Agile BioFoundry

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

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Pseudomonas putida with C6 diacids and branched-chain PHAs

Gregg Beckham, Taraka Dale, John Gladden, Adam Guss, Nathan Hillson, Chris Johnson, Phil Laible, Jon Magnuson

BETO Peer Review 2019

Technology Session Review Area: Agile BioFoundry

March 7, 2019

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.

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 *Pseudomonas putida* KT2440
- Target 1: C6 diacids – muconic, ß–ketoadipic, adipic acids
- Target 2: Branched-chain PHAs

Outcome:

- Increased strain performance to novel targets via DBTL
- Use this system to demonstrable improvements to DBTL cycle times
- Further development of a robust industrially relevant bacterial 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

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	$700k	$2.5 MM	$3.5 MM	$2.8 MM
Partners: LBNL (2%); NREL (38%); PNNL (10%); SNL (11%); LANL (19%); ORNL (16%); ANL (4%); INL (0%)				

Barriers

Ct-L. Decreasing Development Time for Industrially Relevant Microorganisms

- Developing an industrially-relevant host microbe, *P. putida*, via the DBTL concept

Ct-D. Advanced Bioprocess Development

- Increasing TRY of novel bioproducts via DBTL

Objective:

Improve critical performance metrics for T-H pairs in *P. putida* 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 at the inception of the Agile BioFoundry

- *P. putida*-adipate(s) were first T-H from the ABF pilot project, shovel-ready
- Achieved Go decision in ABF pilot with muconate, ß-ketoadipate

Context: *P. putida* offers a robust host for producing shikimate-derived compounds

- Easy to engineer, aromatic-catabolic microbe, robust growth on glucose
- Leverage BETO investment in lignin
- Cannot natively utilize pentoses

Project goals:

- Engineer KT2440 to consume hydrolysate
- Employ DBTL and advanced tools for C6 diacids, branched-chain PHAs
- Main initial target is muconate productivity (shown to be a key cost driver)
- Provide products to ChemCatBio, Performance-Advantaged Bioproducts

Project overview: Why *P. putida*?

Pseudomonas putida

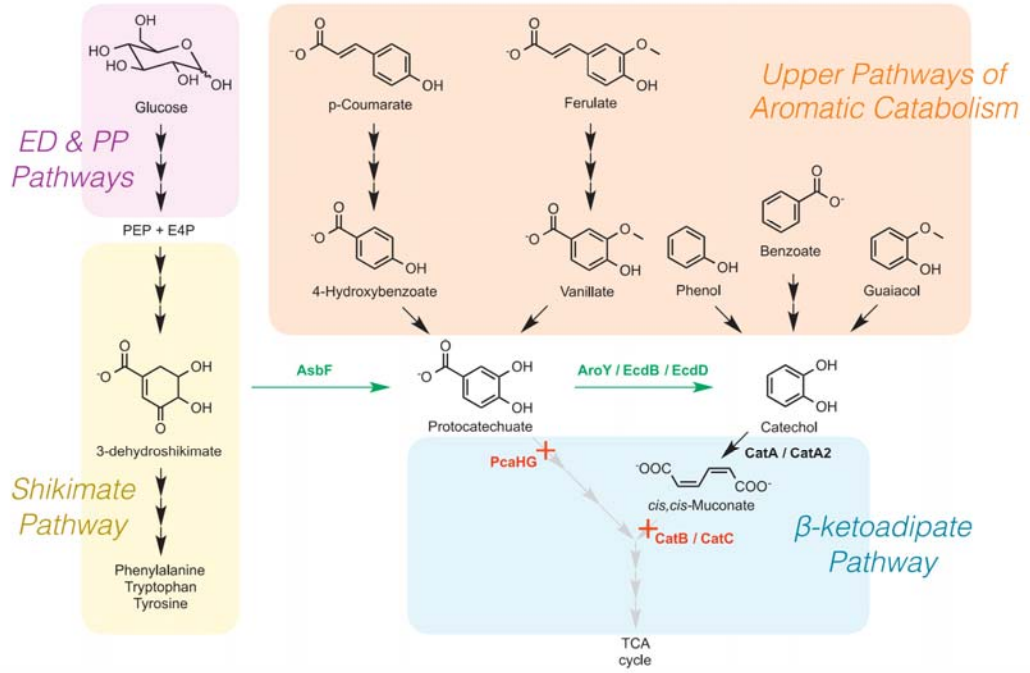
- Soil bacterium
- Gram-negative aerobe
- Fast growing
- Stress tolerant
- Metabolically versatile
- Genetically tractable

Project overview: Why these products?

In *P. putida:*

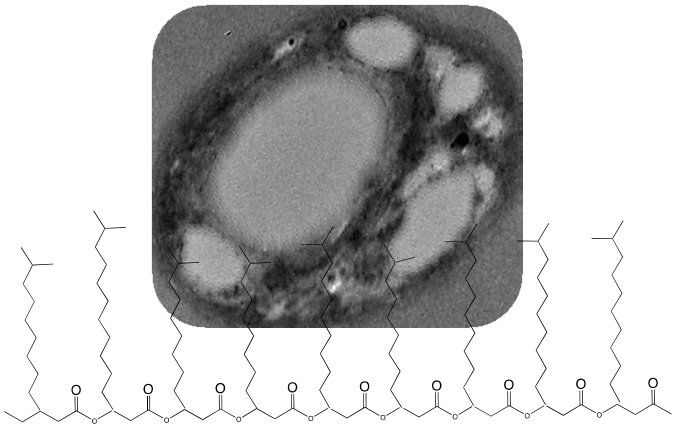
Cis,cis-muconic acid

- Natural intermediate in the breakdown of lignin monomers
- Readily accessed from the native shikimate pathway



Branched-chain polyhydroxyalkanoates

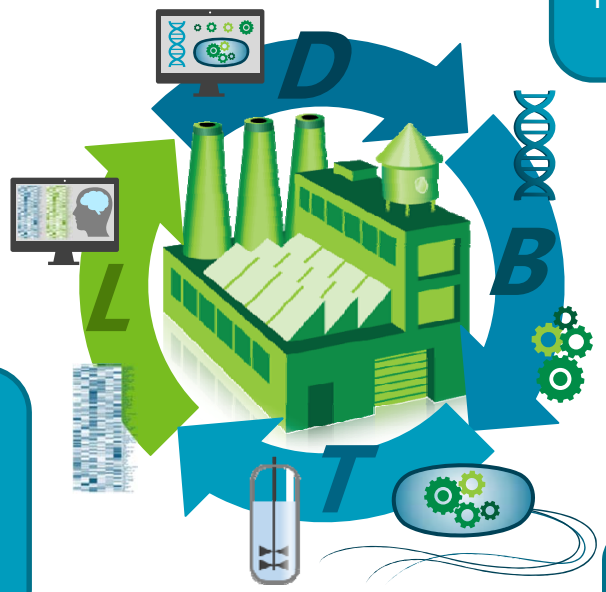
- *P. putida* naturally accumulates PHAs
- *Pseudomonas oleovorans* can make BCPHAs from fatty acid feedstock, suggesting feasibility



2 – Approach

Management approach

- **Virtual meetings:** weekly calls with *P. putida* team
- **F2F 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 *P. putida*
- **Milestones:** DBTL cycle times, product performance metrics
- **Project interfacing:** *ad hoc* meetings with IA, I&S, other BETO consortia
- **Software**: Experimental Data Depot, DIVA, ART, etc.



Gregg Beckham, Chris Johnson

Lead, DBTL tools, applications

Adam Guss

DBT applications, hydrolysate utilization

Nathan Hillson, Hector Garcia-Martin

Build, Learn tools

Taraka Dale

In vivo biosensors, DBT tools, applications

Phil Laible

In vitro biosensors, Learn tools, applications

John Gladden

DBT applications

Jon Magnuson, Kristin Burnum-Johnson

-omics for Test

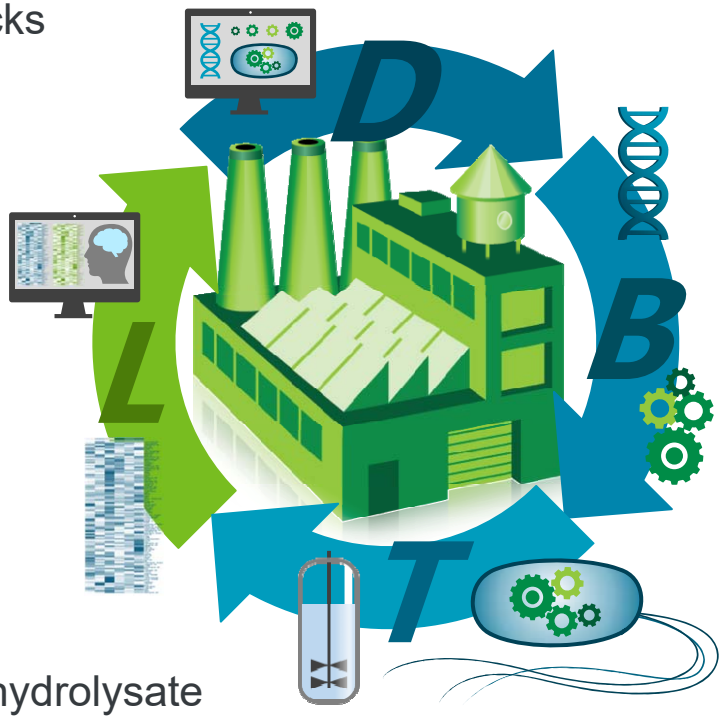
Technical approach

Critical success factors

- Demonstrable improvements to 2 targets enabled by DBTL
- Meaningful DBTL cycles with output from Learn leading to strain improvements
- Identification and mitigation of key DTBL bottlenecks

Challenges

- Deploying Learn tools in development in parallel with Learn-friendly Test experiments
- Product quantification and identification when targeting novel bioproducts
- Overcoming metabolic regulation of glucose consumption in *P. putida* KT2440



