Agile BioFoundry

U.S. DEPARTMENT OF ENERGY | Energy Efficiency & Renewable Energy

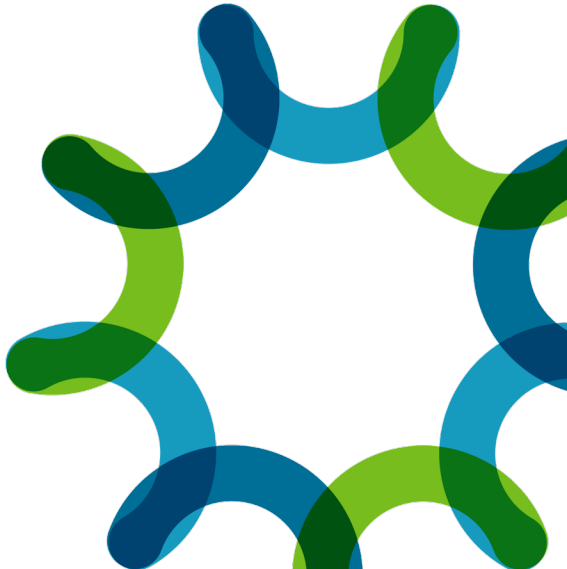
BIOENERGY TECHNOLOGIES OFFICE

Host Onboarding Task

Adam Guss (ORNL)

Taraka Dale (LANL)

BETO Peer Review 2019
Conversion Technologies
2:20-2:50PM
March 7, 2019
Denver, CO



ABF Goal Statement

- **Goal**: Enable biorefineries to achieve 50% reductions in time to bioprocess scale-up as compared to the current average of around 10 years by establishing a distributed Agile BioFoundry that will productionize synthetic biology.

- **Outcomes**: 10X improvement in Design-Build-Test-Learn cycle efficiency, **new host organisms**, new IP, and manufacturing technologies effectively translated to U.S. industry ensuring market transformation.

- **Relevance**: Public infrastructure investment that increases U.S. industrial competitiveness and enables new opportunities for private sector growth and jobs.

Host Onboarding Goal Statement

- **Goal**: Evaluate and improve tools for new, non-model host organisms that would be advantageous for synthesis of new bioproducts.

- **Outcomes**: Suite of organisms and tools made publicly available to the ABF and external stakeholders.

- **Relevance**: Industry has specifically identified a need for new organisms for bioprocessing. The Host Onboarding task aims to fill this gap with the long-term goal of reducing bioprocessing costs and advancing the bioeconomy.

Quad Chart Overview

Timeline

- Start: October 1, 2016
- End: September 30, 2019
- 83% complete

	Total Costs Pre FY17**	FY 17 Costs	FY 18 Costs	Total Planned Funding (FY 19-Project End Date)
DOE Funded	$138k	$736k	$654k	$1.57M
Partners: LBNL (6%); NREL (18%); PNNL (0%); SNL (11%); LANL (20%); ORNL (36%); ANL (8%); INL (1%)				

Barriers

- *Ct-L*. Decreasing Development Time for Industrially Relevant Microorganisms
- *Ct-D*. Advanced Bioprocess Development

Objective:

To evaluate, improve, deliver new host organisms and tools to facilitate cost-effective production of biofuels/bioproducts.

End-of-project goal:

Accelerate tool development in non-model organisms that will benefit both BETO programs as well as external stakeholders; Design, build, and test the strength of at ≥ 20 promoters, with the aim of demonstrating an ≥ 20-fold range in expression for *Z. mobilis* and *C. tyrobutyricum*

1 – Project Overview

Project overview: History & context

- **Non-model organisms** are attractive as potential industrial platforms for bioconversion because they often **possess complex phenotypes** that are not currently feasible to engineer into model organisms.
  - Low pH for producing acids
  - Robustness / toxicity tolerance
  - Syngas utilization
- Use is nascent – **molecular/genetic tools often not available**.
- **Tool development** (e.g. genetic transformation, CRISPR, modular parts for tunable gene expression, genomic integration systems) is necessary to **couple advanced metabolic engineering with the physiological advantages** that these organisms bring to the table.

Quotes from Industry

"Expand host range and make new organisms scalable ….Great use of national lab resources"

"Onboard a bunch of organisms with a lot of tools. Avoid companies needing to license and go into different organisms to avoid IP issues"

"Organisms that represent a broad range of metabolic space and manufacturing potential"

"Make a database. Standardized strain descriptions. Growth conditions. How made. Tools used. Substrate ranges. How transformable."

Project overview: Project goals

Organism Evaluation

- Determine readiness of proposed hosts for DBTL within the ABF
- Identify knowledge and tool gaps

Tools and Technologies

- Public set of tools and technologies for new hosts
- Deliver genetically-tractable, industrially-relevant host organisms

Support BETO Portfolio

- Accelerate progress in “State of Technology” (SOT) projects by developing tools for easier genetic manipulation

2 – Approach (Management)

Management approach

- **Virtual meetings:** monthly HO Team calls
- **F2F meetings**: ABF annual all-hands
- **Updates**: reported progress at Task Lead meetings
- **Team Leads:** experts in non-model host development
- **Milestones:** Reports developing the Tier System
- **Project interfacing:** Participate in the ABF Management structure, interact regularly with the DBTL Team

Adam Guss

SOT interface, transformation tools, promoter libraries, anaerobes

Taraka Dale, Chris Yeager

Tier System, protein design, reporters, HT screening, sensor tools, expression tools

Gregg Beckham
Phil Laible
John Gladden
Dayna Dubaras

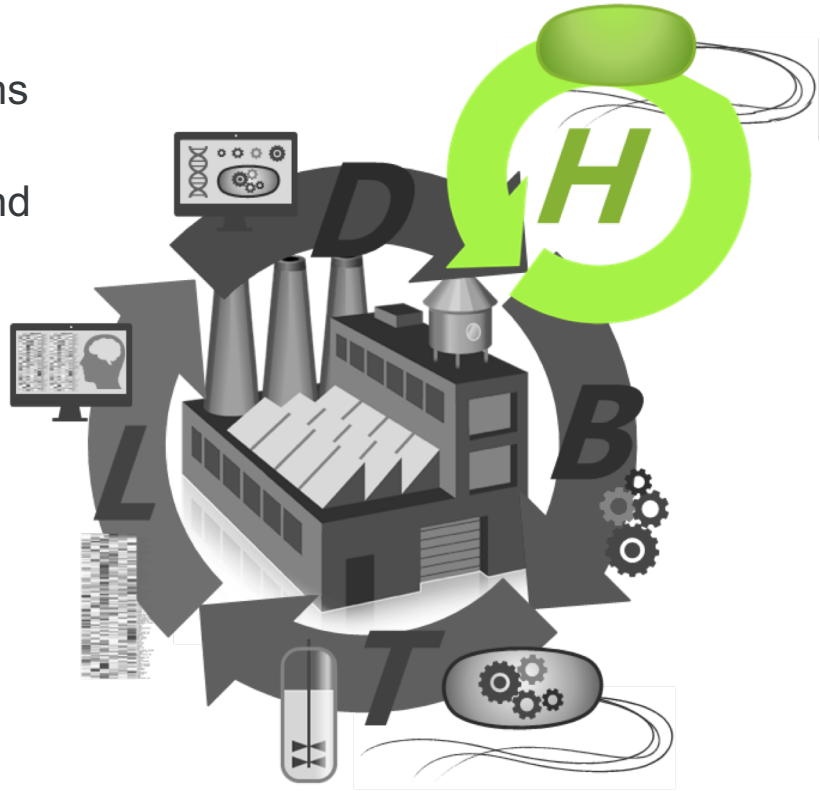
Development of hosts with varied properties: anaerobes/aerobes, product tolerance, rapid screening

3 – Approach (Technical)

Technical approach

Critical success factors

- Developing key criteria for onboarding organisms to DBTL
- Identification of organism-specific challenges and developing broadly applicable solutions where possible



Challenges

- Start almost at “square one” with each new organism
- Choosing the most important phenotypes and/or organisms to pursue

Technical approach

- Develop **criteria and a ranking process** for T-H Pairs
- Develop a **Tier System** for tracking available tools for non-model organisms
- Identify **tool gaps across a diverse set of organisms** and begin to address those
- Identify and address needs of **SOT** Team

3 – Technical Accomplishments/ Progress/Results

Outline of technical accomplishments

Organism Evaluation

- Criteria and Ranking: Host-Target Pair Evaluation
- Tier System

Tools and Technologies

- Host Diversity
- Host and Tool Development

Support BETO Portfolio

- New scope (see Future Work)

Technical accomplishments: developed a process for ranking organisms for target/host pair selection

- Evaluated each organism for readiness for use in DBTL cycle
- Sufficient genetic tools
  - Transformation methods
  - Gene deletion tools
  - Characterized promoters
  - Gene integration tools
- Baseline knowledge
  - Metabolic reconstruction/model
  - Inhibitor and product tolerance
  - Nutrient requirements

Criteria for evaluating initial host-target pairs: "Hostability"

