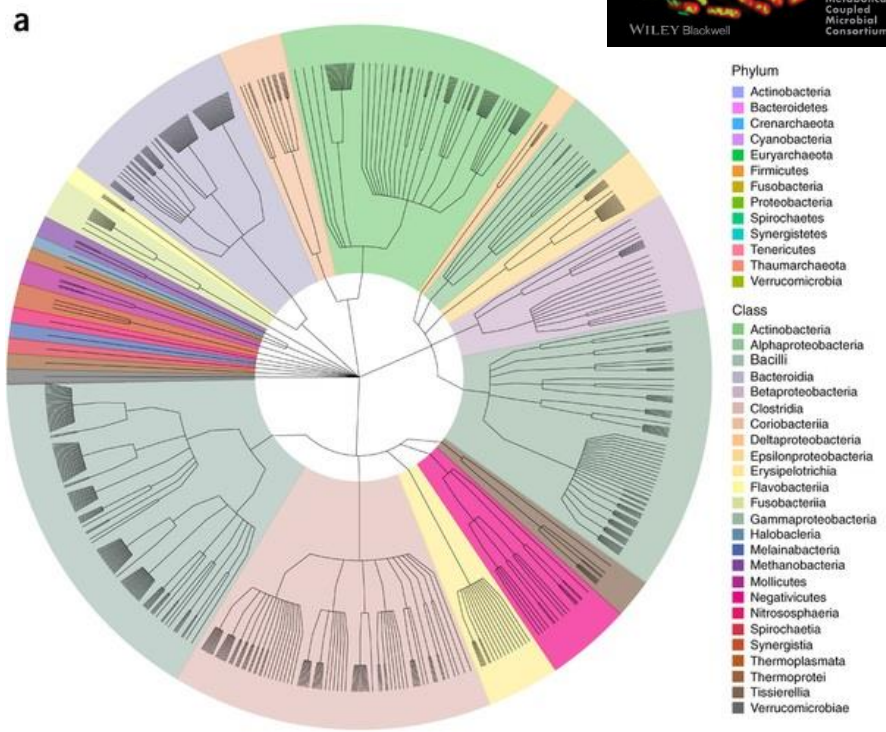
- Over 60 apps spanning assembly, annotation, comparative genomics, metabolic modeling, expression analysis, RNA-seq, and more
- Enhanced RNA-seq and metabolic modeling
- Upload large data objects from the web
- Upload and download select data in bulk
- Greatly enhanced tools supporting 3rd-party software tool development

- Modeled and predicted interactions between heterotrophic and autotrophic species in a simple community (Henry et al., ***J. of Cellular Physiology***)





- Constructed, compared and analyzed core metabolic models of over 8000 microbes (Edirisinghe et al., ***BMC Genomics***)

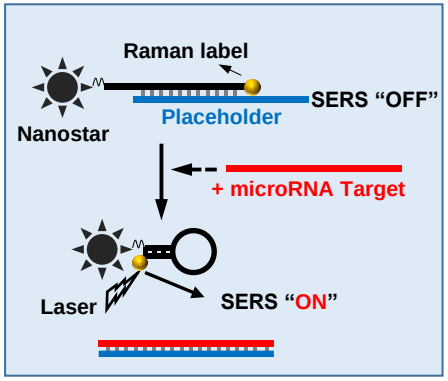


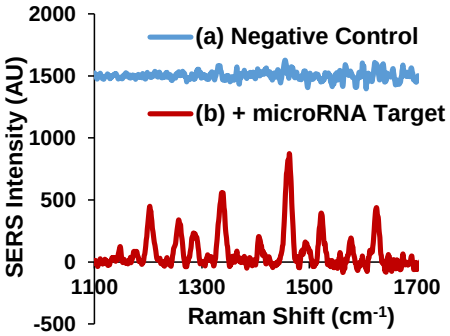
- Reconstructed 773 metabolic models of microbiome isolates (Magnúsdóttir et al., ***Nature Biotech***)

BER M2M
Bioimaging Technologies

DUKE UNIVERSITY
Fitzpatrick Institute for Photonics

Multiplexed Detection of MicroRNA Biomarkers Using SERS-Based Inverse Molecular Sentinel (iMS) Nanoprobes