Technical approach

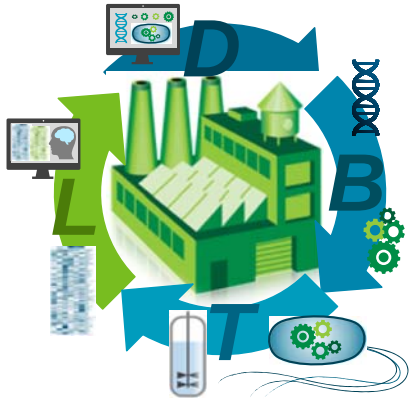
- Expand sugar utilization in *P. putida* for DMR-EH hydrolysate
- Use DBTL to identify rate and regulatory bottlenecks, off-target carbon sinks
- Employ advanced tools (e.g., biosensors) to increase DBTL strain generation efficiency
- On-board new Learn algorithms and co-design Learn-friendly Test experiments

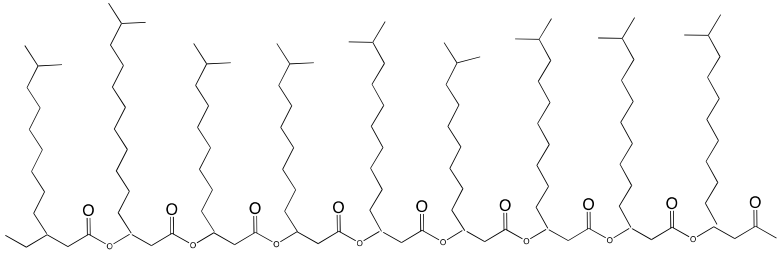
3 – Technical Accomplishments/ Progress/Results

Outline of Technical Accomplishments

DBTL for Target 1: C6 Diacids

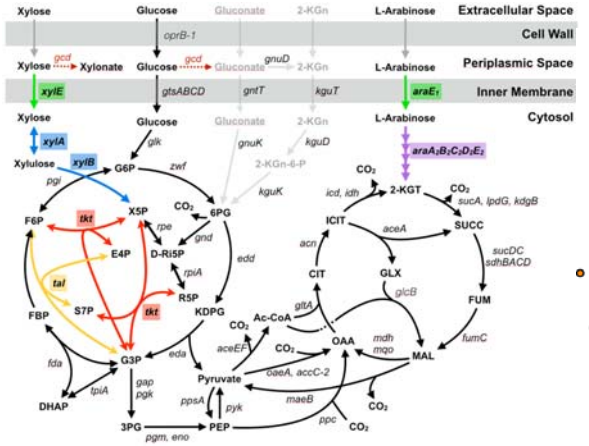
- Baselining muconic acid production
- Improving rate of muconate production
- Successful Learn cycles for strain improvements



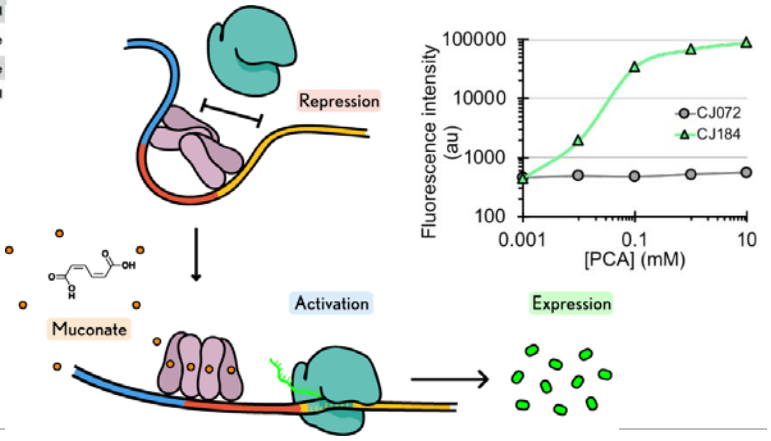


DBTL for Target 2: BCPHAs

DBTL for sugar utilization



New tools for *P. putida*



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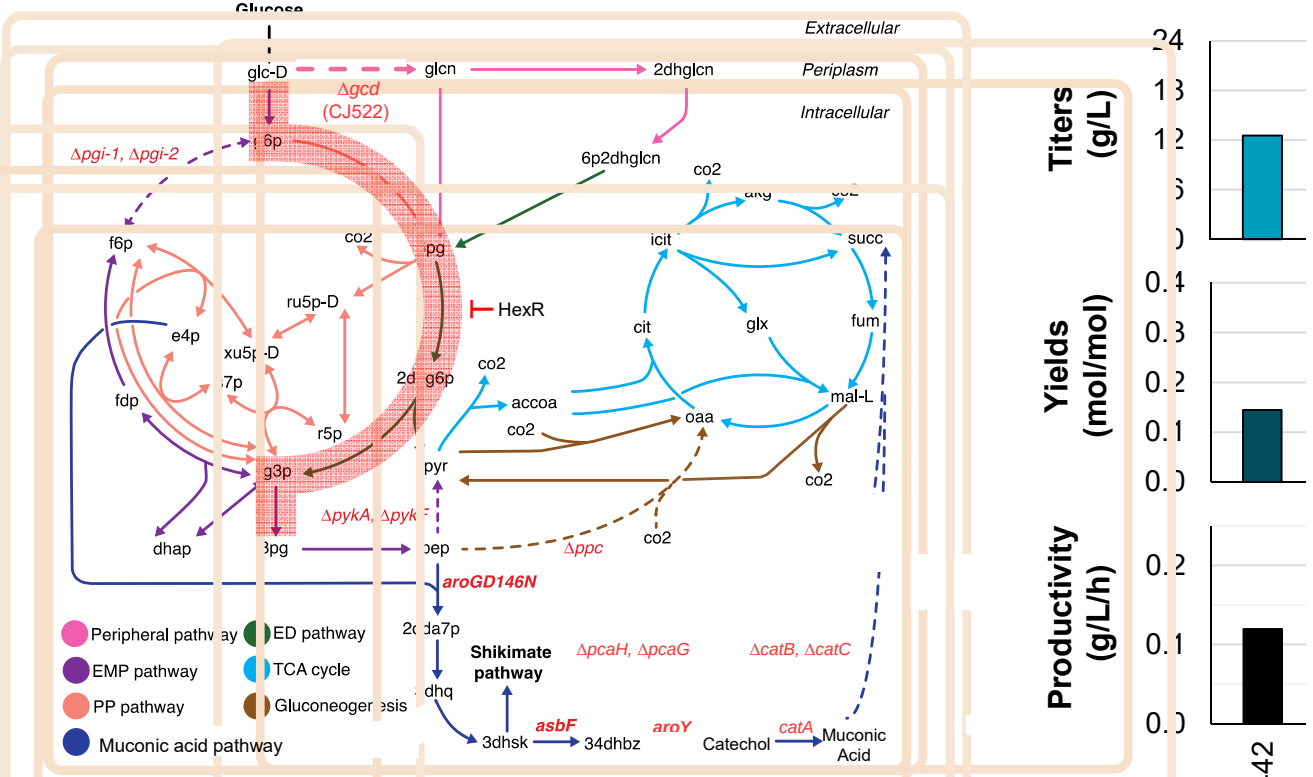
Baseline strain for muconic acid production



Fed-batch

Batch:
25 g/L glucose

Feeding:
500 g/L glucose

- Baseline strains emerged from pilot ABF project that differ in off-target carbon sink (2-ketogluconate) and muconate rate
- TEA predicted that rate should be the highest priority DBTL target
- **Outcome:** Platform strains that achieve high muconate yield but low rates

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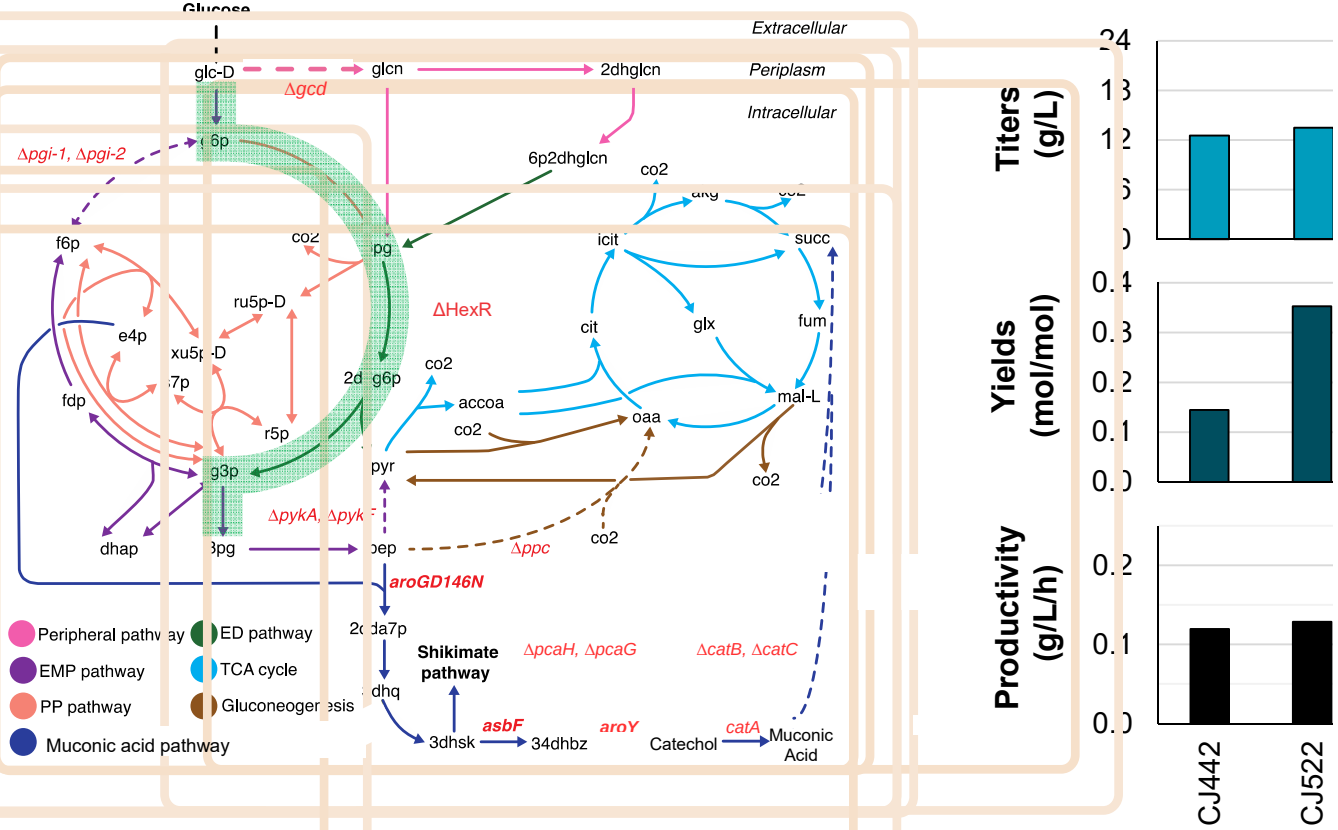
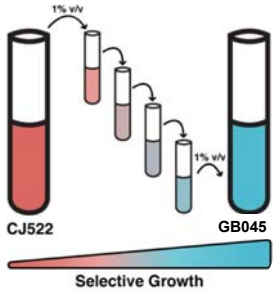
DBTL cycle to improve muconate rate