		Basic Molecular Tools							Advanced Molecular Tools							
Host Name	Example Target Molecule	Genome Sequence Available? Y/N	Transformation Protocol? Y/N	Plasmids/ Vectors available? Y/N	Antibiotic Resistance Markers available Y/N	Other Markers availabl e	Expression Parts (Promoters etc)	Onboardable	Genome integration systems?	Induction Systems?	Strain Stability Low/Med/High	Genome Scale Models	Nutrient Utilization Known?	Product Tolerance Known?	Tier 2 Sum	Sum Score
	POSSIBLE SCORE	**0/1**	**0/1**	**0/1**	**0/1**	**0/1**	**0/1**		**0/1**	**0/1**	**0, 0.5, 1**	**0/1**	**0/1**	**0/1**		
Alicyclobacillus acidocaldarius ATCC 27009	none provided	Y		N	Y; Kan	N	N	0/5	N	N	3	Y	Y	N	0-5	
		1	0	0	1	0	0	0	0	0	1	1	1	not scored	3.0	**3.0**
Aspergillus niger	3-hydroxypropionic acid	Y	Y	Y	Y	Y	Y		Y	Y	H	Y	Y	Y		
		1	1	1	1	1	1	5	1	1	1	1	1	not scored	5.0	**10**
Aspergillus pseudoterreus ATCC 32359	Itaconic acid	Y	Y	Y	Y	Y	Y		Y	Y	H	Y	Y	Y, 10s of g/L		
		1	1	1	1	1	1	5	1	1	1	1	1	not scored	5.0	**10**
C. carboxidivorans	Ethyl butyrate	Y	N	N	N	N	N		N	N		N				
		1	0	0	0	0	0	0	0	0	0	0	0	not scored	0.0	**0**
C. glutamicum ATCC 13032	D-lactic acid	Y	Y	Y	Y	Y	Y		Y	Y	H	Y	Y	Y		
		1	1	1	1	1	1	5	1	1	1	1	1	not scored	5.0	**10**
bruxellensis CBS2499	3-hydroxybutanone (acetoin)	Y	Y	Y	Y	?	Y/N		Y	Y	M	No	Y	Y High		
		1	1	1	1	0	1	0	1	0	0.5	0	1	not scored	2.5	**2.5**
elongata	Ectoine and Levan	Y	Y	Y	Y	Y	Y		y	?	y	n	y	y		
		1	1	1	1	1	1	5	1	0	0.5	0	1	not scored	2.5	**7.5**
Lactobacillus rhamnosus	Lactic acid	Y	Y	Y	Y	Y	Y		Y	Y	H	Y	Y	Y		
		1	1	1	1	1	1	5	1	1	1	1	1	not scored	5.0	**10.0**
P. putida KT2440	Terephthalic acid	Y	Y	Y	Y	Y	Y		Y	Y	H	Yes	Y	High		
		1	1	1	1	1	1	5	1	1	1	1	1	not scored	5.0	**10**
R. toruloides	Farnesene	Y	Y	Y	Y	Y	Y		Y	Y	H	Y	Y	Y		
		1	1	1	1	1	1	5	1	1	1	1	1	not scored	5.0	**10**
Rhodobacter sphaeroides DeltarshI	isoprene	Y	Y	Y	Y	Y	Y		Y	Y	H	Y	Y			
		1	1	1	1	1	1	5	1	1	1	1	1	not scored	5.0	**10.0**
Streptomyces albus J1074	methylpentanoic acid	Y	Y	Y	Y	Y	Y		Y	Y	H	N	?	?		
		1	1	1	1	1	1	5	1	0	1	0	0	not scored	2.0	**7.0**

Criteria for evaluating initial host-target pairs: "Hostability"

Basic Molecular Tools | Advanced Molecular Tools

Host Name	Example Target Molecule	Genome Sequence Available? Y/N	Transformation Protocol? Y/N	Plasmids/ Vectors available? Y/N	Antibiotic Resistance Markers available Y/N	Other Markers availabl e	Expression Parts (Promoters etc)	Onboardable	Genome integration systems?	Induction Systems?	Strain Stability Low/Med/High	Genome Scale Models	Nutrient Utilization Known?	Product Tolerance Known?	Tier 2 Sum	Sum Score
POSSIBLE SCORE		**0/1**	**0/1**	**0/1**	**0/1**	**0/1**	**0/1**		**0/1**	**0/1**	**0, 0.5, 1**	**0/1**	**0/1**	**0/1**		
Alicyclobacillus acidocaldarius ATCC 27009	none provided	Y		N	Y; Kan	N	N	0/5	N	N	3	Y	Y	N	0-5	
		1	0	0	1	0	0	0	0	0	1	1	1	not scored	3.0	**3.0**
Aspergillus niger	3-hydroxypropionic acid	Y	Y	Y	Y	Y	Y		Y	Y	H	Y	Y	Y		
		1	1	1	1	1	1	5	1	1	1	1	1	not scored	5.0	**10**
Aspergillus pseudoterreus ATCC 32359		Y	Y	Y	Y	Y	Y		Y	Y	H	Y	Y	Y, 10s of g/L		
C. carboxidivorans																
C. glutamicum ATCC 13032																
bruxellensis CBS2499																
elongata																
Lactobacillus rhamnosus																
P. putida KT244																
R. toruloides																
Rhodobacter sphaeroides Deltarshl																
Streptomyces																
J1074	acid	Y	Y	Y	Y	Y	Y		Y	Y	H	N	?	?		
		1	1	1	1	1	1	5	1	0	1	0	0	not scored	2.0	**7.0**

Host Name	Example Target Molecule	Genome Sequence Available? Y/N	Transformation Protocol? Y/N	Plasmids/ Vectors available? Y/N	Antibiotic Resistance Markers available Y/N	Other Markers availabl e	Expression Parts (Promoters etc)	Onboardable
POSSIBLE SCORE		**0/1**	**0/1**	**0/1**	**0/1**	**0/1**	**0/1**	
Alicyclobacillus acidocaldarius ATCC 27009	none provided	Y		N	Y; Kan	N	N	0/5
		1	0	0	1	0	0	0
Aspergillus niger	3-hydroxypropionic acid	Y	Y	Y	Y	Y	Y	
		1	1	1	1	1	1	5

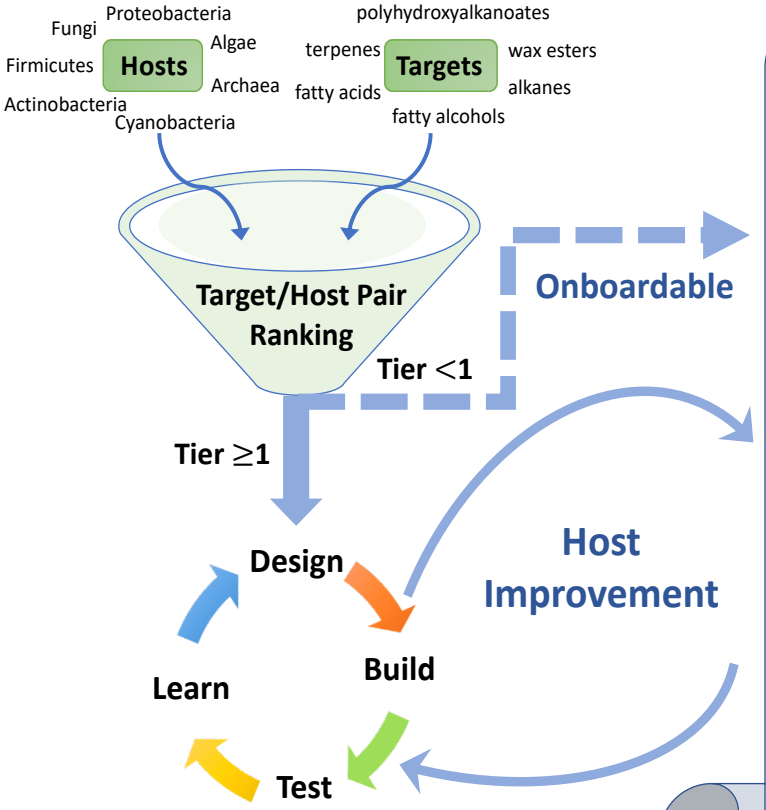
U.S. DEPARTMENT OF ENERGY | Energy Efficiency & Renewable Energy
BIOENERGY TECHNOLOGIES OFFICE

Agile BioFoundry

Technical accomplishments – Tier system for host development

- Develop criteria to quickly **evaluate current state of organism tool and knowledge development**
- **Identify tool and knowledge gaps** in current and future ABF host organisms
- Develop an **organizational framework** for thinking about development of new microbial hosts
- Develop a web-based portal to **organize and advertise capabilities** within the ABF

Overview of Tier system



Tier System Criteria - "Hostability"

Tier 1

Annotated genome; growth conditions; growth kinetics and simple growth models; antibiotic susceptibility; selectable markers; transformation methods; plasmids/vectors; basic expression parts; biosafety/biosecurity information

Tier 2

Substrate utilization panel; toxicity profiles; bioreactor growth; counter-selectable markers; genome integration system; chromosomal safe sites/landing pads; induction systems; panel of constitutive promoters, RBSs, terminators; models of promoters and RBSs/Kozak sequences; genome-scale models; pan genome analysis; transcriptomic, proteomic, metabolomic datasets

Tier 3

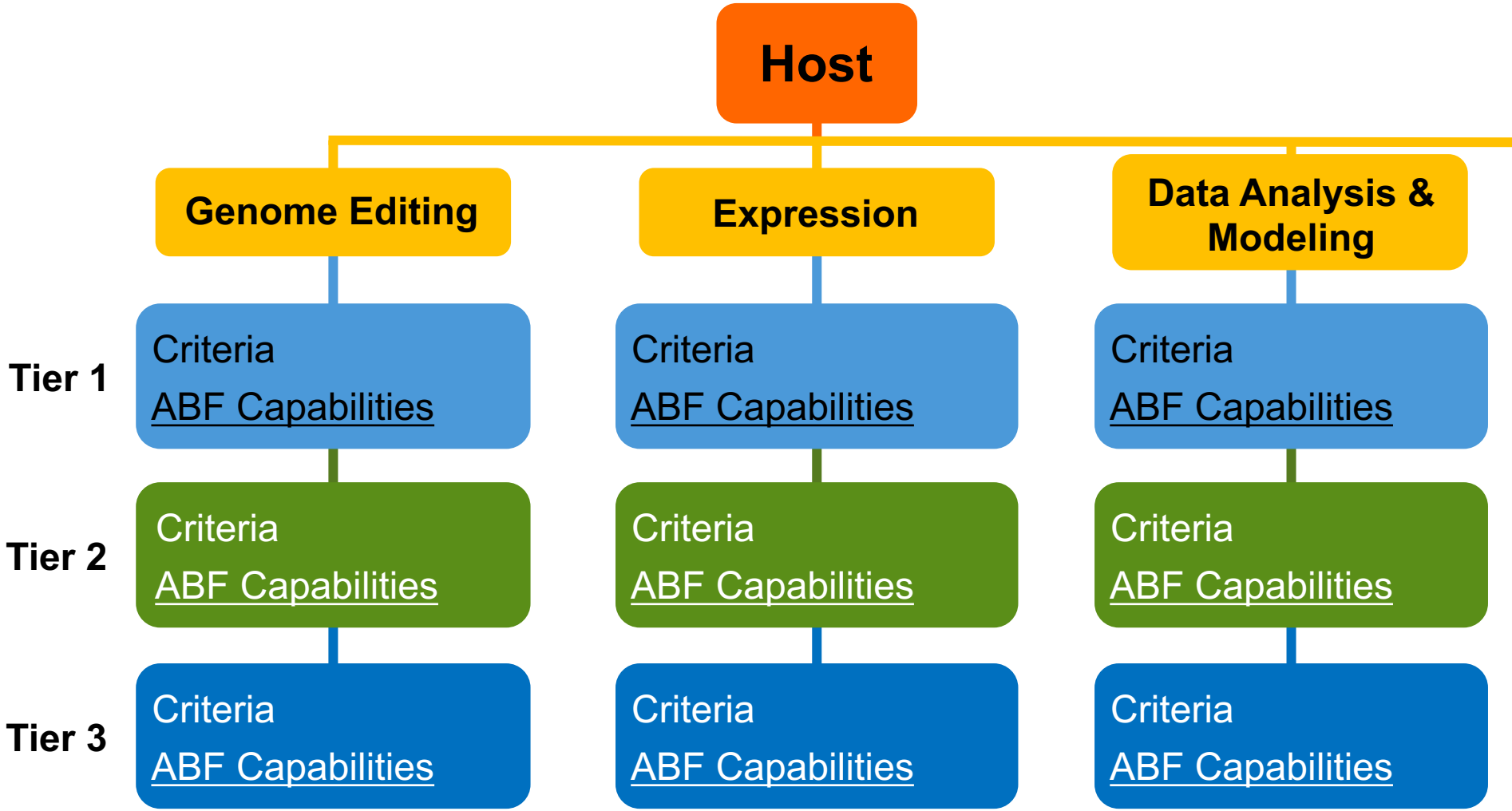
Biosensors; cellular stress monitoring; CRISPR/CAS, Lambda Red, Cre-*lox* systems; advanced genomic integration platforms; gene expression tuning; high throughout protein engineering platform; lipidomic and glycomic datasets; centralized omics databases; multi-omic data integration and analysis; protein localization; protein degradation tags; protein interactome datasets; ^{13}C-MFA experiments and model; kinetic model; population balance model