Objective Probe development for microRNAs detection in plants

Approach

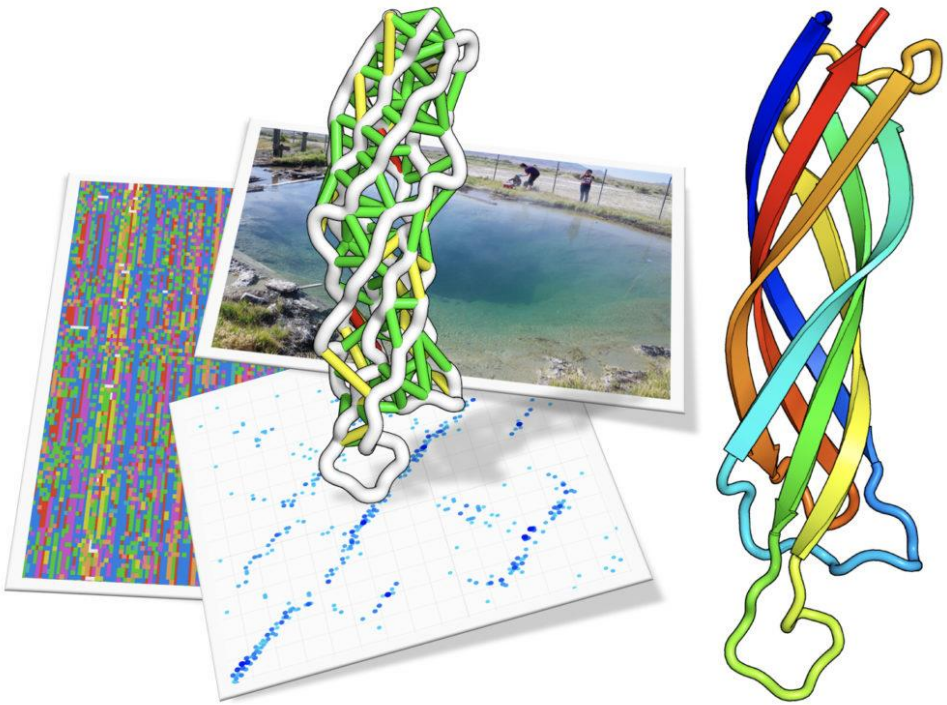
- MicroRNAs play an important role in plant development such as plant floral transition
- SERS-based Inverse Molecular Sentinel (iMS) nanoprobes were developed with plasmonic-active nanostars as the sensing platform to detect microRNAs
- Differently-labeled iMS nanoprobes were designed and developed for multiplexed detection of miR-21 and miR-34a microRNAs in extracted RNA samples.

Results/Impact

- The iMS nanoprobe as a homogeneous assay for multiplexed detection of microRNAs in extracted RNA samples without target amplification steps. The iMS biosensing platform could provide a useful tool to investigate microRNA expression.

H. N. Wang *et al.* (2016). "Multiplexed Detection of MicroRNA Biomarkers Using SERS-Based Inverse Molecular Sentinel (iMS) Nanoprobes " **J. Phys. Chem. C** 2016, 120, 21047−21055 | DOI: 10.1021/acs.jpcc.6b03299

Seeking Structures With Metagenome Sequences



Objective Use metagenomic sequences to fill gaps in structural information for known protein families.

Approach

- Integrate metagenome data, contact-based structure matching, and Rosetta structure calculations to model unknown proteins.

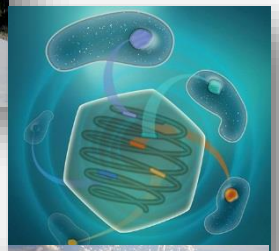
Results/Impact

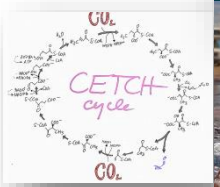
- Rosetta structure predictions are able to accurately model proteins that associate to large families
- Metagenome sequence data more than tripled the number of protein families with sufficient sequences for accurate modeling
- Generated models for 614 protein families with currently unknown structures; 206 putative membrane proteins and 137 with folds not represented in the Protein DataBase

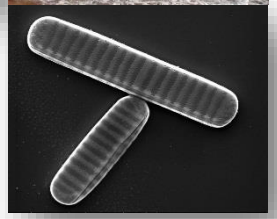
Ovchinnikov et. al. “Protein Structure Determination Using Metagenome Sequence Data.” ***Science*** 355. 6322 (2017) [DOI:10.1126/science/aah4043]

JGI JOINT GENOME INSTITUTE

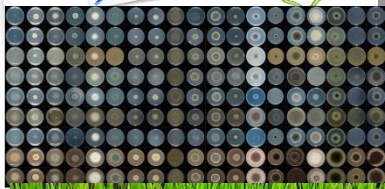
A DOE OFFICE OF SCIENCE USER FACILITY







- *Novel group of giant viruses discovered*, ***Science***
- *Engineering a more efficient system for harnessing carbon dioxide*, ***Science***
- *First CRISPR-Cas9 system in Archaea discovered*, ***Nature***
- *Tracking Antarctic adaptations in Diatoms*, ***Nature***
- *Metagenomics database helps fill in 10 percent of previously unknown protein structures*, ***Science***
- *Harnessing Aspergillus diversity for industrial applications*, ***Genome Biology***
- *Speciation driven by alleles adapted to local conditions*, ***Nature Ecology***
- *IDing grass gene for stomatal morphology underscores importance of developing mutant gene index*, ***Science***
- *Novel mechanism in bacterial-fungal symbiosis could have biodiesel production applications*, ***PNAS***



77 papers published in Q1/Q2 (through April 7, 2017)

New Structural Biology Portal

- "One stop shop" for information about BER structural biology resources
- Highlights of the latest science developments
- Descriptions of capabilities
- Information for new users

https://www.berstructuralbioportal.org

Systems science to meet DOE mission needs in bioenergy, climate and the environment.

http://science.energy.gov/ber

Thank you!

http://genomicscience.energy.gov