- Evolution performed on strains to improve muconate rate
- Several improved strains with changes in glucose regulation
- **Outcome:** Improved strain for muconate production, further rate increases needed



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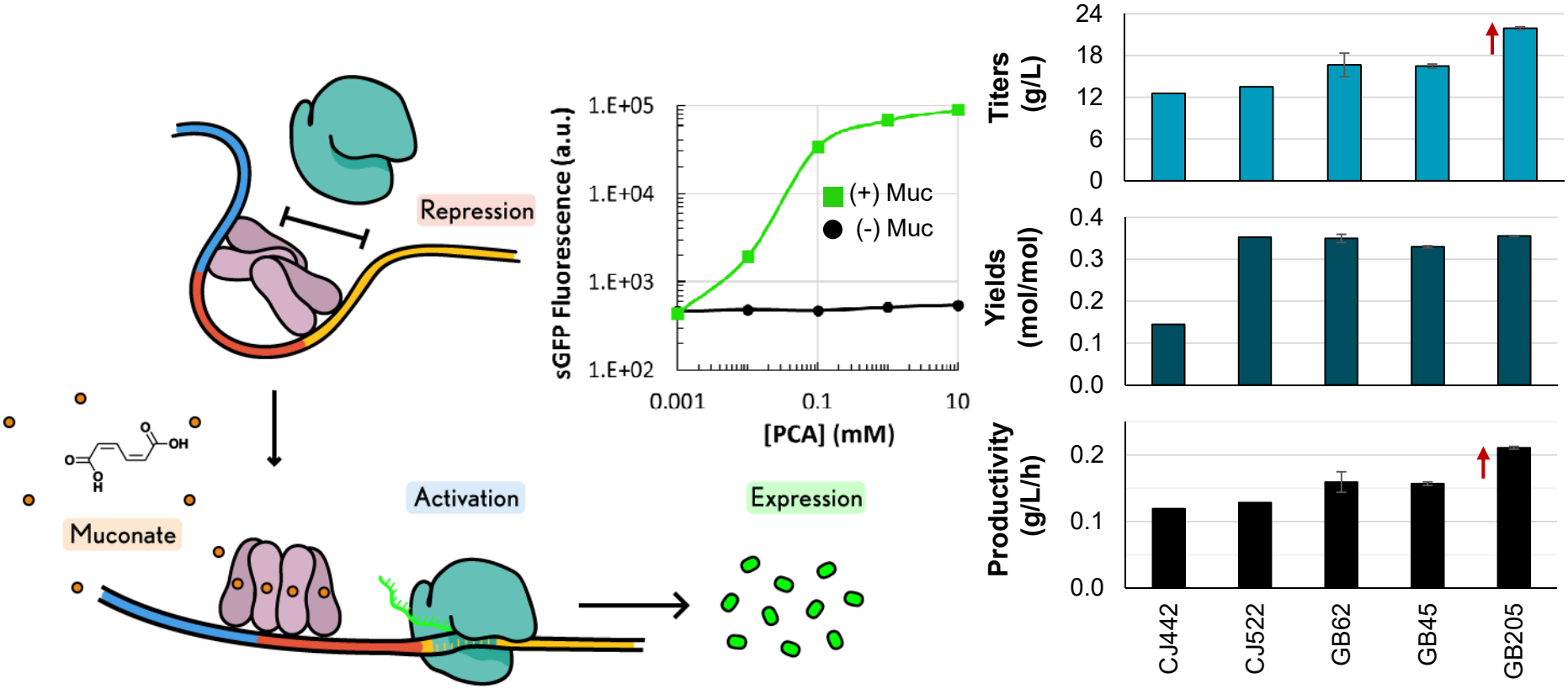
DBTL cycle to improve muconate rate



- Developed a muconate-responsive biosensor to isolate cells with improved muconate production.
- **Outcome:** Biosensor selection on muconate isolated a strain GB205 with improved productivity even beyond previous evolved isolate GB045

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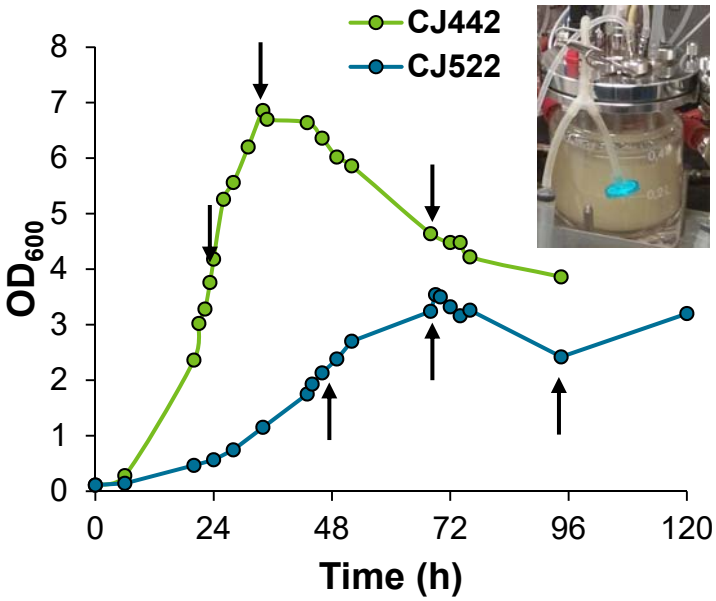
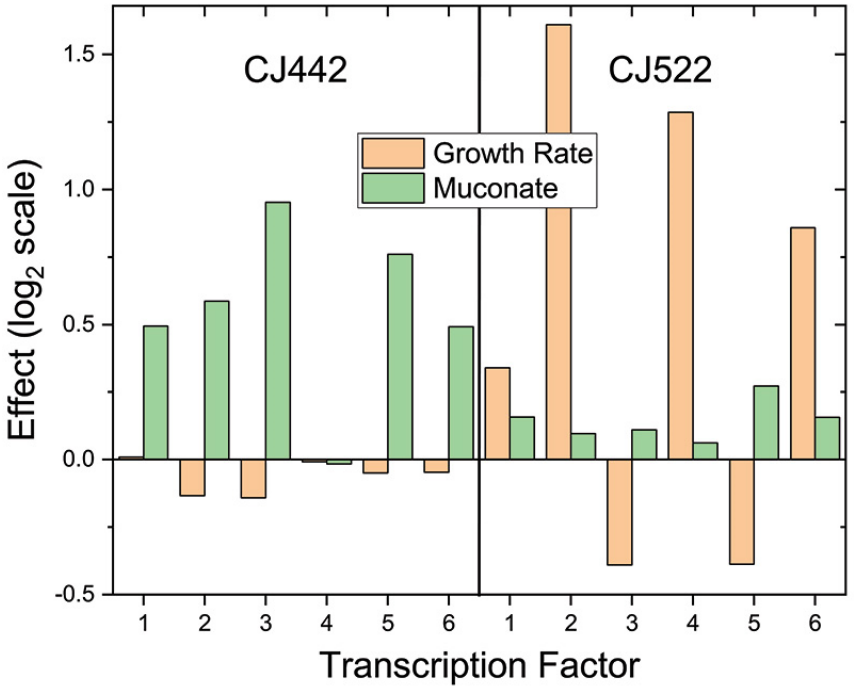
Omics-driven Test-Learn to further improve rate