Tier 4

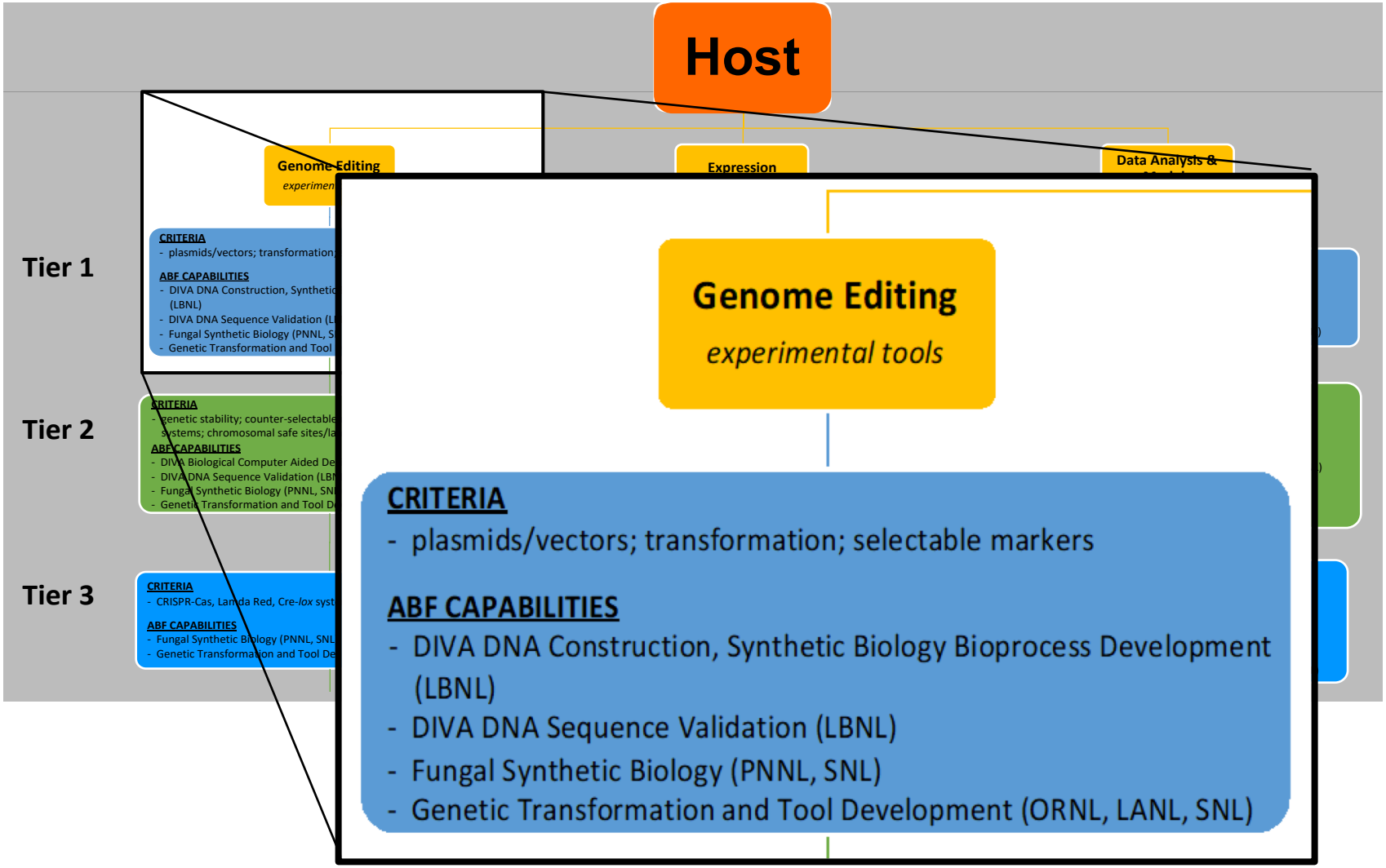
Culture scalability; saturated deletion/loss of function libraries; genomic overexpression platform; adaptive laboratory evolution/cell sorted libraries; baseline strains for maximal flux to metabolic nodes; cellular state sensors and dynamically regulated production strains; signaling model, gene regulation model, multi-scale model; predictive cellular model

- Tier 1 represents the basic tools needed for DBTL
- Hosts that do not meet Tier 1 require further development prior to usage
- Tools increase in sophistication as an organism moves up Tiers
- Not all tools in all Tiers are required for all organisms

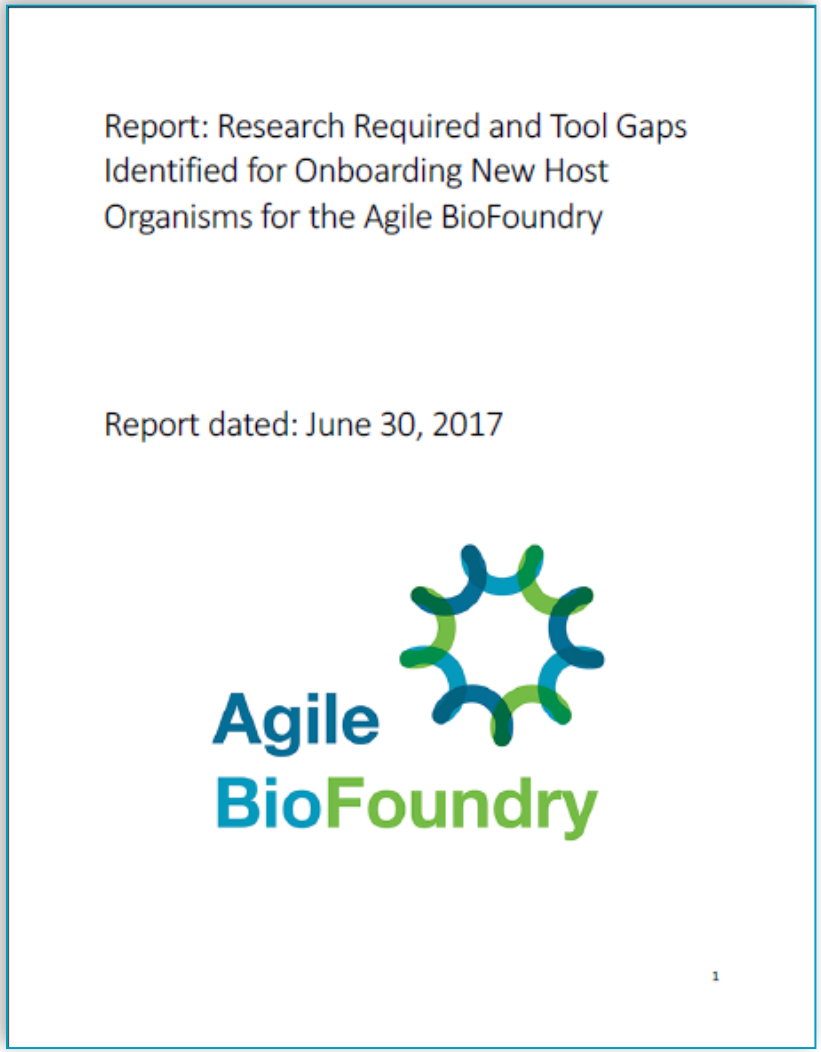
Concept for host development web-based portal



Concept for host development web-based portal



Host onboarding was responsible for two project-wide milestones

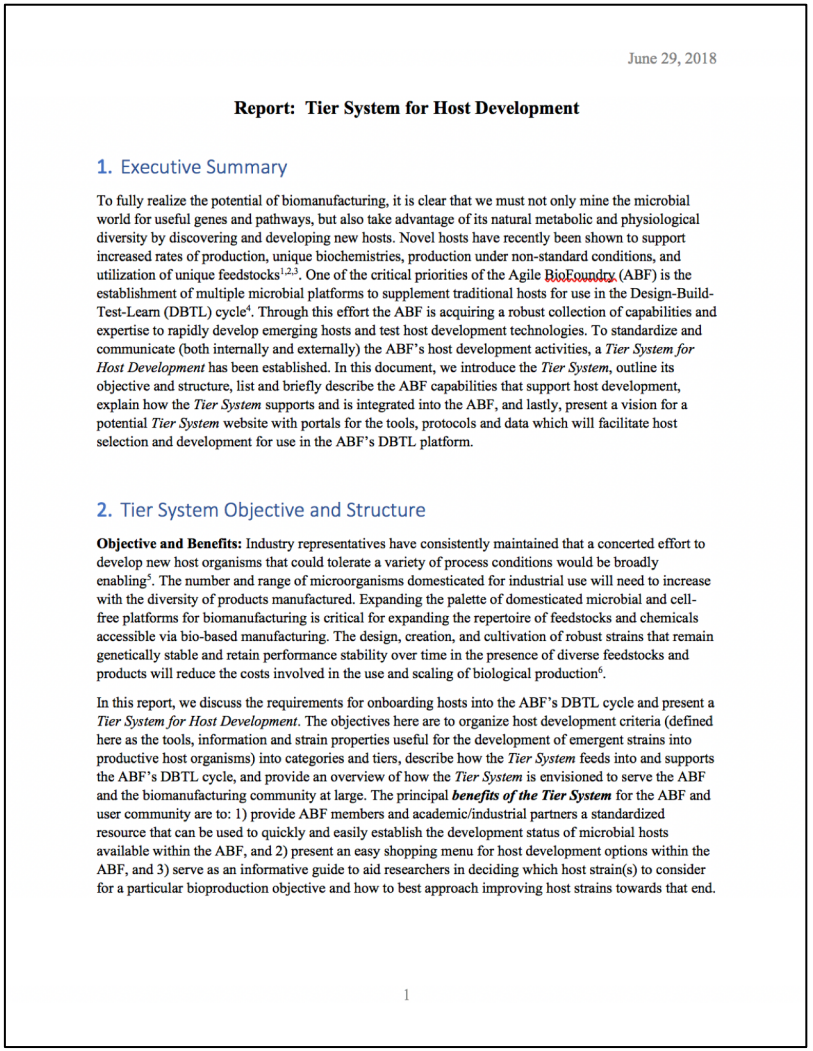


Report: Research Required and Tool Gaps Identified for Onboarding New Host Organisms for the Agile BioFoundry

