Agile BioFoundry

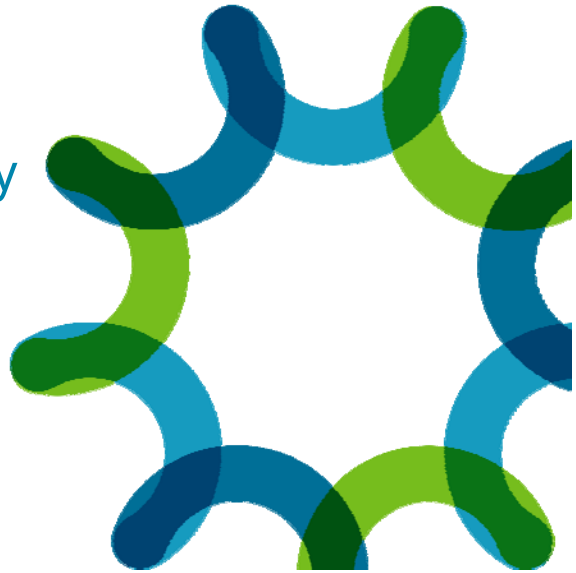
U.S. DEPARTMENT OF ENERGY | Energy Efficiency & Renewable Energy

BIOENERGY TECHNOLOGIES OFFICE

Target/Host: *Aspergillus pseudoterreus* for Organic Acids: 3-Hydroxypropionic and Aconitic Acid

Jon Magnuson, Nathan Hillson, Phil Laible, John Gladden, Gregg Beckham

BETO Peer Review 2019
Technology Session Review Area: Agile BioFoundry
March 7, 2019



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.

Target-Host pair Goal Statement

Goal:

- Validate the Foundry concept by testing the ABF DBTL infrastructure using complementary T-H pairs
- Demonstrate improved efficiency of DBTL cycle and Foundry concept via target-host pair work with *Aspergillus pseudoterreus*
- Target 1: 3-hydroxypropionic acid
- Target 2: aconitic acid

Outcome:

- Increased strain performance to novel targets via DBTL
- Use this system for demonstrable improvements in DBTL cycle times
- Further development of a robust industrially relevant fungal host
- Developing highly relevant datasets for Learn team

Relevance:

- Benchmark DBTL cycle performance and improvement across scales with real-world substrates and process configurations
- Information from DBTL and Integration efforts will be critical to predictive scale-up and scale-down

Quad Chart Overview: T/H *A. pseudoterreus*

Timeline

- Start: October 1, 2016
- End: September 30, 2019
- 81% complete

Budget

	Total Costs Pre FY17	FY17 Costs	FY18 Costs	Total Planned Funding (FY17-19)
DOE Funded	$0M	$1.4M	$2.2M	$5.9M

Partners

- LBNL (15%); PNNL (84%); ANL (0.35%)

Barriers

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

Objective:

Improve critical performance metrics for T-H pairs in *A. pseudoterreus* enabled by the DBTL cycle

End-of-project goal:

Demonstrate T-H pair production of at least 3 molecules at 10 g/L, 100 mg/L/hr, at 40% of theoretical yield from DMR-EH at 10 L

1 - Project Overview

Project overview

History: Task initiated in FY17

- *A. pseudoterreus* Target1 is 3-hydroxypropionic acid, Target 2 is aconitic acid
- Exceeded FY18 annual milestone targets on hydrolysate

Context: *A. pseudoterreus* is an **industrially relevant** filamentous fungus that grows down to pH 2 and produces organic acids in their protonated form for ease of separation and minimal waste generation

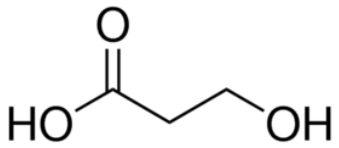
Task specific goals:

- Engineer new or improved organic acid pathways, and increase TRY
- Employ DBTL to produce non-native molecule 3-hydroxypropionic acid (Target 1), and aconitic acid (Target 2)
- Advancements in genetic engineering tools for *A. pseudoterreus*
- Develop and apply array of Learn techniques to identify further targets

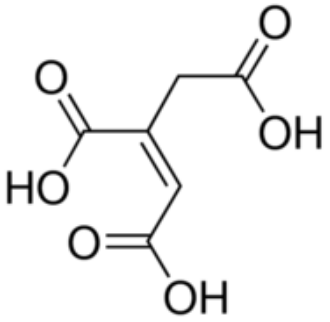
Aspergillus pseudoterreus Host Relevance

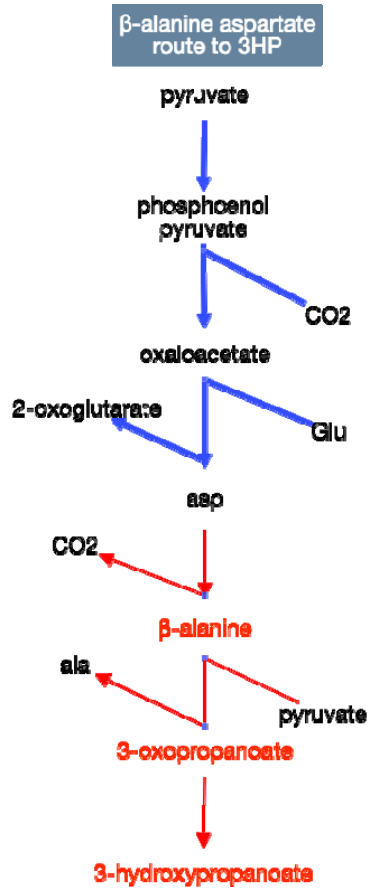
- *Aspergillus* spp. are **industrially relevant**: used for producing small molecules and enzymes in large bioreactors,
  e.g., citric acid in 100,000L airlift reactors, ~3M ton market
- **Genetically tractable**, genome sequenced, genome scale **metabolic model developed**
- **High flux** through glycolysis toward TCA cycle derived **organic acids;**
  A. pseudoterreus ATCC 32359 makes 60 g/L itaconic acid
- Grows and produces at pH 1-3, hence
  it **produces acids, not salts**
  - **Separations** impact: high titer, free acid, crystallization possible
  - Does not require lime to maintain neutral pH and sulfuric acid for post processing acidification, generating gypsum waste
- **Purpose**:
  - Develop **advanced DBTL tools** for *Aspergillus* spp.
  - and show the strength of the platform for producing **organic acids**

Relevance of targets (crops): organic acids



- **Target 1** (began FY17): **3-hydroxypropionic acid**
  Intermediate to acrylic acid and acrylonitrile. NREL developed process to produce acrylonitrile would benefit from a renewable source of 3HP
- **Target 2** (began FY18): **aconitic acid**
  A 6-carbon tricarboxylic acid, like citrate. Beverage acidulant, industrial chelator/modifier (cement) etc.
- **Purpose**: developing concrete examples of **organic acids**