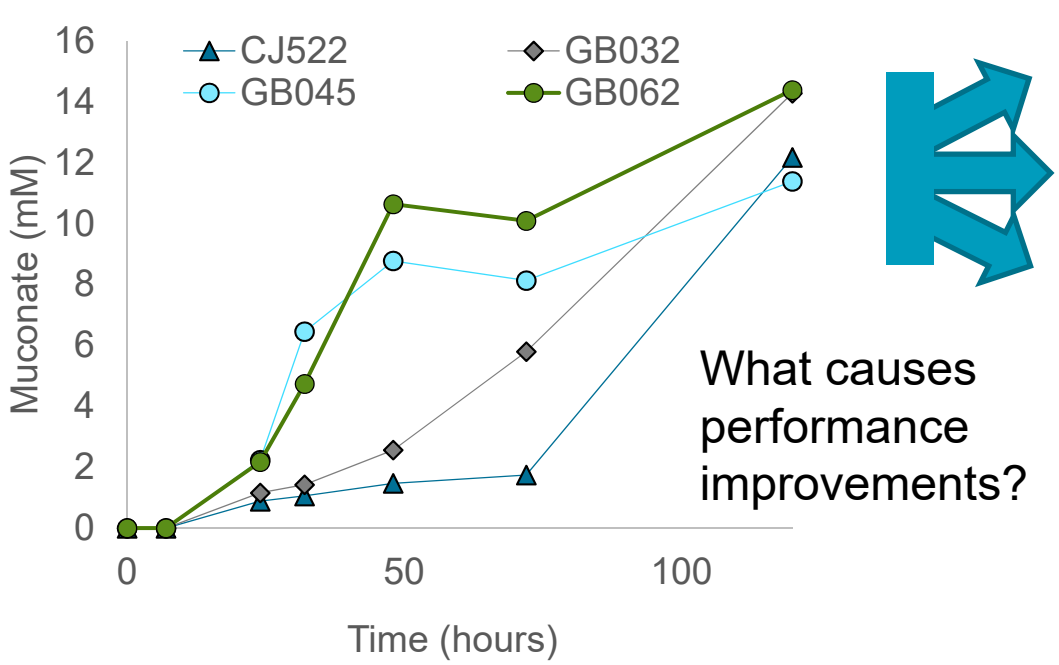


Multi-omics at different growth phases:
exponential, early, and late-stationary

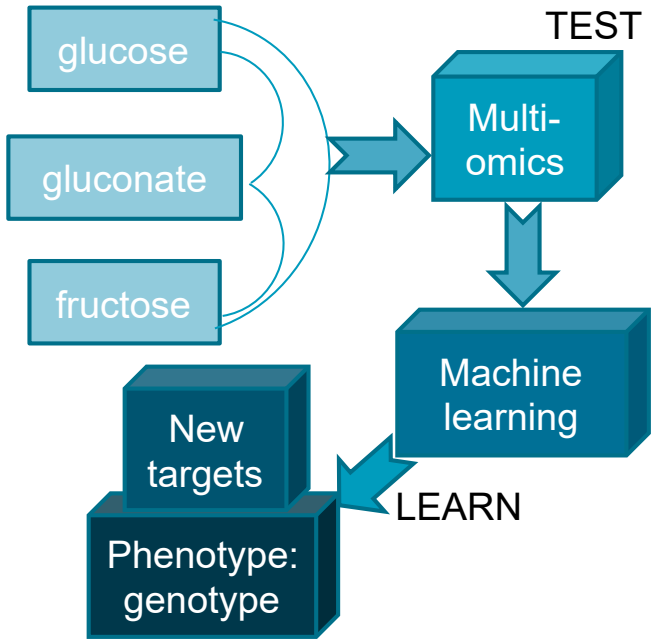


- Conducted a parallel, multi-omics investigation of CJ442 and CJ522
- **Outcome:** Predicted non-intuitive TFs to improve muconate rate, several show improved muconate productivity
- **Lesson learned:** Test and Learn experiments must be closely coordinated

New DBTL cycle with Learn-friendly Test



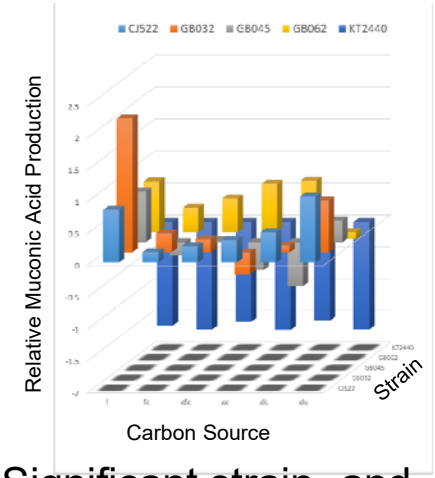
What causes performance improvements?



- Experiment designed closely with Learn team to ensure machine learning can effectively identify novel engineering targets
- **Outcome:** Large experiment completed, omics data collected. KT2440 and 4 engineered strains were tested on 6 carbon source combinations
- *Ongoing :* assay targets identified by machine learning

Sugar Utilization in *P. putida*: Initial Learn

1. Relative Production of Muconic Acid



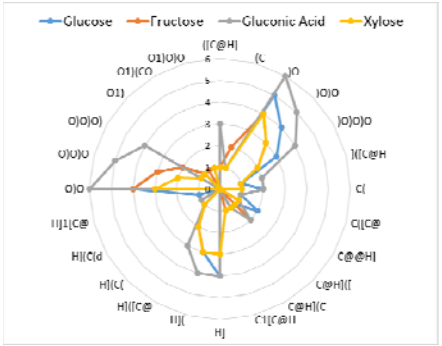
Significant strain- and media-specific effects

2. Significantly Different Omics Features

	Strain	Media	Interaction
Int Metabolome	85	54	59
Ext Metabolome	51	81	56
Proteome	79	55	45
Transcriptome	90	74	78

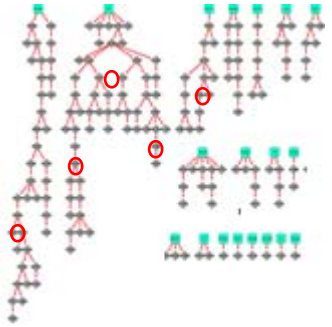
Significant impact of carbon source on all omics datatypes

3. Carbon Source Structural Attributes



Carbon source defined as vector of chemo-informatic attributes

4. Belief Networks link carbon sources to TFs



Attributes have causal effects on regulatory sub-networks

- Computational approaches that lead to specific actionable targets for strain improvement
- **Outcome:** 'Learn Enabled' experimental design maximizes application of AI/ML methods
- *Ongoing:* Metabolomics observations being validated; modeling strategies being solidified

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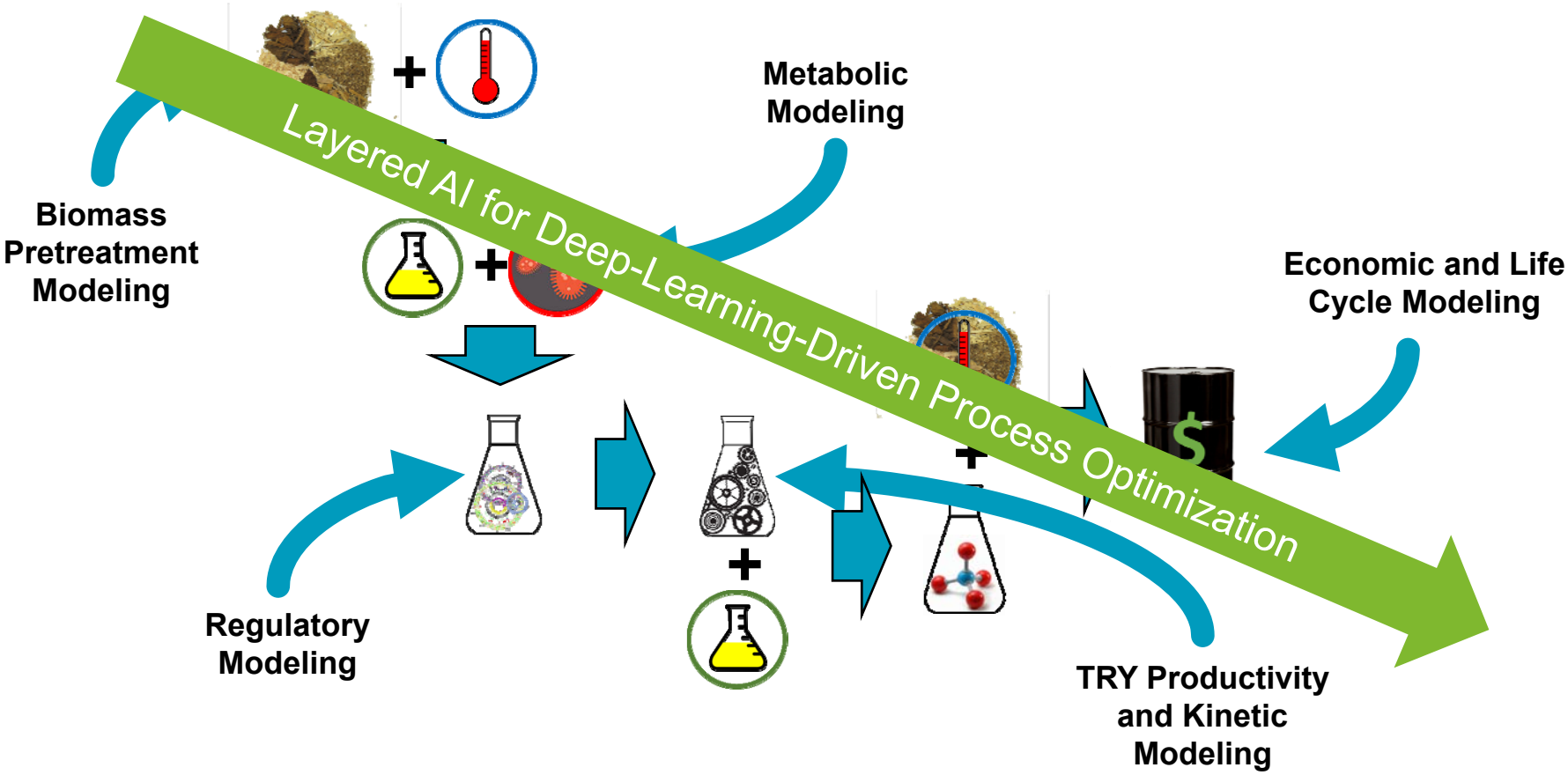
Integrated AI subsystems for Deep Learning in Biomanufacturing



- An ecosystem of learn models for continuous data collection and integration
- **Outcome:** Integrated modules where output of one is input of next
- *Ongoing:* Required complexity and interlab coordination being established