Report dated: June 30, 2017

Agile BioFoundry

1



June 29, 2018

Report: Tier System for Host Development

1. Executive Summary

To fully realize the potential of biomanufacturing, it is clear that we must not only mine the microbial world for useful genes and pathways, but also take advantage of its natural metabolic and physiological diversity by discovering and developing new hosts. Novel hosts have recently been shown to support increased rates of production, unique biochemistries, production under non-standard conditions, and utilization of unique feedstocks[1,2,3]. One of the critical priorities of the Agile BioFoundry (ABF) is the establishment of multiple microbial platforms to supplement traditional hosts for use in the Design-Build-Test-Learn (DBTL) cycle[4]. Through this effort the ABF is acquiring a robust collection of capabilities and expertise to rapidly develop emerging hosts and test host development technologies. To standardize and communicate (both internally and externally) the ABF's host development activities, a *Tier System for Host Development* has been established. In this document, we introduce the *Tier System*, outline its objective and structure, list and briefly describe the ABF capabilities that support host development, explain how the *Tier System* supports and is integrated into the ABF, and lastly, present a vision for a potential *Tier System* website with portals for the tools, protocols and data which will facilitate host selection and development for use in the ABF's DBTL platform.

2. Tier System Objective and Structure

Objective and Benefits: Industry representatives have consistently maintained that a concerted effort to develop new host organisms that could tolerate a variety of process conditions would be broadly enabling[5]. The number and range of microorganisms domesticated for industrial use will need to increase with the diversity of products manufactured. Expanding the palette of domesticated microbial and cell-free platforms for biomanufacturing is critical for expanding the repertoire of feedstocks and chemicals accessible via bio-based manufacturing. The design, creation, and cultivation of robust strains that remain genetically stable and retain performance stability over time in the presence of diverse feedstocks and products will reduce the costs involved in the use and scaling of biological production[6].

In this report, we discuss the requirements for onboarding hosts into the ABF's DBTL cycle and present a *Tier System for Host Development*. The objectives here are to organize host development criteria (defined here as the tools, information and strain properties useful for the development of emergent strains into productive host organisms) into categories and tiers, describe how the *Tier System* feeds into and supports the ABF's DBTL cycle, and provide an overview of how the *Tier System* is envisioned to serve the ABF and the biomanufacturing community at large. The principal ***benefits of the Tier System*** for the ABF and user community are to: 1) provide ABF members and academic/industrial partners a standardized resource that can be used to quickly and easily establish the development status of microbial hosts available within the ABF, and 2) present an easy shopping menu for host development options within the ABF, and 3) serve as an informative guide to aid researchers in deciding which host strain(s) to consider for a particular bioproduction objective and how to best approach improving host strains towards that end.

1

Technical accomplishments: adding host diversity to the ABF

Host/Target Organisms

- *Pseudomonas putida*
- *Rhodosporidium toruloides*
- *Aspergillus pseudoterreus*

HO Team Organisms

- *Clostridium carboxidivorans*
- *Bacillus coagulans*
- *Corynebacterium glutamicum*

CRADA Organisms

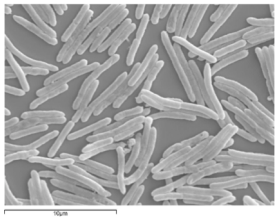
- *Acinetobacter baylyi* ADP1
- *Pichia kudriavzevii*
- *Clostridium ljungdahlii*
- *Clostridium autoethanogenum*
- *Cupriavidus necator*
- *Bacillus sp.*

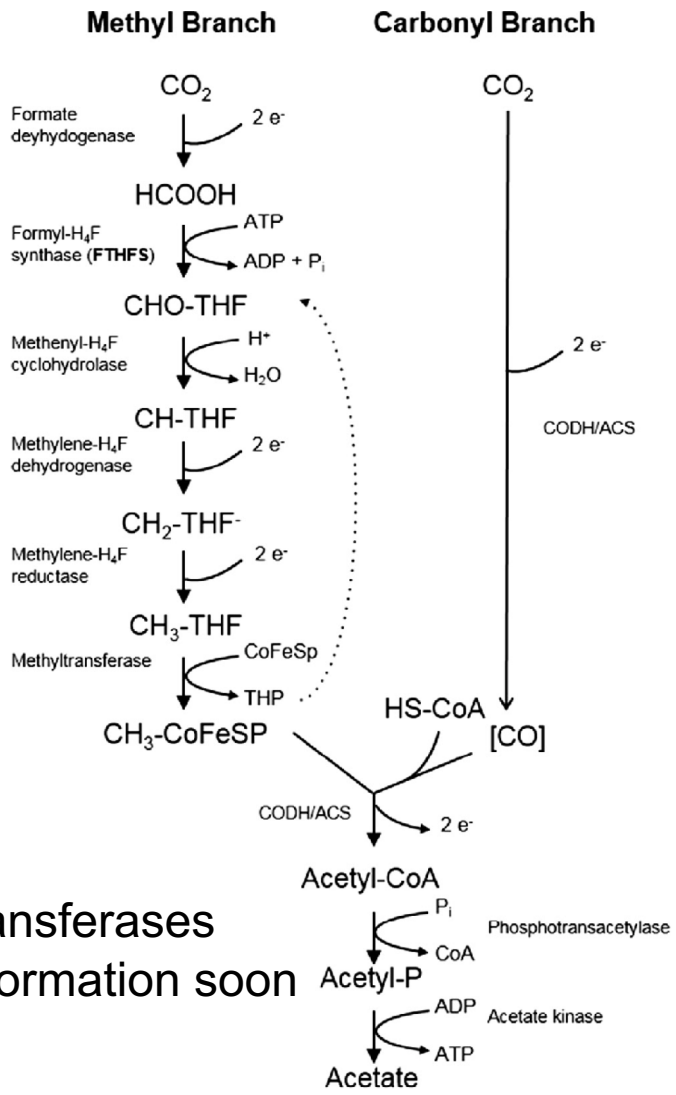
SOT Organisms

- *Zymomonas mobilis*
- *Clostridium tyrobutyricum*

Under development: *C.carboxidivorans*

- Able to robustly utilize syngas and hydrolysate sugars
- Never-before transformed
- Obligate anaerobe
- Natively produces ethanol and acetic acid with lower levels of butyrate, n-butanol, and n-hexanol





Goals

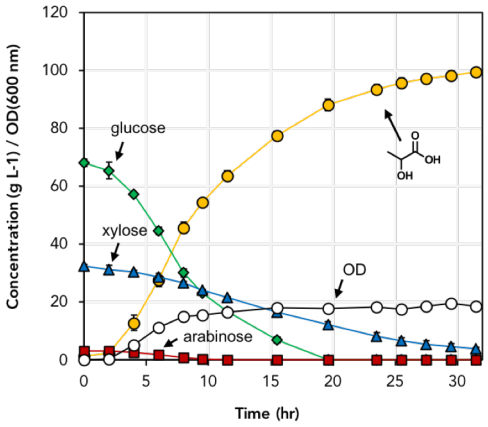
- Develop initial genetic transformation
- Develop enhanced tools to accelerate engineering

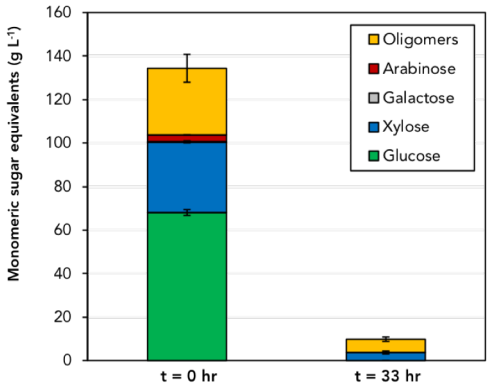
Progress

- Have cloned 5 and expressed 3 of the 7 DNA methyltransferases in *E. coli* to evade host defense systems, testing transformation soon
- Characterized antibiotic sensitivity

Under development: *Bacillus coagulans*

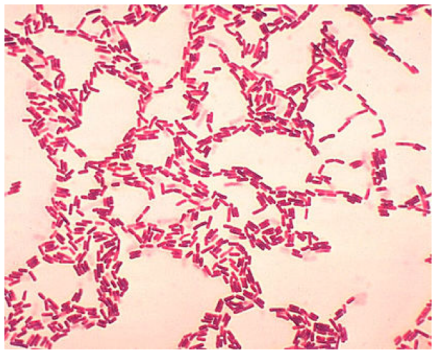
- Able to rapidly utilize hydrolysate sugars, including oligomers
- Never-before transformed
- Facultative anaerobe
- Can produce 100 g/L lactic acid





Goals

- Develop initial genetic transformation
- Develop enhanced tools to accelerate engineering



Progress

- Have cloned and expressed all three DNA methyltransferases in *E. coli* to evade host defense systems, and are testing transformation now
- Characterized antibiotic sensitivity

4 – Relevance

Relevance to BETO goals

Goal:

Develop the tools needed to leverage the unique phenotypes in non-model organisms in order to enable a diverse portfolio of cost-effective biofuels and bioproducts

Relevance to BETO/bioenergy goals / Why is this project important?

Contributing directly to 2020 BETO Milestone to “provide enabling capabilities in synthetic biology for industrially relevant, optimized chassis microorganisms”

Examples of cost savings by developing new host organisms:

- Eliminate costly separations steps by directly producing acids at low pH
- Engineering of hosts that can consume atypical substrates
- Higher substrate uptake rates decreasing fermentation times
- Accelerate strain construction, allowing rapid screening of pathways in parallel

Enhanced genetic tools enables more rapid screening of engineered strains, thereby accelerating the advancement of the SOT

Relevance to broader community

How does this project advance the SOT, contribute to commercial viability of biofuels production?