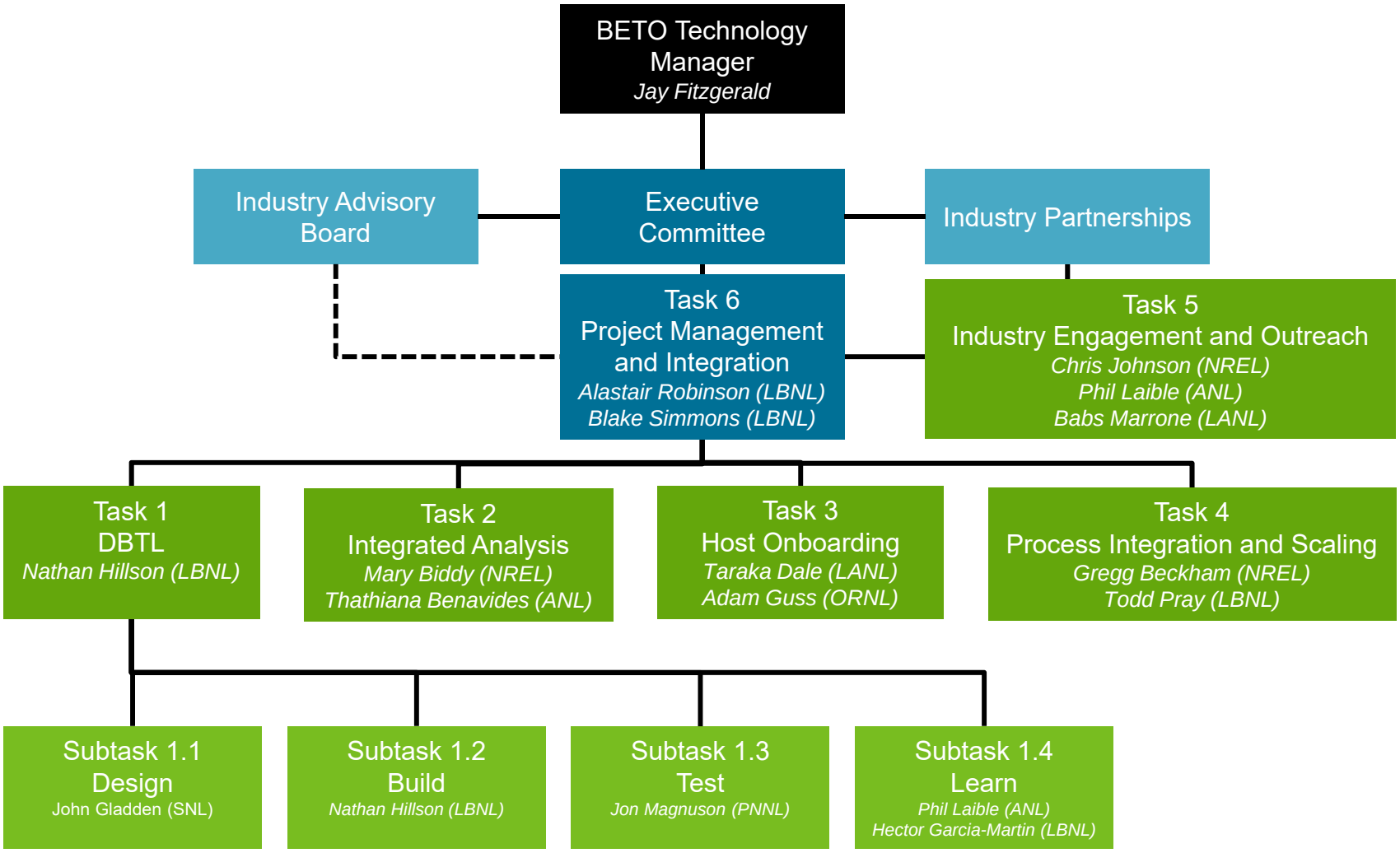


2 – Approach

Six Tasks for Overall Project

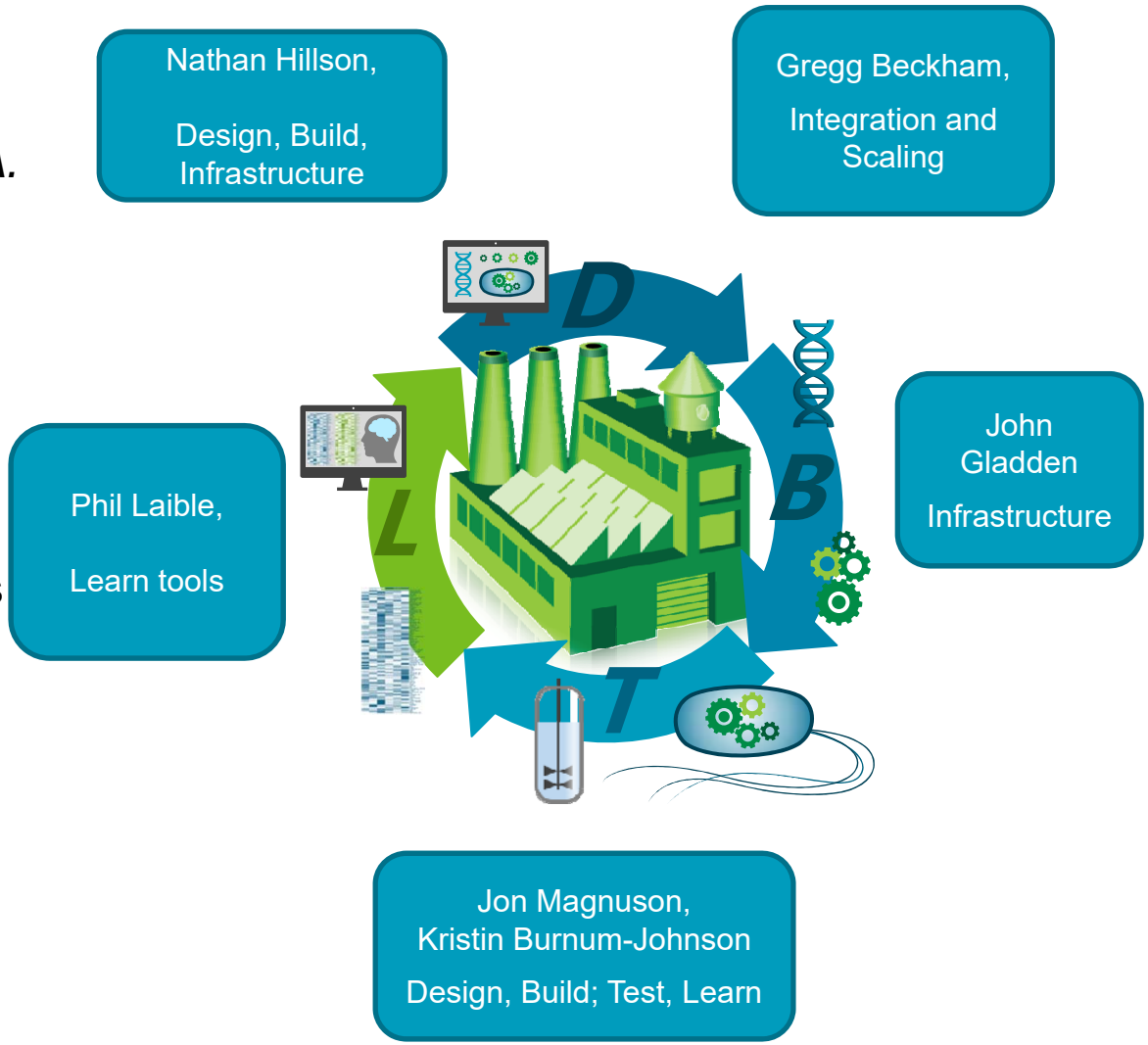
- **Task 1: Design-Build-Test-Learn (*Nathan Hillson* - lead)**
  - **Integrate design-build-test-learn cycle with process automation and sample tracking.**
- Task 2: Integrated Analysis (*Mary Biddy/Thathiana Benavides* – co-leads)
  - Evaluate proposed molecules; develop, update, and improve existing process designs and LCA.
- Task 3: Host Onboarding (*Taraka Dale*/*Adam Guss* – co-leads)
  - Evaluate possible host organisms to determine which on-boarding criteria are not yet met, and fill these gaps through tool development and data collection.
- Task 4: Process Integration and Scale-up (*Gregg Beckham*/*Todd Pray* – co-leads)
  - Standardize, produce, ship, and store hydrolysates; compare clean sugar processes with hydrolysates; **test and scale fermentation to improve titer, rate, and yield; provide integrated, bench-scale data for TEA and LCA; scale fermentation to produce data for Learn.**
- Task 5: Industry Engagement (*Babs Marrone/Chris Johnson/Phil Laible* – co-leads)
  - Identify barriers to industry adoption of synthetic biology technologies, expand number and diversity of industry partnerships, and establish a set of metrics for determining impact of project technologies on industry.
- Task 6: Management (*Blake Simmons* - lead)
  - Manage project management, develop internal and external communications, provide deliverables to BETO, and make some capital equipment purchases.

Project Management – Org Chart



Management approach

- **Virtual meetings:** monthly calls with wider *A. pseudoterreus* DB team
- **F2F meetings**: weekly local *A. pseudoterreus* DB and TL meetings, ABF annual all-hand, during year as needed
- **Updates**: monthly team updates on task lead call, monthly DBTL tracking
- **Team Leads:** experts in fields of work in *A. pseudoterreus*
- **Milestones:** DBTL cycle times, product performance metrics
- **Project interfacing:** *ad hoc* meetings with Integrated Analysis, Integration and Scaling, other BETO consortia



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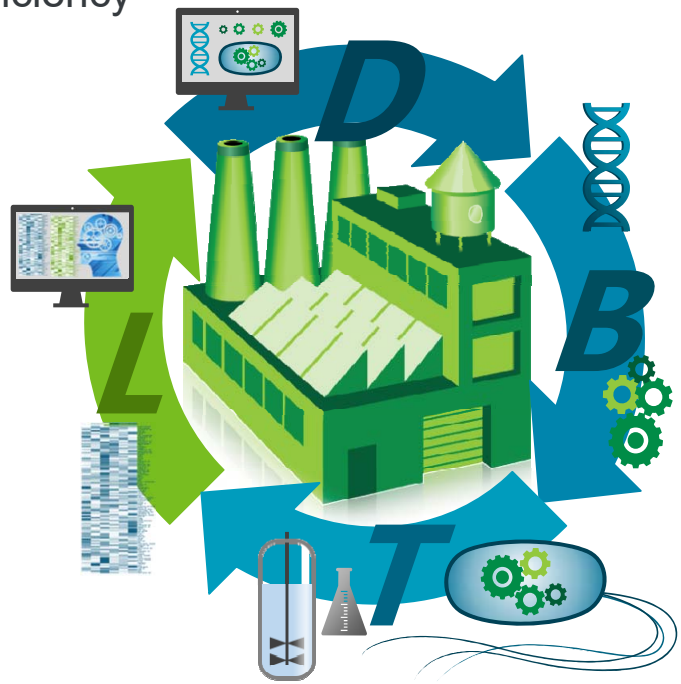
Technical approach

Critical success factors

- Demonstrable improvements in production of Targets 1 and 2 enabled by DBTL
- Meaningful DBTL cycles with output from **Learn** leading to strain improvements
- Identification and mitigation of DBTL bottlenecks; DBTL efficiency

Challenges

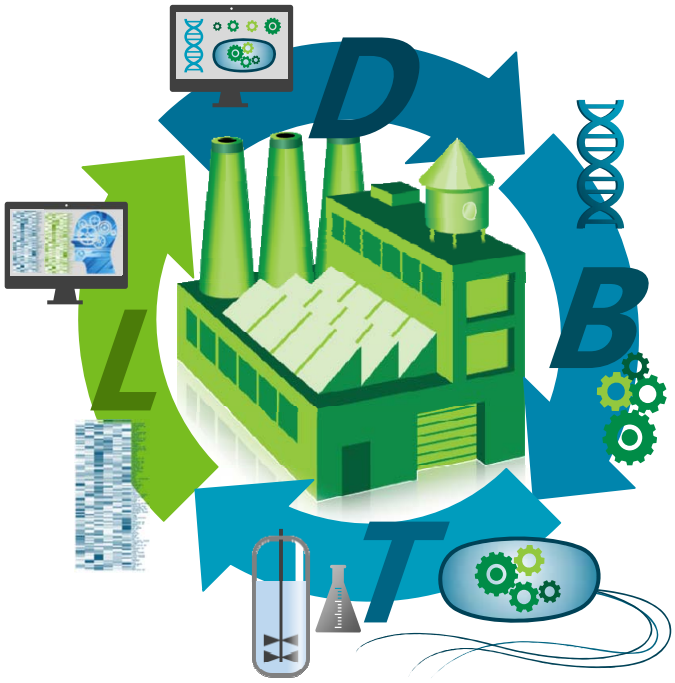
- Industrial host but lacking synthetic biology level tools, hence emphasis on developing the system in ABF
- Genetic engineering in filamentous fungi takes longer but is worth the effort for organic acid targets
- Product identification and quantification when targeting novel bioproducts
- Decreasing side-product organic acids, and catabolism of targets
- Parallel host development *and* application of Learn tools in a developing host organism: models, neural networks…
- Appetite of Learn for data vs. number of Test experiments/samples possible



Technical approach

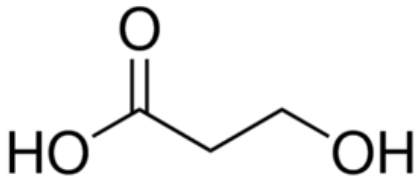
Technical approach

- Increasing metabolic carbon flux to non-native organic acid pathways—3HP
- Increasing production and export of a central metabolite—aconitic acid. Important challenges with compartmentalization and transporters.
- Use TL to identify rate and regulatory bottlenecks, side product acid carbon sinks and suggest new targets for DB
- Design Learn-friendly Test experiments and utilize the array of ABF Learn tools for target identification
- Implement both intuitive and non-intuitive gene target testing for deeper learning about the *Aspergillus* system and about our Learn tools
- A Target/Host goal is to use and improve the DBTL cycle coupled with integration/scaling to increase TRY of relevant small molecule targets by the *Aspergillus* host