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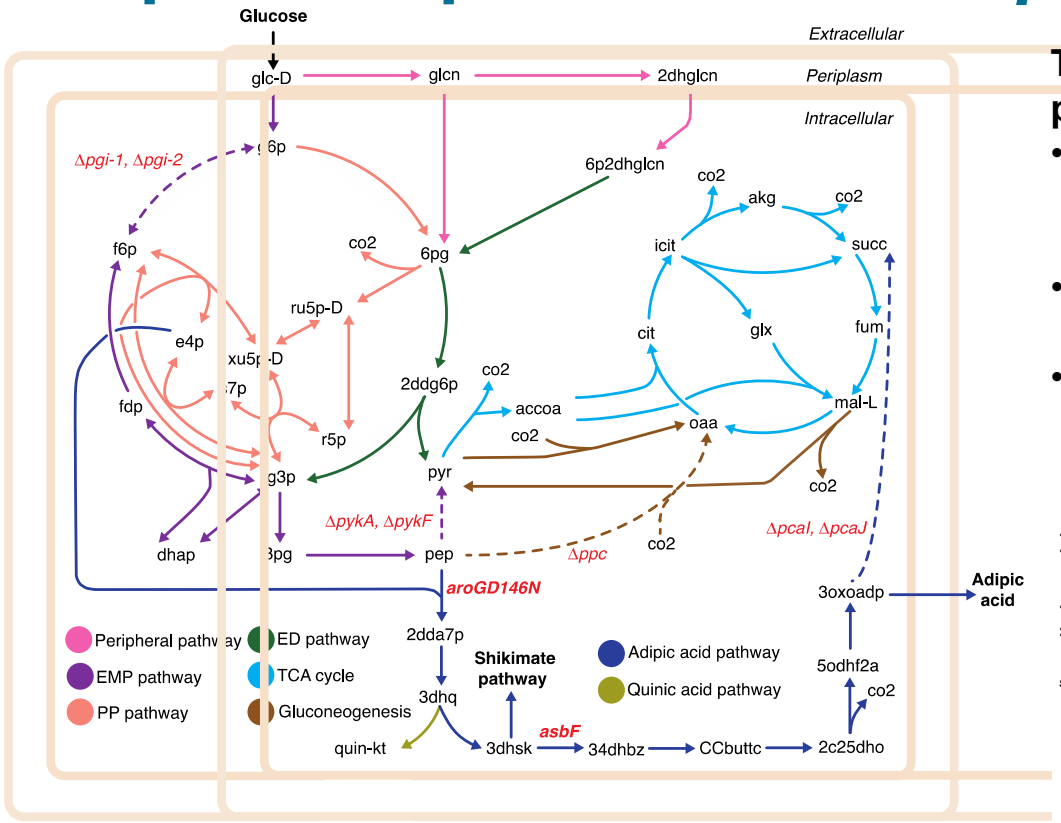
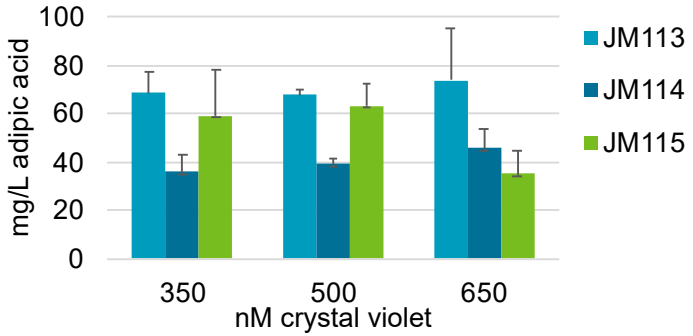
Adipic acid production in *P. putida* (mini DBTL)



Original figure by Jon Magnuson, et al., PNNL

Total of 30 engineered strains tested for production of adipic acid

- 2 modified strains - accumulate precursor β-ketoadipate or β-ketoadipyl-CoA
- 3 different vectors – inducible and constitutive
- 5 different pathways – 3-5 enzymes to convert βKA/βKA-CoA to adipic acid



- Employed DBTL for reversing adipic acid catabolic pathway from ß-ketoadipate
- **Outcome: Highest amount of adipic acid produced was ~70 mg/L**
- Ended this effort, pivoted to adipic acid precursors, muconate and ß-ketoadipate

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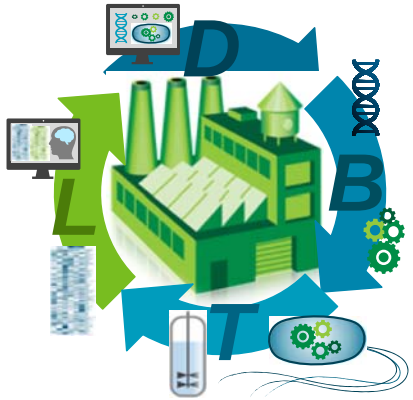
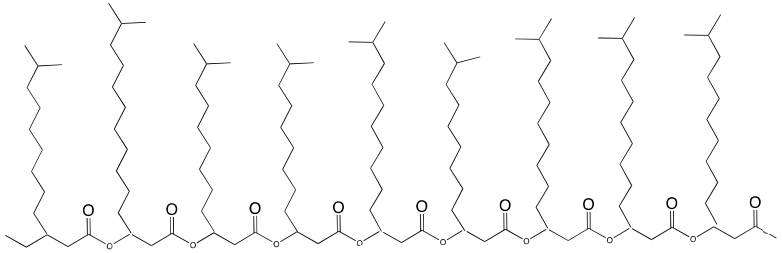
Outline of Technical Accomplishments

DBTL for Target 1: C6 Diacids

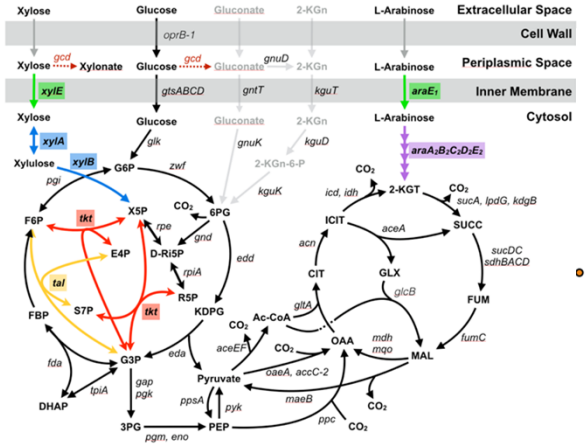
- Baselining muconic acid production
- Improving rate of muconate production
- Successful Learn cycles for strain improvements



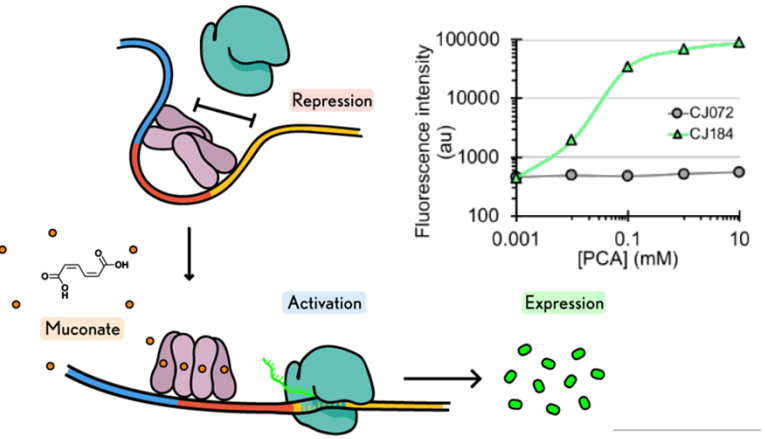


DBTL for Target 2: BCPHAs

DBTL for sugar utilization



New tools for *P. putida*



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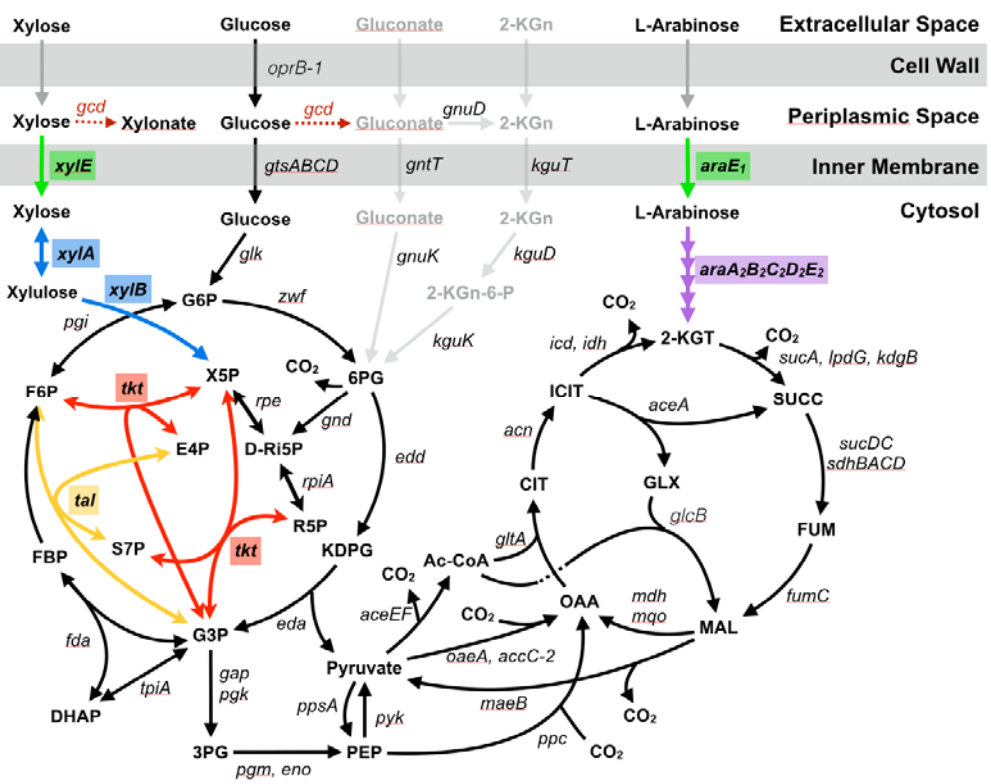
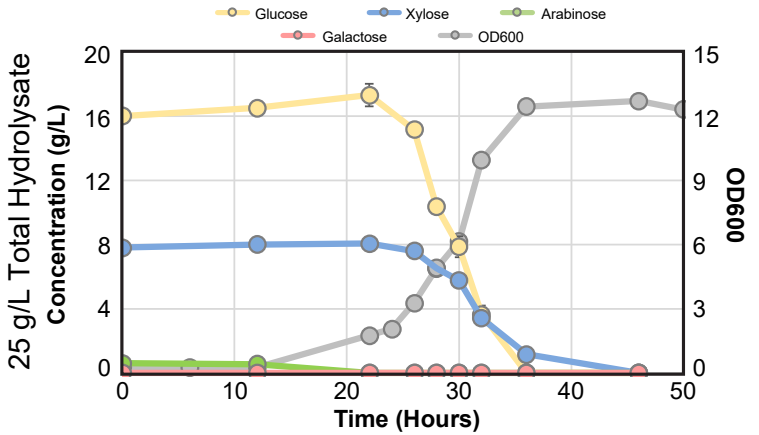
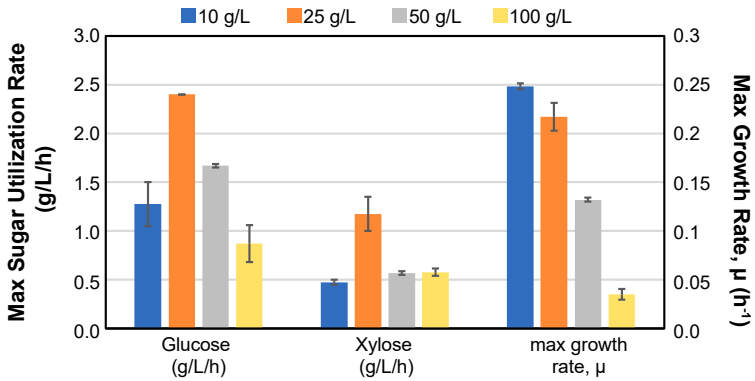
Sugar utilization in *P. putida* (mini DBTL)