- Enhanced genetic tools will allow more rapid screening of engineered strains, thereby accelerating the advancement of the SOT
- Supports industry need for publicly available non-standard hosts and tools

Technology transfer activities

- Publications, patent applications
- Industry collaboration through DFOs and BEEPs projects

5 – Future Work

Future Work

Overall Vision: Develop new tools in non-model host organisms to enable bioengineering by both the ABF as well as external stakeholders

Organism Evaluation

- FY19: evaluate hosts, publish Tier system
- Post-'19: support ABF teams as needed, develop interactive web portal for Tier system

Tools and Technologies

- FY19: Develop genetic tools for 3 hosts with unique phenotypes
- Post-'19: Provide protocols, tools, and new hosts to the biomanufacturing community

Support BETO Portfolio

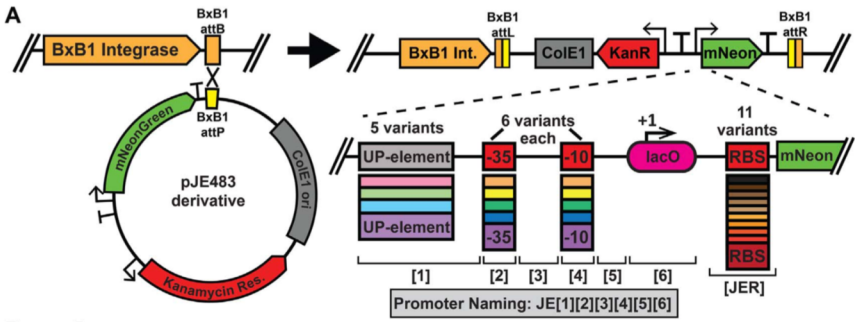
- FY19: host development for SOT
- Post-'19: stay engaged with SOT projects and support as appropriate

ABF: *C. carboxidivorans & B. coagulans*

Goal: Finish developing hosts to the point where they can be used in DBTL

Tools needed:

- Demonstration of initial transformation
  - Replicating plasmid or chromosomal insertion
- Develop characterized gene expression “parts”
  - e.g., promoters, terminators, ribosome binding sites
- Develop tools for simple genome modification
  - e.g., counter-selectable markers for gene deletions, DNA integration system, possibly CRISPR-based editing and regulation
- Publish and advertise availability within the ABF



SOT: *Zymomonas mobilis*

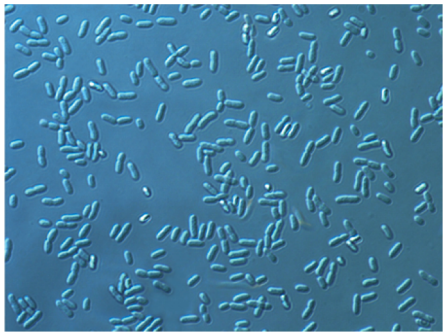
Goal: Make *Z. mobilis* genetic tools better to increase DBTL cycle efficiency

Potential benefits:

- Catabolizes glucose very rapidly with high product yield
- Natively produces ethanol; has recently been engineered to make butanediol

Needs:

- Tools for more rapid engineering progress:
  - Stronger promoters/RBS combinations, trying to match plasmid-based expression levels
  - Counter selection for unmarked genome modifications
  - Better regulated expression
  - Improving transformation efficiency
  - High efficiency DNA integration system (e.g., phage integrases)



SOT: *Clostridium tyrobutyricum*

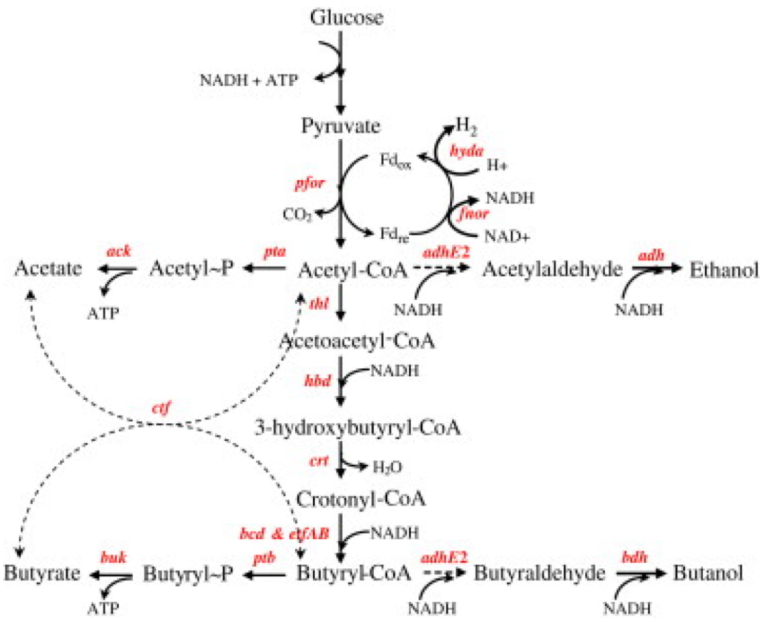
Goal: Make *C. tyrobutyricum* genetic tools better to accelerate DBTL cycle efficiency

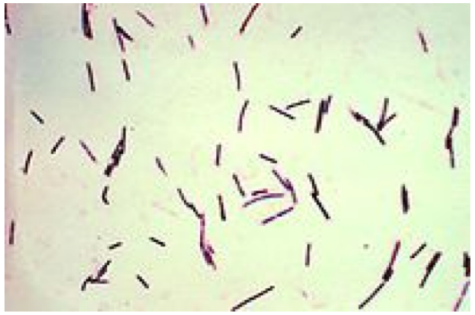
Potential benefits:

- Ferments hydrolysate sugars
- Natively produces butyrate as a product at high yield

Needs:

- Needed tools for more rapid engineering progress:
  - Improve transformation efficiency and reliability
  - Counter selectable markers for easier gene deletions
  - High efficiency DNA integration system for screening heterologous expression constructs
  - Better characterized promoters
  - High throughput reporter systems for anaerobes





U.S. DEPARTMENT OF ENERGY | Energy Efficiency & Renewable Energy
BIOENERGY TECHNOLOGIES OFFICE

Agile BioFoundry

Summary

Overview
- Evaluate and improve tools for new, non-model host organisms

Approach
- Develop genetic tools in potential new hosts and create system for evaluating prospective hosts

Technical Accomplishments
- Created Tier System for evaluating new hosts
- Created *E. coli* strains to enable transformation of new target hosts

Relevance
- The biotechnology industry and other stakeholders need advanced new host organisms for conversion of renewable feedstocks to fuels and chemicals

Future Work
- Develop new hosts for the ABF and expand the genetic tools available for BETO SOT projects

Acknowledgements

- Gregg Beckham
- Dayna Daubaras
- Jim Elkins
- Joshua Elmore
- John Gladden
- Annie Hatmaker
- Scott Hennelly
- Ray Henson
- Ramesh Jha
- Chris Johnson
- Phil Laible
- Jon Magnuson
- Thom Mand
- Isabel Pardo
- Lauren Riley
- Rose Wilton
- Neely Wood
- Chris Yeager

U.S. DEPARTMENT OF ENERGY | Energy Efficiency & Renewable Energy
BIOENERGY TECHNOLOGIES OFFICE

Agile BioFoundry

Additional Slides

Responses to Previous Reviewers' Comments

- Weaknesses include geographic separation
  - As a distributed effort, we clearly have faced operational challenges, although these have more than been made up for by the Agile BioFoundry's ability to leverage physical and human resources across distributed national laboratories. The Agile BioFoundry's program manager, together with regular communications across the consortium (via teleconferences, webinars, informatics servers, SharePoint, annual in-person meetings), have helped mitigate communications risks. Sample transfer risks (i.e., sample stability, sample loss) will continue to be assessed through local/proximal compared with remote sample analysis, and to date we have not suffered from any notable sample losses. We are continuing to make progress in addressing disconnects in technology adoption, and it continues to be an operational imperative to standardize workflows and data-exchange formats wherever possible.
- Do not yet have a compelling argument as to why and how their approach will be better than other potential approaches to the problem
  - What sets the Agile BioFoundry apart from other foundries is that we develop and distribute publicly available tools, methods, and strains aimed at broadly benefiting the biofuels and bioproducts industry. Whereas private foundries are incentivized to develop proprietary tools and organisms, the Agile BioFoundry is a publicly funded effort aimed at delivering technology that will enable industry to either leverage our resources through partnership or adopt our methodologies for developing bioproducts. In comparison to the publicly funded Defense Advanced Research Projects Agency Living Foundries program, there are distinct programmatic and technical differences between the aims of the two efforts. Where the Living Foundries program is primarily focused on developing biological pathways to materials that cannot be achieved through transformations of petroleum feedstocks, the Agile BioFoundry is focused developing biological pathways for producing advanced biofuels and renewable, high-volume chemicals.

Responses to Previous Reviewers' Comments (cont.)

- Rationale for their choice of product targets needs to be strengthened
  - The Agile BioFoundry is pursuing multiple target/hosts to demonstrate that the methods, software, and technologies can be productively applied across product classes. The process and rationale for selecting the three target/hosts pairs for FY 2017 (and the 15 pairs for initially prioritized for FY 2017 – FY 2019) was described during the 2017 Peer Review, and the details were provided to BETO. For our FY 2018 and FY 2019 target/host selection processes, in addition to quantitative technical assessments across multiple categories (TEA and Market, LCA, Strategic Value, Scientific Novelty, DOE Relevance, How Designable, How Buildable, How Hostable, How Testable, How Scalable, and Chemical and Biological Safety), we proactively consulted with the Agile BioFoundry Industry Advisory Board to ensure that our prioritized targets and hosts remain aligned with industry's needs.

- Isn't clear that reducing the cycle time to, say, adipic acid, would be generally applicable to other material
  - As will be / has been presented in the Target/Host ABF presentations at the 2019 Peer Review, we have started to diligently measure cycle times across targets and hosts. This is the pre-requisite step to measuring improvements in (i.e., reductions to) cycle time. It should be noted that we are now pursuing multiple targets in the same host (which could suggest how cycle times for the second target have benefitted from improvements for the first target) and the same target in multiple hosts (which could suggest how cycle times in the second host have benefitted from improvements for the first host). While the former is more directly relevant for this previous reviewer's comment, both are important to capture and understand as they both directly affect the Agile BioFoundry's ability to broadly accelerate biomanufacturing process development across targets and hosts.

Responses to Previous Reviewers' Comments (cont.)

- More emphasis should be placed on the performance gap between small-scale culturing and bench-scale fermentation, which is a well-known problem in the field
  - We recognize that there are challenges associated with each increase in process scale, including the transition from high-throughput, small-scale culturing to bench-scale fermentation. Agile BioFoundry workflows leverage design of experiments and small-scale culture to select strains to grow in bench-scale bioreactors. Bench-scale fermentation provides critical data for the "Learn" component of Design-Build-Test-Learn, both to inform future designs and to develop predictive models that may be applied to small-scale experiments. Agile BioFoundry facilities have recently procured Robo/Biolector(Pro) and Ambr250 instrumentation which both serve to bridge the gap between small-scale culturing and bench-scale fermentation.