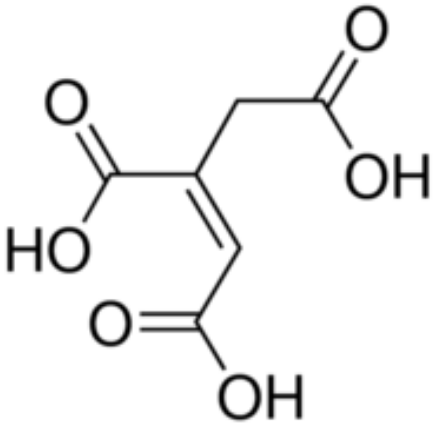


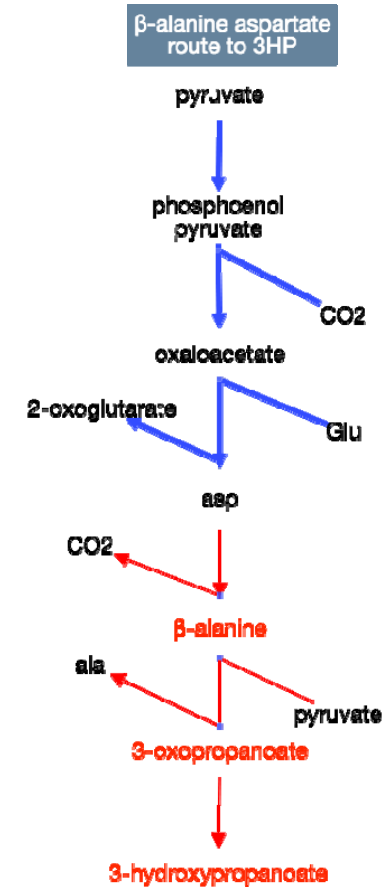
3 – Technical Accomplishments/ Progress/Results

Host: *Aspergillus pseudoterreus*



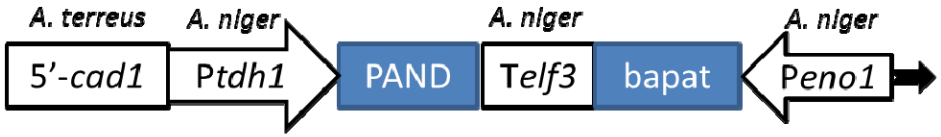
- **Target 1 (FY17): 3-hydroxypropionic acid**
- Target 2 (FY18): *cis*-aconitic acid

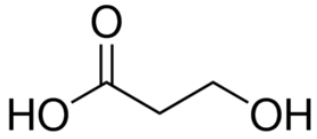


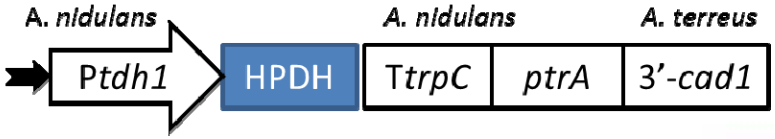


Target 1: 3-HP

Inserting a pathway in *A. pseudoterreus*

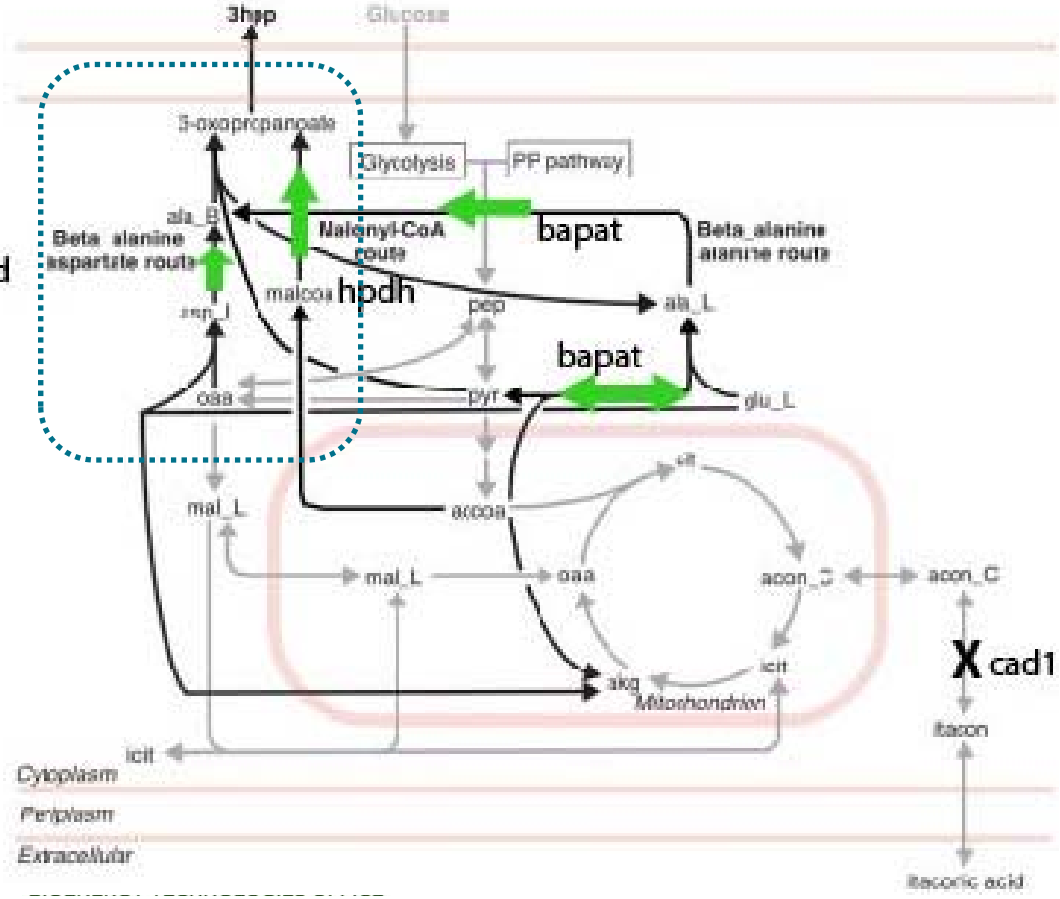






P: promoter
T: terminator

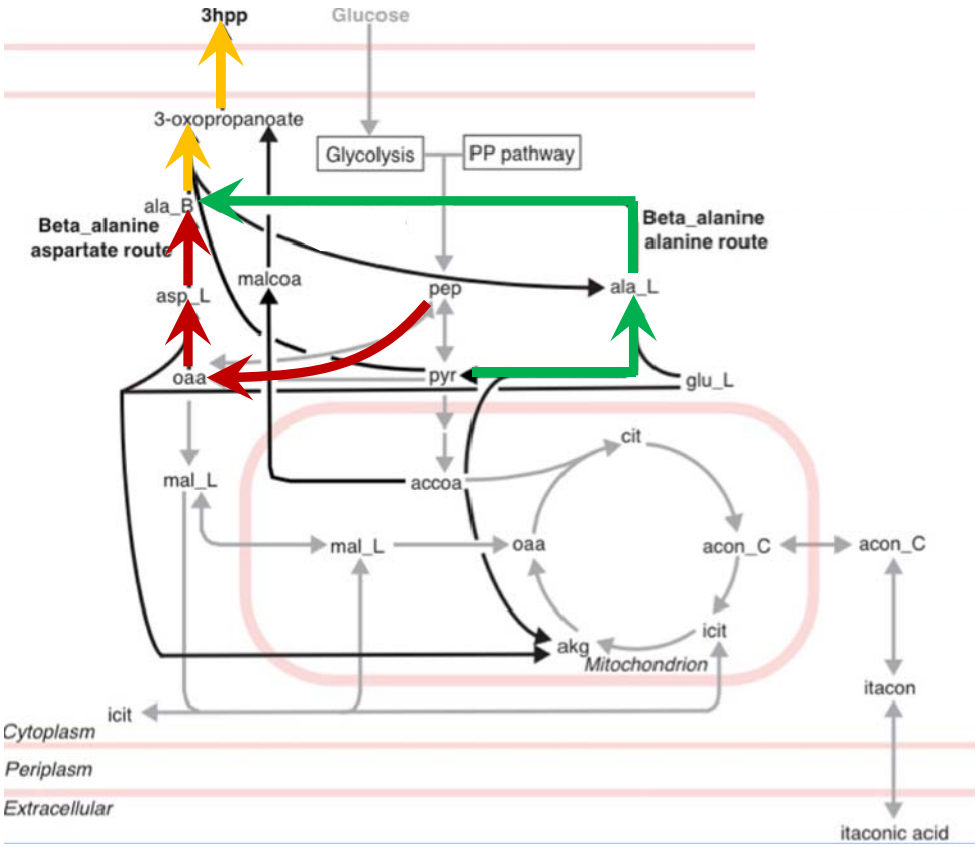
Expression cassette designed to eliminate itaconic acid production by insertion of the β-alanine-aspartate pathway construct into *cad1* gene by Homologous Recombination



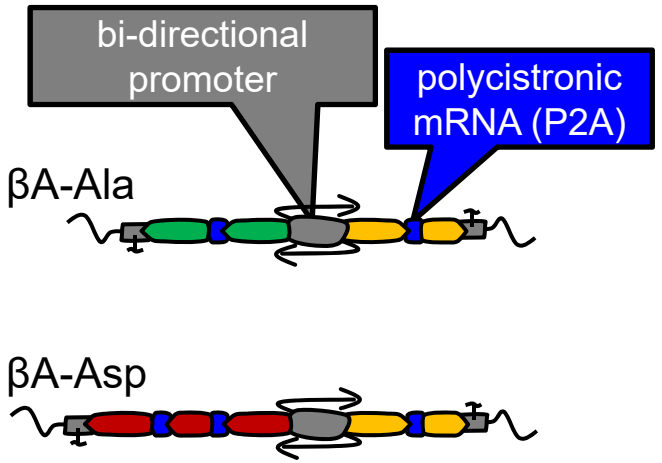
pand

1. **PAND**: aspartate decarboxylase
2. **BAPAT**: β-alanine-pyruvate aminotransferase
3. **HPDH**: 3-hydroxypropionate dehydrogenase

Target 1, 3HP: Sophisticated Designs



Design Strategy

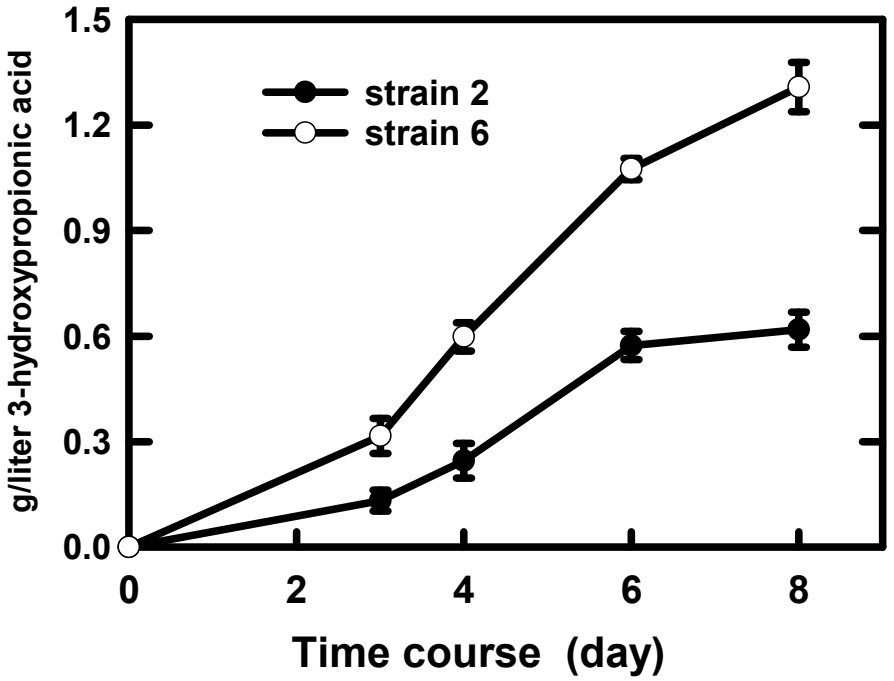


- Bi-directional promoters proven functional
- P2A allowed for reduced pathway size and complexity by expressing multiple proteins per promoter