- Engineered *P. putida* to utilize major C5 sugars present in corn stover hydrolysate
- **Outcome:** *P. putida* strain that co-utilizes glucose, xylose, and arabinose
- *Ongoing*: galactose utilization, C5 sugar conversion to muconate in *P. putida*

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Crop 1 DBTL cycle time progress

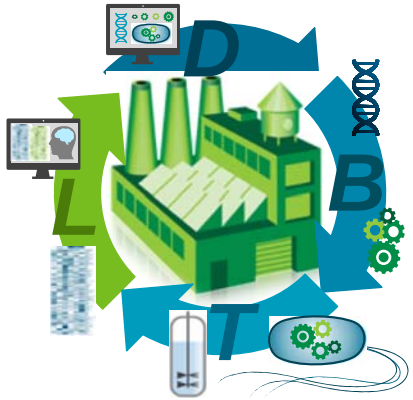
Cycle Time (days)	Design	Build	Test	Learn	Outcomes
Cycle 1	54	130	283	93	40% yield of muconic acid from glucose
Cycle 2	23	130	454	41	Productivity increased from 0.15 to 0.21g/L/h
Cycle 3a	4	42	106		Pentose sugar utilization
Cycle 3b	1	157	302	102	In vivo biosensor development
Cycle 3c					In vitro biosensor applications
Cycle 4	11				New targets generated from from Cycle 1 Learn
Cycle 5	6	104			New targets generated from from Cycle 2

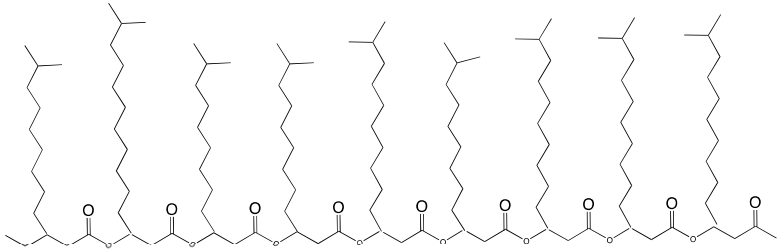
- Multiple, complementary DBTL cycles initiated in parallel
- New cycles ongoing that take Learn predictions from extensive Test experiments
- **Outcome:** Identifying key bottlenecks in DBTL interfaces to increase efficiency

Outline of Technical Accomplishments

DBTL for Target 1: C6 Diacids

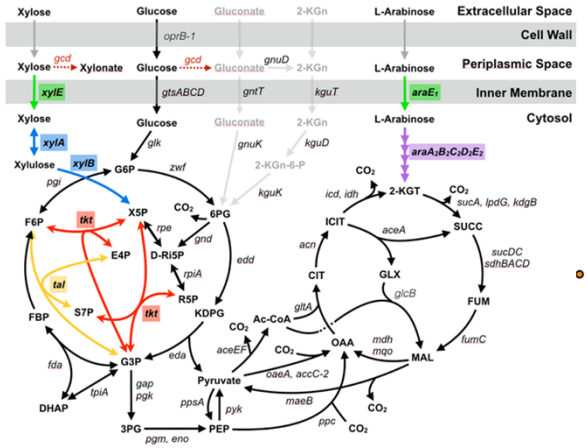
- Baselining muconic acid production
- Improving rate of muconate production
- Successful Learn cycles for strain improvements



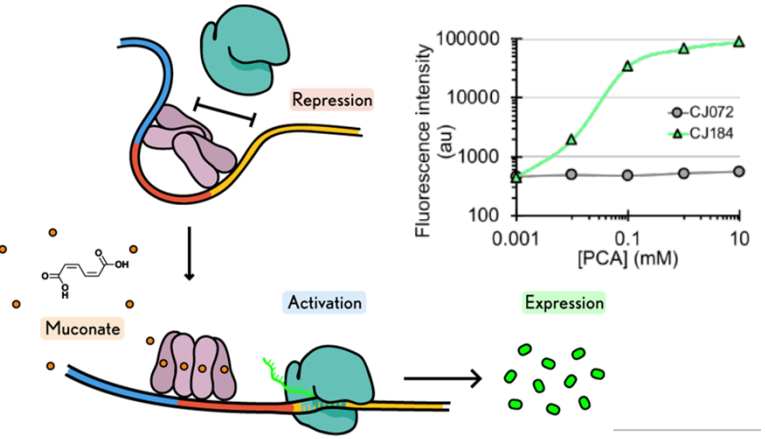


DBTL for Target 2: BCPHAs

DBTL for sugar utilization



New tools for *P. putida*



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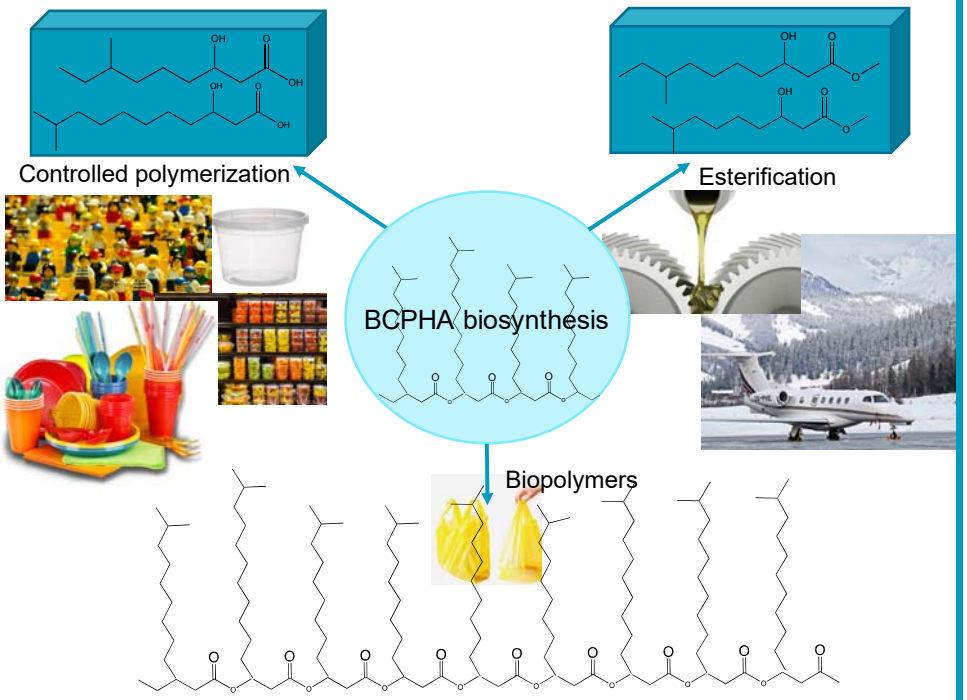
Target 2: Branched-chain PHAs



Strains built for Test

Target 2, Cycle 1: 210 total modifications in 47 strains

- BCPHA may directly replace LDPE in addition to wide-ranging applications
- **Outcome:** strains generated to convert glucose into BCPHA biosynthesis
- *Ongoing:* developing analytical technique for this novel class of molecules

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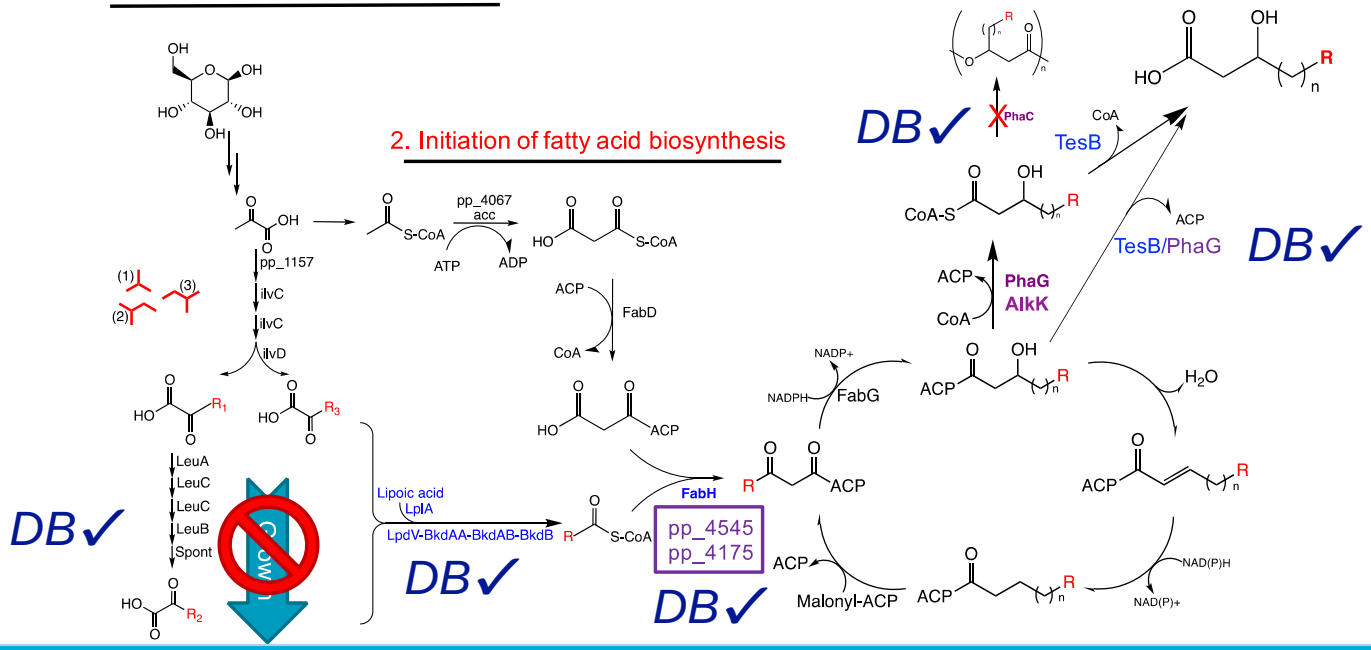
Crop 2 DBTL cycle time progress