- PI is encouraged to look deeply into high-throughput fermentation techniques mastered by enzymes and biobased chemicals and fuels companies
  - As mentioned above, towards adopting the techniques practiced and mastered by companies, Agile BioFoundry facilities have recently procured Robo/Biolector(Pro) and Ambr250 high-throughput fermentation instrumentation.

- Encourage the PI to form a strong liaison between fermentation and the high-throughput team
  - There are strong connections between Agile BioFoundry high-throughput and bio-reactor fermentation teams, with staff shared in common between them.

Publications, Patents, Presentations, Awards, and Commercialization

Publications

- Garima Goyal, Zak Costello, Jorge Alonso Guitierrez, Aram Kang, Taek Soon Lee, Hector Garcia Martin, and Nathan J Hillson. (2018) "Parallel Integration and Chromosomal Expansion of Metabolic Pathways" ACS Synthetic Biology DOI: 10.1021/acssynbio.8b00243
- Costello, Zak, and Hector Garcia Martin. "A machine learning approach to predict metabolic pathway dynamics from time-series multiomics data." NPJ systems biology and applications 4.1 (2018): 19. https://doi.org/10.1038/s41540-018-0054-3
- Oyetunde, Tolutola, et al. "Leveraging knowledge engineering and machine learning for microbial bio-manufacturing." Biotechnology advances (2018). https://doi.org/10.1016/j.biotechadv.2018.04.008
- Amin Zargar, Jesus F. Barajas, Ravi Lal, Jay D. Kealsing. “Polyketide Synthases as a Platform for Chemical Product Design” AIChE (2018) https://doi.org/10.1002/aic.16351
- Jha RK*, Bingen JM, Johnson CW, Kern TL, Khanna P, Trettel DS, Straus CEM, Beckham GT, Dale T* (2018). A protocatechuate biosensor for Pseudomonas putida KT2440 via promoter and protein evolution. Metabolic Engineering Communications (6) 33-38. https://doi.org/10.1016/j.meteno.2018.03.001
- Mitchell G. Thompson, Nima Sedaghatian, Jesus F. Barajas, Maren Wehrs, Constance B. Bailey, Nurgul Kaplan, Nathan J. Hillson, Aindrila Mukhopadhyay & Jay D. Keasling. (2018) "Isolation and characterization of novel mutations in the pSC101 origin that increase copy number". Scientific Reports 8, 1590 doi:10.1038/s41598-018-20016-w
- Jesus F. Barajas, Amin Zargar, Bo Pang, Veronica T. Benites, Jennifer Gin, Edward E. K. Baidoo, Christopher J. Petzold, Nathan J. Hillson, and Jay D. Keasling. (2018) "Biochemical Characterization of β-Amino Acid Incorporation in Fluvirucin B2 Biosynthesis". ChemBioChem 10.1002/cbic.201800169
- Denby, Charles M., et al. "Industrial brewing yeast engineered for the production of primary flavor determinants in hopped beer." Nature communications 9.1 (2018): 965
- Garber ME, Rajeev, Kazakov AE, Trinh J, Masuno D, Thompson M, Kaplan, N, Novichkov PS and Mukhopadhyay A. (2018) "Multiple signaling systems target a core set of transition metal homeostasis genes using similar binding motifs” Mol Microbiol. 107(6):704-717. doi: 10.1111/mmi.13909
- Ando, D., Garcia Martin, H. (2018) "Two-Scale 13C Metabolic Flux Analysis for Metabolic Engineering". In "Synthetic Metabolic Pathways - Methods and Protocols", Springer Protocols - Methods in Molecular Biology, Jensen, Michael Krogh, Keasling, Jay D (Eds.) ISBN 978-1-4939-7295-1 http://www.springer.com/us/book/9781493972944
- Backman TWH, Ando D, Singh J, Keasling JD, García Martín H. (2018) “Constraining Genome-Scale Models to Represent the Bow Tie Structure of Metabolism for (13)C Metabolic Flux Analysis”. Metabolites. 2018 Jan 4;8(1). pii: E3. doi: 10.3390/metabo8010003
- Yuzawa S, Bailey CB, Fujii T, Jocic R, Barajas JF, Benites VT, Baidoo EEK, Chen Y, Petzold CJ, Katz L, Keasling JD. Heterologous Gene Expression of N-Terminally Truncated Variants of LipPks1 Suggests a Functionally Critical Structural Motif in the N-terminus of Modular Polyketide Synthase. ACS Chem Biol. 2017 Nov 17;12(11):2725-2729. doi: 10.1021/acschembio.7b00714

Publications, Patents, Presentations, Awards, and Commercialization (cont.)

Publications (cont.)

- Morrell, W., Birkel, G., Forrer, M.,; Lopez, T., Backman, T.W.H, Dussault, M., Petzold, C., Baidoo, E., Costello, Z., Ando, D., Alonso Gutierrez, J., George, K., Mukhopadhyay, A., Vaino, I., Keasling, J., Adams, P., Hillson, N., Garcia Martin, H. "The Experiment Data Depot: a web-based software tool for biological experimental data storage, sharing, and visualization" (2017) ACS Synthetic Biology DOI: 10.1021/acssynbio.7b00204
- Eng, C.H.*, Backman, T.W.H.*, Bailey, C.B., Magnan, C., Garcia Martin, H.G., Katz, L., Baldi, P., Keasling, J.D. "ClusterCAD: a computational platform for type I modular polyketide synthase design." (2017) Nucleic Acids Research DOI: 10.1093/nar/gkx893 *Contributed equally
- Barajas, J.F., Blake-Hedges, J., Bailey, C.B., Curran, S., Keasling, J.D. (2017). "Engineered polyketides: Synergy between protein and host level engineering" Synthetic and Systems Biotechnology doi.org/10.1016/j.synbio.2017.08.005
- Shymansky, Christopher M., et al. "Flux-enabled exploration of the role of Sip1 in galactose yeast metabolism." Frontiers in Bioengineering and Biotechnology 5 (2017)

Presentations

- Gregg Beckham, Hybrid biological and catalytic processes to manufacture and recycle plastics, Princeton University, November 28th, 2018
- Garcia Martin, H. "Towards a predictive synthetic biology enabled by machine learning and automation". Ginkgo Bioworks, Boston, MA, November 12, 2018
- Nathan J. Hillson. "DIVA (DNA Design, Implementation, Validation Automation) Platform". Invited Talk, 2nd Darmstadt RoboWorkshop, Darmstadt, Germany, November 8, 2018
- Nathan J. Hillson. "Recent developments at the U.S Department of Energy Agile BioFoundry". Invited Talk, 2nd Darmstadt RoboWorkshop, Darmstadt, Germany, November 7, 2018
- Garcia Martin, H. "Towards a predictive synthetic biology enabled by machine learning and automation". AIChE annual meeting, Pittsburgh, PA, October 31 2018
- Garcia Martin, H. "Towards a predictive synthetic biology enabled by machine learning and automation". Thermo Fisher, San Jose, CA, October 19, 2018
- Garcia Martin, H. "Towards a predictive synthetic biology enabled by machine learning and automation". DTRA Tech Watch, Ft. Belvoir, VA, October 10, 2018
- Nathan J. Hillson. "DOE Agile BioFoundry Overview". Invited Talk, SynBioBeta 2018 visit to ESE, Emeryville, CA, October 1, 2018
- Nathan J. Hillson. "ABF Organization, Progress, and FY19 Plans". Invited Talk, ABF All Hands Annual Meeting 2018 (Industry Day), Emeryville, CA, September 12, 2018
- Nathan J. Hillson. "Agile BioFoundry Overview". Invited Talk, ABF All Hands Annual Meeting 2018, Emeryville, CA, September 10, 2018
- Garcia Martin, H. "A new approach to flux analysis". Invited Talk, ABF All Hands Annual Meeting 2018, Emeryville, CA, September 10, 2018

Publications, Patents, Presentations, Awards, and Commercialization (cont.)

Presentations (cont.)

- Hector Plahar. “DIVA Software Platform”. Invited Talk, ABF All Hands Annual Meeting 2018, Emeryville, CA, September 10, 2018
- Tijana Radivojevic. “Automatic Recommendation Tool”, Invited Talk, ABF All Hands Annual Meeting 2018, Emeryville, CA, September 10, 2018
- Jennifer Chiniquy. “DIVA DNA-Seq and DNA Construction”, Invited Talk, ABF All Hands Annual Meeting 2018, Emeryville, CA, September 10, 2018
- Garcia Martin, H. “A New Approach to Flux Analysis". ABF Annual Meeting, Berkeley CA, September 7, 2018
- Garcia Martin, H. “Towards a predictive synthetic biology enabled by machine learning and automation". Invited talk, Machine learning for science workshop, Berkeley, CA, September 5, 2018
- Nathan J. Hillson. “Agile BioFoundry Overview”. Invited Lightning Talk, LBNL BioSciences Area Retreat 2018, Lafayette, CA, August 30, 2018
- Garcia Martin, H. “Modeling from molecules to ecosystems : opportunities, challenges and vision". Invited talk, BioEpic meeting, Berkeley, CA, August 23, 2018
- Garima Goyal “DIVA DNA Construction”. Invited Talk, JBEI Annual Meeting 2018, Sonoma, CA, August 20-22, 2018
- Tijana Radivojevic. “Automatic Recommendation Tool”, Invited Talk, JBEI Annual Meeting 2018, Sonoma, CA, August 22, 2018
- Garcia Martin, H. “Opportunities in the intersection of synthetic biology, machine learning and automation". Invited talk, JBEI Annual Meeting, Berkeley, CA, August 20, 2018
- Garcia Martin, H. “Towards a predictive synthetic biology enabled by machine learning and automation". Invited talk, SIMB, Chicago, IL, August 15, 2018
- Garcia Martin, H. “Towards a predictive synthetic biology enabled by machine learning and automation". Invited talk, International Workshop for BioDesign and Automation (IWBDA), Berkeley, CA, August 2nd, 2018
- Garcia Martin, H. “Towards a predictive synthetic biology enabled by machine learning and automation". Invited talk, Biocruces, Bilbao, Spain, July 20, 2018
- Garcia Martin, H. “Machine Learning to Predict Metabolic Pathway Dynamics from Multiomics Data". Invited talk, AI for synthetic biology, Stockholm, Sweden, July 15, 2018
- Garcia Martin, H. “Towards a predictive synthetic biology enabled by machine learning and automation". Invited talk, BCAM, Bilbao, Spain, July 3, 2018
- Nathan J. Hillson, "Berkeley (and other) National Lab(s): Current Biosecurity Frameworks and Strategies in Action", Invited Talk, EBRC meeting - Improving Security Considerations in Engineering Biology Research, Emeryville, CA, June 26, 2018
- Nathan J. Hillson and Hector A. Plahar, "ICE Software Platform", Invited Talk, Software for Synthetic Biology Workflows Workshop, SEED 2018, Scottsdale, Arizona, June 7, 2018
- Gregg Beckham. Developing new processes to valorize lignin and sugars to building-block chemicals and materials, RWTH Aachen University, May 28th, 2018

Publications, Patents, Presentations, Awards, and Commercialization (cont.)