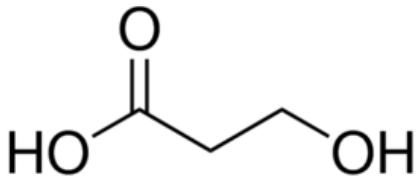
- Developing **advanced engineering tools**
- Testing **alternative pathways** to produce 3HP

Target 1, 3-HP production determined by LC

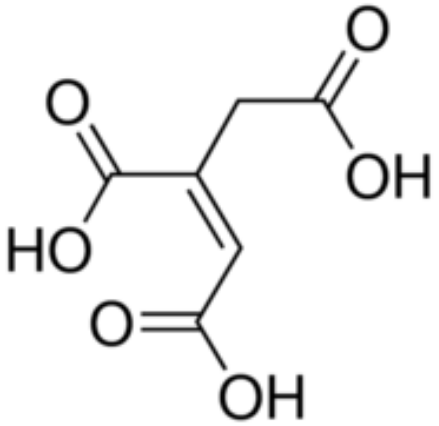
Strain 2
Strain 6



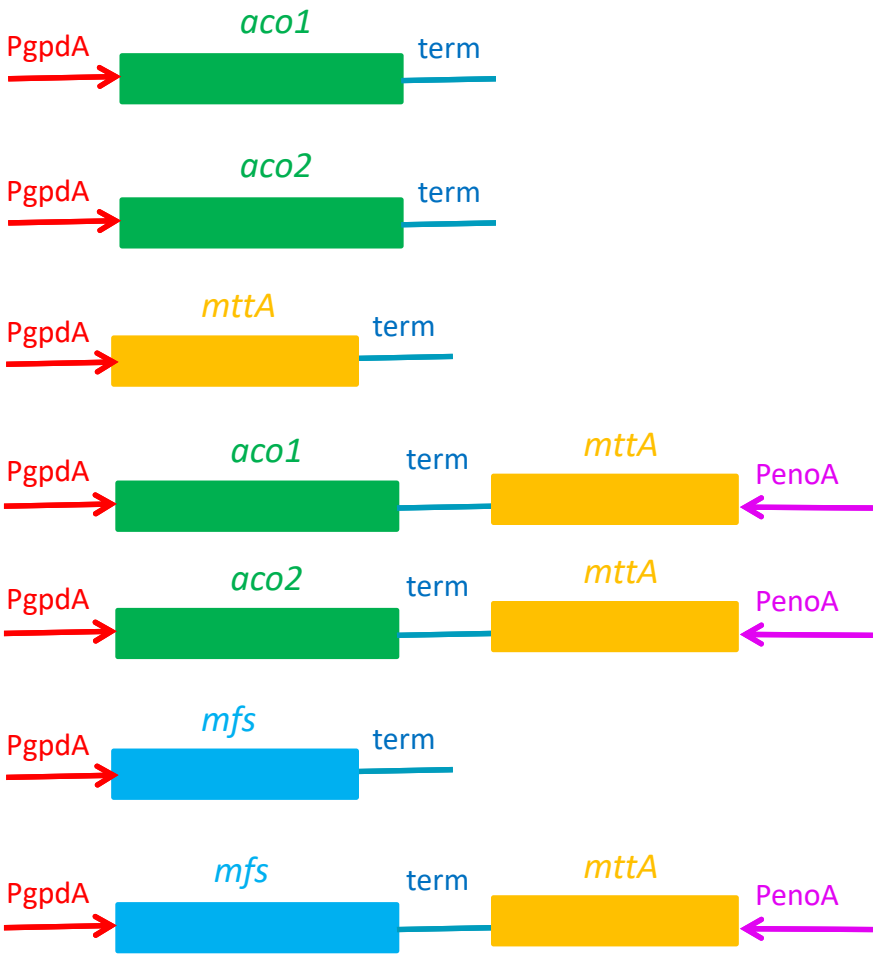
Host: *Aspergillus pseudoterreus*



- Target 1 (FY17): 3-hydroxypropionic acid
- **Target 2 (FY18): *cis*-aconitic acid**

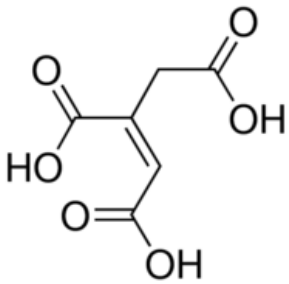


Target 2, Design/Build Strategy: Overexpression constructs targeting biosynthesis and transporter candidates



Construct components

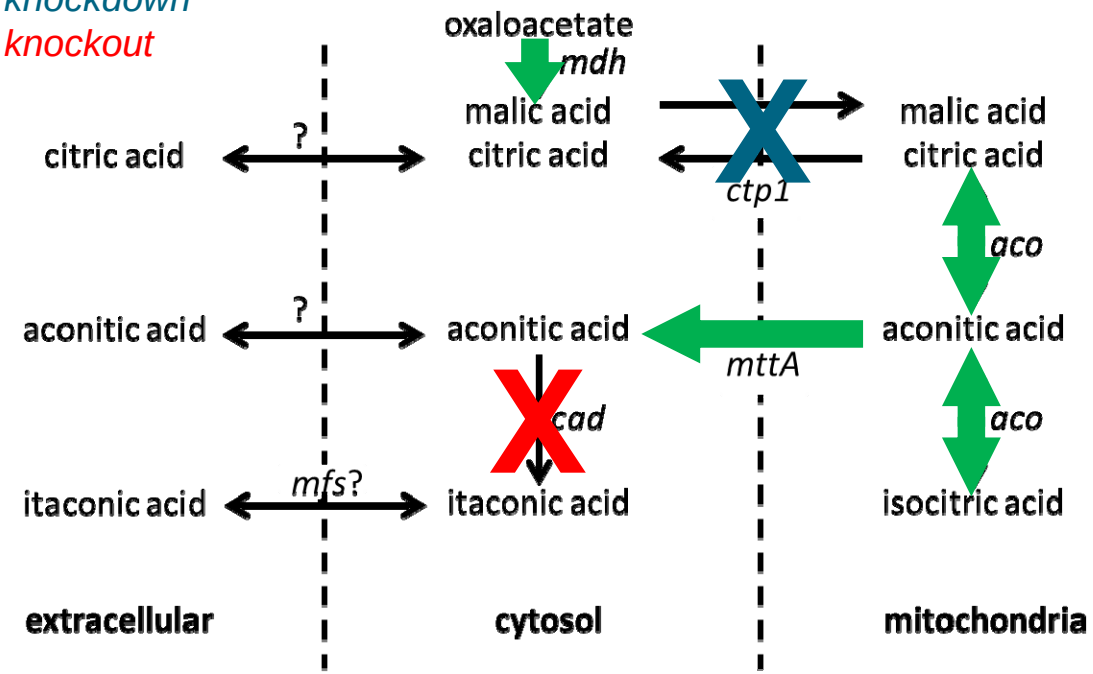
- *aco1*, *aco2*: conitase variants
- *mttA*: mitochondrial transporter
- *mfs*: plasma membrane transporter
- Strong constitutive promoters
  - PenoA: enolase
  - PgpdA: glyceraldehyde-3-P DH



Target 2: *cis*-Aconitic Acid, Complex Designs

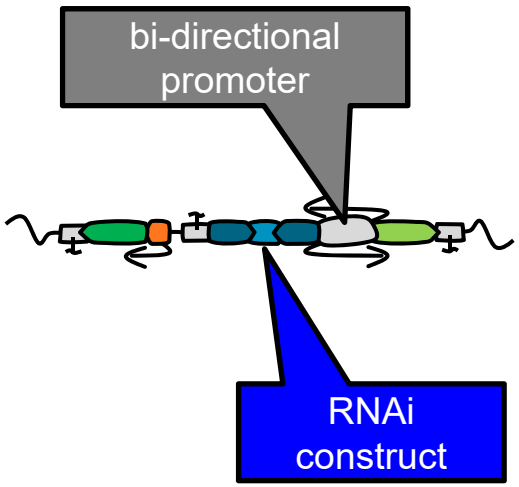
knock-up
knockdown
knockout

Pathway visualization



Design Strategy

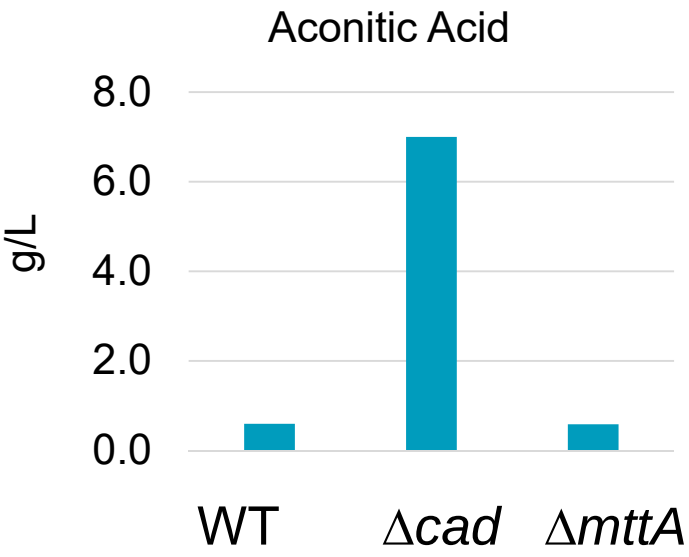
(largest)



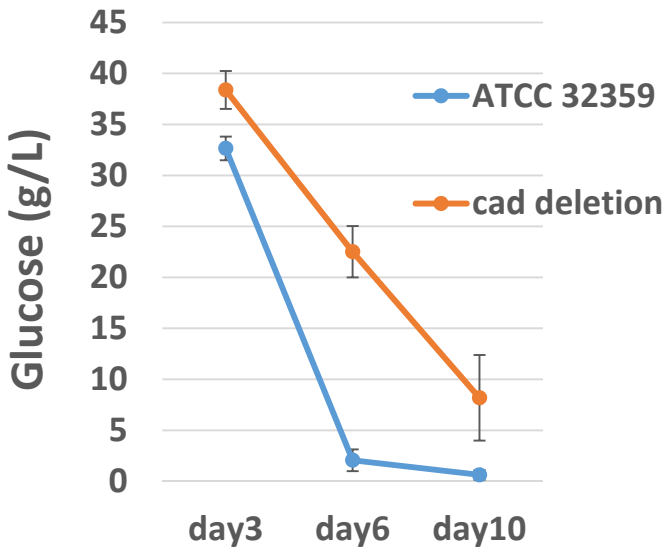
- Reuse of Bi-directional promoter!
- RNAi constructs design!