Cycle Time (days)	Design	Build	Test	Learn	Outcomes
Cycle 1	94	69	125	41	Build baseline BCPHA strains and characterize
Cycle 2	91	12			Develop autolysis system

- Multiple, complementary DBTL cycles initiated in parallel
- New cycles ongoing that take Learn predictions from extensive Test experiments
- **Outcome:** Identifying key bottlenecks in DBTL interfaces to increase efficiency

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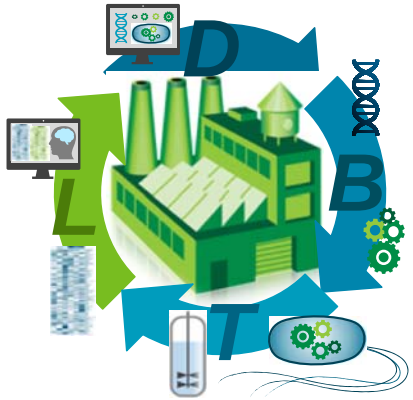
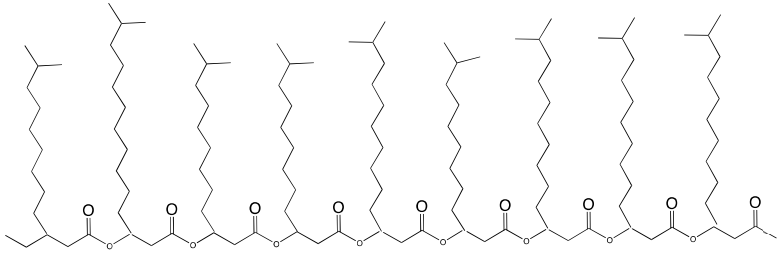
Outline of Technical Accomplishments

DBTL for Target 1: C6 Diacids

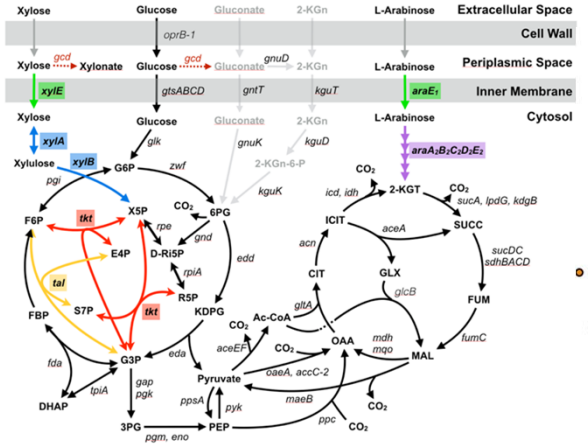
- Baselining muconic acid production
- Improving rate of muconate production
- Successful Learn cycles for strain improvements



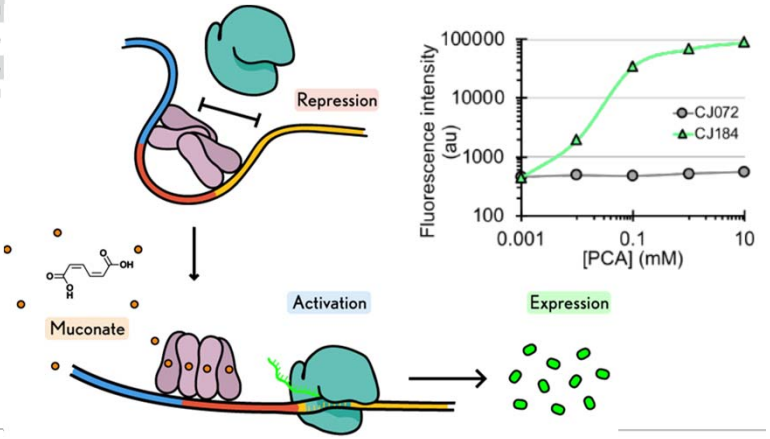


DBTL for Target 2: BCPHAs

DBTL for sugar utilization



New tools for *P. putida*



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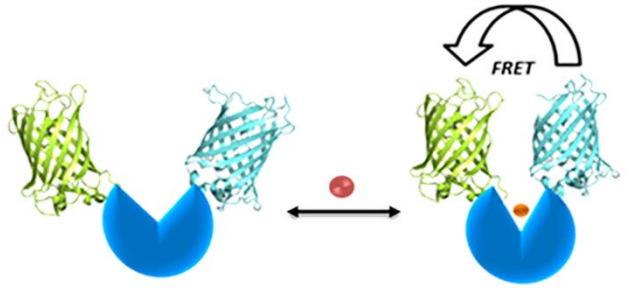
Ongoing tool development

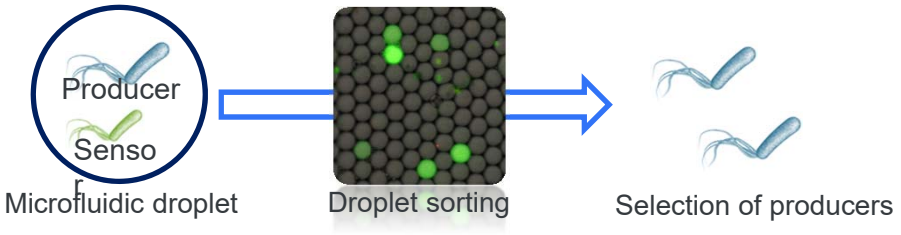
FRET biosensors for strain optimization

- Real–time signal response
- Follow metabolic or catabolic processes
- Adaptable to a wide range of targets
- Family of muconate sensors for multiple applications



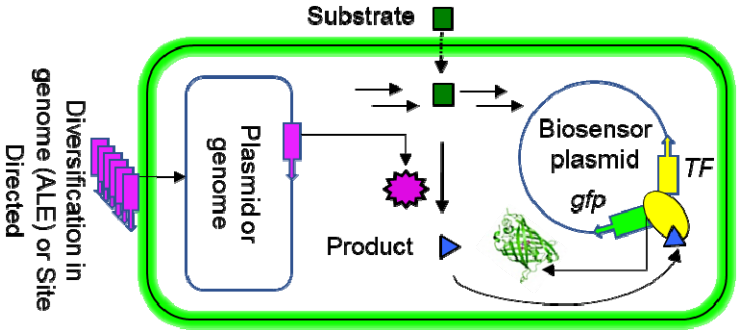
Enzyme-linked biosensors

- TF sensors with >100-fold increase in fluorescence

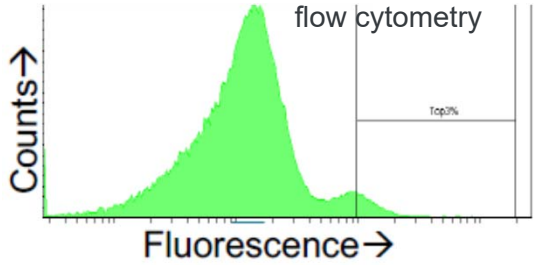


TF biosensors for strain optimization

- Reports on *in vivo* metabolic activity
- Can be tuned for different target concentrations
- Coupled to flow cytometry for rapid isolation of top performers.



Observed variation in fluorescence level



- New biosensors developed for optimization of biocatalysts and production strains
- **Outcome:** Ligand reporting systems for high-throughput *in vitro* and *in vivo* screening
- *Ongoing:* Development and application for new targets and intermediates

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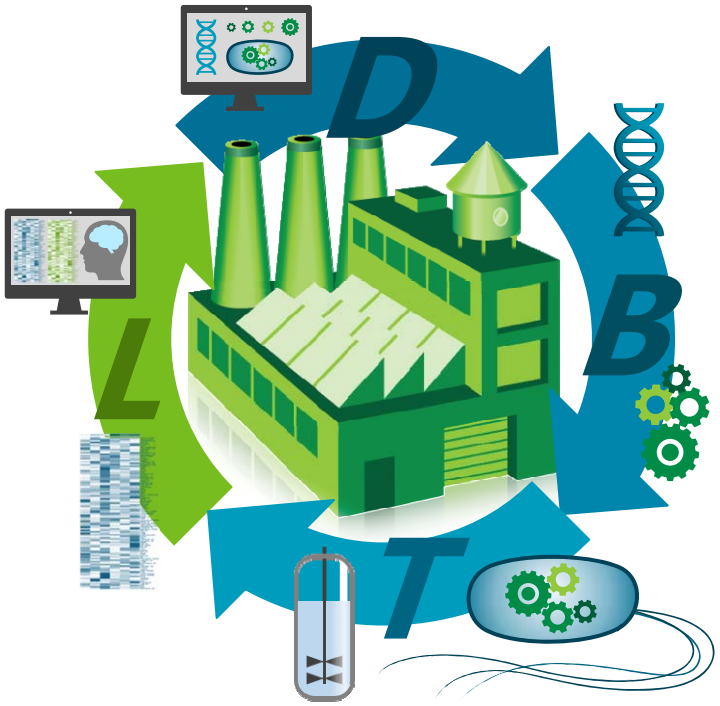
4 – Relevance