Presentations (cont.)

- Gregg Beckham. Adventures in engineering Pseudomonas putida for expanded substrate specificity and improved tolerance, RWTH Aachen University, May 28th, 2018
- Hillson, N.J. “Berkeley Lab project activities, biosecurity practices, and their roles within the larger biosecurity landscape”. Invited Talk, Working Group on Automation in SynBio, Gryphon Scientific, Takoma Park, MD, May 23, 2018
- Hillson, N.J. “Recent developments at the Agile BioFoundry”. Invited Talk, Diligence Ventures/Suzhou Government visit to ABF, Emeryville, CA, May 2, 2018
- Gregg Beckham. Hybrid biological and catalytic processes to manufacture and recycle plastics, MIT, April 27th, 2018
- Hillson, N.J. “Recent developments at the Agile BioFoundry”. Invited Talk, 2018 Life Science Symposium - Synthetic Biology and Metabolic Engineering, MilliporeSigma Innovation Center, St. Louis, MO, April 27, 2018
- Garcia Martin, H. " A Machine Learning Approach to Predict Metabolic Pathway Dynamics from Time Series Multiomics Data". Invited talk at Madison Microbiome Meeting at University of Wisconsin, Madison, WI, April 25, 2018.
- Jennifer Chiniquy, Cindi Hoover, Joel Guenther, Nurgul Kaplan, Garima Goyal, Mark Kulawik, Hector Plahar, Zachary Costello, Brian Bushnell, Samuel Deutsch, and Nathan J. Hillson. “Overcoming Challenges in MiSeq DNA Construct Sequence Validation”. Invited Poster, DOE JGI User Meeting 2018, San Francisco, CA, March 14, 2018
- "Test" and "Learn" in process research informs design strategy Sundstrom, E. R.,, M. Mirsiaghi, F. Tachea, N. Sun, T.R. Pray, D. Tanjore. ECO-BIO, Dublin, Ireland, March 5, 2018.
- Garcia Martin, H. "EDD as a data warehouse and Learn facilitator". Invited talk at Argonne National Lab, St. Louis, Lemont, IL, March 5, 2018
- Garima Goyal, Nurgul Kaplan, Jennifer L. Chiniquy, Hector A. Plahar, Annabel Large, Lisa Simirenko, Samuel Deutsch, and Nathan J. Hillson. “DIVA Services: PCR, Full DNA Construction, and MiSeq Validation”. Invited Poster, DOE BER GSP Contractor’s Meeting 2018, Tysons Corner, VA, February 27, 2018
- Hillson, N.J. “Three synthetic biology design challenges we face, and how we are approaching them”. Invited Talk, Dagstuhl Seminar 18082, Wadern, Germany, February 19, 2018
- Jennifer Chiniquy, Nurgul Kaplan, Garima Goyal. “DIVA DNA-Seq Service”, JBEI User Meeting presentation, February 12, 2018.
- Garcia Martin, H. "Metabolic Modeling of –omics Data for Biofuel Production". Invited talk at Bayer, Sacramento, CA, February 2, 2018.
- Garcia Martin, H. " Machine Learning and Mechanistic Models to Predict Biological Outcomes using ‘omics Data". Invited talk at Environmental Genomics and Systems Biology retreat, Berkeley, CA, January 19, 2018
- Jesus F. Barajas. “Current progress towards engineered PKS lactam pathways”. JBEI/BBD group meeting presentation, December 13, 2017
- Hillson, N.J. “Agile BioFoundry Overview”. Invited Talk, iSynBio/SIAT visit to JGI, Walnut Creek, CA, December 9, 2017
- Jennifer Chiniquy, Nurgul Kaplan. “DIVA DNA-Seq Service”. ESE User Meeting presentation, November 20, 2017

Publications, Patents, Presentations, Awards, and Commercialization (cont.)

Presentations (cont.)

- Hillson, N.J. “Agile BioFoundry Overview”. Invited Talk, Cargill visit to ESE, Emeryville, CA, November 17, 2017
- Hillson, N.J. “Flanking Homology DNA Assembly, Protocol Design Software, and Synthetic DNA”. Invited Talk, Bitesize Bio Webinar, November 15, 2017
- Simmons, B.A. and Hillson, N.J. “The BioDefense Foundry”. Invited Talk, DTRA Tech Watch Briefing, Springfield, VA, November 8, 2017
- Hillson, N.J. “Agile BioFoundry Overview”. Invited Talk, University of Wyoming, Laramie, WY, November 3, 2017
- Hillson, N.J. “Parallel Integration and Chromosomal Expansion of Metabolic Pathways”. Invited Talk, University of Wyoming, Laramie, WY, November 3, 2017
- Hillson, N.J. “Agile BioFoundry Overview”. Invited Talk, Braskem Zoom Teleconference, November 1, 2017
- Hector Garcia Martin. “Modeling of -omics data for Biofuel Production through Synthetic Biology”. EECE Department seminar, Washington University, St. Louis MO, October 20th, 2017
- Hillson, N.J. “Agile BioFoundry Overview”. Invited Talk, ABLC Next Tour of ESE (ABF/ABPDU/JBEI), Emerville, CA, October 16, 2017
- Hillson, N.J. “Agile BioFoundry Overview”. Invited Talk, Berkeley Lab Workshop: Industrialization of engineering biology: from discovery to scale-up, SynBioBeta SF 2017, UCSF Mission Bay, San Francisco, CA, October 3, 2017
- Hillson, N.J. “How the Agile BioFoundry Thinks About Paths to Commercialization”. Invited Talk, SynBio for Defense, Arlington, VA, September 27, 2017
- Hillson, N.J. “BioDefense – the Agile BioFoundry and Predictive Biology”. Invited Talk, Presentation for Dimitri Kusnezov (Chief Scientist, DOE NNSA), Berkeley, CA, September 21, 2017
- Hillson, N.J. “Sustainable development through a synthetic biology foundry”. Invited Talk, CellPress LabLinks - Basic to Applied Science for Sustainable Development, Berkeley, CA, September 18, 2017
- Plahar, H.A. “Software Session: Recent DeviceEditorjs/DIVA/ICE improvements”. Invited Talk, JBEI Annual Meeting, Monterey, CA, September 15, 2017
- Costello, Z. “Software Session: The Automatic Recommendation Tool”. Invited Talk, JBEI Annual Meeting, Monterey, CA, September 15, 2017
- Backman, T.W.H. “ClusterCAD: a computational platform for type I modular polyketide synthase design.” Invited Talk, JBEI Annual Meeting, Monterey, CA, September 14, 2017
- Hillson, N.J. “Agile BioFoundry Update”. Invited Talk, JBEI Annual Meeting, Monterey, CA, September 13, 2017
- Plahar, H.A. “ICE/DIVA Software Tutorial”. Invited Talk, Agile BioFoundry Annual Meeting, NREL IBRF, Golden, CO, August 29, 2017
- Hillson, N.J. “Agile BioFoundry Overview”. Invited Talk, Agile BioFoundry Annual Meeting, NREL IBRF, Golden, CO, August 28, 2017
- De Paoli, H.C. “A. pseudoterreus 3HP Design and Build”. Invited Talk, Agile BioFoundry Annual Meeting, NREL IBRF, Golden, CO, August 28, 2017.
- Chiniquy J., “DIVA DNA-Seq Service”. Invited Talk, Agile BioFoundry Annual Meeting, NREL IBRF, Golden, CO, August 28, 2017

Publications, Patents, Presentations, Awards, and Commercialization (cont.)

Presentations (cont.)

- Garcia Martin, H. "Predicting Metabolic Pathway Dynamics by Combining Multiomics Data with Machine Learning and Kinetic Modeling". Invited talk at "Multi-omics for Microbiomes" conference, Pasco, WA, July 31, 2017.
- Johnson, C.W. “Metabolic engineering of Pseudomonas putida KT2440 for production of muconic acid from sugar”, SIMB Annual Meeting, July 31, 2017
- Hillson, N.J. "j5 Software Through the Years: Insights from Aggregate Public Usage Metrics". Invited lightning talk, World Metrology Day Symposium, Stanford, CA, May 22, 2017.
- Beckham, G.T. "The Agile BioFoundry: Investing in Biomanufacturing Infrastructure”, TechConnect World, May 16, 2017
- Derek Vardon. Potential commercialization opportunities for valorization of biomass to polymer precursors. Invited Seminar. Alliance Commercialization and Deployment Committee Meeting, NREL. May 2017.
- Gregg Beckham. The Agile BioFoundry: Investing in Biomanufacturing Infrastructure, TechConnect World, May 16, 2017
- Hillson, N.J. "Overview of the Agile BioFoundry". Invited talk, IMP (Mexican Petroleum Institute) Visit to JBEI, Emeryville, CA, April 21, 2017.

Posters

- J. Meadows, C. Johnson, S. Notonier, YM. Kim, S.Tripathy, K. Burnam-Johnson, M. Burnet, J. Magnuson, G. Beckham, N. Hillson, J. Gladden. “Engineering Pseudomonas putida KT2440 to produce adipic acid from lignocellulosic components”. Invited Poster, ABF All Hands Annual Meeting 2018, Emeryville, CA, September 10, 2018
- Jesus F. Barajas, Jingwei Zhang, Amin Zargar, Bo Pang, Huaxiang Deng, Veronica T. Benites, Edward E. K. Baidoo, Christopher J. Petzold, Nathan J. Hillson, Jay D. Keasling. “Development of Valerolactam and Caprolactam Biosynthetic Routes”. Invited Poster, ABF All Hands Annual Meeting 2018, Emeryville, CA, September 10, 2018
- Garima Goyal, Nurgul Kaplan, Jennifer L. Chiniquy, Jonathan Diab, Joel M. Guenther, Hector A. Plahar, Joanna Chen, Manjiri Tapaswi, Nina Stawski, Lisa Simirenko, Samuel Deutsch, and Nathan J. Hillson. “DIVA (Design Implementation Validation Automation) DNA Construction”. Invited Poster, ABF All Hands Annual Meeting 2018, Emeryville, CA, September 10, 2018
- Jonathan Diab, Jennifer Chiniquy, Cindi Hoover, Joel Guenther, Nurgul Kaplan, Garima Goyal, Mark Kulawik, Hector Plahar, Zachary Costello, Brian Bushnell, Samuel Deutsch, and Nathan J. Hillson. “MiSeq DNA Construct Sequence Validation”. Invited Poster, ABF All Hands Annual Meeting 2018, Emeryville, CA, September 10, 2018
- Edward E.E.K. Baidoo and Veronica Teixeira Benites. “High throughput analysis of isoprenoid pathway intermediates by HILIC-QTOF-MS”. Invited Poster, ABF All Hands Annual Meeting 2018, Emeryville, CA, September 10, 2018.
- Isaac Wolf, Carolina Barcelos, Shawn Chang, Nilufer Oguz, Matt Dorsey, Davinia Salvachua, Robert Nelson, Todd Pray, Eric Sundstrom and Deepti Tanjore. “Harmonization of Fermentation for Production of P. putida-derived Muconic Acid”. Invited Poster, ABF All Hands Annual Meeting 2018, Emeryville, CA, September 10, 2018

Publications, Patents, Presentations, Awards, and Commercialization (cont.)