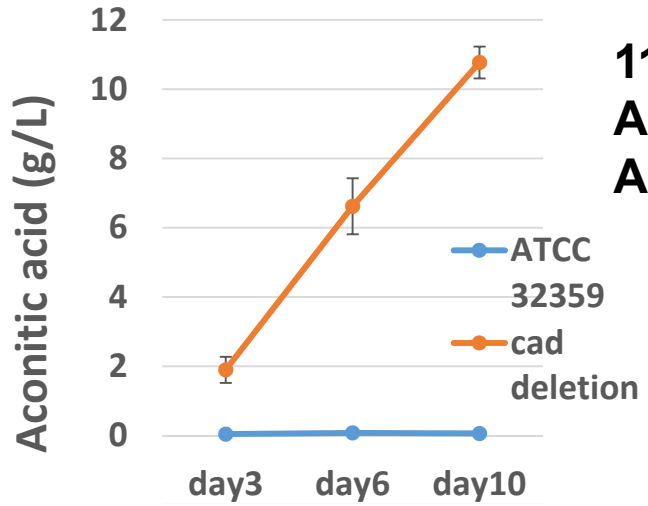
1) Delete *cad* to eliminate flux to itaconic acid—starting strain
*2) Overexpress *mttA* to isolate aconitic acid from mitochondrial aconitase (*aco*)
3) Decrease expression of citrate/malate antiporter (*ctp1*) to keep citric acid mitochondrial
*4) Overexpress *aco* to increase redistribution rate of mitochondrial organic acids
5) Overexpress *mdh* to increase *mttA* transport (may be an aconitate/malate antiporter)

Target 2: Aconitic acid production in *A. pseudoterreus*



- *mttA*: mitochondrial aconitic acid transporter is essential
- Need to identify other transporters that can boost TRY

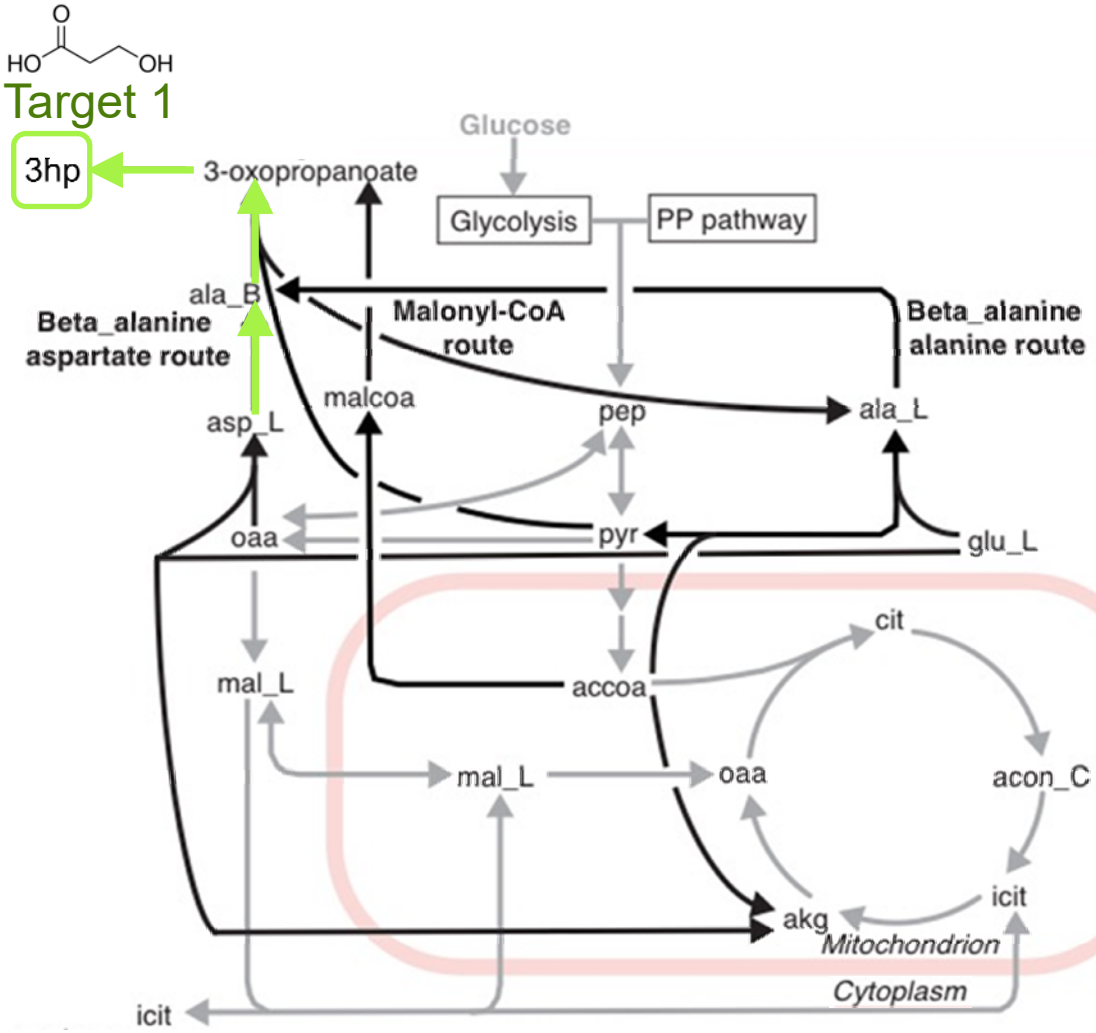




11 g/L Aconitic Acid

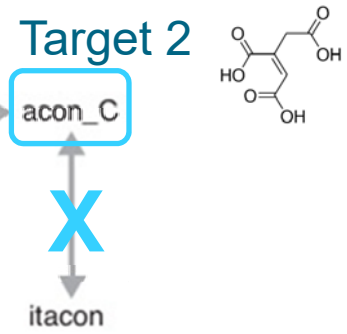
- Good baseline titer
- Room to improve yield and hence titer

TEST and LEARN
Metabolic analysis of strains for Targets 1 & 2



Strain for TL	Organic Acid
1. wild-type	itaconic
2. 3HP+	3HP
3. *cad*	aconitic
4. *cad*::3HP+	3HP
5. *cad*::3HP+(2x)	3HP

- *4 time points, quadruplicates*



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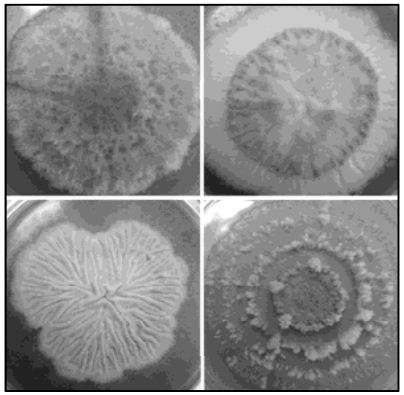
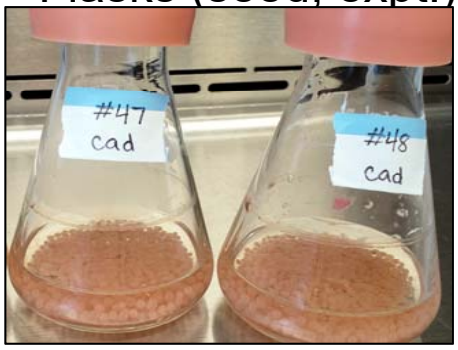
TEST: Metabolic analysis of engineered strains

- Work across scales depending on experimental requirements
  - 40-120 shake flasks for surveying conditions, **replicates of multiple time points**
  - 6x0.5L reactors for a few conditions in stirred tank reactor environment
  - 30L reactors: **real time measurement & control** of multiple parameters, **feeding** expts…

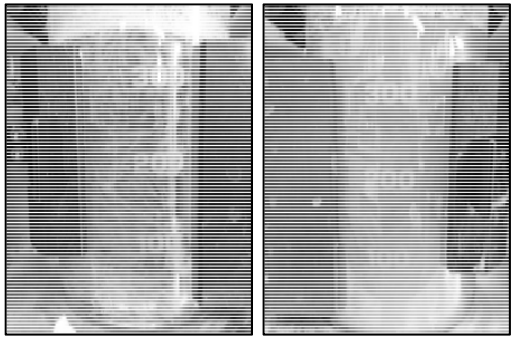
Agar plates (seed)



Flasks (seed, expt.)