Relevance

Goal: Employ targets in robust host, *P. putida* KT2440, to demonstrate the ABF concept towards improved strain performance

- Crop 1: C6 diacids (muconic, ß-ketoadipic, adipic)
- Crop 2: Branched-chain PHAs
- Can be used as performance-advantaged bioproducts or direct replacements



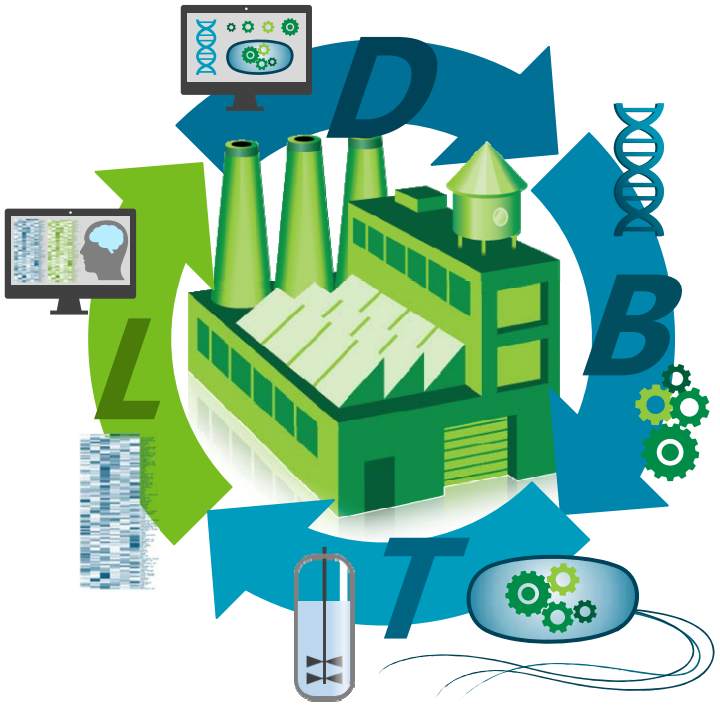
Why is this project important? What is the relevance to BETO/bioenergy goals?

- 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 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
- *P. putida* is an promising chassis for bioproduction



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

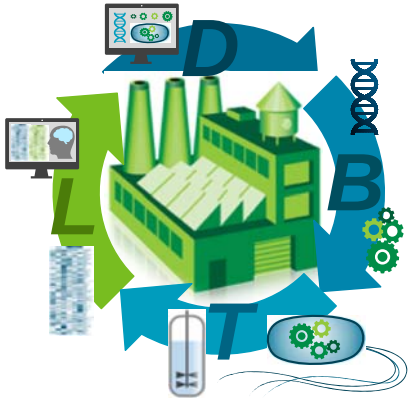
5 – Future Work

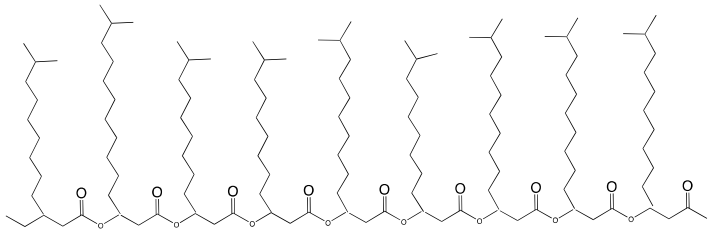
Future Work

Project-end milestones: ≥ 10 g/L in DMR-EH hydrolysate, 100 mg/L/hr

DBTL for Target 1: C6 Diacids

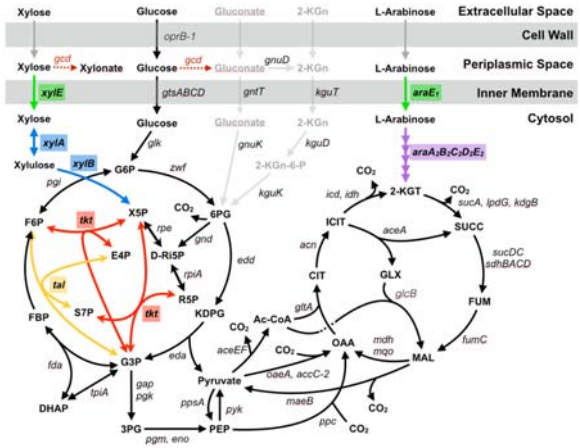
- Testing new, non-intuitive Learn targets
- Improving rate of muconate production
- Successful Learn cycles for improvements
- Expand muconate to new host: *C. glutamicum*



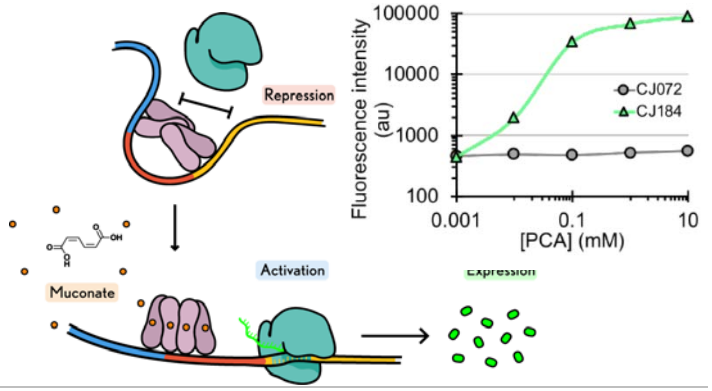


Initiate new DBTL cycles for BCPHAs

Utilization of galactose and conversion of C5/C6 sugars to C6 diacids



Continued **tool development** and applications to enable DBTL



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Future Work beyond FY19

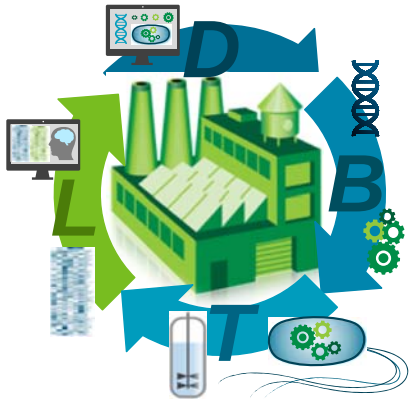
Standardization of DBTL workflow across T/H pairs

- Towards automation – increase focus on high throughput Design/Build workflows compatible with automation
- Develop SOPs for advanced Test/Learn functions
- Streamline DBTL function, reduce time/resources, increase capacity

Host Development

- Tools – expand basic toolset (parts, establish plasmids) and implement advanced genome editing tools
- Standardized library of parts and high-throughput DNA assembly methods
- Host versatility- expand metabolic space to reach new “nodes” for novel heterologous bioproducts

Work more closely with other BETO consortia to inform DBTL



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Co-Optimization of Fuels & Engines

ChemCatBio

BIOPROCESSING SEPARATIONS CONSORTIUM

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Summary

Overview

– Aim to demonstrate ABF concept via *P. putida* KT2440 with two novel molecule targets

Approach

– Employ DBTL cycle for increasing C6 diacid rate, BCPHA yield

– Accelerate DBTL efforts with advanced tool development

Technical accomplishments

– Baseline strains for muconate production, highest yields reported to date

– Enabled pentose and hexose utilization in *P. putida*

– Employed Learn to make non-intuitive predictions that lead to improved production rate

– Demonstrated BCPHA production, deployed advanced tools for DBTL

Relevance

– DBTL demonstrations in non-standard host bacterium

– Performance-advantaged co-products essential to meet DOE cost targets

Future work

– New DBTL cycles for Targets 1 (rate) and 2 (yield), informed by Test-Learn

– Work towards performance targets on DMR-EH for Targets 1 and 2

Acknowledgements

- Phil Laible
- Peter Larsen
- Gyorgy Babnigg
- Rosemarie Wilton
- Deborah Hanson
- Martyna Michalska
- Taraka Dale
- Ramesh Jha
- Scott Hennelly
- Niju Narayanan
- Naresh Pandey
- Carol Kay Carr
- Sean Reardon
- Jon Magnuson
- Kristin Burnum-Johnson
- Young-Mo Kim
- Jeremy Zucker
- Nathan Hillson
- Alastair Robinson
- Blake Simmons
- John Gladden
- Hector Garcia Martin
- Chris Johnson
- Davinia Salvachua
- Gayle Bentley
- Brenna Black
- Rita Clare
- Graham Dominick
- Ray Henson
- Bill Michener
- Marykate O'Brien
- Isabel Pardo
- Darren Peterson
- Peter St. John
- Adam Guss
- Josh Michener
- Joshua Elmore
- Quint Peabody
- Julie Chavez
- Jessica Martinez
- Gara Wolff
- Swarnendu Tripathi
- Mark Butcher
- Jamie Meadows
- Todd Pray
- Deepti Tanjore

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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.

T/H Project Milestones

- **FY17 Annual SMART milestone**
  - Demonstrate the Agile BioFoundry process by successfully completing one or more Design, Build, Test, Learn cycles for 5 3? molecules in their designated onboarded hosts, hitting baseline titers of 100 mg/L in mock or DMR-EH hydrolysate for at least 2 molecules.

- **FY18 Q1 Regular Milestone**
  - Increase the DBTL throughput capacity 1.5-fold by initiating the DBTL cycle for an additional 3 molecules in FY18. Initiate host onboarding for any additional FY18 hosts.

- **Go/No-Go Decision, Q2 FY18**
  - Demonstrate process integration and scaling in 2 L bioreactors in DMR-EH hydrolysate using a target molecule introduced into the BioFoundry in FY17 with a target titer of at least 1 g/L.

- **FY18 Annual SMART milestone**
  - From a set of 10 6? target molecules, demonstrate successful production of 40% with titers for FY18 target molecules of at least 100 mg/L in mock or DMR-EH hydrolysate, and titers for FY17 target molecules of at least 500 mg/L in DMR-EH hydrolysate.

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.