Posters (cont.)

- J. Prahl, S. Coradetti, D. Liu, G. Geiselman, T. Pray, J. Gladden, E. Sundstrom, and D. Tanjore. “Insights from Bioreactors make Scale-Down Modeling more Effective”. Invited Poster, ABF All Hands Annual Meeting 2018, Emeryville, CA, September 10, 2018
- Garima Goyal, Nurgul Kaplan, Jennifer L. Chiniquy, Jonathan Diab, Joel M. Guenther, Hector A. Plahar, Joanna Chen, Manjiri Tapaswi, Nina Stawski, Lisa Simirenko, Samuel Deutsch, and Nathan J. Hillson. “DIVA (Design Implementation Validation Automation) DNA Construction”. Invited Poster, JBEI Annual Meeting 2018, Sonoma, CA, August 20-22, 2018
- William Morrell, Mark Forrer, Garrett Birkel, Traci Lopez, Nathan J Hillson, Hector Garcia Martin. “Collaboration with the Experiment Data Depot”. Invited Poster, JBEI Annual Meeting 2018, Sonoma, CA, August 20-22, 2018
- Jonathan Diab, Jennifer Chiniquy, Cindi Hoover, Joel Guenther, Nurgul Kaplan, Garima Goyal, Mark Kulawik, Hector Plahar, Zachary Costello, Brian Bushnell, Samuel Deutsch, and Nathan J. Hillson. “MiSeq DNA Construct Sequence Validation”. Invited Poster, JBEI Annual Meeting 2018, Sonoma, CA, August 20-22, 2018
- Sarah A LaFrance, Jacob Coble, Thomas Rich, Hector Plahar, Joshua Nixon, Nathan J. Hillson. “VectorEditor: Freely Open-Source Javascript Webapp for DNA Visualization, Annotation, and Editing”. Invited Poster, JBEI Annual Meeting, Monterey, CA, September 13, 2017
- Annabel Large, Nurgul Kaplan, Jennifer Chiniquy, Garima Goyal, and Nathan Hillson. “Expansion and Optimization of DIVA DNA Sequence Validation Services”. Invited Poster, JBEI Annual Meeting, Monterey, CA, September 13, 2017
- Garima Goyal, Nurgul Kaplan, Jennifer L. Chiniquy, Joel M. Guenther, Hector A. Plahar, Joanna Chen, Manjiri Tapaswi, Nina Stawski, Lisa Simirenko, Samuel Deutsch, and Nathan J. Hillson. “DIVA (Design Implementation Validation and Automation) DNA Construction”. Invited Poster, JBEI Annual Meeting, Monterey, CA, September 13, 2017
- Nurgul Kaplan, Garima Goyal, Jennifer L. Chiniquy, Joel M. Guenther, Hector A. Plahar, Joanna Chen, Manjiri Tapaswi, Nina Stawski, Lisa Simirenko, Samuel Deutsch, and Nathan J. Hillson. “Using DIVA, DeviceEditor, and j5 for DNA Construction”. Invited Poster, JBEI Annual Meeting, Monterey, CA, September 13, 2017
- William Morrell, Garrett Birkel, Mark Forrer, Traci Lopez, Nathan J Hillson, Hector Garcia Martin. “The Experiment Data Depot platform”. Invited Poster, JBEI Annual Meeting, Monterey, CA, September 13, 2017
- Backman, T.W.H., Eng, C.H., Bailey, C.B., Keasling, J.D., Garcia Martin, H. “Software for polyketide synthase (PKS) design”. Invited Poster, JBEI Annual Meeting, Monterey, CA, September 13, 2017
- Garima Goyal, Nurgul Kaplan, Jennifer L. Chiniquy, Joel M. Guenther, Hector A. Plahar, Joanna Chen, Manjiri Tapaswi, Nina Stawski, Lisa Simirenko, Samuel Deutsch, and Nathan J. Hillson. “DIVA (Design Implementation Validation and Automation) DNA Construction”. Invited Poster, Agile BioFoundry Annual Meeting, NREL IBRF, Golden, CO, August 28, 2017
- Nurgul Kaplan, Garima Goyal, Jennifer L. Chiniquy, Joel M. Guenther, Hector A. Plahar, Joanna Chen, Manjiri Tapaswi, Nina Stawski, Lisa Simirenko, Samuel Deutsch, and Nathan J. Hillson. “Using DIVA, DeviceEditor, and j5 for DNA Construction”. Invited Poster, Agile BioFoundry Annual Meeting, NREL IBRF, Golden, CO, August 28, 2017

Publications, Patents, Presentations, Awards, and Commercialization (cont.)

Posters (cont.)

- Jennifer L. Chiniquy, Cindi A. Hoover, Joel M. Guenther, Nurgul Kaplan, Christopher W. Beitel, Samuel Deutsch, and Nathan J. Hillson. “Towards a High-Throughput Low-Cost Automated DNA Sequence Validation Workflow”. Invited Poster, Agile BioFoundry Annual Meeting, NREL IBRF, Golden, CO, August 28, 2017
- William Morrell, Garrett Birkel, Mark Forrer, Traci Lopez, Nathan J Hillson, Hector Garcia Martin. “The Experiment Data Depot platform”. Invited Poster, Agile BioFoundry Annual Meeting, NREL IBRF, Golden, CO, August 28, 2017
- Hector A. Plahar, Elena Aravina, Oge Nnadi, Joanna Chen, Paul D. Adams, Jay D. Keasling, and Nathan J. Hillson. “ICE: A Distributed and Interconnected Biological Part Registry”. Invited Poster, Agile BioFoundry Annual Meeting, NREL IBRF, Golden, CO, August 28, 2017
- Jha, R., Narayanan, N., Johnson, C., Beckham, G., Dale, T. “Whole cell biosensing in Pseudomonas putida KT2440”. Invited Poster, Agile BioFoundry Annual Meeting, NREL IBRF, Golden, CO, August 28, 2017
- Pandey N., Krishnamurthy, M., Jha, Ramesh., Hennelly, S., Dale, T. “Riboregulator Development To Increase Metabolic Flux Towards Muconate Production”. Invited Poster, Agile BioFoundry Annual Meeting, NREL IBRF, Golden, CO, August 28, 2017
- John Meng, Angela Tarver, Matthew Hamilton, Robert Evans, Lisa Simirenko, Nathan J. Hillson, Jan-Fang Cheng, and Samuel Deutsch. “SynTrack 2: A Scalable DNA Assembly Production Workflow Management”. Invited Poster, 2017 Synthetic Biology: Engineering, Evolution & Design (SEED), Vancouver, British Columbia, Canada, June 20-23, 2017.
- Sarah A LaFrance, Jacob Coble, Thomas Rich, Hector Plahar, Joshua Nixon, Nathan J. Hillson. “VectorEditor: Freely Open-Source Javascript Webapp for DNA Visualization, Annotation, and Editing”. Invited Poster, 2017 Synthetic Biology: Engineering, Evolution & Design (SEED), Vancouver, British Columbia, Canada, June 20-23, 2017.
- William Morrell, Garrett Birkel, Mark Forrer, Traci Lopez, Nathan J Hillson, Hector Garcia Martin. “The Experiment Data Depot platform”. Invited Poster, 2017 Synthetic Biology: Engineering, Evolution & Design (SEED), Vancouver, British Columbia, Canada, June 20-23, 2017.
- Nurgul Kaplan, Garima Goyal, Jennifer L. Chiniquy, Joel M. Guenther, Hector A. Plahar, Joanna Chen, Nina Stawski, Manjiri Tapaswi, Lisa Simirenko, Samuel Deutsch, and Nathan J. Hillson. “DIVA (Design, Implementation, Validation Automation) DNA Construction: Wet-Lab Workflow and Software Platform”. Invited Poster, 2017 Synthetic Biology: Engineering, Evolution & Design (SEED), Vancouver, British Columbia, Canada, June 20-23, 2017.
- Philip C. Gach, Manasi Raje, Nurgul Kaplan, Sangeeta Nath, Samuel Deutsch, Jay D. Keasling, Paul D. Adams, Nathan J. Hillson and Anup K. Singh. “A Microfluidic Platform for Combinatorial Gene Assembly, Transformation, Culture and Assay”. Invited Poster, 2017 Synthetic Biology: Engineering, Evolution & Design (SEED), Vancouver, British Columbia, Canada, June 20-23, 2017.
- Hillson, N.J. "j5 Software Through the Years: Insights from Aggregate Public Usage Metrics". Invited Poster, World Metrology Day Symposium, Stanford, CA, May 22, 2017.
- Jennifer L. Chiniquy, Cindi A. Hoover, Joel M. Guenther, Nurgul Kaplan, Christopher W. Beitel, Samuel Deutsch, and Nathan J. Hillson. “Towards a High-Throughput Low-Cost Automated DNA Sequence Validation Workflow”. Invited Poster, World Metrology Day Symposium, Stanford, CA, May 22, 2017.

Publications, Patents, Presentations, Awards, and Commercialization (cont.)

Posters (cont.)

- G. Goyal, Z. Costello, J.A. Gutierrez, A. Kang, T.S. Lee, H.G. Martin, and N.J. Hillson. “PIACE: Parallel Integration and Chromosomal Expansion of Biofuel Pathways in E. coli”. Invited Poster, World Metrology Day Symposium, Stanford, CA, May 22, 2017.
- Nurgul Kaplan, Garima Goyal, Jennifer L. Chiniquy, Joel M. Guenther, Hector A. Plahar, Joanna Chen, Nina Stawski, Manjiri Tapaswi, Lisa Simirenko, Samuel Deutsch, and Nathan J. Hillson. “DIVA (Design, Implementation, Validation Automation) DNA Construction: Wet-Lab Workflow and Software Platform”. Invited Poster, World Metrology Day Symposium, Stanford, CA, May 22, 2017.