0.5L Bioreactors



30L Bioreactors

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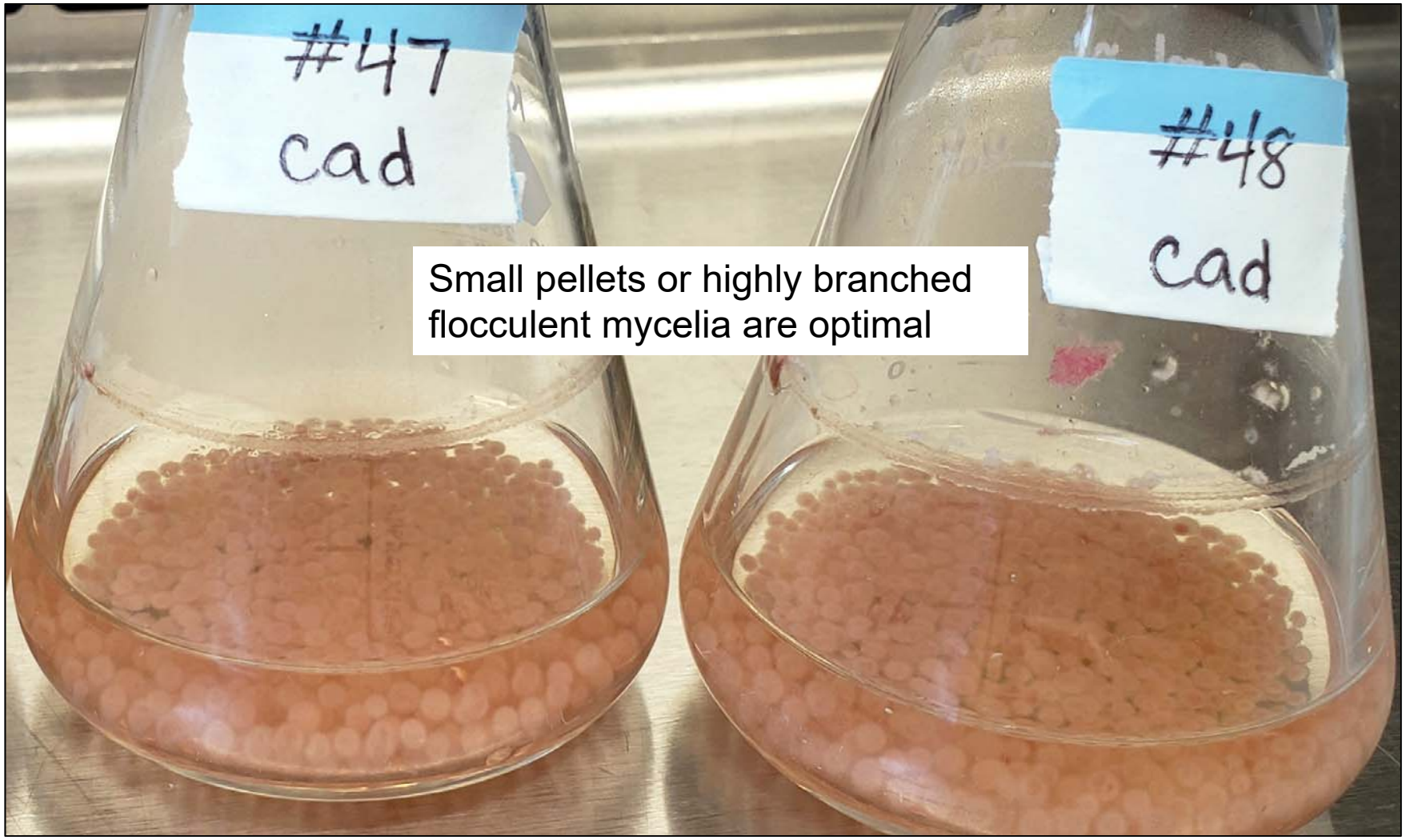
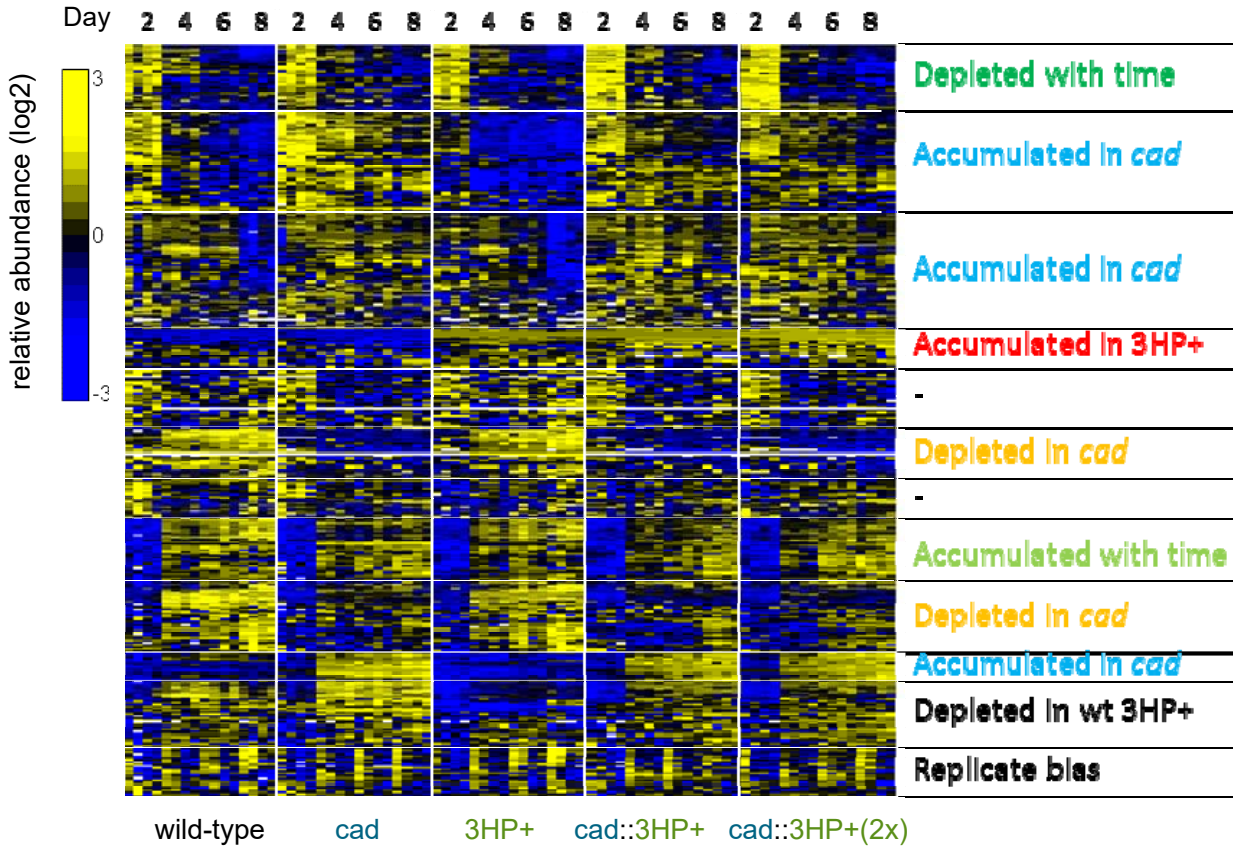
Sidebar: *A. pseudoterreus*
1-5mm Diameter Pellet Morphology



TEST: Omics data for *Aspergillus pseudoterreus* Learn

5 strains x 4 time points x 4 replicates = 80 samples

Large sets of statistically robust data needed for advanced **Learn** approaches



- **Proteomics**
- 7178 **global** proteins
- 79 **targeted** proteins

- **Metabolomics**
- 122 identified **intracellular** metabolites
- 198 unknown intracellular metabolites

- 14 **extracellular** metabolites + biomass

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LEARN: Clustering on the metabolic network

Depleted with time

Accumulated in *cad*

Accumulated in *cad*

Accumulated in 3HP+

-

Depleted in *cad*

-

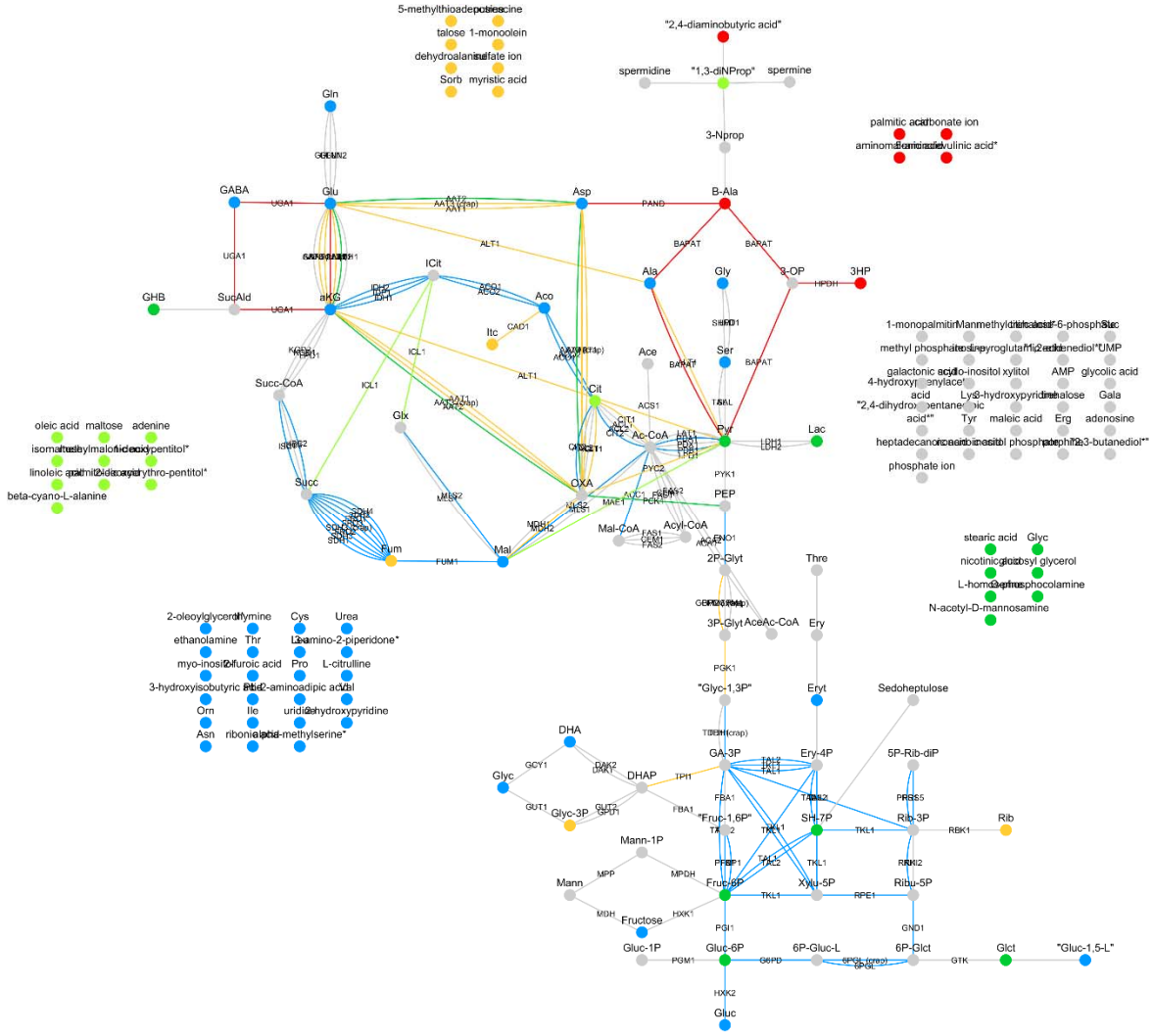
Accumulated with time

Depleted in *cad*

Accumulated in *cad*

Depleted in wt 3HP+

Replicate bias



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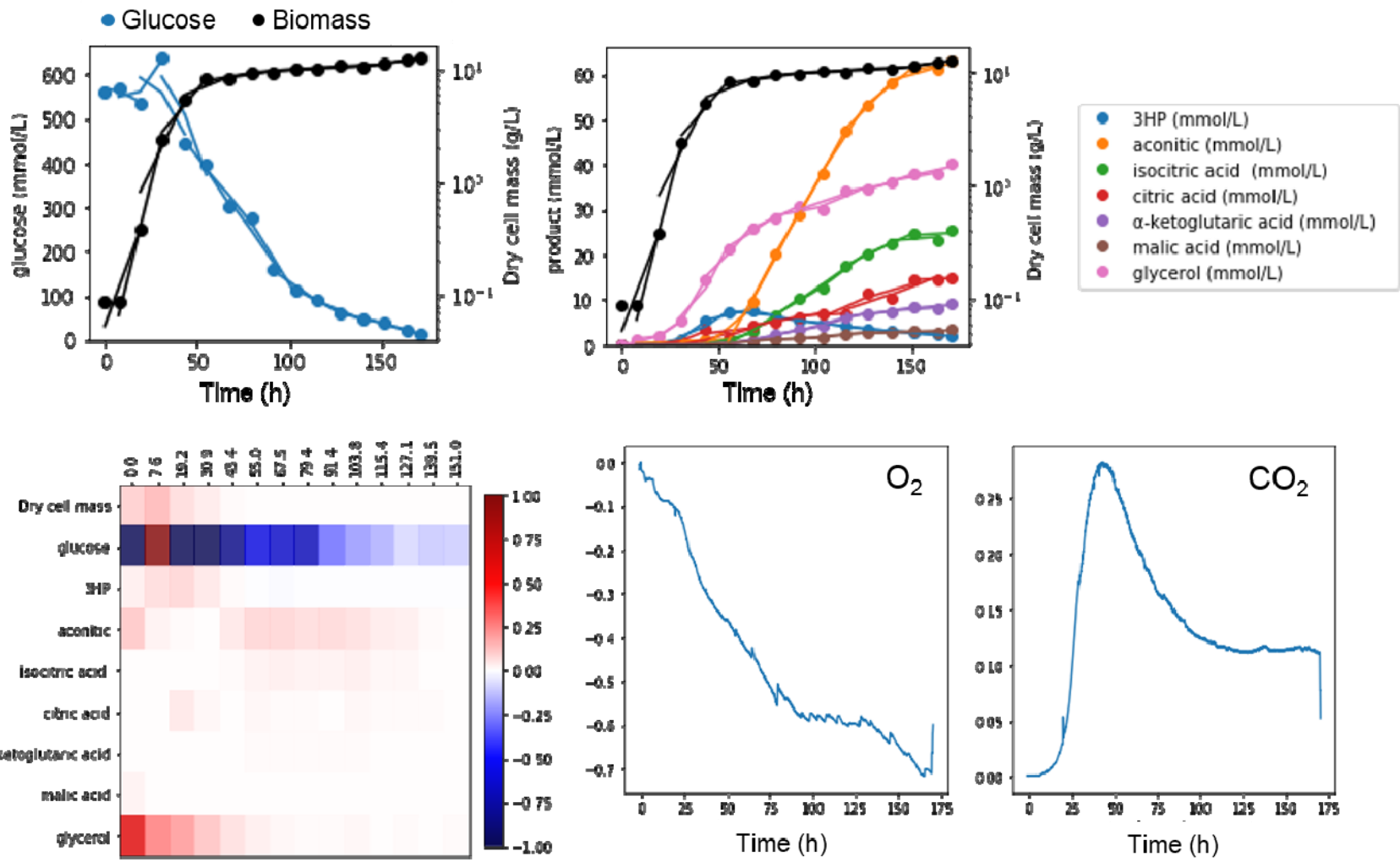
LEARN: Extracellular metabolomics for modeling dynamic fluxes during bioreactor cultivation

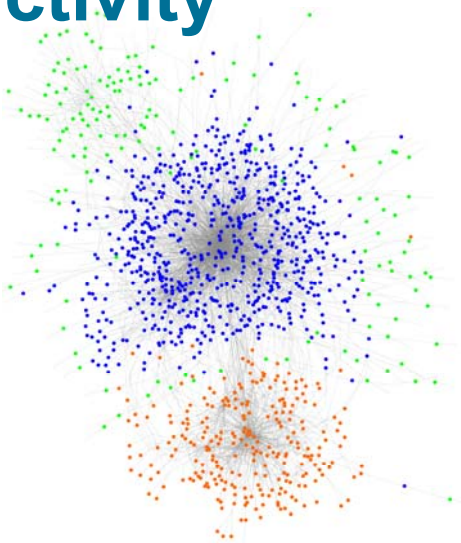


- Concentrations of key substrates/products
- Overall **carbon balance to constrain FBA**

LEARN: Flux variability analysis identifies fluxes that must change to maximize productivity

Fluxes to maximize aconitic acid (target 2)

		cad		max aconitic acid	
rxnID	Gene	min	max	min	max
R_rx10	Alcohol transporter	0.07	0.23	0	0
R_rx11	2-oxoglutarate transporter	-0.1	-0	-0	0
R_rx11	Citrate transporter	-0.1	-0	-0	0
R_rx11	Isocitrate transporter	-0.1	-0	-0	0
R_rx11	CO2 transporter	-0.6	-0.3	-0	0
R_rx11	Dicarboxylate:Pi antiporter	0.02	0.1	0	0
R_rx11	Dicarboxylate:Pi antiporter	0.02	0.1	0	0
R_rx11	Glycerol:H symporter	-0.1	-0	-0	0
R_rx12	Isocitrate transporter	-0.1	-0	-0	0
R_rx12	Cis-aconitate transporter	0.05	0.11	0.22	0.22
R_rx12	2-Oxoglutarate exchange	0.02	0.02	0	0
R_rx12	Citrate exchange	0	0	0	0
R_rx12	Isocitrate exchange	0	0.01	0	0
R_rx13	(S)-Malate exchange	0.02	0.03	0	0
R_rx13	Succinate exchange	0.02	0.02	0	0
R_rx13	Ethanol exchange	0.07	0.09	0	0
R_rx13	Glycerol exchange	0.01	0.02	0	0
R_rx14	Aconitate hydratase	0.02	0.2	0	0.01
R_rx14	CO2 exchange	0.29	0.38	0	0.03
R_rx14	Cis-aconitate transporter	-0.1	-0.1	-0.2	-0.2
R_rx14	Cis-aconitate exchange	0.05	0.07	0.22	0.22



Mitochondrial organic acid transporters as a target to control organic acid flux

Next round of genes for Target 2 DB:

- 3 mitochondrial antiporters
- 1 specific organic acid transporter in plasma membrane

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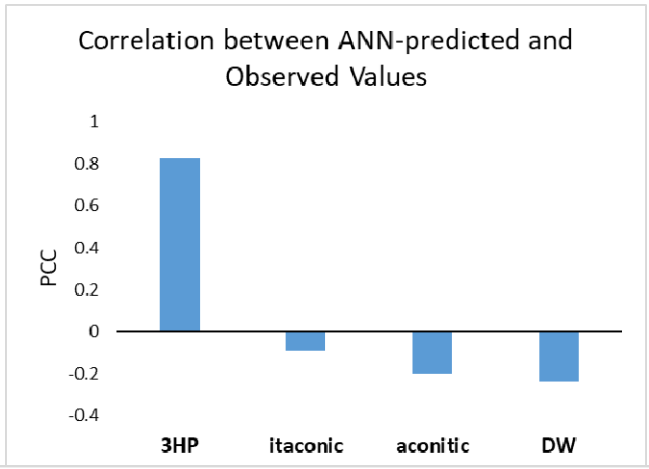
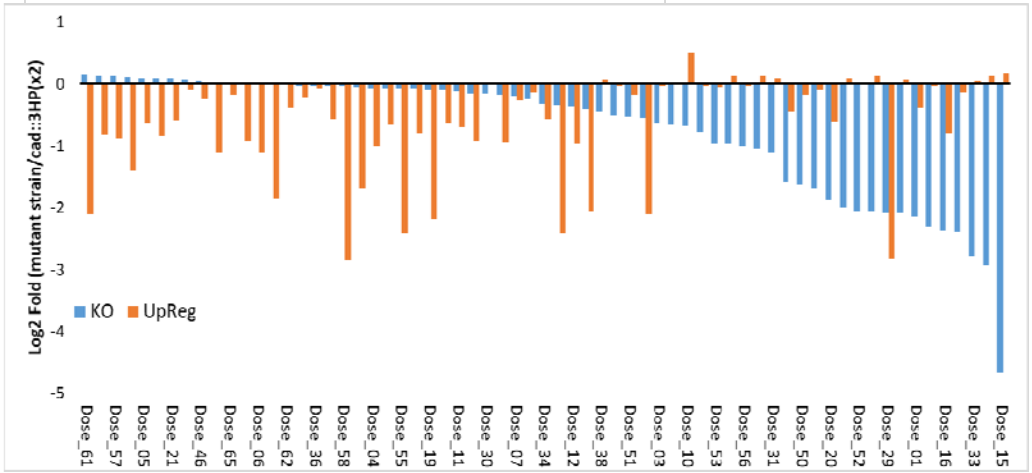
LEARN: Artificial Neural Network (ANN)





Input

- Omics data
- Culture data

Potential

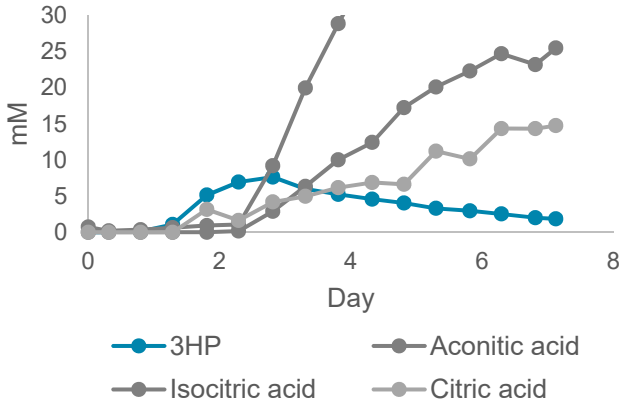
- ID regulatory network vs. genes regulated
- e.g., transcription factors, transceptors

Non-intuitive candidate genes for improving 3HP TRY:

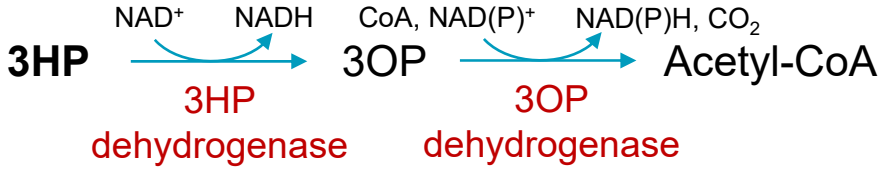
- Hypothetical gene E: over-expression
- Hypothetical gene F: deletion

Proposed pathways for 3HP degradation in *A. pseudoterreus*

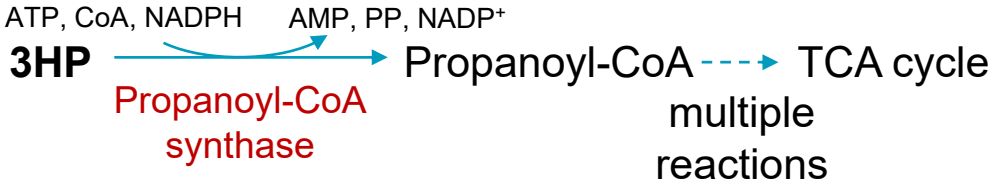
3HP is metabolized during bioreactor production with the *cad*::3HP+(2x) strain



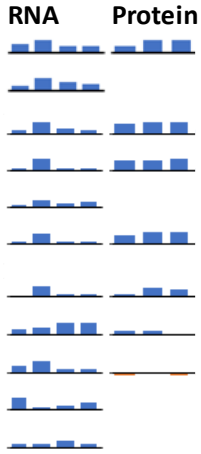
oxidative pathway



reductive pathway



Gene	BlastP Evalue
3HP dehydrogenase candidate 1	1.79E-57
3HP dehydrogenase candidate 2	1.14E-08
3OP dehydrogenase candidate 1	6.19E-62
3OP dehydrogenase candidate 2	1.54E-54
3OP dehydrogenase candidate 3	7.22E-39
3OP dehydrogenase candidate 4	2.35E-114
propanoyl-coa synthase candidate 1	3.82E-16
propanoyl-coa synthase candidate 2	1.50E-108
propanoyl-coa synthase candidate 3	2.28E-16
propanoyl-coa synthase candidate 4	2.38E-07
propanoyl-coa synthase candidate 5	6.05E-13



A. pseudoterreus genes with homology to bacterial 3HP degradation pathways were identified by blastP resulting in 119 gene candidates for the above three **unknown enzymes**.

Candidate genes significantly up-regulated in the presence of spiked 3HP (RNA measurements) or endogenously produced 3HP (protein measurements) reduced the number of candidates for the next DBTL cycle.

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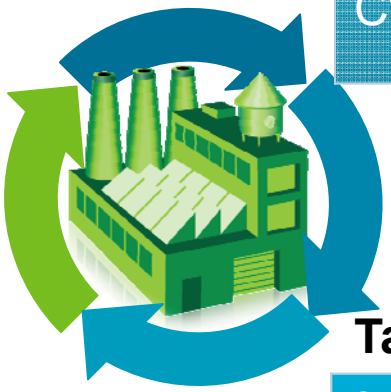
Outline of Target 1 and 2 DBTL

Target 1: 3-Hydroxypropionic Acid

Cycle Time (days)	Design	Build	Test	Learn	Outcomes
Cycle 1	89	250	279	83	Demonstrated 2 g/L production
Cycle 2	31	317	92+		Alternative 3HP pathway variants
Cycle 3	58				Intuitive and non-intuitive targets in DB based on Cycle 1 DBTL



Note: "mini-DBTL cycles" are not broken out

Target 2: Aconitic Acid

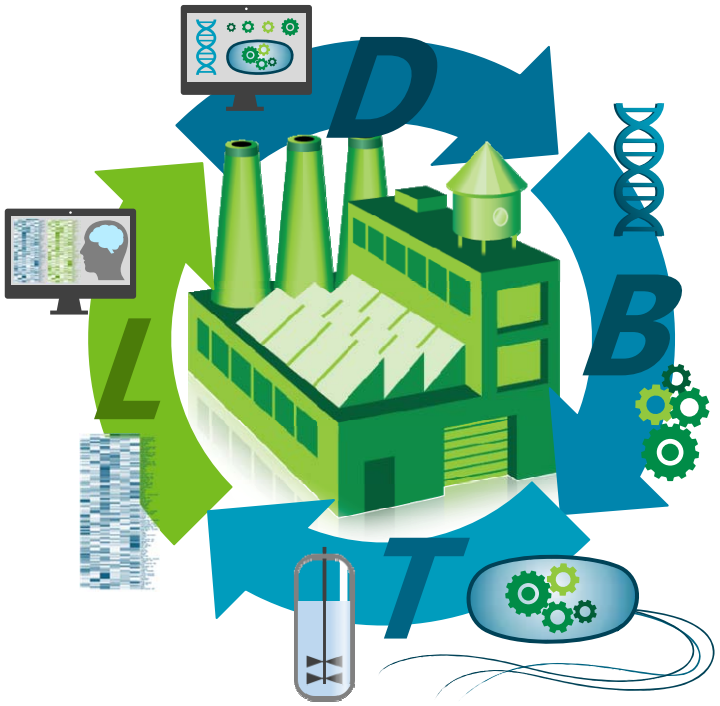
Cycle Time (days)	Design	Build	Test	Learn	Outcomes
Cycle 1	1	43	259		Demonstrated 11 g/L with base strain
Cycle 2	42	274	29+		Multiple transporter and aconitase variants in testing

4 – Relevance

Relevance

Goal: Employ targets in robust highly acid tolerant host, *A. pseudoterreus*, to demonstrate the ABF concept towards improved strain performance

- Target 1: 3-hydroxypropionic acid
- Target 2: aconitic acid
- Can be used as performance-advantaged bioproducts or direct replacements

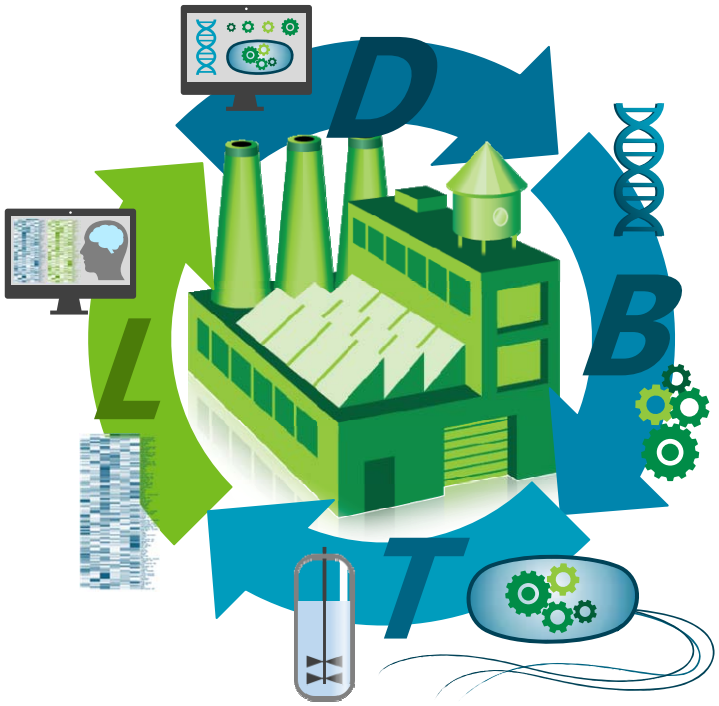


Why is this project important? What is the relevance to BETO/bioenergy goals?

- Improved strain performance enabled by DBTL
- Demonstrated ability to make non-intuitive predictions from Learn for strain engineering
- Contribute to overall BETO and bioeconomy goals of using non-standard strains to produce drop-in replacements and performance-advantaged bioproducts
- Learn can inform scaling activities and vice versa

Relevance

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



- Synthetic biology towards valuable co-products:
  - Will be critical for the viability of the US and global bioeconomy
- Learn activities directly advance “State of Technology” over solely rational strain engineering approaches
- *A. pseudoterreus* is a promising chassis for bioproduction, especially of organic acids at low pH—ease of separation, purity, low waste, low contamination risk

Technology transfer activities

- Patent applications on engineered strains, enzymes, and new pathways
- Peer-reviewed publications in the pipeline describing work in collaboration with other BETO projects and across the ABF tasks (e.g., IA, I&S)
- Industry collaboration through DFOs and BEEPs projects

5 – Future Work

5-Future Work

Goals:

- Through multiple DBTL cycles with different Target/Hosts, provide data to challenge and improve the Test and Learn tools for broad applicability--beyond the current Hosts to onboarding hosts within the ABF and through Industry projects (CRADAs)
- Continue to build the synthetic biology tool set to make *A. pseudoterreus* an agile host
- Strengthen **Learn** methods to facilitate intuitive gene discoveries and especially **non-intuitive** gene targets
- Incorporate **Scaling & Integration** capabilities to improve bioprocess parameters, check robustness and reproducibility of process across ABF facilities (NREL, LBNL)

5-Future Work

Specifics for Target 1, 3HP:

- **Test-Learn** process has identified multiple targets for the next DBTL cycle to increase TRY
- **Learn**: 2 genes from the Artificial Neural Network Learn approach, and 3 to 4 top tier genes from genome scale metabolic modeling are proceeding to next DBTL cycle
- **Scaling**: Additional 0.5 and 30L bioreactor experiments to improve process parameters and 3HP TRY: feeding DMR, lowering pH since it improves 3HP output, adjusting aeration etc.
- FY19 and beyond, Test-Learn: Comparative RNA-Seq experiment has identified candidate genes involved in undesirable 3HP catabolism = additional genes to delete to increase 3HP TRY

5-Future Work

Specifics for Target 2, aconitic acid:

- Testing of strains from current DBTL cycle:
- **Test-Learn:** (RNA-Seq, proteomics and metabolomics) of aconitic acid strains with transporter mutant strains vs. base strain, to identify aconitic transporter candidates in mitochondria and plasma membrane
- Learn: full omics experiments to feed Artificial Neural Network and Kinetic Modeling approaches
- Beyond FY19: Next cycle of Design-Build with non-intuitive gene candidates from ANN and metabolic modeling analysis of these Test results

Summary

- **Overview**
  - Utilizing industrially relevant acid-tolerant host organism for ease of production of commodity organic acid targets
  - Improved genetic engineering tools (DB) and analytical/computational (TL) methods for more rapid optimization of *Aspergillus* for various target molecules
- **Approach**
  - Integration of strengths of ABF partners for advanced DB tool development and Learning
  - Strong collaborative ABF team accelerates DBTL for each T/H
- **Technical Accomplishments**
  - 2-12 g/L titers of two organic acids in *Aspergillus*
  - Multiple models and Learn approaches developed and applied
- **Relevance**
  - Industrial fungus with increasingly well developed DBTL tool set
  - Low pH for organic acid separation and purification with little waste generation
- **Future Directions**
  - Additional targets identified by Learn to improve TRY
  - Scaling to optimize bioprocess and test for robustness
  - Advanced Learn tools will only improve with more data from multiple DBTL cycles

ABF Team Acknowledgements

- Scott Baker
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- Robby Robinson
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- Swarnendu Tripathi
- Bobbie-Jo Webb-Robertson
- Jeremy Zucker

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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
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- 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
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- 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
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- 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.